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Environment/climate change

Air pollution exposure and reproductive hormonal levels across the menstrual cycle in a time-to-pregnancy cohort Kaniz Rabeya*, Kaniz Rabeya, Gabrielle Johnson, Timothy Canty, Karen Schliep, Rachael Hemmert, Pauline Mendola, Neil Perkins, Akanksha Singh, Allison Ring, Carrie Nobles,

Background: Ambient air pollution has been associated with adverse reproductive and pregnancy outcomes; however, the role of hormones is underexplored. We investigated the association between ambient air pollution and reproductive hormones among women attempting pregnancy.

Methods: The EAGeR trial (2007-2011), a prospective time-to-pregnancy study, enrolled 1,001 women (18-40 years) from the Intermountain West, with the majority residing along the Wasatch Front. Daily diaries and fertility monitors tracked timing of menstrual cycles and ovulation. Estrone-3-glucuronide (E1G), follicle-stimulating hormone (FSH), luteinizing hormone (LH), & pregnanediol glucuronide (PdG) were measured in urine at early follicular phase, ovulation, & luteal phase. Residential air pollution exposure was estimated from Air Quality Data for Health-Related Applications (AQDH) Models, including ozone (O3), fine particulate matter (PM2.5), & nitrogen dioxide (NO2), and averaged across the late luteal phase in the prior cycle (0-7 days before menses), early to mid-follicular phase (1-10 days after menses), & ovulation (11-16 days after menses). Generalized linear models estimated the association between air pollutants and hormones, adjusting for age, income, education, and race/ethnicity.

Result: We observed a trend of air pollution with lower hormone levels across the menstrual cycle. Women exposed to a 5 ppb increase in O3 during the late luteal phase in the prior cycle had 1.56 (95% CI -2.90, -0.22) ng/mg Cr lower E1G and 0.23 (95% CI -0.42, -0.04) µg/mg Cr lower PdG in the early follicular phase. Similarly, women exposed to a 5 ppb increase in PM2.5 during the early to mid-follicular phase had 0.45 (95% CI -0.9, -0.01) mIU/mg Cr lower FSH and 0.48 (95% CI -0.99, 0.02) mIU/mg Cr lower LH at ovulation.

Conclusion: Ambient air pollution was associated with hormone levels across the menstrual cycle, suggesting hormones may be a susceptible pathway for impacts on women’s reproductive health.

Genetics/Molecular/Omics

Extreme Heat Exposure Before Conception Shapes Placental Transcriptomic Signatures

Kimi Van Wickle*, Kimi Van Wickle, Lauren A. Eaves, Cassandra O'Lenick, Kyle Roell, Claire Jensen, Tracy A. Manuck, Stephanie Engel, Michael O'Shea, Rebecca C. Fry,

Introduction. Extreme heat exposure during pregnancy is a growing concern with climate change and is linked to preterm birth. The placenta may be a key driver, but few human studies have examined the impact of heat on placental function. We tested whether extreme heat exposure is associated with placental mRNA expression and whether responses vary by exposure timing and heat metric.

Methods. We analyzed data from the ELGAN cohort, a prospective, multi-site study of children born before 28 weeks' gestation, including those with valid address history and placental mRNA data (n=186). We used NASA's Daymet product and geocoded residential address to reconstruct heat exposure. Daily ambient heat metrics (mean, minimum, maximum temperature, and mean heat index) were aggregated to represent mean exposure and any days above the 95th and 99th percentile of the heat during critical windows: 3 months preconception, 2 weeks preconception, first trimester, and 2 weeks before birth. Differential expression analyses were conducted using DESeq2 with multiple test correction.

Results. We identified 996 differentially expressed genes (DEGs) across all heat metrics, corresponding to 300 unique genes. Nearly all were related to preconception exposure (979 DEGs; 98.3%), primarily in the 2 weeks preconception (816 DEGs, 81.9%). Key epigenetic regulator *DNMT1* was 2.3-fold higher among participants with any days >99th percentile minimum temperature 2 weeks preconception (log2FC=1.50; BH p=0.002). The most significant DEG was *HMGN5* in response to any days >99th percentile heat index 2 weeks preconception (log2 fold change (log2FC)=-16.03; BH p=7.7×10-57), a gene linked to uterine decidualization.

Conclusions. Extreme heat exposure, particularly during periconception, is associated with altered gene expression in very preterm placentas. Minimum temperatures and heat index had particularly robust effects, suggesting physiologic overnight recovery and heat burden may be important contributors.

Big Data/Machine Learning/AI

Precision Medicine Approach to Elective Induction Decisions: Secondary Analysis of A Randomized Trial of Induction Versus Expectant Management (ARRIVE) Yuri V. Sebastião*, Yuri V. Sebastião, Katelyn J. Rittenhouse, Jackie K. Patterson, Teeranan Pokaprakarn, John M. Thorp Jr., Stephen R. Cole, Jeffrey S.A. Stringer,

Elective induction at 39 weeks reduces cesarean risk among low-risk pregnancies, but outcome heterogeneity may be masked. We evaluated whether individualized treatment rules could improve outcomes.

We analyzed ARRIVE trial data (N=6,106 low-risk nulliparas randomized at 38 weeks' gestation to undergo either elective induction at 39 weeks or expectant management) using intention-to-treat. Baseline covariates included maternal age, height, weight, BMI, cervical dilation, Bishop score, assisted conception, substance use, marital status, employment, insurance, prior pregnancy loss, and fetal anomaly. We estimated individualized treatment effects on cesarean delivery and a perinatal (fetal/neonatal) morbidity/mortality composite using causal forests. Three individualized policies were defined: (A) induce if lower cesarean risk for induction versus expectant management, (B) induce if lower perinatal composite risk, and (C) induce if lower cesarean risk without increased perinatal risk. Expected risks under each policy, including universal induction and expectant management, were estimated via augmented inverse-probability-weighting with 5-fold cross-fitted SuperLearner. Missing data were replaced by 20 imputations using chained equations.

Compared to universal expectant management, universal induction had 18.6% cesarean (Risk Difference, RD: −3.6% [95% Confidence Interval: -5.6, -1.7]) and 4.3% perinatal composite risk (RD: -1.1% [-2.2, 0.0]). Individualized policies (A-C) recommended induction for 75.1-85.6% of participants, achieving 19.0-19.7% cesarean and 4.4-4.6% perinatal risk.

In ARRIVE, universal induction achieved the lowest cesarean risk, but individualized policies reduced inductions by 14–25 percentage points while maintaining lower cesarean and perinatal risks than universal expectant management. Individualized strategies may support patient-centered decision-making by identifying those unlikely to benefit from elective induction.

Methods

Regression-Based Proximal Reconciliation of Conflicting Randomized Trials with Unmeasured Effect Modifiers Daniel Xu*, Daniel Xu, Eric Tchetgen Tchetgen, Enrique Schisterman, Ellen Caniglia,

Conflicting randomized controlled trial (RCT) results complicate evidence synthesis and regulatory decision making. One example is the RCTs evaluating 17-α-hydroxyprogesterone caproate for preventing recurrent preterm birth (PTB). The Meis trial reported a meaningful reduction in recurrent PTB, whereas the confirmatory PROLONG trial found no benefit despite identical protocols. Differences in study populations, specifically heterogeneity in baseline PTB risk, are a hypothesized reason for this discrepancy. Existing transportability-based approaches to assess reconcilability are underpowered and do not account for unmeasured effect modifiers (EMs).

We propose a regression-based proximal causal inference framework for reconciling RCTs that leverages proxies for unmeasured EMs. We develop two frameworks for formalizing a hypothesis test of reconcilability of conditional causal effects on additive and multiplicative scales under generalized linear models. The first extends transportability methods to account for unmeasured EMs; the second directly tests equality of model coefficients, yielding improved power. To provide evidence for rather than against reconcilability, we also introduce an equivalence test based on the mean squared distance (MSD) between conditional causal effects.

Simulations show that while both coefficient-based and transportability tests control Type I error, the former approach is more powerful (power: 0.846 vs. 0.252 for n=3000). We apply the methods to the PTB trials, using gestational age at prior PTB and BMI as proxies for hypothesized unmeasured EMs, e.g., cervical length. The coefficient-based test provided stronger evidence against reconcilability (p=0.018) than the transportability test (p=0.243), while equivalence testing yielded no evidence of similarity (normalized MSD 7.17; one-sided 95% CI 15.75). These findings suggest residual heterogeneity in unmeasured EMs and show how the proposed methods can clarify conflicting RCT results.

Pregnancy outcomes

A Mendelian Randomization Study of Maternal Thyroid Function and Cerebral Palsy

Yuewen Ge*, Yuewen Ge, Andrew Dewan, Zeyan Liew,

Background

Cerebral palsy (CP) is a neuromotor disorder that is strongly associated with adverse perinatal conditions. Maternal thyroid dysfunction in pregnancy is suggested to increase CP risk, but the evidence is not yet conclusive.

Methods

We conducted a two-sample MR study to investigate the causal effect of maternal thyroid function on the risk of CP in offspring, and to explore potential pregnancy-related factors as potential mediators of this association. Genetic instruments for hyperthyroidism and hypothyroidism were obtained from a large European genome-wide association study (GWAS) by Sakaue et al. (2021), instruments for free thyroxine (FT4) and thyrotropin (TSH) were derived from the ThyroidOmics Consortium, and the genetic data for CP were obtained from FinnGen. Genetic instruments for potential mediators, including preterm birth, gestational duration, and maternal birthweight, were derived from the Early Growth Genetics Consortium. Primary analyses were performed using the inverse variance weighted method, with sensitivity tests using MR Egger, weighted median, and weighted mode approaches. Heterogeneity and horizontal pleiotropy were assessed using Cochran's Q statistic and the MR Egger intercept.

Results

Genetically-predicted hyperthyroidism was associated with increased odds of CP (IVW OR=1.09, 95% CI 1.01–1.18; p=0.030), but no association was found between the mediators evaluated and genetically-predicted hyperthyroidism. In contrast, while higher FT4 levels were associated with preterm birth (OR=1.13, 95% CI 1.04–1.23; p=0.006) and gestational weight gain (β=0.13, p=0.035), and genetically-predicted hypothyroidism was associated with a lower birthweight (β=-0.019, p=0.041), no evidence of an overall effect on CP was observed for FT4, TSH, and hypothyroidism.

Conclusions

Genetic liability to maternal hyperthyroidism may increase the risk of CP, but the association was not mediated through the pregnancy factors examined. Our results support the importance of maternal thyroid function in the etiology of CP.

Paternal/Men’s health

Residential Proximity to Major Roads and Semen Quality in a U.S. Preconception Cohort

Eliza Pentz*, Eliza Pentz, Mary Willis, Kipruto Kirwa, Greg Sommer, Michael Eisenberg, Lauren Wise, Amelia Wesselink,

Background: Exposure to traffic-related air pollution, some components of which have been shown to reduce sperm production, may contribute to poorer semen quality.

Methods: We analyzed data from Pregnancy Study Online (PRESTO), a preconception cohort study of female pregnancy planners (ages 21-45) and their male partners (ages ≥21). Using a home-testing protocol, 878 men provided 1,578 semen samples during preconception. We assessed semen volume, total sperm count (TSC), sperm concentration, total motile sperm count (TMSC), and percent motility. Participants reported home addresses and covariate data on baseline questionnaires. We geocoded addresses and calculated distances to major roads. We categorized participants as living close to a major road if their residence was <50m from a state or county road or <100m from an interstate or limited-access highway. We estimated percent differences (%D) and 95% confidence intervals (CIs) using linear regression models with generalized estimating equations, adjusting for individual- and neighborhood-level sociodemographic characteristics.

Results: Living close to a major road (vs. not) was associated with slightly lower TMSC (%D: -7.7, 95% CI: -23.2, 10.8) and percent motility (%D: -5.0, 95% CI: -10.4, 0.3). However, when we considered 5 levels of road proximity (reference: ≥400m), there was no clear dose-response association for TMSC (%D [95%CI]; <50m: -11.7 [-29.1, 10.1]; 50-99m: 4.6 [-16.4, 31.0]; 100-199m: -8.5 [-25.0, 11.7]; 200-399m: 0.4 [-17.8, 22.6]) or percent motility (%D [95%CI]; <50m: -2.5 [-9.5, 4.5]; 50-99m: 0.5 [-6.9, 7.]; 100-199m: 7.1 [0.8, 13.4]; 200-399m: 3.3 [-2.9, 9.5]). Living close to a major road (vs. not) showed little association with semen volume (%D: 0.8, 95% CI: -5.7, 7.4), sperm concentration (%D: -1.8, 95% CI: -15.0, 13.4), and TSC (%D: -2.2, 95% CI: -16.3, 14.4).

Conclusion: Our preliminary findings do not support an association between residential proximity to major roads and semen quality.

Social determinants of health

PM2.5 and Preterm Birth by Neighborhood Racial and Economic Composition in Florida, 2010 to 2022 *, Jessica Broach, Maeve Wallace, Emily Harville, Xiuling Zhao, Christopher Uejio,

Background: Current research has failed to explore the intersection of harmful physical and social environments with regard to reproductive health outcomes which are sensitive to both in isolation. The objective of this study was to evaluate whether the association between PM2.5 pollutant exposure and preterm birth differs by neighborhood racial and economic composition, as measured by the Index of Concentration at the Extremes (ICE).

Methods: We conducted a retrospective cohort study of 2,124,840 births using birth certificate data obtained from the Florida Department of Health (2010 to 2022). Average PM2.5 concentrations in each trimester were obtained from the North America Chemical Reanalysis dataset and linked with geographic coordinates for mother's residential address. We spatially joined geographic coordinates for mother's residential address to Census tract shapefiles and estimated annual census tract ICE values based on the American Community Survey 5-year estimates for population by race and income. ICE values ranged from -1 to 1 and we grouped births within tracts into three levels: <-0.0782 (concentrated deprivation) -0.0781<0<0.0964 (intermediate), and >0.0964 (concentrated privilege). ICE-stratified logistic regression models estimated adjusted odds ratios (aOR) and 95% confidence intervals (CIs) for the association between trimester-specific PM2.5 levels and odds of preterm birth.

Results: PM2.5 exposure in the first trimester was associated with greater odds of preterm birth with incrementally increasing magnitudes across each level of ICE: concentrated deprivation (aOR 1.005, 95% CI 1.001, 1.009), intermediate (aOR 1.009, 95% CI 1.004, 1.013), and concentrated privilege (aOR 1.015, 95% CI 1.010, 1.019). Similar results were observed in the second and third trimesters.

Conclusions: Exposure to PM2.5 contributes to preterm birth and is moderated by composition of the social environment, although not in the hypothesized direction.

Social determinants of health

Neighborhood and Individual Food Insecurity, Federal Food Assistance Programs, and Gestational Diabetes Rana F. Chehab*, Rana F. Chehab, Amanda L. Ngo, Mara B. Greenberg, Liwei Chen, Assiamira Ferrara, Yeyi Zhu,

Introduction
Gestational diabetes mellitus (GDM) may be shaped by food access barriers at both neighborhood and individual levels. We examined how neighborhood food access and individual food insecurity (FI) may jointly influence GDM risk, and whether federal food assistance mitigates this risk.

Methods
We conducted a population-based cohort study of 13,927 pregnant individuals at Kaiser Permanente Northern California between 2020 and 2022. Neighborhood food access was assessed at pregnancy onset using the USDA census tract–level low-income, low–food access (LILA) indicator. FI during pregnancy was assessed using the validated two-item Hunger Vital Sign screener. Using modified Poisson regression models that accounted for clustering at the neighborhood level, we estimated relative risks (RRs) and 95% confidence intervals (CIs) for GDM, comparing individuals with LILA only, FI only, both, or neither, while adjusting for key covariates including age at delivery, education, insurance type, parity, and smoking and alcohol use during pregnancy.

Results

Overall, 15.6% of pregnant individuals lived in LILA neighborhoods, 9.0% reported FI, and 3.7% had both. Compared with neither exposure, LILA only was modestly associated with GDM (RR 1.15 [95% CI 0.98–1.34]), while FI only (1.47 [1.23–1.77]) and both LILA-FI (1.39 [1.04–1.86]) showed stronger associations. Associations were attenuated to null among those who received federal food assistance in pregnancy (FI only: 1.28 [0.72–2.27]; both LILA-FI: 1.29 [0.66–2.53]), and persisted for non-recipients (FI only: 1.52 [1.25–1.85]; both LILA-FI: 1.46 [1.06–2.01]).

Conclusion
Neighborhood and individual FI were associated with higher GDM risk, with receipt of federal food assistance potentially mitigating this risk.

Women’s/Gynecologic Health

Neighborhood Typology and A1C Trajectories among Women with Gestational Diabetes in New York City: A Longitudinal Study Teresa Janevic*, Bohao Wu, Natalie Boychuk, Shelley Liu, Frances Howell, Andrew Rundle, Teresa Janevic,

Background: Neighborhood environments are associated with type 2 diabetes (T2D), yet prior studies have focused on single neighborhood determinants rather than multidimensional profiles. Women with gestational diabetes (GDM) experience heterogeneous postpartum glycemic trajectories. We used a data-driven approach to classify New York City (NYC) neighborhoods into distinct profiles and examined their associations with postpartum A1C trajectories among women with GDM.

Methods: Using 2009-2021 linked NYC birth, hospital discharge, and NYC A1c Registry data, we identified GDM cases in birth/hospital data. Women with pre-pregnancy diabetes were excluded. We applied latent profile analysis to 10 social and built environment characteristics in 2010 to classify neighborhoods. The profile with the most average neighborhood characteristics was used as the reference. Participants’ residential addresses were updated at each A1C test to assign neighborhood profiles as the time-varying exposure. We used linear mixed-effects models with random intercepts at the census block and individual levels to estimate adjusted differences in repeated A1C measurements across neighborhood profiles, adjusting for maternal age, race and ethnicity, educational attainment, nativity, and parity.

Results: Among 13,231 women with GDM at baseline, seven distinct neighborhood profiles were identified. Compared with the Profile 5 neighborhoods (the most average), residence in Profile 1 neighborhoods (“Green and Wealthy”, mean difference [β]: -0.11, 95% CI -0.21, -0.01), Profile 4 neighborhoods (“Unhealthy Built Environment and Wealthy”, β: -0.11, 95% CI -0.21, -0.02), and Profile 7 neighborhoods (“Affluent Urban”, β: -0.16, 95% CI -0.25, -0.07) was associated with lower A1C levels.

Conclusions: Considering multidimensional neighborhood environments revealed distinct A1C trajectories after GDM, underscoring the value of neighborhood-based glycemic control.

Environment/climate change

Residential mobility and exposure misclassification of PM2.5 among pregnant Medicaid enrollees from 2001-2014 Stefania Papatheodorou*, Stefania Papatheodorou, Yinying Qian, Krista Huybrechts, Sonia Hernandez Diaz, Matthew Shupler, Wanyu Huang, Xinye Qiu, Michael Leung, Yaguang Wei, Joel Schwartz, Brent Coull, Christopher J. McDougle, Antonella Zanobetti, Marc Weisskopf, Hayon Michelle Choi,

Background:
Residential mobility during pregnancy can introduce exposure misclassification in environmental epidemiology studies and is socially patterned. However, large-scale characterizations of prenatal mobility and the direction and magnitude of associated changes in air pollution exposure remain limited.

Methods:
We analyzed 1,548,297 Medicaid-covered pregnancies in the United States from 2001–2014. Residential mobility was defined as a change in ZIP code between the last menstrual period (LMP) and delivery. Movers were further classified by directional change in ambient $PM_{2.5}$ exposure between LMP and delivery (High→High, High→Low, Low→High, Low→Low), based on the median annual ZIP code $PM_{2.5}$ (10.8 µg/m3). Maternal sociodemographic, neighborhood, and clinical characteristics were compared using standardized mean differences (SMDs).

Results:
Overall, 259,918 pregnancies (16.8%) involved residential mobility. Movers were younger (mean age 23.4 vs. 24.8 years; SMD −0.23), more likely to be Black (37.0% vs. 31.6%), compared with non-movers, and the median (IQR) move distance was 12.4 (6.5–23.8) km. Most people moved from high-to-high (n=85,101, 32.7%) and low-to-low (n=83,021, 31.9%) PM2.5 areas. The overall mean $PM_{2.5}$ difference between delivery and LMP ZIP codes was −0.55 µg/m³ (SD 4.12), masking substantial heterogeneity by direction of move. Moves from low- to high-$PM_{2.5}$ areas (n=33,628, 13%) were associated with a mean increase of 3.9 µg/m³, whereas moves from high- to low-$PM_{2.5}$ areas (n=47,152, 18%) were associated with a mean decrease of 4.7 µg/m³. Moves into higher-exposure areas were characterized by higher population density and greater neighborhood disadvantage, whereas moves into lower-exposure areas were associated with higher household income, homeownership, and lower neighborhood poverty. Movers also exhibited modestly higher prevalence of selected comorbidities than non-movers (all SMDs <0.20).

Conclusions:
Approximately one in six Medicaid-covered pregnancies involved residential mobility, most often over short distances, yet frequently accompanied by important changes in $PM_{2.5}$ exposure and neighborhood socioeconomic context. These transitions highlight residential mobility as an important source of differential exposure misclassification in perinatal environmental health studies.

Birth defects

Community Influenza Activity During Pregnancy and Cerebral Palsy in Offspring Cole King*, Cole King, Haoran Zhuo, Zeyan Liew,

Background:

Cerebral palsy (CP) is the most common childhood movement disorder, and its incidence varies seasonally. Influenza, a common seasonally varying pathogen, has been associated with poor birth and neurodevelopmental outcomes. However, no studies have examined whether community influenza activity is associated with CP risk.

Methods:

A cohort of 4.47 million live births in California from 2007-2015 was linked to CP diagnostic records through 2021 from a statewide diagnostic system, yielding 4,679 cases. Weekly influenza-like illness (ILI) surveillance data were obtained from the California Department of Public Health and averaged for each pregnancy and trimester to estimate community influenza circulation. Logistic regression was used to estimate the odds ratio (OR) and 95% confidence intervals (CI) for CP diagnosis based on community influenza activity, adjusted for maternal, neighborhood, and environmental factors. Temporal negative controls were used to evaluate uncontrolled confounding bias, and causal mediation analyses were conducted to identify potential causal pathways for the associations found.

Results:

Increased influenza activity during the first trimester was associated with CP diagnosis (OR 1.07 [95% CI 1.02-1.13]), especially for years dominated by the H1N1 viral subtype (OR = 1.18 [95% CI 1.11-1.26]). This relationship was robust to temporal negative controls that assessed community influenza activity before and after pregnancy. Mediating effects were noted for preterm birth and very preterm birth (mediated percentages 9.6% and 17.92%, respectively) but not for preeclampsia (mediated percentage <1%).

Conclusions:

Maternal exposure to increased community influenza during the first trimester of pregnancy is associated with increased CP risk, especially in years dominated by descendants of the 2009 novel H1N1 virus. Given continued emergence of novel respiratory pathogens, the potential implications of these findings merit further investigation.

Environment/climate change

Prenatal and postnatal exposure to ambient temperature and risk of autism spectrum disorder and attention-deficit/hyperactivity disorder among Medicaid recipients Stefania Papatheodorou*, Stefania Papatheodorou, Matthew Shupler, Xinye Qiu, Krista Huybrechts, Sonia Hernandez Diaz, Hayon Michele Choi, Michael Leung, Wanyu Huang, Yaguang Wei, Joel Schwartz, Antonella Zanobetti, Marc Weisskopf,

Background: Studies on the association between ambient temperature and risk of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) have been limited, especially among low-income populations who may be particularly vulnerable to environmental exposures.

Methods: The Medicaid Analytic eXtract (MAX) was used to generate a mother-infant longitudinal cohort from 2001-2013. Cases of ASD within the cohort were identified via ICD-9/10 codes. Ambient temperature exposure was assigned at the zip-code of residence. Cox proportional hazard models examined the association between both average zip-code level prenatal and postnatal ambient temperature exposure with the risk of developing ASD and ADHD. Distributed lag non-linear models were used to characterize temperature exposures (prenatal: 0-to-37-week lag; postnatal: 0-to-3-year lag). Cox models were stratified by county, birth year and race and adjusted for demographics, behavioral risk factors, ambient fine particulate matter concentration, season of delivery, and area-level socioeconomic status.

Results: A total of 1,548,303 births were included in the modeling. A 1-degree Celsius increase in average weekly prenatal temperature exposure was associated with 1.05 (95% CI: 1.00–1.11) and 0.99 (95%CI: 0.97-1.00) times the risk of ASD and ADHD, respectively, at the cumulative lag (0-37 weeks). A 1-degree Celsius increase in average annual postnatal temperature exposure was associated with 1.02 (95% CI: 0.96–1.08) and 1.02 (95% CI: 0.98–1.05) times the risk of ASD and ADHD, respectively, at the cumulative lag (0-3 years).

Conclusion: Among low-income children, prenatal temperature exposure was associated with elevated risk of ASD but not ADHD risk. There was no association between postnatal temperature exposure and ASD risk. Although there were potentially sensitive windows of exposure in early childhood for ASD and ADHD, cumulative postnatal temperature exposure was not associated with ASD and ADHD risk.

Funding: This study was supported by the National Institute of Health grant R01-ES034038.

Child health and development

Neonatal functional brain network maturation, prematurity, and early language development Ayesha Sania*, Ayesha Sania, Nicolò Pini, Alice Zhou, Hyun Kim, Lynn Chen, Seonjoo Lee,

Background: Functional brain networks mature rapidly during the final weeks of gestation, with large-scale networks present at birth in term infants. Preterm birth may alter early functional brain organization and neurodevelopmental outcomes by shortening the intrauterine developmental period.

Methods: Resting-state magnetic resonance imaging data were analyzed from 645 infants enrolled in the Developing Human Connectome Project in the United Kingdom. Imaging was performed between 28 and 45 weeks postmenstrual age. Functional connectivity was quantified using persistent-homology–based metrics, including backbone dispersion, backbone strength, and cycle strength. Developmental trajectories were estimated using smoothing splines. Differences between preterm (gestational age <37 weeks; n=128) and full-term infants (n=501) were examined at term-equivalent age, adjusting for sex and radiology score. Neurodevelopmental outcomes were assessed at 18–24 months using the Bayley Scales of Infant and Toddler Development, Third Edition.

Results: Backbone dispersion and backbone strength demonstrated nonlinear maturation across postmenstrual age (all $p<0.0001$), with rapid increases between 30 and 40 weeks postmenstrual age and plateauing near term. At term-equivalent age, preterm infants had lower backbone dispersion (standardized $\beta = -0.58$; 95% Confidence Interval, CI: −0.78, −0.38) and backbone strength ($\beta = -0.96$; 95% CI: −1.14, −0.78) compared with full-term infants. In mediation analyses, both backbone strength and cycle strength showed significant indirect effects; backbone strength fully mediated the association between prematurity and Bayley language scores at 18–24 months.

Conclusions: Functional brain network organization at term-equivalent age differed by gestational age. Network metrics mediated the association between prematurity and early language development, identifying early network topology as a mechanistic pathway linking preterm birth to neurodevelopmental risk.

Child health and development

Effectiveness of developmental screening and early intervention for communication delays
Diane Putnick*, Diane Putnick, Akhgar Ghassabian, Pauline Mendola, Kirsten Sigenthaler, Xuanxuan Zhu, Rajeshwari Sundaram, Edwina Yeung,

Few have quantified and demonstrated the impact of universal screening for communication delays on intervention uptake or eventual remission. Despite calls for research, the U.S. Preventative Services Task Force finds insufficient evidence to recommend universal screening for speech/language delay in children 5 years and younger. We hypothesized that children who failed a communication screener would be more likely to have poor language performance, and to receive a communication diagnosis and speech/language intervention than those who passed. Finally, we hypothesized that receiving speech/language intervention before 3 years would increase the likelihood that a diagnosis remits by age 7.

Children (n=1474) and parents from the Upstate KIDS birth cohort (2008-2010) were followed longitudinally from 4 months to 7 years. Ages and Stages Questionnaire (ASQ) screeners were administered repeatedly and parents reported about speech/language intervention, diagnoses, and remittance of diagnoses. A selected sample (n=586) attended a clinic visit for testing with the Battelle Developmental Inventory (BDI-2).

Failing any ASQ communication screener from 4 months to 3 years had 0.81 sensitivity and 0.75 specificity for scoring 2 standard deviations below the BDI-2 communication domain mean at 4 years. Children who failed a communication screener were more than twice as likely to receive a communication diagnosis (adjusted RR=2.47, 95%CI=2.03-3.00) and more than three times as likely receive speech/language intervention by age 3 (adjusted RR=3.71, 95%CI=3.04-4.53) than those who did not fail. Among children who were ever diagnosed with a communication delay (n=231), those who received speech/language intervention by age 3 were 47% more likely to have their diagnosis remit by age 7 (adjusted RR=1.47, 95%CI=1.13-1.91).

This study supported universal screening for identifying communication delays, moving children into early intervention, and subsequently ameliorating those delays.

Methods

Separating causal questions from statistics with application to dietary interventions in Project Viva cohort offspring Soren Harnois-Leblanc*, Soren Harnois-Leblanc, Izzuddin Aris, Karen Switkowski, Wei Perng, Sheryl Rifas-Shiman, Emily Oken, Marie-France Hivert, Jessica Young, Lan Wen,

Causal inference methods for observational data, including g-computation, inverse probability weighting (IPW), and doubly-robust/machine learning (DML), are increasingly applied in practice. However, they are often limited to strict interventions forcing all individuals to the same exposure level, which lack policy relevance and are susceptible to positivity problems. In this study, we show that these methods can be generalized to more pragmatic questions, such as effects of dietary interventions that consider the individual's natural intake level.

Using data from 944 adolescents (mean age: 13.2 yrs, SD: 0.9) in the Project Viva cohort (MA, USA), we estimated effects of strict interventions of consuming fast-food <1x/wk vs >=3x/wk, and <1x/wk vs 1-2x/wk, on average 5-year homeostatic assessment model for insulin resistance (HOMA-IR, mean 2.5, SD: 1.8). We then estimated effects where consumption depends on the individual's "natural" level: reduce to <1x/wk and 1-2x/wk if naturally consuming 1-2x/wk and >=3x/wk, respectively, with no change if naturally consuming <1x/wk. This was compared to average HOMA-IR under no intervention.

Prevalence of fast-food consumption was 62.5%, 32.6%, 4.9% for frequencies of <1x/wk, 1-2x/wk and >=3x/wk, respectively. Under the strict static intervention comparing <1x/wk vs >=3x/wk, we observed a difference in 5-year HOMA-IR of -0.39 (95% CI: -3.43, 1.13) with IPW, -0.03 (-0.73, 0.72) with g-computation, and -0.18 (-0.51, 0.15) with DML. Effects when comparing <1x/wk vs 1-2x/wk ranged from -0.10 to -0.48, with narrower CIs. Effects under the pragmatic intervention on HOMA-IR were as follows: 0.03 (-0.14, 0.23) with IPW, -0.05 (-0.17, 0.09) with g-computation, and -0.01 (-0,18, 0.16) with DML.

In conclusion, estimated effects from pragmatic interventions were less method-dependent and more precise. Strict interventions produced inconsistent estimates across methods due to greater susceptibility to positivity violations, particularly IPW.

Child health and development

Dietary intake and childhood adiposity beyond BMI: the Upstate KIDS study Xuanxuan Zhu*, Xuanxuan Zhu, Diane Putnick, Priscilla Clayton, Tzu-Chun Lin, Edwina Yeung,

Background. Childhood adiposity is associated with increasing risks of insulin resistance, liver diseases, and cardiovascular diseases. Although emerging studies have studied the association between diet and childhood obesity, most studies have focused on single foods or nutrients and measured adiposity by body mass index (BMI). Little is known about the dietary intake of food groups. Further, BMI is an imperfect proxy for adiposity because it may not reflect body fat distribution. Our study aimed to examine the association between dietary intake of food groups and childhood adiposity measured by fat mass and fat mass index (FMI).
Methods. Data came from Upstate KIDS, a prospective cohort study, where mothers reported children's daily servings for specific foods on 7- and 9-year questionnaires such as fruits, vegetables, and grains. We categorized foods into available food groups including fruits, vegetables, dairy, protein, and grains and calculated their total dietary intake (servings/day). Fat mass was measured by the Quantum V portable device at clinic visits at 9-10 years. FMI was calculated as fat mass/height2. Generalized linear models were used to estimate associations with covariates adjusted, such as sociodemographics, maternal pre-pregnancy BMI, and child moderate-to-vigorous physical activity.
Results. Among 347 children, the mean fat mass was 8.41±5.20 kg, and the mean FMI was 4.51±2.91 kg/m2. Higher servings of fruits were associated with lower fat mass (B=-0.79, 95% CI: -1.4, -0.18) and FMI (B=-0.43, 95% CI: -0.77, -0.09) crudely, similarly for whole grains. However, the associations were attenuated to null after adjusting for covariates. Daily dietary intake of vegetables, dairy, protein, and grains were not associated with fat and FMI.
Conclusion. No associations were observed of dietary intake of food groups with fat mass and FMI in children. A larger sample size and more detailed diet measures are needed to study the association in the future.

Nutrition/obesity

Pericconceptional plant-based dietary patterns and cardiometabolic risk at 3 years postpartum Qianhui Jin*, Qianhui Jin, Lisa Bodnar, Ashley Naimi, Sara Parisi,

Background: The periconceptional period represents a critical window for primordial prevention of cardiometabolic conditions, which are increasingly prevalent among US reproductive-aged women. Plant-based dietary patterns may reduce cardiometabolic risk, yet little is known about whether these dietary patterns during the periconceptional period are associated with postpartum cardiometabolic conditions.

Objective: To evaluate the association between periconceptional plant-based dietary patterns and cardiometabolic risk at 3 years postpartum.

Methods: We used data from the Nulliparous Pregnancy Outcomes Study: monitoring mothers-to-be Heart Health Study, a pregnancy cohort study that followed participants from pregnancy to a median of 3 years postpartum (n=3776). Usual dietary intake during the 3 months around conception was estimated from a food frequency questionnaire. We used k-means clustering on the percent of total energy contributed by 17 food groups and 3 dietary components to identify dietary patterns, which were then characterized by percent of total energy derived from plant sources. Associations between dietary patterns and new-onset postpartum hypertension, metabolic syndrome were estimated using a doubly robust estimator and an ensemble of machine learning algorithms to account for confounders including sociodemographic, medical and neighborhood factors.

Results: Three dietary patterns were identified: “Animal foods, high refined grains, and added sugars” (48%); “Plant-forward, high fruits and vegetables” (14%); and “Plant-forward, high grains” (36%), with mean percent of total energy from plant sources of 62%, 67%, and 72%, respectively. Approximately 15% of participants met the criteria for metabolic syndrome (n=551) and 20% had hypertension (n=752). The unadjusted prevalence of metabolic syndrome was highest in the “Animal foods, high refined grains, and added sugars” pattern (20%) and approximately half as high in the plant-forward patterns (9-11%), while unadjusted hypertension prevalence was modestly lower in the plant-forward patterns (17-18%) than in the “Animal foods, high refined grains, and added sugars” pattern (22%). After adjusting for confounders, compared with the “Animal foods, high refined grains, and added sugars” pattern, the “Plant-forward, high grains” pattern was associated with 2.7 fewer cases of metabolic syndrome per 100 participants (adjusted risk differences [RD]: -2.7, (95% confidence interval [CI]: -5.4, -0.1), whereas the “Plant-forward, high fruits and vegetables” pattern was not meaningfully associated with metabolic syndrome (RD: -2.4; 95% CI: -5.5, 0.7). No meaningful associations across dietary patterns were observed for hypertension.

Conclusions: Periconceptional dietary patterns that emphasize plant foods may be linked to a reduced postpartum metabolic syndrome risk. Structural interventions that improve access to and affordability of nutrient-dense plant foods may help support shifts toward plant-forward dietary patterns during the reproductive years and promote postpartum cardiometabolic health.

Pregnancy outcomes

Pre-pregnancy calcium supplementation on the risk of gestational hypertension and proteinuria: A per-protocol analysis of a randomized trial Chase Latour*, Chase Latour, Kyle Busse, Gabriela Cormick, Stefanie Hinkle, José Belizán, Enrique Schisterman, Sunni Mumford, Ellen Caniglia,

Introduction: Adhering to pre- and early-pregnancy low-dose calcium supplementation may reduce the risk of preeclampsia. However, its effect on preeclampsia physiology—specifically, gestational hypertension and proteinuria—is unclear.

Methods: We analyzed data from a double-blind, placebo-controlled trial of daily, low-dose calcium supplementation from pre-conception through 20 weeks' gestation among women with prior preeclampsia in Zimbabwe, South Africa, and Argentina (2011-16). Persons with chronic hypertension and proteinuria at screening were excluded. Gestational hypertension and proteinuria were assessed during study visits at 20 and 32 weeks', from medical records, and at delivery based on blood pressures (systolic ≥140 or diastolic ≥90 mmHg) and urine protein (≥2 on urine dipstick or elevated urinary protein lab values). Adherence was defined as taking assigned tablets at least 5 days/week, on average, as determined by 12-weekly counts. We estimated per-protocol risk ratios (RRs) with parametric g-computation. We addressed missingness via multiple imputation (m=10) and estimated confidence intervals (CIs) via bootstrap (n=500).

Results: Among 1,355 participants (678 calcium, 677 placebo), 60% adhered to assigned treatment. Gestational hypertension and proteinuria were imputed for 573 and 978 persons, respectively, for ≥1 month of follow-up. Adhering to pre- and early-pregnancy calcium supplementation (vs placebo) had minimal to no effect on risk of gestational hypertension (33.6% vs 35.2%; RR=0.95 [95% CI: 0.90, 1.05]) or proteinuria (20.7% vs 21.6%, RR=0.95 [95% CI: 0.87, 1.04]).

Conclusions: Though prior analyses found adherence to pre- and early-pregnancy low-dose calcium associated with reduced preeclampsia risk, we found no associations with gestational hypertension or proteinuria, though estimates were in the same direction. These differences may reflect bias towards the null from non-differential outcome misclassification in secondary trial outcomes.

Social determinants of health

The association between social supports in the perinatal period and breastfeeding status in the MAASTHI cohort in Southern India Andrew Williams*, Andrew Williams, Prafulla Shriyan, Deepa Ravi, Marta Hill, Maithili Karthik, Vishrutha Thulasiram, Giridhar Babu,

Background: Social support (emotional, informational, or practical assistance, from friends or healthcare professionals), may promote breastfeeding. In India, breastfeeding rates have increased over the past 30 years, yet progress has stagnated. This analysis quantified the association of social support during pregnancy and postpartum with breastfeeding among a cohort of Indian mothers and their children.

Methods: The sample consisted of 851 pregnant women from the MAASTHI birth cohort in Southern India who completed social support assessments (during pregnancy and one-year postpartum), and with consistent breastfeeding data through one year postpartum. Composite social support scores were categorized into four groups as low social support at both time points, high social support only during pregnancy, high social support only at one-year and high social support at both timepoints. Regression models estimated the association between social support and breastfeeding at one-year, adjusted for sociodemographic and obstetric factors.

Results: Average duration of breastfeeding was 199 days. In regression analyses, breastfeeding support at birth was associated with breastmilk being the child's first food (AOR=2.37, 95%CI:1.84,3.05) and breastfeeding initiation within 1 to 4 hours of birth (AOR= 5.60, 95%CI:2.96,10.57). Compared to women with low social support at both pregnancy and one year postpartum, women with high social support during pregnancy had greater odds of breastfeeding at one year (AOR=1.45, 95%CI:1.02,2.06).

We did not find any significant association for women with high social support at both pregnancy and one year, or high social support at one year alone.

Discussion: Breastfeeding support at birth was associated with early initiation of breastfeeding. High levels of social support during pregnancy was associated with breastfeeding at one year. Timing and type of social support may determine how beneficial social supports are to a breastfeeding mother.

Pregnancy outcomes

Heatwave Exposure During Pregnancy and Risk of Gestational Diabetes Mellitus in Arizona (2014-2021) Paulina Luna Ramirez*, Paulina Luna Ramirez, Rietta Wagoner, Melissa Furlong,

Exposure to extreme heat during pregnancy has been associated with a higher risk of adverse perinatal outcomes, but evidence regarding gestational diabetes mellitus (GDM) remains limited. The purpose of this study was to identify the association between heatwave exposure during pregnancy and odds of GDM, while identifying gestational weeks of susceptibility.

The analytical sample included 536,621 singleton births from Arizona birth certificates and a total of 43, 481 GDM cases. Heatwaves were defined as 3,4, and 5 consecutive days of a temperature higher than 42 degrees Celsius. Distributed non-linear lag models were utilized to estimate the odds ratios (OR) and 95% confidence intervals (CI) across gestational weeks. Models were adjusted for birth year, infant sex, county, month of conception and maternal demographic characteristics such as age, race/ethnicity, and education. Additional heat index models were incorporated to assess temperature and humidity.

For the maximum temperature models, positive associations were observed for 3-day, 4-day and 5-day heatwaves between gestational weeks 11 and 27 with odds ratios of 1.02-1.03 and a 95 %CI (1.01-1.03).

Heat index models showed significant associations earlier in pregnancy. The highest associations were observed between gestational weeks 0-15 with an OR of 1.03 and a 95% CI (1.01- 1.05).

These findings suggest that heatwave exposure during early and middle pregnancy are associated with the odds of developing GDM. Heat index models identified an association earlier, possibly indicating that combining temperature and humidity may be better at capturing the physiological response of heat stress. This highlights the importance of considering the gestational period and heatwave duration when identifying pregnancy outcomes related to heat.

Environment/climate change

Air Pollution Exposure Across Spermatogenesis and Sperm DNA Methylation Carrie Nobles*, Carrie Nobles, Timothy Canty, Karolina Nowak, Neil Perkins, Pauline Mendola, Lindsey Russo, Kaniz Rabeya, Gabrielle Johnson, Karen Schliep, Rachael Hemmert, May Shaaban, Akanksha Singh, Allison Ring, C Matthew Peterson, Erica Johnstone, Richard Pilsner,

Introduction: While air pollution is associated with decrements in semen quality, underlying mechanisms and downstream impacts on fertility and offspring health remain underexplored. We evaluated the association of air pollution with sperm DNA methylation as a potential pathway for adverse impacts of air pollution on men's reproductive health.

Methods: This ancillary study included 1,220 men from the Folic Acid and Zinc Supplementation Trial (2013-2017) enrolled in Salt Lake City with a semen sample collected 6 months after enrollment. Residential air pollution exposure during spermatogenesis, including nitrogen dioxide, ozone, and fine particulate matter, was estimated using the Community Multiscale Air Quality model. Sperm DNA methylation was previously assessed using the Illumina EPIC v1 array platform. Linear regression identified the CpGs (CpGassoc) and Differentially Methylated Regions (DMR, Aclust2.0) falling below the false discovery rate (FDR, $q<0.05$) and nominal $p<0.0001$ per increase in each air pollutant, adjusted for co-pollutants, age, and season. Gene set enrichment analyses (GSEA) retained genes with $q<0.05$ and normalized enrichment score >1.8 or <-1.8.

Results: While only one CpG site fell below FDR significance, we observed a relationship of air pollutants with 121 CpGs and 30 DMRs at $p<0.0001$, annotated to 104 and 11 individual genes, respectively. DMRs were annotated to several genes implicated in spermatogenesis, including DNA transcription and repair (RIOX1, FANCL), proteostasis (RPL39P25), mitotic division and microtubule assembly (ANKRD53, TUBB4A), and cell adhesion and immune response (ST8SIA2, PLA2G4D). GSEA identified upregulated pathways associated with detection of chemical stimuli and downregulated pathways associated with mitochondrial translation during spermatogenesis.

Conclusions: Findings add to emerging evidence suggesting men's air pollution exposure may be associated with differential methylation of genes linked to spermatogenesis.

Environment/climate change

Per- and Polyfluoroalkyl Substances (PFAS), Perceived Stress, and Miscarriage in a Cohort of U.S. Black Women Samantha Schildroth*, Samantha Schildroth, Birgit Claus Henn, Victoria Fruh, Amelia K Wesselink, Anissa I Vines, Antonia M Calafat, Julianne Cook Botelho, Alexander P Keil, Chandra L Jackson, Anne Marie Jukic, Quaker E Harmon, Donna D Baird, Ganesa Wegienka, Lauren A Wise,

Background: Per- and polyfluoroalkyl substances (PFAS) can dysregulate hormonal and metabolic processes supporting healthy pregnancies. PFAS exposure has been associated with miscarriage risk but less is known about co-exposure to multiple PFAS and psychosocial stressors, especially among Black women.

Methods: We used prospective data from 538 participants from the Study of Environment, Lifestyle, and Fibroids who self-identified as Black/African American. We measured concentrations of six PFAS in baseline plasma samples and participants completed the Perceived Stress Scale-4 (PSS-4) at baseline. Participants reported pregnancy outcomes (miscarriage, induced abortion, ectopic/tubal pregnancy, live birth, stillbirth) at follow-up study visits (~20, 40, and 60 months). We used Cox proportional hazards models, using gestational week as the time scale, to estimate hazard ratios (HRs) with 95% confidence intervals (CIs) characterizing miscarriage risk associated with PFAS concentrations and PSS-4 scores. We also used the survival extension of quantile-based g-computation to estimate associations of the mixture (PFAS and PSS-4 scores) with miscarriage risk.

Results: Ninety-five miscarriages were reported in the study. In Cox models, perfluorohexanesulfonic acid (PFHxS) was associated with 99% (95% CI=1.10, 3.58) and 52% (95% CI=0.73, 3.17) higher risk for miscarriage at the 50th-74th and ≥75th percentiles (vs. <50th percentile), respectively. Other PFAS were not strongly associated with miscarriage. PSS-4 scores (per 1-standard deviation increase) were associated with 23% (95% CI=0.98, 1.53) higher risk for miscarriage. The mixture (PFAS and PSS-4 scores) was non-linearly associated with higher miscarriage risk, but associations were imprecise.

Conclusions: PFHxS and experience of perceived stress were associated with higher risk of miscarriage in a cohort of Black women.

Environment/climate change

The role of early-life lead exposure on allergic endpoints among disadvantaged children residing in Philadelphia, PA Greta Ziegler*, Greta Ziegler, Jing Nie, Heather Lehman, Marina Oktapodas Feiler,

Introduction

There is limited evidence that early life low-level lead exposure, even below the current set action level, may be associated with allergic disease. The present study investigated this association among a low-income, inner-city cohort of children residing in Philadelphia, PA.

Methods

Electronic medical charts of children <10 years of age who presented to the Temple University Hospital System from 2010-2020 were retrospectively reviewed. Laboratory-measured blood lead levels (BLLs) were pulled from medical records and allergy outcomes were defined using ICD-10 codes. Log-binomial regression models were fit adjusting for child age at lead exposure, race, and ethnicity to estimate prevalence ratios (PR) and 95% confidence intervals (CIs) for the association between BLLs and allergic outcomes.

Results

There were 14,217 children that met the inclusion criteria. In this cohort, 58% (n=8,356) were Black. After adjustment, children with the highest categorical BLLs (≥ 3.5 µg/dL) had 2.58 (95% CI: 2.15, 3.10) times greater risk of having any allergic outcome. When stratified by asthma status, the association was stronger for those without asthma (PR=2.28) than those with asthma (PR=1.70). Children with BLLs between 1-3.4 µg/dL had a positive association with food allergies (PR=1.73, 95% CI=1.08, 2.80), compared to those with BLLs <1 µg/dL. In children with BLLs between 1-3.4 µg/dL and ≥3.5 µg/dL, higher risks of plant allergy were observed (PR=2.61, 95% CI=2.11, 3.23; PR=2.54, 95% CI=2.04, 3.16, respectively), compared with children with levels <1 µg/dL.

Conclusion

Children in this low-income, inner-city cohort with elevated BLLs, even those below the public health action value, have significantly increased risk of any allergic disease. These findings indicate a high-risk group of children for adverse allergic outcomes who could benefit from targeted clinical, community, and policy interventions to reduce lead exposure or prevent allergic outcomes.

Child health and development

Gestational Exposure to Organophosphate Esters and Adiposity at 7–9 Years: Evidence from a pan-Canadian Birth Cohort Yohane Vincent Abero Phiri*, Yohane Vincent Abero Phiri, Aimin Chen, Jillian Ashley-Martin, Tye E. Arbuckle, Joseph Braun, Sheniz Moonie, Youssef Oulhote, William Fraser, Melissa Legrand, Michael M. Borghese, John Krzeczkowski, Maria Velez, Bruce Lanphear, Katherine Morrison, Mandy Fisher, Mark R. Palmet, Maryse Bouchard, Ann M. Vuong,

Background
Organophosphate esters (OPEs) are ubiquitous chemicals with obesogenic properties; but evidence regarding the association between prenatal exposure and childhood adiposity is limited.
Methods
Using data from 306 mother-child dyads in the Maternal Infant Research on Environmental Chemicals (MIREC) cohort, we examined associations between prenatal urinary concentrations of OPE metabolites, including bis(2-chloroethyl) phosphate (BCEP), bis(1-chloro-2-propyl) phosphate (BCIPP), bis(1,3-dichloro-2-propyl) phosphate (BDCIPP), di-n-butyl phosphate (DNBP), and diphenyl phosphate (DPHP), measured at 6-13 and 16-21 weeks of gestation, and ten indicators of adiposity in children aged 7-9 years. Covariate-adjusted linear and logistic regression models were used to estimate metabolite-specific associations and effect measure modification by sex as well as quantile g-computation to assess joint (i.e., mixture) effects.
Results
First trimester BCIPP concentrations were associated with higher odds of overweight or obesity [adjusted odds ratio (aOR) = 2.51; 95% CI: 1.01, 7.77] and higher body fat percentage [β = 0.90; 95% CI: 0.18, 1.62], while DNBP was positively associated with waist-to-height z-scores [β = 0.64; 95% CI: 0.12, 0.86] and body fat percentage [β = 0.20; 95% CI: 0.14, 1.48]. Second trimester results showed similar patterns, with BCIPP associated with higher overweight/obesity risk [aOR = 1.66; 95% CI: 1.02, 3.09] and DNBP associated with higher fat mass index and waist-circumference Z-scores. Mixture effects were largely null; however, BCIPP and DNBP contributed most strongly to the positive mixture associations with increased adiposity. Some of the aforementioned associations were stronger among girls.
Conclusion
Prenatal exposure to OPE metabolites, particularly BCIPP and DNBP, was associated with higher mid-childhood adiposity in this Canadian birth cohort, suggesting that early-life OPE exposure are obesogens.

Gender and sexual identity

Intersectional Disparities in Perinatal Outcomes among Ethnoracial Minority Same-Gender Couples Diana Tordoff*, Diana Tordoff, Stephanie Leonard, Safyer McKenzie-Sampson, Mekhala Dissanayake, Juno Obedin-Maliver, Suzan Carmichael,

Background: Sexual minority women experience higher risk of adverse pregnancy outcomes compared to heterosexual women. Both sexual minority and ethnoracial minority women have higher risk of adverse pregnancy outcomes, but whether and how these identities intersect is largely unknown. We used a quantitative intersectionality approach to describe perinatal outcomes at the intersection of ethnoracial group and family structure, focusing on mother-mother partnerships.

Methods: We used linked vital records and hospitalization discharge data for live births in California 2016-2020. We considered two maternal outcomes (postpartum hemorrhage [PPH] and severe maternal morbidity [SMM]) and two infant outcomes (preterm birth <37 weeks and low birth weight <2500g [LBW]). We estimated adjusted predicted probabilities and risk differences (RD) from logistic regression models adjusted for maternal age, nulliparity, multifetal gestation, education level, and insurance.

Results: The analytic sample included 1,916,822 births to mother-father couples and 4,105 births to mother-mother couples. Maternal ethnoracial identities included 16% Asian, 5% Black, 45% Hispanic of any race, and 31% White. Women in mother-mother partnerships had higher rates of PPH and SMM than women in mother-father couples across all ethnoracial groups. Among White women, births to mother-mother couples were more likely to be preterm (RD 1.1 per 100 births, 95%CI 0.1-2.3)) and LBW (RD 0.7 per 100 births, 95% CI 0.1-1.7), but this disparity was not observed for other ethnoracial groups. Black women in mother-mother partnerships had the highest prevalence for all outcomes: 6.9% PPH, 5.5% SMM, 10.2% preterm birth, 10.2% LBW.

Conclusions: Ethnoracial minority women in same-gender couples experience compounded disparities in PPH and SMM, but we did not observe this pattern for infant outcomes. Our findings highlight the need for future work focused on improving maternal outcomes for Black sexual minority women.

Health equity

Reducing maternal health disparities for Asian American/Pacific Islanders: the role of comorbidities Mekhala Dissanayake*, Mekhala Dissanayake, Maya Mathur, Suzan Carmichael, Elliott Main,

Asian American/ Pacific Islander (AAPI) groups experience different burdens of severe maternal morbidity (SMM), as well as comorbidities that contribute to SMM, such as hypertensive disorders of pregnancy (HDP) and diabetes. We sought to determine the extent to which differences in the prevalence of comorbidities explain disparities in SMM among AAPI groups. We analyzed linked vital statistics records and maternal hospital discharge records from California from 2011-2019, examining SMM from delivery to 42 days postpartum among White (referent), Chinese, Indian, Filipina, and Pacific Islander women. We examined the presence of any comorbidity (HDP: chronic/gestational hypertension, pre-eclampsia; Diabetes: chronic /gestational diabetes) as a mediator and controlled for maternal age, parity, pre-pregnancy body mass index, education, and insurance. We used inverse odds weights to balance mediator distributions between AAPI groups and Whites, estimating total effects (existing disparity) and direct effects (unexplained disparity) with risk ratios. Our sample included 1,686,972 births. Chinese and Indian women had lower prevalences of HDP (White 10.3%, Chinese 4.5%, Indian 7.6%), higher prevalences of diabetes (White 8.4%, Chinese 15.0%, Indian 20.8%) and similar prevalences of SMM (White 1.6%, Chinese 1.7%, Indian 1.8%) compared to Whites. Filipina and Pacific Islander women had higher prevalences of HDP (Filipina 15.1%, Pacific Islander 14.2%), diabetes (16.3% and 20.9%, respectively) and SMM (2.6% and 2.6%, respectively). Balancing mediators did not reduce disparities among Chinese and Indian women. Among Filipinas, balancing mediators reduced the existing disparity of 1.64 (95% Confidence Interval (CI): 1.57, 1.71) to 1.47 (95% CI: 1.39, 1.53). Among Pacific Islanders, the existing disparity of 1.47 (95% CI: 1.04, 1.60) was reduced to 1.37 (95% CI: 1.07, 1.56). Overall, our results suggest a need for tailored interventions to prevent SMM among AAPI groups.

Health equity

Decomposition of the Black-White Disparity in Vaginal Birth after Cesarean with a Trial of Labor Lindsay Mallick*, Lindsay Mallick, Marie Thoma, Katherine Grantz, Rajeshwari Sundaram, Bizu Gelaye,

Vaginal birth after cesarean (VBAC) is associated with a lower risk of maternal morbidity, though concern for uterine rupture often motivates a planned repeat cesarean section (CS). Though VBAC rates are similar between Black and White women in the US, rates diverge among those with a trial of labor after CS (TOLAC). Given pervasive maternal mortality disparities, examining unplanned CS with TOLAC is critical.

We used 2017-2021 natality data to examine factors explaining the Black-White disparity in VBAC among singleton, vertex births at 39-41 weeks' gestation to those with one prior birth undergoing TOLAC (N=159,238). Adjusted linear probability models estimated race-stratified risk difference (RD). Oaxaca-Blinder decomposition quantified the proportion of the disparity in VBAC explained by group differences in covariate distributions rather than RD alone. Covariates (21 total) included socioeconomic, health, risk behavior, state, and urbanicity.

An unplanned CS with TOLAC occurred in 46% of Black and 31% of White parturients, leaving a 15-percentage point (ppt) disparity in VBAC. There were noted differences in risk factor prevalence and RDs in delivery mode by race, for example, larger RDs for some states of residence for Black parturients. Factors that contributed most to the disparity were BMI (15%), insurance (7%), long birth interval (5%), education (4%), and residence state (3%), though younger maternal age and lower birthweight reduced the gap (-13%). In total, 22% of the VBAC disparity could be explained by the modeled factors, such that, if all were equal, the disparity would only lower from 15 to 12 ppt.

Though underreporting of risk factors and unobserved clinical predictors like cervical favorability may differ slightly by race, it is unlikely that unmeasured factors contributing to this disparity are solely physiological. Rather, the substantial unexplained portion may reflect structural influences and warrants further investigation using clinical data.

Obstetric health

Timing of Sepsis and Progression to Septic Shock During Pregnancy and Postpartum Hiluf Ebuy Abraha*, Hiluf Ebuy Abraha, Hale Teka, Bisrat Tesfay Abera1,

Background

Sepsis remains a leading cause of maternal morbidity and mortality worldwide. Although sepsis can occur across all stages of pregnancy, less is known about whether its timing influences progression to severe disease, including septic shock. This study examined the association between sepsis timing and progression to septic shock.

Methods

We conducted a retrospective cohort study of 298 pregnant or postpartum women with sepsis at Ayder Hospital in Tigray, Ethiopia, between 2015 and 2021. The primary outcome was progression to septic shock. Sepsis timing was categorized as abortion-related, pregnancy-associated (during pregnancy or labor), or postpartum. To address small-sample bias and potential separation, we used Firth penalized logistic regression. The primary model adjusted for maternal age, parity, residence, antenatal care visits, and baseline obstetric morbidities. A secondary model additionally adjusted for focus of infection.

Results

Overall, 38 (12.8%) women progressed to septic shock. In the primary adjusted model, sepsis during pregnancy was associated with higher odds of septic shock compared with postpartum sepsis (adjusted Odds Ratio [aOR] = 3.4, 95% Confidence Interval [CI]: 1.4-8.1). Abortion-related sepsis was associated with higher but non-significant odds of shock (aOR = 1.7, 95% CI: 0.6-4.9). After adjustment for focus of infection, the association for sepsis during pregnancy was attenuated but remained significant (aOR = 2.8, 95% CI: 1.1-6.6). Non-obstetric infection focus was associated with increased odds of septic shock (aOR = 3.5, 95% CI: 1.6-7.4).

Conclusions

Sepsis during pregnancy was associated with increased odds of septic shock compared with postpartum sepsis. Partial attenuation after adjustment for infection focus suggests differences in infection source may contribute to timing-related severity. These findings underscore the need for early recognition and timely escalation of care for sepsis during pregnancy and labor.

Pregnancy outcomes

Exploring Temporal Trends in Ectopic Pregnancy Using Electronic Health Record Data *, Kirsten Hepburn, Tiffany Moore, Neeharica Kodali, Dominic Apio, Alexandra Hergenrader, Melissa Mathes, Emma Buddenhagen, Sydni Springer, Zoe Keese, Quinlan Couch, Christopher Wichman, Elizabeth Reisher, Elizabeth Weedin, Carol Geary,

Background: Ectopic pregnancy (EP) remains a leading cause of early pregnancy morbidity and mortality, and is a serious condition necessitating medical intervention. However, its etiology is largely unknown. Monthly or seasonal incidence patterns have been noted but are poorly understood due to inconsistencies in data capture and analytical methods. Better-defined temporal patterns could guide research on underlying causal mechanisms. Using diagnoses, care, and date/time data, we aimed to characterize EP incidence temporal trends.

Methods: Using an algorithm based on billing and diagnosis codes, we identified unique pregnancies and their outcomes from a U.S. Midwestern academic medical center between 2014-2023. Estimated pregnancy start date was derived from embryo transfer, last menstrual period or ultrasound documentation from within the EHR. Manual chart review was used to confirm EP diagnosis, complete missing data, and perform random data quality checks. Periodic and binomial logistic regression modeling was used to examine month-to-month and annual ectopic pregnancy trends, adjusting for EP-related covariates.

Results: Among the 20,290 pregnancies identified, 1.9% were ectopic. EP was more commonly associated with being self-identified as Black, invitro fertilization, a history of sexually transmitted infection history or smoking, and advancing maternal age. EP rates rose from 1.3% in 2014 to ~2% in 2019, when rates plateaued. Wide variation in absolute EP counts (range: 0-8 per month) was noted. However, there were not statistically significant monthly or seasonal trends in EP incidence across the study period, before or after covariate adjustment.

Conclusions: EP estimates aligned with those reported nationally. Although there were no consistent monthly or seasonal trends, EP case clustering may represent non-annually cyclical factors. In addition, we found an increase in incidence during the second half of the study period, warranting further investigation.

Big Data/Machine Learning/AI

Accelerating Pediatric Epidemiologic Research Through AI-Powered Research Management Systems Allison Curry*, Allison Curry, Ryan Warren, Johnathon Ehsani, Dominique Ruggieri, Joel Hillier,

Epidemiologic research infrastructure remains fragmented across recruitment, screening, consent, and data collection—creating major operational barriers. Concurrently, rising personnel costs, compliance requirements, and funding instability mean fewer studies, longer timelines, and staff effort diverted from science to documentation—inefficiencies that compound in under-resourced settings where pediatric disease burden is highest.

We developed a HIPAA-compliant Research Management System to accelerate participant-based pediatric epidemiologic studies while meeting institutional governance requirements. The RMS consolidates operations with role-based access, immutable audit trails, and IRB-ready documentation. Protocol-grounded AI capabilities enable multilingual participant recruitment, automated consent/assent with comprehension validation (including automated reconsent when minors reach age 18), and real-time tracking of engagement metrics. Security architecture supports academic implementation. We evaluated multi-institutional feasibility and preliminary performance.

Five institutions—Harvard, Johns Hopkins, UWash, UIowa, Nationwide Children's Hospital—completed independent security, AI governance, and IRB reviews, and then initiated epidemiologic projects. UIowa's feasibility study (n=20 young adults) showed clear AI interactions, 2-day completion versus 4-week conventional estimate, and coordinator effort reduced from 50 to 4 hours. Ongoing validation studies include Johns Hopkins' longitudinal adolescent driving cohort (n=256) and Nationwide Children's pediatric injury research.

A governance-first AI platform successfully implemented across diverse academic settings demonstrated feasibility for accelerating pediatric epidemiologic operations. Preliminary findings suggest substantial efficiency gains; ongoing validation studies are assessing methodological rigor, representativeness, and equity implications.

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Child health and development

Pregnancy and childhood health behaviors modify associations of maternal obesity with childhood obesity and adiposity Sylvia Badon*, Sylvia Badon, Monique Hedderson, Emily Knapp, Ben Marafino, Rana Chehab, Bethany Hallenbeck, Michelle Katzow, Wei Perng, Yeyi Zhu, Assiamira Ferrara,

Background: Exposure to maternal obesity during gestation is associated with childhood obesity and adiposity; there is a need to identify modifiable behaviors that mitigate these obesogenic effects. We evaluated whether sleep, physical activity (PA), or diet during pregnancy or in childhood modified these relationships.
Methods: We used harmonized data from the Environmental Influences on Child Health Outcomes (ECHO) Cohort [n ranged from 4,027 (for pregnancy PA) to 18,507 (for childhood sleep)]. We ran separate mixed effects models for each outcome (childhood obesity based on BMI; waist circumference as a measure of adiposity) and effect modifier (self- or parent-reported sleep, PA, diet) with a product term between maternal BMI category and each effect modifier. We used a p-value threshold of 0.1 for evidence of effect modification.
Results: The association of maternal obesity with childhood obesity was modified by pregnancy diet ($p=0.04$) and childhood PA ($p=0.06$). Associations of maternal obesity with childhood obesity were attenuated in those with exposure to high vs low quality pregnancy diet [OR(95% CI): 1.6(0.9-2.9) vs 3.3(2.8-3.9)] and in those meeting/exceeding vs below recommended childhood PA [3.5(2.9-4.2) vs 3.7(3.2-4.2)]. The association of maternal obesity with childhood waist circumference was modified by pregnancy and childhood diet ($p=0.05$, 0.07) and childhood sleep ($p<0.001$). Associations of maternal obesity with childhood waist circumference were attenuated in those with high vs low diet quality [mean difference(95%CI):1.8cm(0.1-3.6) vs 4.5(3.9-5.1) for pregnancy; 4.0(3.2-4.8) vs 5.8(4.8-6.8) for childhood] and below vs meeting/exceeding recommended childhood sleep [3.4(2.8-4.0) vs 5.7(5.3-6.2)].
Conclusions: A high quality diet in pregnancy or childhood and recommended levels of childhood PA may mitigate the associations of maternal obesity with childhood obesity and adiposity. These findings suggest opportunities for early behavioral intervention.

Child health and development

Maternal Nitrosatable Drugs Use in Pregnancy and Risks of Autism Spectrum Disorders and Attention Deficit Hyperactivity Disorders in Offspring. Zeyan Liew*, Eugenia Chock, Ya-Hui Hu, Pengfei Guo, Chuanjie Deng, Julia Heck, Pei-Chen Lee, Zeyan Liew,

Background:

Nitrosatable drugs (NSDs) are increasingly used in pregnancy and have been linked with adverse pregnancy outcomes, birth defects, and childhood cancers. Whether maternal use of NSDs affects the risk for offspring's neurodevelopmental disorders is unknown.

Objective:

We evaluated the association between maternal antenatal prescriptions of NSDs and diagnoses of autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) among offspring in Taiwan.

Design, Setting, and Participants:

We conducted a nationwide cohort study of 2,093,821 mother-child pairs linking the Taiwan National Birth Certificate database (2004-2015) and the Taiwan National Health Insurance Research Database (2004-2019). We estimated the Incidence Rate Ratio (IRR) for childhood ASD or ADHD according to maternal claims of at least two prescriptions of NSDs during pregnancy as being exposed. The NSD medications were further categorized as amides, secondary, or tertiary amides. We used standard outcome regression and propensity score (PS) analyses to control for a range of confounding factors, including sociodemographic, pregnancy morbidities, and use of other medications.

Results:

Inverse relationships were observed between maternal claims of two prescriptions of any NSD in pregnancy and childhood ASD (IRR: 0.88, 95% CI 0.84-0.91) and ADHD (IRR: 0.82, 95% CI 0.80-0.83) after controlling for confounders. The associations were similar for amides and tertiary amides, but a small increase in risks was noted for secondary amines and ASD (IRR: 1.12, 95% CI 1.07-1.18); or ADHD (IRR:1.18, 95% CI 1.15-1.21).

Conclusion:

We found no strong evidence that NSD use during pregnancy affects the risks of childhood ASD and ADHD, while the roles of maternal exposure to secondary amines and childhood neurodevelopment impairments need further scrutiny.

Child health and development

Exploring New Opportunities for Epidemiological Research using HBCD Biospecimens

Darci Johnson*, Darci Johnson, Kimberly LeBlanc, Katherine Cole, Traci Murray, Christopher Sarampote,

The HEALthy Brain and Child Development (HBCD) Study, the largest long-term study of early brain and child development in the U.S., aims to identify variability in neurodevelopmental trajectories and investigate how risk and resilience factors may impact these trajectories. This multi-site, longitudinal cohort study sponsored by over a dozen National Institutes of Health (NIH) Institutes, Centers, and Offices has enrolled over 4,600 families during pregnancy and will follow them throughout childhood. HBCD participants include over 35% who have been exposed to substances prenatally. Measures for parents include pregnancy information, biospecimens, and medical and family history. Measures for children include anthropometrics, biospecimens, social, emotional, and cognitive function, and EEGs and MRIs from early infancy to assess brain activity and growth.

HBCD data is available publicly on the NIH Brain Development Cohorts (NBDC) Data Hub, where researchers can apply for access to this rich dataset. HBCD Data Release 2.0, scheduled for February 2026, will include cumulative information on over 3,500 pregnancies, 2,200 infants aged 0-1 month, 1,300 infants aged 3-9 months, 600 infants aged 9-15 months, and 450 infants aged 10-17 months.

In addition to the NBDC Data Hub, researchers will soon be able to apply for access to HBCD biospecimens. Samples include saliva, DNA from saliva, plasma, serum, whole blood, placenta, umbilical cord, and cord blood from moms, and saliva, DNA from saliva, stool, and urine from children, which researchers will apply for access to through an X01 at the NIH. Increasing access to these specimens will support further research into areas such as epigenetics, environmental exposures, and biological function.

This unprecedented resource of data and biospecimens provides new epidemiological opportunities for studying the neurodevelopmental trajectories of children, both exposed and unexposed to substances.

Child health and development

Prenatal Phthalate Exposure, Child Adiposity, and Executive Function in Middle Childhood

Joana Amankwaa*, Joana Amankwaa, Stephanie Engel, Amanda Ramos,

Phthalates are endocrine-disrupting chemicals widely used in consumer products. Prenatal exposure to phthalates has been associated with long-term cognitive deficits. However, factors that shape individual susceptibility to phthalate-related neurodevelopmental risk are still being explored. Because phthalates are lipophilic and have been linked to metabolic disruption and increased adiposity, and childhood adiposity has been associated with EF deficits, child fat mass may be a relevant biological factor that moderates this relationship. Using data from the Mount Sinai Children's Environmental Health Study, we examined whether child adiposity moderates the relationship between prenatal phthalate exposure and EF in middle childhood.

This sample includes 404 mother–child dyads, with the analytic sample including 86 children with complete data on phthalate exposure, fat mass, and EF. Prenatal phthalate exposure was assessed using maternal spot urine samples collected between 25 and 40 weeks' gestation, and composite log scores were created for low molecular weight (LMW) and high molecular weight (HMW) phthalates. Child adiposity was assessed at age 4 using bioelectrical impedance analysis to estimate fat mass percentage. EF was measured between ages 6-9 using the Behavior Rating Inventory of Executive Function (BRIEF). For children with EF data at multiple waves, the oldest available BRIEF assessment was used, resulting in a single EF score per child. Analyses controlled for creatinine, race, sex, marital status, smoking during pregnancy, and education.

Across separate moderation models examining LMW and HMW phthalates, higher fat mass percentage at age 4 showed positive associations with Global Executive Composite T scores (LMW: $\beta = 0.25$, 95% CI [−0.04, 0.54]; HMW: $\beta = 0.19$, 95% CI [−0.10, 0.48]). There was no evidence of moderation by fat mass percentage for LMW phthalates ($\beta = 0.10$, 95% CI [−0.10, 0.29]) or HMW phthalates ($\beta = 0.10$, 95% CI [−0.09, 0.29]).

While results did not suggest that fat mass moderated the association between prenatal phthalate exposure and EF, results suggested a positive association between child adiposity and EF difficulties in middle childhood. This may indicate that fat mass might act as a mechanism through which phthalates might influence EF, and future analyses will examine this.

Child health and development

Concordance with pediatric urinary tract infection clinical guidelines and short-term outcomes in children in the US Military Health System Yixin Chen*, Yixin Chen, Clinton Hall, Celeste Romano, Chrystelle Kiang, Anna Bukowinski, Zeina Khodr, Gia Gumbs, Ava Conlin, Nanda Ramchandar,

Background: Urinary tract infection (UTI) is a common bacterial infection in early childhood. Inappropriate treatment may lead to adverse short-term outcomes. We assessed concordance with American Academy of Pediatrics guidelines for UTI testing, treatment, and management, and evaluated the risk of selected adverse outcomes associated with treatment nonconcordance in US military-connected children.

Methods: We used Birth and Infant Health Research program data to identify children born January 2012–October 2021 and aged 2–24 months at first UTI diagnosis. Using administrative medical data, we defined testing concordance as having both a urine culture and urinalysis within ± 3 days of diagnosis, treatment concordance as being prescribed proper antibiotics with recommended duration (i.e., 7–14 days) within 5 days of diagnosis, and management concordance as having a renal and bladder ultrasound (RBUS) within 90 days of diagnosis or before a second UTI. Selected adverse health outcomes included antibiotic allergy within 14 days, Clostridium difficile, diarrhea, ER visit, or hospitalization within 30 days of antibiotic dispensation. Adjusted modified Poisson models estimated the risk of any adverse outcome with treatment nonconcordance.

Results: A total of 14,112 children with first UTI treated with antibiotics were included. For testing, 8038 (57.0%) infants had both a urine culture and urinalysis done. For treatment, 12,180 (86.3%) infants had proper antibiotics with recommended duration. For management, 3697 (26.2%) had RBUS. We observed 2056 (14.6%) infants with any of the selected adverse outcomes and estimated a null association with treatment nonconcordance (RR=1.00, 95% CI: 0.89-1.12).

Conclusion: Many infants with an initial UTI are not receiving recommended diagnostic tests or follow-up imaging, highlighting the need for improved practice guidance. High treatment concordance may limit the power to detect differences in short-term adverse outcomes.

Child health and development

Association between infant consumption of water during the Flint water crisis and child development measures Nicole Jones*, Nicole Jones, Brittany Tayler, Jenny LaChance, Diana Haggerty, Eric Finegood, Julia Felton, Crystal Cederna, Mona Hanna,

Objective
The Flint water crisis (April 2014–October 2015) exposed residents to water contaminated with lead. The relationship between infant water consumption during the crisis and childhood socio/emotional skills and executive function remains unexplored. Our objectives were to: (1) describe infant consumption of unfiltered tap water and (2) test associations between infant water consumption and early childhood screening measures.

Methods
This cross-sectional study used data from the Flint Registry. Eligible participants were children exposed to Flint water as infants (0-12 months old) during the crisis whose caregivers completed surveys between 2019–2022 (n=1149). Water consumption was categorized based on caregiver report. Social/emotional and executive function outcomes were assessed using nationally normed tools: the Behavior Assessment System for Children, 3rd Edition (BASC-3), and the Behavior Rating Inventory of Executive Function Screener, 2nd Edition (BRIEF-2). Logistic regression models were adjusted for child age, caregiver education, income, breastfeeding, and material hardship.

Results
Most infants (66%) consumed unfiltered tap water daily during the crisis. Daily consumption was more common among children from lower-income households, with lower caregiver educational attainment, lower household income, higher material hardship, and not breastfed. In adjusted analyses, daily consumption was associated with at-risk or clinically concerning scores on the BRIEF-2 (OR=1.54, 95% CI: 1.07–2.23), BASC-3 internalizing problems (OR=1.93, CI: 1.23–3.03), and BASC-3 adaptive skills (OR=2.02, CI: 1.23–3.31).

Conclusion
This study is the first to describe infant tap water consumption during the Flint water crisis and its association with child social/emotional and executive functions. Findings highlight the need for the need for ongoing lead in water elimination and prevention efforts and early intervention to mitigate long-term health impacts.

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Disability status

Mid-frequency hearing loss in the US pediatric population: Prevalence of an important disability you've never heard about Diana Haggerty*, Diana Haggerty, Nicole Talge,

Mid-frequency hearing loss (MFHL) selectively impacts hearing at frequencies typical of human speech (1000 kHz, 2000 kHz, and sometimes 4000 kHz), and children with MFHL are disadvantaged with respect to communication-driven development and learning. MFHL prevalence in clinical samples is <1%, but prevalence estimates in the general pediatric population are limited and use varying definitions.

To address these issues, we used pediatric audiometry data from the National Health and Nutrition Examination Survey (NHANES; 2017-2020 cycle). Our sample included children (6-18 years) with a complete audiometric exam and no indication of middle ear dysfunction (n=1451). We identified MFHL if the difference between the mean of low and high frequency thresholds and the mean of mid-frequency thresholds exceeded 10 dB in either ear. We considered two existing definitions to generate prevalences: 1) (500 Hz+4,00 kHz)/2 – (1,000 kHz+2,000 kHz)/2, and 2) (500 Hz+ 8,000 kHz)/2 – (1,000 kHz+2,000 kHz+4,000 kHz)/3. We examined the concordance between these definitions using Cohen's kappa and the overlap of each definition with caregiver- or self-reported hearing difficulties. We weighted all estimates to account for the complex study design.

Definitions 1 and 2 classify 5.1% (95%CI 3.7, 6.5) and 5.2% (95%CI 3.8, 6.6) of children with MFHL, respectively. Approximately 51% (definition 1) and 73% (definition 2) of these mid-frequency losses fall above pediatric clinical thresholds (> 15 dB). However, the concordance between definitions 1 & 2 was poor (kappa=0.173, 95%CI 0.172, 0.174). Caregiver or self-reported hearing difficulties were reported in 3% of children with MFHL under definition 1 and 5% under definition 2.

MFHL may be more common in the general pediatric population than previously reported in clinical samples. Developing a validated definition of MFHL is essential to screen, treat, and support children with MFHL during foundational phases of their development.

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Environment/climate change

Interconceptional Exposure to Common Plasticizers and Fetal Growth Kim Nail Cajachagua Torres*, Kim Nail Cajachagua Torres, Linda G. Kahn, Teresa Herrera, Hediyeh Baghsheikhi, Shilpi Mehta-Lee, Yuyan Wang, Wenging Yang, Kurunthachalam Kannan, Mengling Liu, Leonardo Trasande, Akhgar Ghassabian,

Background Maternal exposure to common plasticizers prior to conception may impact fetal growth, but evidence outside of subfertile populations remains limited.

Methods Participants were women with two successive pregnancies enrolled in a NYC birth cohort (2016-2021, interpregnancy interval median=2.5 years, 90% range=0.99-4.9). Exposure data from the first pregnancy or pregnancy 1 (up to three measurements) were used as the interconceptional exposure for the second pregnancy or pregnancy 2, for which fetal growth and birth outcome data were available in 139 and 173 dyads, respectively. We averaged concentrations of urinary phthalate metabolites and bisphenols across timepoints, adjusted for urinary dilution, and natural log-transformed them. Repeated fetal biometry measures from clinical ultrasounds were used to predict growth parameters at 20, 30, and 36 weeks using linear mixed-effects models assuming nonlinear effects of gestational age. Information on birth outcomes was obtained from electronic health records. We used mixed models to test associations with fetal growth across gestation and linear regression for birth outcomes. Since the health effects of phthalates and bisphenols are sexually dimorphic, we examined interactions with fetal sex, which was significant, so we conducted sex-stratified models.

Findings In male fetuses, higher maternal interconceptional levels of mono-ethyl phthalate were positively associated with estimated fetal weight, biparietal diameter, and head circumference. We also found positive associations of mono(2-ethylhexyl) phthalate with abdominal circumference and femur length. In contrast, higher mono-(2-carboxyheptyl) phthalate was associated with shorter femur length. In female fetuses, higher mono(2-carboxymetylhexyl) phthalate was associated with smaller abdominal circumference. Interconceptional levels of phthalate metabolites were positively associated with gestational length but negatively associated with birth length z-scores. There were no associations with bisphenols.

Interpretation Interconceptional exposure to phthalates may influence fetal growth, with males and females affected differently.

Environment/climate change

Using cycle-timed air pollutant estimates to model fecundability Gabrielle Johnson*, Gabrielle Johnson, Kaniz Rabeya, Timothy Canty, Karen Schliep, Rachael Hemmert, Pauline Mendola, Neil Perkins, Akanksha Singh, Allison Ring, Sunni Mumford, Carrie Nobles,

Background: Accounting for sensitive windows of reproduction is crucial for understanding how timing of underlying biologic processes impacts the overall effect of environmental exposures, such as air pollution, on odds of pregnancy.

Methods: We included 1001 women from the Effects of Aspirin in Gestation and Reproduction (EAGeR) trial who lived in the Intermountain West and had residential georeferenced pollutant estimates. We abstracted pollutant data from the Air Quality Data for Health-Related Applications (AQDH) and Community Multiscale Air Quality Modeling System (CMAQ), including ozone (O3), particulate matter 2.5 (PM2.5), nitrogen dioxide (NO2), sulfur dioxide (SO2), and carbon monoxide (CO). We estimated biologically relevant sensitive windows to air pollution timed to cycle start date including pre-ovulation and implantation as well as the corresponding broader follicular and luteal phases, respectively. We constructed a multi-pollutant discrete-time Cox proportional hazards model to predict fecundability odds ratio (FOR) per inter-quartile range (IQR) increase in pollutants. Models adjusted for age, treatment status, income, education, and smoking.

Results: Multi-pollutant models using CMAQ data found that during pre-ovulation, O3 decreased odds of pregnancy by 20% (FOR 0.80, 95% CI 0.67, 0.96 per 15.6 ppb) and NO2 by 20% (FOR 0.8, 95% CI 0.56, 1.13 per 7.1 ppb). During implantation, O3, PM2.5, NO2, and SO2 were associated with trends of lower odds of pregnancy while CO increased odds of pregnancy by 43% (FOR 1.43, 95% CI 1.08, 1.91 per 80.6 ppb). Findings during pre-ovulation and implantation were consistent with follicular and luteal phases, respectively. AQDH data produced similar results.

Conclusion: Our findings account for sensitive windows of reproduction and suggest that air pollution may impact fecundability. Next steps include evaluating pollutant mixtures to further characterize pollutants associated with pregnancy.

Environment/climate change

Examining early gestational susceptibility to ambient air pollutants and risk of pregnancy loss in a time-to-pregnancy cohort Kaniz Rabeya*, Kaniz Rabeya, Gabrielle Johnson, Timothy Canty, Karen Schliep, Rachael Hemmert, Pauline Mendola, Neil Perkins, Akanksha Singh, Allison Ring, Sunni Mumford, Carrie Nobles,

Background: Early pregnancy is a highly sensitive developmental period in relation to pregnancy loss. We examined air pollution exposure during the earliest gestational weeks encompassing implantation, placentation, and embryogenesis.

Methods: A preconception time-to-pregnancy study (EAGeR trial, 2007-2011) enrolled 1,001 women (18-40 years) from the Intermountain West, with most residing along the Wasatch Front. Residential air pollution exposure was estimated from Air Quality Data for Health-Related Applications (AQDH) & Community Multiscale Air Quality (CMAQ) Models, including ozone (O3), fine particulate matter (PM2.5), & nitrogen dioxide (NO2) and averaged across gestational weeks encompassing pre-ovulation & early embryo development (weeks 1-3), implantation & early loss (4&5), & clinical pregnancy loss (6-9). Pregnancy loss was defined as an observed loss after detection of pregnancy using human chorionic gonadotropin. Generalized linear models estimated relative risk for pregnancy loss per interquartile range increase in pollutants, adjusting for age, income, education, race/ethnicity, and season.

Result: A trend of increasing risk of pregnancy loss was observed during the earliest gestational weeks, including pre-ovulation & early embryo development for both models, although estimates were imprecise. In gestational week 4, PM2.5 was associated with a 29% higher risk of pregnancy loss (RR 1.29, 95% CI 1.00, 1.66 per 2.4 µg/m^3 for CMAQ model) while O3 showed no clear association and NO2 was associated with a non-significant risk decrease. Conversely, during weeks encompassing clinical pregnancy loss, NO2 was associated with an imprecise trend of higher pregnancy loss (RRs ranging from 1.20 to 1.45), while PM2.5 RRs ranged from 0.65 to 0.92.

Conclusion: Exposure to air pollution early in pregnancy may be associated with pregnancy loss, although interdependencies among pollutants may limit inferences. Next steps include evaluating broader air pollution mixtures.

Environment/climate change

Prenatal drinking water nitrate and preterm birth in the Agricultural Health Study Cherrel K. Manley*, Cherrel K. Manley, Jessie P. Buckley, Lawrence S. Engel, Mary H. Ward, Dale P. Sandler, Laura E. Beane Freeman, Paul A. Romitti, Stephanie M. Engel,

Prenatal exposure to drinking water nitrate has been associated with increased risk of congenital malformations. Evidence for other birth outcomes has been less consistent. Few studies have evaluated these associations among agricultural workers, who may experience elevated exposures due to use of private wells and proximity to farming activities. We examined the association of prenatal drinking water nitrate exposure with risk of preterm birth in the Agricultural Health Study (AHS), a prospective cohort of licensed pesticide applicators and their spouses in Iowa (IA) and North Carolina (NC). AHS participants reported residential histories and drinking water sources via questionnaire. For private well users, we estimated nitrate levels at enrollment addresses using state-specific random forest models. Models were trained and tested using available well nitrate measurements in each state, and accounted for well depth, soil characteristics, nitrogen inputs, and other predictors. For public water supply (PWS) users, we linked geocoded enrollment addresses to municipal nitrate monitoring data and computed yearly average concentrations for years with available data (IA: 1970-2018, NC: 1978-2018). AHS applicators and spouses were linked to birth certificate records to identify births and ascertain birth outcomes. Births were linked by year to nitrate concentrations. Among these births, birth years ranged from 1988-2011. Of 7,473 (IA: 6,864, NC: 609) total births, 385 (IA: 343, NC: 42) were preterm. Median nitrate concentrations were 1.51 mg/L NO3-N (interquartile range [IQR]:3.8) in IA and 1.96 mg/L (IQR:1.18) in NC among well users, and 1.00 mg/L NO3-N (IQR:3.0) in IA and 0.18 mg/L (IQR:0.54) in NC among PWS users. Using binomial regression, the risk ratio for preterm birth per IQR increase was 1.03 (95% confidence interval: 0.95, 1.12), after adjusting for year and state. We observed limited evidence of an association of prenatal nitrate exposure with preterm birth.

Environment/climate change

Prenatal exposure to air pollution and term low birthweight among Latinas: The role of ethnic enclaves Valerie Martinez*, Valerie Martinez, Asa Bradman, Maria-Elena Young, Andrew Williams, Sandie Ha,

Background: Low birthweight (LBW, <2,500 g) is associated with maternal health and socioeconomic factors. Prenatal air pollution exposure is linked to increased LBW risk, while residence in ethnic enclaves (areas with ethnically similar residents) have been linked to favorable outcomes. Few studies have examined whether the air pollution-LBW association differs by enclave residence.

Objective: To evaluate associations between prenatal particulate matter <2.5 microns (PM2.5) and ozone (O3) exposures and term LBW (tLBW), and whether associations vary by enclave status.

Methods: This retrospective cohort study included 901,135 Latina singleton births in California from 2014-2018. tLBW was defined as a birth >37 weeks of gestation and <2,500 g, from birth certificates. Daily air pollutant concentrations from US Environmental Protection Agency regulatory monitors were linked to maternal residential ZIP codes at delivery, averaged across trimesters and whole pregnancy, and categorized into quartiles (Q). Enclaves were defined as ZIP codes ≥66th percentile on three American Community Survey-based metrics (2018): population density, dissimilarity, and isolation. Generalized linear mixed models estimated adjusted odds ratio (aOR) and 95% confidence intervals, adjusting for confounders, with Quartile 1 (low air pollution as reference).

Results: PM2.5 associations were null. O3 was associated with higher odds of tLBW: first trimester aORs: Q2:1.05(1.01–1.10), Q3:1.04(1.00–1.09), and Q4:1.07(1.03–1.12); second trimester aOR: Q4:1.11(1.04–1.19); whole-pregnancy aORs: Q3:1.09(1.04–1.14) and Q4:1.10(1.04–1.16), respectively. Associations were observed in Latino enclaves and non-enclaves, with associations in enclaves for select windows (e.g., second trimester Q4 aOR: 1.15(1.02-1.29) vs 1.09(1.01–1.18) in non-enclaves).

Conclusion: These findings support the need to reduce O3 exposures and strengthen protections for pregnant populations, especially in marginalized areas.

Environment/climate change

Using cycle-timed air pollutant estimates to model fecundability Gabrielle Johnson*, Gabrielle Johnson, Kaniz Rabeya, Timothy Canty, Karen Schliep, Rachael Hemmert, Pauline Mendola, Neil Perkins, Akanksha Singh, Allison Ring, Sunni Mumford, Carrie Nobles,

Background: Accounting for sensitive windows of reproduction is crucial for understanding how timing of underlying biologic processes impacts the overall effect of environmental exposures, such as air pollution, on odds of pregnancy.

Methods: We included 1001 women from the Effects of Aspirin in Gestation and Reproduction (EAGeR) trial who lived in the Intermountain West and had residential georeferenced pollutant estimates. We abstracted pollutant data from the Air Quality Data for Health-Related Applications (AQDH) and Community Multiscale Air Quality Modeling System (CMAQ), including ozone (O3), particulate matter 2.5 (PM2.5), nitrogen dioxide (NO2), sulfur dioxide (SO2), and carbon monoxide (CO). We estimated biologically relevant sensitive windows to air pollution timed to cycle start date including pre-ovulation and implantation as well as the corresponding broader follicular and luteal phases, respectively. We constructed a multi-pollutant discrete-time Cox proportional hazards model to predict fecundability odds ratio (FOR) per inter-quartile range (IQR) increase in pollutants. Models adjusted for age, treatment status, income, education, and smoking.

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Environment/climate change

Prenatal exposure to air pollution and term low birthweight among Latinas: The role of ethnic enclaves Valerie Martinez*, Valerie Martinez, Asa Bradman, Maria-Elena Young, Andrew Williams, Sandie Ha,

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Conclusion: These findings support the need to reduce O3 exposures and strengthen protections for pregnant populations, especially in marginalized areas.

Environment/climate change

Interconceptional Exposure to Common Plasticizers and Fetal Growth Kim Nail Cajachagua Torres*, Kim Nail Cajachagua Torres, Linda G. Kahn, Teresa Herrera, Hediyeh Baghsheikhi, Shilpi Mehta-Lee, Yuyan Wang, Wenging Yang, Kurunthachalam Kannan, Mengling Liu, Leonardo Trasande, Akhgar Ghassabian,

Background Maternal exposure to common plasticizers prior to conception may impact fetal growth, but evidence outside of subfertile populations remains limited.

Methods Participants were women with two successive pregnancies enrolled in a NYC birth cohort (2016-2021, interpregnancy interval median=2.5 years, 90% range=0.99-4.9). Exposure data from the first pregnancy or pregnancy 1 (up to three measurements) were used as the interconceptional exposure for the second pregnancy or pregnancy 2, for which fetal growth and birth outcome data were available in 139 and 173 dyads, respectively. We averaged concentrations of urinary phthalate metabolites and bisphenols across timepoints, adjusted for urinary dilution, and natural log-transformed them. Repeated fetal biometry measures from clinical ultrasounds were used to predict growth parameters at 20, 30, and 36 weeks using linear mixed-effects models assuming nonlinear effects of gestational age. Information on birth outcomes was obtained from electronic health records. We used mixed models to test associations with fetal growth across gestation and linear regression for birth outcomes. Since the health effects of phthalates and bisphenols are sexually dimorphic, we examined interactions with fetal sex, which was significant, so we conducted sex-stratified models.

Findings In male fetuses, higher maternal interconceptional levels of mono-ethyl phthalate were positively associated with estimated fetal weight, biparietal diameter, and head circumference. We also found positive associations of mono(2-ethylhexyl) phthalate with abdominal circumference and femur length. In contrast, higher mono-(2-carboxyheptyl) phthalate was associated with shorter femur length. In female fetuses, higher mono(2-carboxymetylhexyl) phthalate was associated with smaller abdominal circumference. Interconceptional levels of phthalate metabolites were positively associated with gestational length but negatively associated with birth length z-scores. There were no associations with bisphenols.

Interpretation Interconceptional exposure to phthalates may influence fetal growth, with males and females affected differently.

Environment/climate change

Prenatal drinking water nitrate and preterm birth in the Agricultural Health Study Cherrel K. Manley*, Cherrel K. Manley, Jessie P. Buckley, Lawrence S. Engel, Mary H. Ward, Dale P. Sandler, Laura E. Beane Freeman, Paul A. Romitti, Stephanie M. Engel,

Prenatal exposure to drinking water nitrate has been associated with increased risk of congenital malformations. Evidence for other birth outcomes has been less consistent. Few studies have evaluated these associations among agricultural workers, who may experience elevated exposures due to use of private wells and proximity to farming activities. We examined the association of prenatal drinking water nitrate exposure with risk of preterm birth in the Agricultural Health Study (AHS), a prospective cohort of licensed pesticide applicators and their spouses in Iowa (IA) and North Carolina (NC). AHS participants reported residential histories and drinking water sources via questionnaire. For private well users, we estimated nitrate levels at enrollment addresses using state-specific random forest models. Models were trained and tested using available well nitrate measurements in each state, and accounted for well depth, soil characteristics, nitrogen inputs, and other predictors. For public water supply (PWS) users, we linked geocoded enrollment addresses to municipal nitrate monitoring data and computed yearly average concentrations for years with available data (IA: 1970-2018, NC: 1978-2018). AHS applicators and spouses were linked to birth certificate records to identify births and ascertain birth outcomes. Births were linked by year to nitrate concentrations. Among these births, birth years ranged from 1988-2011. Of 7,473 (IA: 6,864, NC: 609) total births, 385 (IA: 343, NC: 42) were preterm. Median nitrate concentrations were 1.51 mg/L NO3-N (interquartile range [IQR]:3.8) in IA and 1.96 mg/L (IQR:1.18) in NC among well users, and 1.00 mg/L NO3-N (IQR:3.0) in IA and 0.18 mg/L (IQR:0.54) in NC among PWS users. Using binomial regression, the risk ratio for preterm birth per IQR increase was 1.03 (95% confidence interval: 0.95, 1.12), after adjusting for year and state. We observed limited evidence of an association of prenatal nitrate exposure with preterm birth.

Fertility and fecundity

Total motile sperm count as a predictor of pregnancy from timed intercourse in subfertile couples Shahpar Najmabadi*, Shahpar Najmabadi, Joseph Stanford, Mckay Hatch,

BACKGROUND

Total motile sperm count (TMSC), an aggregate measure of sperm concentration, motility, and semen volume, is widely used as an overall indicator of semen quality, yet its ability to predict pregnancy from timed intercourse is not well studied.

OBJECTIVE

To assess the predictive value of TMSC for spontaneous pregnancy in subfertile couples attempting conception with timed intercourse and supportive medical treatment.

METHODS

We conducted a retrospective study of heterosexual couples experiencing subfertility and seeking natural conception between 2013-2023 at the Restorative Reproductive Medicine (RRM) clinic at the University of Utah. De-identified data were abstracted from the Epic electronic health record. Couples were included if they were attempting spontaneous conception, not pregnant at the first visit, and had at least one semen analysis. Those with absolute infertility (e.g., bilateral tubal blockage, azoospermia) were excluded. TMSC was categorized as ≤5 million, 5-15, 15-50, and >50 million. Descriptive statistics and logistic regression assessed the association between TMSC and spontaneous pregnancy (primary binary outcome), adjusting for male age and female gravidity.

RESULTS

Eighty couples were included; 33 (41%) achieved pregnancy from timed intercourse. The mean prior duration of attempting conception was 1.6 ± 1.4 years. Mean male and female ages were 33.6 ± 6.0 and 31.9 ± 5.5 years, respectively. Mean TMSC was 170.7 ± 214.7 million. Logistic regression confirmed increasing probability of pregnancy with higher TMSC. Couples with TMSC >50 million had an odds ratio of 5.1 (95% confidence interval 0.82, 31.3).

CONCLUSIONS

Higher TMSC was associated with increased likelihood of spontaneous pregnancy, supporting its use as a practical prognostic marker for prognosis in timed intercourse.

Fertility and fecundity

Fecundability in Relation to Use of Fertility Awareness Indicators and Mobile Computing Apps Among Females with Subfertility: an Analysis from the Pregnancy Study Online (PRESTO) Esther Chun-Pin Chang*, Esther Chun-Pin Chang, Shahpar Najmabadi, Saskia Spiess, Kenneth Rothman, Lauren Wise, Joseph Stanford,

Background: Previous studies have shown that the use of fertility awareness indicators and mobile applications (“apps”) can increase fecundability and shorten time-to-pregnancy (TTP) among females without subfertility (≤6 cycles of attempt time). However, evidence on the effect of these methods on TTP among those with subfertility is limited. We evaluated the effect of fertility awareness indicators and mobile fertility apps on fecundability (per-cycle probability of conception) among females with subfertility.

Methods: In Pregnancy Study Online (PRESTO), we analyzed data from 4,670 North American females aged 21-45 years who had been attempting to conceive for >6 cycles at baseline (2013-2025). Participants were followed every two months to assess pregnancy status and were censored after 12 cycles of attempt time. Poisson regression models with an Andersen–Gill data structure were used to estimate fecundability ratios (FRs) and 95% confidence intervals (CIs) for use of fertility indicators and mobile apps, adjusting for potential confounders. We used fully conditional specification to multiply-impute missing data, including missing pregnancy outcome.

Results: Participants who used fertility indicators (N=3,898) had similar, though slightly higher, fecundability than non-users (FR=1.09; 95% CI: 0.92–1.28). Participants who used mobile fertility apps (N=3,671) had similar fecundability to non-users (FR=1.05; 95% CI: 0.91–1.21).

Conclusion: Although use of fertility awareness indicators and mobile apps may shorten TTP among females who have been trying to conceive for ≤6 cycles at baseline, benefit appeared slight among females with subfertility. Because 38% of participants were lost to follow-up, results should be interpreted with caution.

Fertility and fecundity

Are Fasting Glucose and Fasting Insulin Associated With Time to Pregnancy and Time to Live Birth in Subfertile Women Undergoing Restorative Reproductive Medicine? *, Jeanna Ryan, Karen Schliep, Shahpar Najmabadi, Joseph Stanford,

Background: Delayed time to live birth increases relationship stress, emotional strain, and family planning challenges. Prior research suggests that higher fasting glucose and insulin levels may be associated with longer time to pregnancy (TTP) and live birth (TLB). To our knowledge, no prior studies have addressed associations between fasting glucose or fasting insulin and TTP/TLB among women who received treatment for subfertility with restorative reproductive medicine (RRM), which includes metabolic disorder management.

Methods: We conducted preliminary analyses using data from the International NaProTechnology Evaluation and Surveillance of Treatment (iNEST) study, with supplemental electronic health record data. The cohort included subfertile women pursuing RRM for fertility at the Utah site. Using fasting glucose and insulin measured within one year of initial RRM visit, we calculated TTP/TLB from reported start of pregnancy attempts using Cox proportional hazards models (HR) and 95% confidence intervals (CIs) with delayed entry and right-censoring, adjusted for maternal age and parity.

Results: Analyses included 30 women. Median age 30.0 years (interquartile range [IQR]: 25.5-31.9), median BMI was 24.4 kg/m2 (IQR: 22.2-31.2), 63% had at least 1 prior live birth, 67% achieved pregnancy, and 60% achieved a live birth. Higher fasting glucose was associated with an adjusted longer TTP (HR per 10 mg/dL: 0.49; 95% CI: 0.25, 0.96). No associations were observed between fasting insulin and TTP (HR per 10 mg/dL: 0.95; 95% CI: 0.87, 1.03), or between fasting glucose (HR per 10 mg/dL: 0.61; 95% CI: 0.30, 1.22) or insulin (HR per 10 mg/dL: 0.99; 95% CI: 0.96, 1.02) and TLB.

Conclusion: In this initial analysis of subfertile women undergoing RRM, fasting glucose, but not fasting insulin, was associated with TTP; neither was associated with TLB. These findings warrant further investigation in larger cohorts to better understand metabolic factors in reproductive outcomes.

Fertility and fecundity

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Fetal loss/stillbirth/infant mortality

Association between preconception dietary inflammation score and stillbirth among birth defect cases, National Birth Defects Prevention Study, 1997-2011 Sarah Fisher*, Sarah Fisher, Alexandra Videll, Eva Williford, Eleni Papadopoulos, Eirini Nestoridi, Paul Romitti, Kristin Conway, Tania Desrosiers, Uma Reddy, Wendy Nembhard, Meredith Howley,

Stillbirth is more common among infants with birth defects. Others have hypothesized that inflammation may increase risk of birth defects among liveborn infants and, separately, of stillbirth among infants without birth defects. We used data from the National Birth Defects Prevention Study to evaluate the association between preconception dietary inflammation and stillbirth among infants with birth defects ("cases"). Mothers of 13,434 liveborn cases and 320 stillborn cases self-reported exposure information via telephone interview. Mothers reported average dietary intake of 63 food items during the year before pregnancy. We calculated a Dietary Inflammation Score (DIS), adapted from Byrd, et al. (2019), categorized into quartiles. We used log binomial models to estimate the relative risk (RR) and 95% confidence interval (CI) of stillbirth associated with each DIS quartile, compared to the lowest, adjusted for maternal age, race/ethnicity, body mass index (BMI), anti-inflammatory medication use, smoking status, alcohol consumption, and study site. We evaluated interaction between DIS and obesity (yes/no) on both the additive and multiplicative scales. Overall, mothers of stillborn cases were younger, had higher BMI, were more often Black or Hispanic, had lower completed education, and more often reported pregestational diabetes than mothers of liveborn cases. We observed an inverse association between DIS and stillbirth, with a dose-response relationship between DIS quartile and stillbirth risk (25th quartile RR: 0.95, 95% CI 0.71, 1.27; 50th quartile RR: 0.66, 95% CI 0.48, 0.92; 75th quartile RR: 0.53, 95% CI 0.37, 0.74). We did not observe evidence of additive or multiplicative interaction between obesity and DIS. In conclusion, DIS was not associated with increased stillbirth risk among infants with birth defects in our study. However, we cannot rule out the effect of other sources of inflammation on stillbirth risk, or of DIS on stillbirth without birth defects.

References:

1. Byrd DA, Judd SE, Flanders WD, Hartman TJ, Fedirko V, Bostick RM. Development and Validation of Novel Dietary and Lifestyle Inflammation Scores. J Nutr. Dec 1 2019;149(12):2206-2218. doi:10.1093/jn/nxz165

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Genetics/Molecular/Omics

Placental chromatin accessibility patterns associate with DNA methylation in stress-linked genes and birth size measures Nafisa Nawal Islam*, Nafisa Nawal Islam, Nafisa Nawal Islam, Shan Hua, Patrick Murphy, Kieran O'Donnell, Thomas O'Connor,

Objective: We examined whether placental genome-wide chromatin accessibility patterns reflecting greater gene activity associate with i) DNAm of candidate stress biology-related genes that partly govern pregnancy and ii) specific birth size measures.

Methods: DNA sequence data from ATAC-seq (Assay for Transposase-Accessible Chromatin with sequencing) were generated for a subset of placentas (N = 183) from a cohort study in Rochester, New York. Libraries were normalized based on total mapped reads. Targeted placental DNAm was quantified at selected CpG sites within candidate HPA axis-related genes (HSD11B2, FKBP5, NR3C1). Anthropometric outcomes at birth included weight, height, and head circumference, and their z-scores. Spearman correlations tested relationships between placental chromatin accessibility, birth size measures, and average percent DNAm in hypothalamic-pituitary-adrenal (HPA) axis-related genes.

Results: Based on enrichment scores at 'peaks', representing high accessibility regions, we identified four distinct clusters characterized by distinct chromatin accessibility signatures in placental tissue across samples using Uniform Manifold Approximation and Projection, with specific enrichment for CTCF and SP1 transcription factor motifs. Placental HSD11B2 DNAm was positively correlated with average RPKM score across all the samples at highly accessible regions in cluster-4 (rho = 0.18) and negatively correlated with Cluster-1 and 2 (rho = -0.21; -0.17); in sex-stratified analyses, most associations were significant only in males and not in females. Cluster-specific accessibility patterns across all the samples correlated significantly with birth size measures in term births ($p < 0.05$): highly accessible regions in cluster-4 showed a positive correlation with neonatal head circumference and its Z-score, while those in cluster-1 showed a negative correlation.

Conclusions: We report for the first time evidence that chromatin accessibility patterns are reliably associated with important birth outcomes.

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Health equity

“They make us feel inferior”: Black women’s experiences and coping with racism in maternal healthcare in Georgia Ran Zhang*, Ran Zhang, Jasmin Darville, Sheree Boulet, Beverly Bruno, Alexis Kendall, Ifrah Sheikh, Myiera Seymour, Simone Sanders, Chrisma Manley, Gina Northington, Kaitlyn Stanhope, Sierra Carter,

Background Racism embedded in the healthcare system limits access to quality maternal care and adversely affects Black women’s health. Guided by the radical healing framework, this mixed-methods study examined Black women’s experiences of racism in maternal healthcare and identified coping and healing strategies.

Methods Between December 2023 and January 2024, we conducted a survey among Black women aged 18-45 years residing in Georgia. Measures assessed obstetric racism, race-related stress, perceived stress, physical and mental health, social support, Africultural coping strategies, critical consciousness, and Black community activism orientation. We summarized characteristics and scale scores using descriptive statistics and compared groups by age, education, and household income using t-tests. We conducted focus groups to explore experiences of racism in maternal healthcare and coping and healing practices, using inductive thematic analysis.

Results Survey respondents (n=209) were primarily aged 25–34 years (62.7%), non-Hispanic (91.4%), and college-educated (64.1%). Nearly all had been pregnant (98.1%), with 70.1% reporting ≥2 pregnancies. Race-related stress across cultural, individual, and institutional domains was moderate (mean 1.9, SD 1.2), as was perceived stress (mean 25.8, SD 6.8). Mental health showed moderate limitations in energy and fatigue (mean 56, SD 22.1), while physical health was generally good. Obstetric racism was reported infrequently; however, when experienced, respondents reported higher stress levels linked to ceremonies of degradation, racial reconnaissance, and disrespectful treatment. Self-reported social support was high (mean 6.2, SD 0.9). Respondents frequently used cognitive/emotional, spiritual, and Africultural collective coping strategies. Critical consciousness was moderate, with stronger orientation toward low-risk and formal political activism than high-risk activism. Focus groups reinforced survey findings and highlighted four domains: enduring and resisting systemic racism, nurturing self-determination and empowerment, healing through cultural identity and community, and imagining radical hope and transformation.

Conclusion Racism and discrimination impose substantial physical and emotional burdens on Black women. Research that amplifies strategies utilized by Black women, like radical healing, to combat oppression are necessary to support holistic healing. Maternal health research and clinical practice should move beyond individual-level coping frameworks and support approaches that foster collectivism, community-based healing, and structural change to promote more equitable care.

Health equity

Leveraging Medicaid Refugee Flags: Perinatal Outcomes among Refugee Medical Assistance-Eligible Immigrants, Other Immigrants, and US-born Pregnant People, Marion County, Indiana, 2010-2024 Ashley Judge*, Ashley Judge, Sarah Wiehe, Unai Miguel Andres, Ricky Camplain, Molly Rosenberg, Kelli Ryckman, Christina Ludema,

Evidence from Canada and Northern Europe suggests refugees have a higher risk of adverse birth outcomes compared to Other immigrants (Oi). Few US studies exist due to challenges identifying refugees in common data sources, though results could inform targeted intervention.

We conducted a retrospective cohort study of singleton, live births in Marion County, Indiana using linked Medicaid and Vital Records data (2010-2024). Among all Marion County birth records, we identified individuals ever flagged in Medicaid during the study period as Refugee Medical Assistance-eligible immigrants (RMAi) (refugees, asylees, Cuban/Haitian entrants, and special victims of torture). Country of birth on the birth certificate was used classify Oi and US-born people (USb). We compared differences by immigrant status in preterm birth (PTB) using log-binomial generalized estimating equations and in term birthweight (TBW) (in grams) using weighted linear regression each using robust standard errors to account for clustering by mother and adjusted for age-squared and education. We then stratified by race/ethnicity, country of origin, and time since first Medicaid enrollment.

Among 228,007 births (5,512 RMAi, 39,828 Oi, 182,667 USb), contrary to hypotheses, RMAi had the lowest risk of PTB compared to Oi (Risk Ratio (RR)=0.7 (95% Confidence Interval (CI): 0.6, 0.8)) and USb (RR=0.5 (95% CI: 0.4, 0.5)). RMAi had TBW similar to Oi (β= -7 (95% CI: -22, 8)) and higher TBW than USb (β=18 (95% CI: 3, 32)). Some variation existed by race/ethnicity: Latino RMAi had lower TBW than Latino Oi. Outcomes for Burmese RMAi did not vary by time in the US.

In this population, RMAi generally had the lowest risk of PTB and similar/higher TBW, suggesting that the healthy migrant effect may extend to refugees despite premigration adversity. This RMAi flag enables refugee health surveillance with limitations and could be adopted in other states to explore outcomes among this heterogenous population.

Health equity

County-Level Predictors of Hospital-Based Obstetric Unit Closures in the United States, 2010–2022 Rylee Bergeron*, Andrew Williams, Rylee Bergeron,

Background: Hospital-based obstetric unit closures are an increasing concern in the United States, particularly in rural communities where access to maternity care is limited. These closures heighten risks for maternal and infant morbidity and may exacerbate geographic inequities in care. We examined whether county-level rurality, poverty, and racial/ethnic composition are associated with obstetric unit closure between 2010 and 2022.

Methods: County-level data were drawn from the University of Minnesota Rural Health Research Center, American Community Survey, and Decennial Census, with 3,131 counties included in analysis. Percent rural, poverty, and NH White were categorized into population based quartiles (low values as reference). Cox proportional hazards models estimated associations between county-level characteristics and obstetric unit closure from 2010-2022, with counties censored if services were maintained or never present.

Results: Nationally, the proportion of counties with obstetric services declined from 56.1% in 2010 to 49.0% in 2022. In the multivariable model, rurality was the primary driver of closure risk. Compared to urban counties, the most rural (noncore) counties (HR: 10.95; 95%CL: 6.28–19.11). and moderate rural counties (HR: 5.17; 95%CL: 3.12–8.57) faced high hazards of closure High county-level poverty was associated with a lower hazard of closure (HR: 0.50; 95%CL: 0.27–0.90). Percent non-Hispanic White population was not significantly associated with closure risk.

Discussion: In this analysis, rurality was a consistent predictor of obstetric unit loss, independent of county-level poverty and racial/ethnic composition. The observed protective effect of higher poverty warrants further study into how safety-net funding may stabilize services in disadvantaged areas. Policy must prioritize the financial and staffing burdens of noncore rural facilities to prevent expanding maternity care deserts and mitigate geographic inequities in birth outcomes.

Health equity

Reduction of county-level socioeconomic inequity can partially remediate racial disparities in infant mortality and preterm birth Naria Sealy*, Naria Sealy, Heather Burris, Ellen Caniglia, Aimin Chen, Melody Goodman, Katharine Rendle, Stefanie Hinkle,

Background: County-level inequities in socioeconomic indicators of structural racism may explain some of the racial disparities in infant mortality (IM) and preterm birth (PTB, <37 weeks' gestation).

Methods: We used vital statistics (2018-2020) in 1427 US counties (n=6,070,978 Black and White births). Census data were used to calculate poverty inequity by dividing each county's poverty rate for Black residents by the rate for White residents, dichotomized into excess Black poverty (ratio >1) vs. not (≤1). This was repeated for county-level income, education (proportion high school diploma), and unemployment. ICE race-income was dichotomized into privileged (>0) or disadvantaged (≤0). We estimated risk differences (RD) for Black-White disparities in IM and PTB. We used causal mediation models to estimate the IM and PTB inequity that would remain if Black disadvantage in each county-level structural racism indicator were eliminated; race as the exposure and socioeconomic structural racism indicators as the mediators. Inverse probability weighting accounted for mediator-outcome confounding (age, education, parity, payment method, urbanicity, hypertension and diabetes) and a linear probability model with robust standard errors estimated RDs (per 100 births) with 95% confidence intervals (CI).

Results: There were 1,510,977 Black and 4,515,616 White births: the risk of IM was 0.9% vs. 0.4%, respectively (RD=0.53 [95% CI: 0.52, 0.55], and the risk of PTB was 12% vs. 7%, respectively (RD=4.82 [4.76, 4.88]). Eliminating county-level Black disadvantage reduced the IM and PTB disparity for each indicator. Removal of excess Black poverty had the highest reductions in IM and PTB disparities: RD=0.24 (0.12, 0.37) and RD=3.20 (2.72, 3.67), respectively, corresponding to 34% and 55% of the disparities eliminated.

Conclusion: Policies focused on reducing county-level socioeconomic inequities driven by structural racism may substantially narrow racial disparities in IM and PTB.

Health equity

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Infectious disease/COVID 19

Acute Otitis Media Treatment Among Children in the US Military Health System Chrystelle Kiang*, Chrystelle Kiang, Clinton Hall, Celeste J. Romano, Yixin Chen, Anna T. Bukowinski, Zeina G. Khodr, Gia R. Gumbs, Ava Marie S. Conlin, Nanda Ramchandar,

Background: Approximately 60% of children will experience at least 1 episode of acute otitis media (AOM), a middle ear infection, by age 3. AOM is the most common indication for antibiotic treatment in children and proper usage is necessary to prevent antibiotic resistance and risk of adverse events. We sought to characterize AOM treatment among US military-connected children.

Methods: This retrospective cohort study used Birth and Infant Health Research program data to identify children born between March 2013 and June 2021, with follow-up until age 5 or September 2024. We obtained diagnosis and treatment records from administrative medical encounter data and evaluated concordance with American Academy of Pediatrics guidelines among those treated with antibiotics. Guideline-concordant 1st line treatment was amoxicillin for 10 days for those <2 years and 7 days for ≥2 years. We summarized guideline concordance by child, parental, and provider characteristics.

Results: During the study period, 418,896 children had at least 1 outpatient AOM diagnosis and were prescribed an oral antibiotic. For children ages 6 months–2 years old, 68% were prescribed amoxicillin for 10 days. For children 2–5 years old, only 7% were prescribed amoxicillin for the recommended 7 days while 64% were prescribed amoxicillin for 10 days, and the remaining 29% were prescribed non-guideline concordant antibiotics. There were no meaningful differences by child, parent, and provider characteristics.

Conclusion: While most children in our study were prescribed the guideline-concordant agent of amoxicillin, those aged 2–5 were likely to have a non-concordant duration and receive an oversupply. This inappropriate use of antibiotics may lead to adverse outcomes and antimicrobial resistance.

Infectious disease/COVID 19

Pregnant Women’s Experiences During a Public Health Emergency: A Cross-Sectional analysis of the COVID-19 Pregnancy Risk Assessment Monitoring System COVID-19 Supplement Andrew Williams*, Michael Osei, Andrew Williams, Danielson Ramona,

Objectives: The COVID-19 pandemic was associated with increased maternal morbidity and mortality, with racially minoritized women having worse outcomes than other women in the United States. However, there is little understanding of pandemic-specific stressors that may contribute to disparate outcomes. Thus, this analysis provides descriptive statistics of COVID-19 pandemic related factors among a sample of women who recently gave birth in the United States that can inform future public health disaster preparedness.

Methods: Analysis of 2020-2022 Pregnancy Risk Assessment Monitoring System COVID-19 supplement data (n=453,231) identified five pandemic experience factors through factor analysis: family household stressors, housing instability, COVID prevention measures, COVID household exposure, and external exposure. Prevalence of each factor was estimated overall and by demographic factors.

Results: Family household stressors affected 42.1% of women, including increased anxiety (48.5%) and job loss (29.9%). Housing instability impacted 11.3%, while 35.2% struggled accessing prevention supplies. Significant disparities emerged: Black and Hispanic women experienced highest family stress rates (48.5%, 48.0%); American Indian/Alaska Native women faced greatest housing instability (21.6%). Younger, unmarried women and those with lower education, Medicaid enrollment, or pre-existing vulnerabilities experienced disproportionate burdens.

Conclusions: Findings necessitate targeted emergency preparedness protocols prioritizing pregnant women’s social support infrastructure, including housing assistance programs, expanded childcare services, and guaranteed access to prevention resources. The pandemic exacerbated maternal health disparities, with marginalized communities bearing the greatest burden. Medicaid expansion and culturally-responsive interventions should be implemented to support vulnerable populations during public health emergencies.

Infectious disease/COVID 19

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Conclusions: Findings necessitate targeted emergency preparedness protocols prioritizing pregnant women's social support infrastructure, including housing assistance programs, expanded childcare services, and guaranteed access to prevention resources. The pandemic exacerbated maternal health disparities, with marginalized communities bearing the greatest burden. Medicaid expansion and culturally-responsive interventions should be implemented to support vulnerable populations during public health emergencies.

Infectious disease/COVID 19

Effectiveness of maternal influenza vaccination against influenza-associated emergency department and urgent care encounters among infants aged >6 months – VISION Network, 2023–2024 and 2024–2025 seasons Emily Reeves*, Emily Reeves, Emily Reeves, Zachary Weber, Duck-Hye Yang, Shaun Grannis, Toan Ong, Sarah Ball, Malini DeSilva, Kristin Dascomb, Sara Tartof, Stephanie Irving, Karthik Natarajan, Nicola Klein, Caitlin Ray, Amanda Payne, Amanda Payne, Shikha Garg, Samantha Olson, Jennifer DeCuir,

Studies have shown that maternal influenza vaccination during pregnancy provides protection for infants aged <6 months, a population at increased risk of severe influenza and without a licensed influenza vaccine. We evaluated maternal influenza vaccine effectiveness (VE) against influenza-associated emergency department or urgent care (ED/UC) encounters among infants during two U.S. influenza seasons (2023-2025).

A test-negative, case-control study was conducted among infants <6 months with linkage to maternal vaccination records. Infants with acute respiratory illness (ARI)-associated ED/UC encounters who tested positive or negative for influenza and negative for SARS-CoV-2 and RSV via molecular testing at seven VISION Network health systems were included. VE was estimated using logistic regression comparing the odds of maternal influenza vaccination (≥14 days before delivery) in influenza positive cases vs influenza negative controls, adjusting for site, infant age, race/ethnicity, calendar time, and season.

Among 3,815 ARI encounters in infants, 455 (12%) tested positive and 3,360 (88%) tested negative for influenza; 69 (15%) cases vs 1,018 (30%) controls were born to mothers who received an influenza vaccine in pregnancy. Overall VE was 53 (95% CI: 38–64). VE was statistically significant among infants 0–1 month (64%, 95% CI: 40–80), 2-3 months (63%, 95% CI: 39–79), and third trimester maternal vaccination (70%, 95% CI: 56–81). VE was not statistically significant among infants 4-5 months (34%, 95% CI: -1–58), first (29%, 95% CI: -13–57), and second trimester vaccination (25%, 95% CI: -19–55).

Maternal influenza vaccination was effective against influenza-associated ED/UC encounters in infants <6 months. VE point estimates were highest in those 0–3 months and when vaccinated in the third trimester. These findings provide evidence of infant protection from maternal influenza vaccination and may help inform clinical decisions about timing of influenza vaccination during pregnancy.

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Mental health

Beyond Diagnosis: Migraine and Depressive Symptoms in Young Women in the Growing Up Today Study Holly Crowe*, Holly Crowe, Kathryn Rexrode, Janet Rich-Edwards, Alyssa Lebel, Hadine Joffe,

Half of people with migraine or depression are diagnosed before age 18. Adolescence and young adulthood are characterized by neurodevelopmental changes and increased risk of declining mental health, especially among young people with chronic health conditions. However, the link between adolescent-onset migraine and depression is understudied, and research tends to focus on diagnosed depression and migraine, which likely underestimates the true burden. To quantify the association between migraine and depression in young adults, we used data from 15,031 female participants in the ongoing Growing Up Today Study (age 9-17 at enrollment). We used self-reported physician diagnoses, as well as ICHD-3 criteria to categorize headache symptoms as migraine (yes/no) and a CESD-10 ≥10 cutoff to categorize mild depression symptoms during multiple time points from 2007-2016 (ages 11-29). We found that 28% of young adults reported experiencing migraine symptoms (21%) or diagnosis (19%)and 43% reported ever experiencing probable depression (CESD≥10; 33%) or a diagnosis of depression (23%) We used multivariable logistic regression to quantify the association between migraine and depression, adjusting for age at enrollment and menarche, race and ethnicity, diet score, physical activity, and history of trauma and abuse. We found a strong cross-sectional association between any migraine and depression (OR= 3.30, 95 CI: 2.99-3.64). The estimates for migraine and depression symptoms, regardless of diagnoses, were 1.80 (95% CI: 1.51-.2.15). These results indicate that migraine and depression symptoms commonly co-occur in young people, whether subthreshold or diagnosed. Young adulthood is a critical period for mental health screening, particularly among individuals with migraine, who are especially vulnerable.

Mental health

Bidirectional Associations of Migraine and Anxiety Symptoms and Diagnoses Among U.S. Young Adult Women Holly Crowe*, Holly Crowe, Kathryn Rexrode, Janet Rich-Edwards, Alyssa Lebel, Hadine Joffe,

Migraine affects roughly 1 in 6 young adults in the United States, and anxiety nearly 1 in 3, substantially disrupting education, social functioning, and quality of life. Existing research has largely relied on cross-sectional designs and physician diagnoses, likely underestimating disease burden. We used longitudinal self-reported migraine and anxiety symptoms and diagnosis to evaluate the bidirectional association between migraine and anxiety among 15,031 female participants in the ongoing Growing Up Today Study (age 9-17 at enrollment; 25-34 at last assessment). We used ICHD-3 criteria to categorize headache symptoms as migraine (yes/no) and RCMAS-2 scores to categorize anxiety symptoms as probable (≥90th percentile), possible (85-89th), or no anxiety (<85th), along with binary indicators of self-reported physician diagnosis at multiple time points from 2007-2021. We conducted adjusted logistic regression for cross-sectional analyses and log-binomial regression for prospective analyses, excluding those with the outcome at baseline. Models adjusted for age at enrollment and menarche, race and ethnicity, diet score, physical activity, and history of trauma and abuse. Overall, 28% of participants ever reported migraine and 26% ever reported probable anxiety (symptoms or diagnosis). We found strong, consistent bidirectional association between young adult migraine and anxiety. The RR for migraine predicting incident anxiety was 1.50 (95% CI: 1.32-1.71) and the RR for anxiety predicting incident migraine was 2.26 (95% CI: 1.89-2.70). We found consistent estimates in cross-sectional analyses of ever-anxiety among those with any migraine (OR= 3.09, 95% CI 2.78-3.42), symptom-based (OR=1.72, 95% CI: 1.37-2.10), diagnosis-based (OR=1.29, 95% CI: 1.02-1.62) migraine. These findings support adolescence and young adulthood as critical periods during which migraine and anxiety co-occur, though associations may reflect shared vulnerability rather than causal effects

Mental health

American Indian and Alaska Native mothers' experiences of postpartum depression: a systematic review and thematic synthesis Ceco Maples*, Ceco Maples, Danielle Gartner,

Postpartum depression (PPD) disproportionately affects American Indian and Alaska Native (AIAN) mothers, yet how AIAN mothers experience PPD, a necessary step in addressing this health inequity, remains underexplored. To systematically examine AIAN mothers' experiences and experiential knowledge of PPD, we conducted a systematic review and thematic synthesis of qualitative research identified through systematic searching of seven electronic databases (CINAHL, Embase, ProQuest Theses and Dissertations Global, PsycINFO, PubMed, Scopus, and Web of Science) and citation chaining. Following identification, deduplication, and screening, 12 studies met the inclusion criteria; included studies were appraised using the CONSIDER (CONSolIDated critERia for strengthening the reporting of health research involving Indigenous Peoples) checklist and synthesized using Thomas and Harden's (2008) thematic synthesis which identified five analytical themes across studies: (1) *settler-colonial determinants of maternal mental health*, (2) *culturally unsafe clinical encounters*, (3) *postpartum depression as historical trauma*, (4) *silent suffering and epistemic injustices*, and (5) *community, continuity, and kinship as methods of care*. Overall, findings underscore the complex sociocultural and historical factors shaping AIAN mothers' experiences of PPD and highlight the importance of culturally safe interventions and research approaches that center Indigenous knowledge and experiences.

Mental health

Decision Making Involvement and Symptoms of Depression and Anxiety Among a Cohort of Mothers in Rural Pakistan *, Aparna G. Kachoria, Joanna Maselko, Holly M. Burke, Kavita Sigh, Donna R. McCarraher, Angela M. Parcesepe,

Maternal depression and anxiety remain a substantial burden in rural Pakistan. Decision making involvement has been associated with perinatal mental health; less is known about the relationship between decision making involvement and mental health beyond the perinatal period.

Using data from the Bachpan cohort in rural Pakistan we assessed the relationship between decision making and symptoms of depression (Patient Health Questionnaire-9>10) or anxiety (General Anxiety Disorder-7>10) among mothers of children who were 6-7 years old (n=1,154). Decision making was assessed by asking about mothers' involvement in decision making in four parenting scenarios (discipline, education, spending, upbringing) and categorized into three unique exposure variables: lack of decision making, sole decision making, and shared decision making. Linear regression models were used to estimate the relationship between decision making and depression or anxiety symptom severity.

Mothers who lacked decision making in all four scenarios had significantly lower depressive and anxiety scores (i.e., lower symptom severity) compared to mothers who were involved in all four scenarios. Mothers who shared decision making in some or all scenarios had significantly lower depression scores compared to mothers who reported no shared decision making, though this was not observed for anxiety. Notably, sole decision making in all scenarios was associated with significantly higher depressive and anxiety scores compared to those who reported no sole decision making.

Findings support a nuanced relationship between decision making and maternal depression, including a positive relationship between shared decision making and mental health. Future research should study these relationships in other settings, and specifically investigate pathways through which lack of decision making is associated with lower severity and through which sole decision-making is associated with higher severity in depression and anxiety.

Mental health

Disparities in Prenatal Depression Treatment Engagement by Nativity, Race, and Ethnicity

Kendria Kelly-Taylor*, Kendria Kelly-Taylor, Sara Aghaee, Joshua Nugent, Nina Oberman, Ai Kubo, Charles Quesenberry Jr, kathryn Erickson-Ridout, Mibhali Bhalala, Lyndsay Avalos,

Depression severity may play a key role in understanding racial, ethnic, and nativity related disparities in prenatal depression treatment. This study examines differences in treatment initiation and type by maternal nativity (US-born vs. non-US-born) among a diverse cohort of pregnant individuals universally screened for depression. We conducted a retrospective cross-sectional analysis (2013-2019) of Kaiser Permanente Northern California members who were newly diagnosed with depression between the first day of LMP to the day before a live birth (n=27,044). Race and ethnicity, and nativity were obtained from birth records. Treatment initiation (any vs. none), type (antidepressant medication vs. psychotherapy), and covariates (e.g., maternal age, Medicaid, anxiety, parity, substance use, depression severity via Patient Health Questionarrie-9) were extracted from electronic health records. Modified Poisson regression models (one with depression severity included and one without) estimated the adjusted relative risk (aRR); analysis was stratified by race/ethnicity. In the models excluding depression severity, US-born Hispanic and White individuals were significantly less likely to initiate treatment than their non–US-born counterparts (aRR:0.78;95%CI:0.67-0.92, aRR:0.81;95%CI:0.71-0.91, respectively). These associations attenuated and became non- significant after adjusting for depression severity. No significant differences were observed between US-born and non–US-born Black or Asian individuals. Treatment type did not significantly differ by nativity across racial and ethnic groups. Findings suggest depression severity may mediate the relationship between maternal nativity and treatment initiation; further analysis is warranted. In addition, examining this relationship across race, ethnicity, and nativity incorporates an intersectional lens to better understand disparities in perinatal treatment engagement.

Mental health

Trends in Suicide Mortality by Method among US Individuals aged 10-24 Years from 1999 to 2024 Anne Bischops*, Anne Bischops, Marie-Laure Charpignon, Kenneth D. Mandl, Maimuna Majumder,

Background

For over a decade, suicide has been the second leading cause of death among individuals aged 10-24 in the United States (US). From 1999 to 2019, suicide rates increased by 46%. However, recent temporal trends after the COVID-19 pandemic remain unclear. We examined suicide mortality patterns, focusing on method use by sex and age group.

Methods

Using publicly available mortality data from the National Center for Health Statistics (NCHS), we analyzed national-level suicide rates from 1999 to 2024 by method. Four suicide method categories were considered: firearm, poisoning, asphyxiation, and other. For each method, both crude and age-standardized suicide mortality rates were estimated and stratified by sex and age group. Changing trend time points and annual percent change (APC) were determined via Joinpoint regression models, using R and the NCI Joinpoint software.

Results

Following a downward trend from 2018 to 2020, suicide mortality rates have since plateaued. Rates declined among ages 15-19 (APC 2017-2024: -3.3, p=0.027) and 20-24 (APC 2021-2024: -5.8, p=0.038), but not among ages 10-14. Although rates were three times higher among males in 1999-2017, the sex gap decreased by 9.3% since 2017. Firearms remained the leading method, predominantly used by males and 15-to 24-year-olds, although their use was increasing among females and 10-to 14-year-olds. Asphyxiation was most common among females and ages 10-14. Poisoning and other methods showed a steady rise. Results were robust to age standardization.

Discussion

Adolescent suicide mortality rates have plateaued, suggesting that earlier progress in prevention efforts may have leveled off during the pandemic. Firearm-related suicides are rising among individuals aged 10-14 and females. Further, suicides by poisoning are increasing across all age groups and both sexes. The implementation of targeted, sex- and age-sensitive approaches will be key to reinforcing the effectiveness of suicide prevention efforts.

Mental health

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Mental health

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Methods

Ownership, design, and development of mHealth interventions for Indigenous maternal and infant health and wellbeing: a scoping review Ceco Maples*, Danielle Gartner, Ceco Maples, Kehli Henry, Morgan Vigil-Hayes,

Background. Mobile health (mHealth) interventions (apps, remote monitoring tools, and) are increasingly being used to address the ongoing maternal and child health inequities experienced by Indigenous peoples across the world. While effective in changing behaviors some situations, little scholarly attention focuses explicitly on the design and delivery context of the interventions, which for Indigenous communities, can make a big difference in uptake. Therefore, through this scoping review, we seek to answer the following question: What design, content development, and data management principles have been applied in the creation of mobile health interventions that support Indigenous maternal and infant health and wellbeing?

Methods. We searched 7 databases (ACM DL, CINAHL, Embase, PsycInfo, PubMed, Scopus, Web of Science) for empirical, peer reviewed sources published after 2000 that also focus on Indigenous people and perinatal mHealth interventions. After removing duplicates, two co-authors screened titles and abstracts of 122 data sources to identify 33 articles for inclusion. The full team identified relevant information to extract from each article. All co-authors are participating in data extraction.

Results. Twenty-five percent of the included articles were conducted within the U.S.A., and these studies focus on reducing cardiometabolic risk, smoking, alcohol consumption during pregnancy. While data collection is still underway, preliminary results suggest that investigators underreport their data management, co-design, and ownership practices, but that for the studies that include information, considerations are made to uphold Indigenous data sovereignty and governance principles.

Conclusions. This scoping review aims to bridge the gap between the identified data concerns of Indigenous communities and the broader mHealth interventional landscape that may or may not provide culturally safe and acceptable solutions to pressing perinatal health concerns.

Methods

Assessing the Validity of Self-Reported Perinatal Health Outcomes in the San Francisco Abundant Birth Project Pilot Evaluation Study Erin Hubbard*, Erin Hubbard, Emily Boniface, Stephanie Arteaga, Ariana Bennett, Maile Chand, Monica De La Cruz, Breezy Powell, Michaela Taylor, Zea Malawa, Brittany Chambers Butcher, Anu Gomez, Deborah Karasek,

Background:Collecting survey data may be more feasible than other data acquisition approaches for investigators studying perinatal health outcomes among historically oppressed populations. However, data on the validity of self-reported perinatal outcomes and conditions are limited, especially for those at highest risk of poor birth outcomes in the United States.

Methods: We used survey and medical record data from the evaluation study of the San Francisco Abundant Birth Project, a guaranteed income program during pregnancy and the early postpartum period, to assess the validity of self-reported health outcomes from interviewer-administered surveys. Survey data were collected from August 2021 to May 2024. Using data from 114 participants, we calculated sensitivity, specificity, positive predictive value, and negative predictive value for 17 measures with medical record data as the alloyed (generally accurate but imperfect) gold standard. Each measure was categorized as having excellent (>90% for 3 of 4 validity measures), moderate (70-90% for 3 of 4 validity measures), or poor (<70% for 2 of 4 validity measures) overall agreement.

Results: Measures with excellent agreement between self-report and medical records included multiple gestations, delivery mode, preterm birth, previous preterm birth, placenta previa or placental abruption, hospitalization after birth, preexisting diabetes, and neonatal intensive care unit stay. Measures with moderate agreement were low birthweight, small for gestational age, gestational diabetes, and preeclampsia. Measures with poor agreement included gestational hypertension, anemia, depression, anxiety, and hospitalization during pregnancy.

Conclusions: Agreement between self-report and medical records was excellent or moderate for the majority of outcomes assessed. Possible sources of discordance, like poor patient-provider communication, should be further explored for measures with poor overall agreement.

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Methods

Ownership, design, and development of mHealth interventions for Indigenous maternal and infant health and wellbeing: a scoping review Ceco Maples*, Danielle Gartner, Ceco Maples, Kehli Henry, Morgan Vigil-Hayes,

Background. Mobile health (mHealth) interventions (apps, remote monitoring tools, and) are increasingly being used to address the ongoing maternal and child health inequities experienced by Indigenous peoples across the world. While effective in changing behaviors some situations, little scholarly attention focuses explicitly on the design and delivery context of the interventions, which for Indigenous communities, can make a big difference in uptake. Therefore, through this scoping review, we seek to answer the following question: What design, content development, and data management principles have been applied in the creation of mobile health interventions that support Indigenous maternal and infant health and wellbeing?

Methods. We searched 7 databases (ACM DL, CINAHL, Embase, PsycInfo, PubMed, Scopus, Web of Science) for empirical, peer reviewed sources published after 2000 that also focus on Indigenous people and perinatal mHealth interventions. After removing duplicates, two co-authors screened titles and abstracts of 122 data sources to identify 33 articles for inclusion. The full team identified relevant information to extract from each article. All co-authors are participating in data extraction.

Results. Twenty-five percent of the included articles were conducted within the U.S.A., and these studies focus on reducing cardiometabolic risk, smoking, alcohol consumption during pregnancy. While data collection is still underway, preliminary results suggest that investigators underreport their data management, co-design, and ownership practices, but that for the studies that include information, considerations are made to uphold Indigenous data sovereignty and governance principles.

Conclusions. This scoping review aims to bridge the gap between the identified data concerns of Indigenous communities and the broader mHealth interventional landscape that may or may not provide culturally safe and acceptable solutions to pressing perinatal health concerns.

Nutrition/obesity

Examining the role of early pregnancy dietary intake on preterm birth using target trial emulations Kyle Busse*, Kyle Busse, Stefanie Hinkle, Heather Burris, Sara DeMauro, Rana Chehab, Sylvia Badon, Enrique Schisterman, Ellen Caniglia, Yeyi Zhu, Rita Strakovsky, Alison Hipwell, Dana Dabelea, Lynn Yee, Alison Gemmill, Rui Ling, Shalmali Bane, Assiamira Ferrara, Monique Hedderson, Amanda Marma Perak, Zhaozhong Zhu, Nicole Spillane, Anne Lang Dunlop, Joseph Stanford, Sunni Mumford,

Introduction: Adhering to a healthy diet may reduce the risk of preterm birth, but it remains unclear which dietary strategies are most effective, as trials of dietary interventions in pregnancy are often infeasible. We estimated the observational analogs of the intention-to-treat effects of hypothetical interventions to meet 2015-2020 Dietary Guidelines for Americans (DGA) recommendations in pregnancy on the risk of preterm birth.

Methods: We used data from 10,095 pregnancies (10,069 people) in the Environmental influences on Child Health Outcomes (ECHO) Cohort with diet assessed before 20 weeks' gestation. Discrete interventions were defined as: 1) achieving a Healthy Eating Index-2015 (HEI) score ≥60th percentile; 2) meeting recommendations for ≥7 of 13 DGA components; 3) meeting recommendations for total fruits and vegetables; 4) meeting recommendations for all "moderation" components (sodium, refined grains, saturated fats, added sugars); 5) meeting recommendations for ≥2 moderation components. Modified Poisson regression with robust standard errors estimated risk ratios (RR) and 95% confidence intervals (CI) for preterm birth (<37 weeks'), adjusted for age, race, ethnicity, education, parity, pre-pregnancy BMI, household income, alcohol and tobacco use, and plurality. Multiple imputation (m=20) was used for missing covariate data.

Results: 1,044 deliveries (10%) were preterm. Achieving a HEI score ≥60th percentile (score of 67, RR=0.84 [95% CI 0.74-0.94]), meeting recommendations for ≥7 DGA components (17% of pregnancies, RR=0.86 [0.73-1.01]), and meeting recommendations for total fruits and vegetables (24%, RR=0.86 [0.75-0.98]) were associated with a lower risk of preterm birth. Meeting recommendations for all (1%) or ≥2 moderation components (20%) was not associated with preterm birth.

Conclusions: Identifying strategies to help pregnant people meet recommendations for overall diet quality and fruit and vegetable intake may reduce the risk of preterm birth.

Nutrition/obesity

Maternal peanut consumption during pregnancy and birth outcomes Xiaozhong Wen*, Xiaozhong Wen, Fatima Mohammed, Ethan Conner, Akashpreet Grewal, Heath Cottengim, Priyadharshan Manohar, Madison Pompy Madison Pompy, Todd Rideout,

Background: Positive birth outcomes are important for both short-term and long-term health of children. Peanuts are a rich source of macronutrients, micronutrients, and other bioactive constituents, including phytosterols and phenolic compounds.

Objectives: We examined the association between maternal peanut food consumption during pregnancy and birth outcomes.

Methods: We analyzed data from a U.S. cohort of 1,444 mother-infant dyads in the Infant Feeding Practices Study II. In late pregnancy, mothers reported the frequency and portion size of consuming peanut foods in the past month, including peanuts and peanut butter. We used multivariable logistic and linear regression models to examine associations of maternal peanut food consumption with binary (i.e., preterm, small-for-gestational-age [SGA], large-for-gestational-age [LGA]) and continuous (i.e., gestational age, birth weight, and birth length) birth outcomes, respectively, adjusting for socio-demographics, pregnancy-related characteristics, and the Healthy Eating Index.

Results: On average, mothers consumed 0.21 cups/week of peanuts and 2.37 tablespoons/week of peanut butter during pregnancy. Older age, higher education, higher household income, higher Healthy Eating Index, and WIC non-recipient were associated with higher peanut food consumption. Pregnant individuals who consumed a high amount of peanut and peanut butter combined had a significantly lower risk of preterm birth (2.1% vs 5.7%; confounder-adjusted OR, 0.32 [95% CI [0.11, 0.97]; P-value = 0.044). The risk of preterm birth decreased with the amount of peanut and peanut butter combined per 1-gram per day increment, with a confounder-adjusted OR of 0.75 (95% CI, 0.57, 0.97; P-value = 0.031). The associations were not significant for other birth outcomes.

Conclusions: High maternal consumption of peanut foods during pregnancy has a potential benefit in reducing the risk of preterm birth.

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Obstetric health

Cesarean Delivery Risk Following Labor Induction in Low-Risk Pregnancies: A Population-Based Mixed-Methods Study Dovile Vilda*, Dovile Vilda,

Background: Labor induction is increasingly common in low-risk pregnancies, yet its association with cesarean delivery may vary across patient populations. Evidence describing racialized differences in cesarean risk following induction, and the care processes underlying these differences, remains limited.

Methods: We used an explanatory sequential mixed-methods design. Quantitative analyses used Louisiana birth certificate data from 2012–2023 to identify low-risk nulliparous, term, singleton, vertex births without documented pregnancy complications delivered between 39 and 41 6/7 weeks' gestation. Log-linear regression models with a log link and binomial distribution estimated adjusted risk ratios (aRRs) and absolute risk differences (RDs) for cesarean delivery associated with labor induction, stratified by race/ethnicity and gestational age and adjusted for demographic, socioeconomic, and clinical factors. Qualitative data were collected through semi-structured interviews with obstetricians, midwives, labor and delivery nurses, and doulas practicing across hospital and community settings in Louisiana to explore labor management decision-making and perceived drivers of intervention use.

Results: Among 139,274 low-risk births, 46.5% followed labor induction. In adjusted models, induction was associated with higher cesarean delivery risk for Latine/Hispanic (aRR = 1.20; 95% confidence interval: 1.08–1.32), non-Hispanic Black (aRR = 1.15; 95% confidence interval: 1.06–1.25), and Asian patients (aRR = 1.15; 95% confidence interval: 1.03–1.28), but not for non-Hispanic White patients (aRR = 0.95; 95% confidence interval: 0.87–1.04). Elevated risks persisted at both full-term and late-term gestations, corresponding to absolute cesarean risk increases of approximately 3–5% among patients of color. Preliminary qualitative findings suggest that induction-related decision-making is shaped by hospital protocols, fear of adverse outcomes, reimbursement incentives, and limited shared decision-making, contributing to intervention cascades.

Conclusions: Labor induction is differentially associated with cesarean delivery risk across racialized groups among clinically low-risk pregnancies. Integrating population-based estimates with provider perspectives highlights how institutional labor management practices may contribute to observed differences in maternal outcomes.

Obstetric health

Blood pressure trajectories from early pregnancy through early postpartum: A descriptive Latent Class Growth Model analysis Rui Ling*, Rui Ling, Mengling Liu, Yu Chen, Anais Hausvater, Shilpi Mehta-Lee, Leonardo Trasande, Linda Kahn,

Background: Average blood pressure (BP) in pregnancy follows a shallow U-shape, but individual trajectories vary. This study used electronic medical records (EMR) data to investigate characteristics of latent classes of systolic (SBP) and diastolic (DBP) BP from early pregnancy through “the fourth trimester” postpartum, a critical but less studied period of cardiovascular (CV) risk.

Methods: We included women with singleton live births or stillbirths in the NYU Children’s Health and Environment Study (2016–2023). BP from EMR during nonurgent encounters was modeled with latent class growth models separately for pregnancy (N=1,563) and ≤14 weeks postpartum (N=1,326). Inclusion required a baseline and ≥2 additional BP measures per period. We used Bayesian Information Criterion, class sizes, and entropy for model selection; and Chi-square tests and Kruskal–Wallis tests for group differences.

Results: In pregnancy, we identified three classes for SBP: ‘Population average’ (92%), ‘High decrease’ (3%), and ‘Low increase’ (5%); and two for DBP: ‘Population average’ (82%) and ‘Low increase’ (18%). Both ‘Low increase’ SBP/DBP were associated with higher risk of hypertensive disorders of pregnancy (HDP). The SBP ‘High decrease’ class was enriched with prior chronic hypertension. Postpartum SBP and DBP each had three classes: ‘Low stable’ (85% for SBP; 94% for DBP), ‘High decrease’ (8% SBP; 3% DBP), and ‘High increase’ (7% SBP; 3% DBP); both ‘High increase’ and ‘High decrease’ were associated with prior HDP and chronic hypertension. We also observed class differences by race/ethnicity and other sociodemographic factors; and prenatal smoking was more prevalent in higher-risk postpartum DBP classes.

Conclusions: In a diverse, urban pregnancy cohort we identified distinct BP trajectories in pregnancy and early postpartum associated both with HDP as well as sociodemographic and behavioral characteristics that may help identify women at risk of short- and long-term CV complications.

Obstetric health

Gestational Diabetes Rates by County of Residence in the United States Rachael Beer*, Rachael Beer, Lauren Rossen,

Background: Gestational diabetes mellitus (GDM) is linked to many short- and long-term health concerns, including pregnancy complications, adverse pregnancy outcomes, and future type 2 diabetes mellitus in women and their offspring. GDM is estimated to affect approximately 8% of pregnancies in the US, with estimates ranging from 5% to 13% by state. To further assess geographic differences in rates, we estimated GDM rates by county of residence.

Methods: We conducted a descriptive cross-sectional study among live singleton births to US residents using 2024 National Vital Statistics System Natality data. We excluded births to mothers with pre-existing diabetes mellitus (1.2%) and records missing information for GDM (0.2%). The presence of GDM was recorded via a check box on the birth certificate based on information from medical records. We modeled GDM rates by county using Bayesian hierarchical models with spatial random effects that smooth unstable estimates. To assess geographic patterns, we mapped county rates.

Results: The study included 3,460,161 births occurring in 3,141 counties in 2024. Maternal GDM was indicated on 8.5% of birth certificates. There was significant geographic variation in model-based GDM rates by county of residence; county rates ranged from 1.8% to 25.6%, with a median of 8.3% (IQR 6.9-9.8) in 2024. Counties in the Pacific, Midwest, and Northeast regions generally had higher rates than counties in the South and Mountain regions, with some exceptions, including clusters of high rates in Arizona, New Mexico, and Texas.

Conclusions: Model-based GDM rates varied substantially by county of residence. Localized rates can help inform prevention efforts on the populations at highest risk.

Obstetric health

Utility of ACOG Low-Dose Aspirin Guidelines in a Low-Resource Setting: Risk of Preeclampsia in Zambia Madison Calvert*, Madison Calvert, Katelyn Rittenhouse, Yuri Sebastião, Bridget Spelke, Margaret Kasaro, Bellington Vwalika, Bethany Freeman, Christina Perez, Jeffrey Stringer,

Preeclampsia is a leading cause of maternal mortality in low-resource settings. While the American College of Obstetricians and Gynecologists (ACOG) recommends low-dose aspirin prophylaxis, these criteria were derived largely from high-income populations. It remains unknown if ACOG risk stratification accurately captures the burden of disease in settings like Zambia, where distinct maternal risk profiles may alter the utility of these guidelines.

We combined participants from three prospective studies (one cohort, two trials) conducted at the same facilities in Lusaka, Zambia (2015-2022). Participants were classified as high-risk for preeclampsia using demographic and clinical covariates mapping to ACOG risk factors, which recommend low-dose aspirin for individuals with ≥1 high-risk factor or ≥2 moderate-risk factors. The primary outcome was preeclampsia, and the secondary outcome was severe preeclampsia. Inverse probability weighting was used to compare risks, adjusting for maternal age and parity.

Among 3,574 participants, 1049 (29.4%) were categorized as high- and 2525 (70.6%) as low-risk. Absolute risk of preeclampsia was 4.1% (2.5% severe preeclampsia). The absolute risk of preeclampsia was 6.6% among ACOG-eligible individuals compared to 2.8% among those ineligible (RD 3.7%; 95% CI 0.020-0.058). Trends were similar for severe preeclampsia (3.9% severe preeclampsia; RD 2.1%; 0.007-0.036).

Application of ACOG guidelines in this Zambian cohort identified a subset of women with more than double the risk of preeclampsia compared to the low-risk group. However, as the majority of total preeclampsia cases occurred in the “low-risk” group, further research is needed to determine if ACOG criteria alone are sufficient or if context-specific risk models are necessary to optimize aspirin implementation in this setting.

Obstetric health

Biomarkers of early onset and severity of hypertensive disorders of pregnancy: a systematic umbrella review Hiluf Abraha*, Nandita Perumal, Amirhossein Fakhre Yaseri, Hiluf Ebuy Abraha, Neharika Talasila, Spring Griffin, Nyaw Lar Too, Jessica Delgado, Nandita Perumal,

Introduction: Hypertensive disorders of pregnancy (HDP) are among the leading causes of maternal mortality globally. Early identification and management of HDP is important to prevent severe disease. However, the pathophysiology of early onset or severity of HDP remains unclear.

Methods: We systematically searched PubMed, EMBASE, CINAHL, and Web of Science up to July 2025 to identify systematic reviews with meta-analyses that examined the relationship between biomarkers (e.g., angiogenic, inflammatory, metabolic, oxidative stress, endocrine, and micronutrient markers) and HDP. Studies that focused exclusively on interventions, imaging markers alone, diagnostic accuracy of biomarkers, or genetic markers were excluded. Abstract and full-text screening and data extraction were conducted in duplicate, and the data was synthesized qualitatively. The review protocol was registered in the PROSPERO database (ID: CRD42024515952).

Results: Of the 3,823 abstracts screened, 80 reviews were included. Almost all reviews (79/80, 98.7%) evaluated preeclampsia either as a primary outcome or in combination with other HDP. Case-control studies were most common (73/80, 91.2%), followed by cohort studies (55/80, 68.7%). Studies from Europe and Central Asia were most represented across reviews (76/80, 95.0%), followed by studies from East Asia and Pacific (67/80, 83.7%) and from North America. Few reviews included primary studies from South Asia, Latin America and the Caribbean, and Sub-Saharan Africa. Only 16/80 reviews (20%) examined associations between biomarkers of early-onset and/or severe preeclampsia. There was substantial heterogeneity in definitions of early onset preeclampsia (ranging from: <18, 18-25, and <34 weeks, or first or second trimesters). Angiogenic biomarkers were consistently associated with early-onset of preeclampsia; whereas inflammatory markers and markers of oxidative stress were most consistently associated with severe preeclampsia across reviews.

Conclusion: There is substantial primary data on the associations between biomarkers and risk of HDP. However, findings on the association of these biomarkers with early-onset or severity of disease is limited and heterogenous. Further evidence, particularly in diverse populations, is needed to support clinical decision-making.

Obstetric health

Effectiveness of remote blood pressure monitoring in managing and preventing pregnancy-related outcomes – An AI-Assisted Systematic Review Courtney Thomas*, Courtney Thomas, Inngide Osirus, Sherri Longo, Chibuike Chukwunyere, Elizabeth Howard, Emily Harville,

Background Remote blood pressure monitoring (RBPM) in pregnancy enables timely detection of elevated blood pressure (BP) and may support early intervention. Uncertainty remains in regard to the most effective and safest implementation of RBPM in pregnancy management. Existing reviews are limited by a narrow focus on either the pregnancy or postpartum period, high-risk pregnancies, or BP-related outcomes alone.

Objectives We aimed to provide a comprehensive overview of RBPM through the perinatal and postpartum period, including interventions and non-BP related maternal outcomes, evaluating the impact of RBPM compared with standard in-clinic monitoring alone.

Methods This review followed Preferred Reporting Item for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. PubMed was searched in March 2025 for randomized trials and observational studies comparing RBPM with standard care among pregnant and postpartum individuals at all risk levels for hypertensive disorders of pregnancy. Screening, data extraction, and risk of bias assessments (ROBINS-I and RoB2) were conducted using a large language model (LLM) with final decisions by the study team.

Results Of the studies screened, 15 met inclusion. In studies of pregnant women (n=10), RBPM showed small statistical differences in diastolic/systolic BP readings, reduced clinic visits, and no differences in adverse outcomes or prediction of preeclampsia compared to usual care. In studies of postpartum women (n=5), RBPM improved BP control, adherence, and long-term cardiovascular risk profiles. Overall, intervention outcomes, including feasibility, cost-effectiveness, safety, and acceptability, were promising, although outcomes may vary based on HDP status.

Conclusions This review supports the beneficial effects of RBPM in pregnancy and postpartum, but large-scale studies are needed to evaluate outcomes across risk levels, socioeconomic groups, and health disparities.

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Biomarkers of early onset and severity of hypertensive disorders of pregnancy: a systematic umbrella review Hiluf Abraha*, Nandita Perumal, Amirhossein Fakhre Yaseri, Hiluf Ebuy Abraha, Neharika Talasila, Spring Griffin, Nyaw Lar Too, Jessica Delgado, Nandita Perumal,

Introduction: Hypertensive disorders of pregnancy (HDP) are among the leading causes of maternal mortality globally. Early identification and management of HDP is important to prevent severe disease. However, the pathophysiology of early onset or severity of HDP remains unclear.

Methods: We systematically searched PubMed, EMBASE, CINAHL, and Web of Science up to July 2025 to identify systematic reviews with meta-analyses that examined the relationship between biomarkers (e.g., angiogenic, inflammatory, metabolic, oxidative stress, endocrine, and micronutrient markers) and HDP. Studies that focused exclusively on interventions, imaging markers alone, diagnostic accuracy of biomarkers, or genetic markers were excluded. Abstract and full-text screening and data extraction were conducted in duplicate, and the data was synthesized qualitatively. The review protocol was registered in the PROSPERO database (ID: CRD42024515952).

Results: Of the 3,823 abstracts screened, 80 reviews were included. Almost all reviews (79/80, 98.7%) evaluated preeclampsia either as a primary outcome or in combination with other HDP. Case-control studies were most common (73/80, 91.2%), followed by cohort studies (55/80, 68.7%). Studies from Europe and Central Asia were most represented across reviews (76/80, 95.0%), followed by studies from East Asia and Pacific (67/80, 83.7%) and from North America. Few reviews included primary studies from South Asia, Latin America and the Caribbean, and Sub-Saharan Africa. Only 16/80 reviews (20%) examined associations between biomarkers of early-onset and/or severe preeclampsia. There was substantial heterogeneity in definitions of early onset preeclampsia (ranging from: <18, 18-25, and <34 weeks, or first or second trimesters). Angiogenic biomarkers were consistently associated with early-onset of preeclampsia; whereas inflammatory markers and markers of oxidative stress were most consistently associated with severe preeclampsia across reviews.

Conclusion: There is substantial primary data on the associations between biomarkers and risk of HDP. However, findings on the association of these biomarkers with early-onset or severity of disease is limited and heterogenous. Further evidence, particularly in diverse populations, is needed to support clinical decision-making.

Pharmacoepidemiology

From Guideline to Practice: A Quasi-Experimental Evaluation of Hypertensive Disorders of Pregnancy Following the ACOG Low-Dose Aspirin Recommendation in Pregnancies With Pregestational Diabetes Lin-Chieh Meng*, Lin-Chieh Meng, Charles E Leonard, Beth Pineles, Brian Lee, Viktor H. Ahlqvist, Cecilia Magnusson, Enrique F Schisterman, Stefanie N Hinkle, Sunni L Mumford, Ellen C Caniglia,

Background: The American College of Obstetricians and Gynecologists (ACOG) recommends low-dose aspirin (LDA) for the prevention of preeclampsia among high-risk pregnancies, including those complicated by pregestational diabetes (PGD). However, recent randomized controlled trials (RCTs) have questioned the efficacy of LDA in this population. We leveraged the 2016 ACOG guideline update as a natural experiment to evaluate the real-world impact of guideline adoption on maternal outcomes among pregnancies with PGD.

Methods: We conducted a controlled interrupted time-series (CITS) analysis using US National Vital Statistics System birth certificate data. Time was indexed by calendar month at gestational age 12 weeks, spanning September 2015 through December 2018, with the September 2016 ACOG guideline update treated as the intervention point. Pregnancies with PGD were compared with a low-risk control group defined as nulliparous individuals younger than 35 years with a normal pre-pregnancy body mass index and no history of PGD, chronic hypertension, or assisted reproductive technology use. This control group was used to address potential confounding from concurrent interventions or underlying temporal trends. The primary outcome was hypertensive disorders of pregnancy (HDP) recorded on the birth certificate, defined as a composite of gestational hypertension and preeclampsia. Segmented regression models were used to estimate between-group differences in immediate level changes and post-guideline trend changes on the absolute risk scale.

Results: The analysis included 75,123 pregnancies with PGD and 993,450 low-risk control pregnancies. The CITS analysis showed no evidence of a between-group, guideline-associated change in HDP, with an estimated immediate level change of 0.18% (95% CI, −1.13 to 1.48) and no differential post-guideline trend change (0.12% per month; 95% CI, −0.06 to 0.30).

Conclusion: In this population-based CITS analysis, real-world uptake of the 2016 ACOG recommendation for LDA was not associated with a reduction in HDP, including preeclampsia, among pregnancies with PGD. These findings are consistent with recent RCT evidence and underscore the need for further research to evaluate the effectiveness of LDA and alternative preventive strategies in this population.

Pharmacoepidemiology

Characterizing pregnancies with unobserved outcomes in administrative claims data Chase Latour*, Chase Latour, Baijun Zhou, Elizabeth Simmons, Oluwasolape Olawore, Megan Delgado, Jacob Kahrs, Elizabeth Suarez, Ellen Caniglia, Mollie Wood,

Introduction: Including pregnancies with unobserved outcomes (i.e. lost to follow-up [LTFU]) may reduce selection bias but exacerbate measurement error in claims-based studies of prenatal exposures. Evidence is limited on how to best balance these concerns.

Objective: To characterize differences between pregnancies with observed versus unobserved outcomes.

Methods: We identified pregnancies using U.S. commercial insurance claims data based on pregnancy-related diagnosis and procedure codes. We included pregnancies with estimated last menstrual periods (LMPs) from 7/1/2016-2/1/2023 and ≥180 days pre-LMP continuous enrollment. Pregnancy outcomes were classified as observed versus LTFU, and among LTFU, by the presence of ≥1 gestational week-specific diagnosis code (Z3A.08–Z3A.42). We compared demographics, comorbidities, gestational age (GA) at end of pregnancy or LTFU, and timing of disenrollment for observed vs LTFU pregnancies and, among LTFU, by Z3A code presence.

Results: Of 1,818,342 pregnancies, 470,726 (26%) were LTFU. LTFU pregnancies had more comorbidities than observed pregnancies (chronic hypertension: 6% vs 4%). Among LTFU, only 35% had ≥1 Z3A code, and they had fewer comorbidities than those with 0 Z3A codes (chronic hypertension: 3% vs 7%). GA at LTFU differed by strata: 41% of those with ≥1 Z3A code were <20 weeks' gestation at LTFU, compared to 83% of those with 0 Z3A codes. Cumulative incidence of disenrollment within 30 days after LTFU differed: 60% for ≥1 Z3A code versus 24% for 0 Z3A codes.

Conclusions: Pregnancies LTFU differed from those with observed outcomes and by the presence of Z3A codes. Those with ≥1 Z3A code had fewer comorbidities and disenrolled quickly after LTFU, compared to those with none. Excluding pregnancies with such differing characteristics could result in meaningful selection bias in studies of prenatal exposures. Ongoing manual claim review will clarify LTFU pregnancy validity.

Pharmacoepidemiology

Maternal acetaminophen (paracetamol) use in pregnancy and risk of pediatric hepatocellular jaundice Julia Heck*, Julia Heck, Chuanjie Deng, Zeyan Liew, Pei-Chen Lee,

Background: There has been increasing interest in the putative impacts of acetaminophen in pregnancy on offspring, with many studies focusing on neurodevelopmental outcomes. Acetaminophen is the largest cause of liver failure worldwide, yet possible hepatic effects of pregnancy acetaminophen intake have been underreported in the literature.

In Taiwan, acetaminophen is only available at pharmacies; it cannot be obtained at convenience stores. All medications prescribed by a physician are free. Women average 22 prenatal care visits, suggesting sufficient opportunity to obtain prescriptions.

Methods: We conducted a population-based cohort study in Taiwan using data from the Maternal and Child Health Database linked to National Health Insurance Database to identify children diagnosed with hepatocellular jaundice (ICD-9 573.8) between 2004-2017. A hepatocellular jaundice diagnosis does not occur without hepatocellular damage, and diagnosis occurs after assessing alanine transaminase (ALT), aspartate transferase (AST), ultrasound, and/or MRI results. The study included 2,294,292 mother-child pairs (births 2004-2015), of which 5308 children had a diagnosis of hepatocellular jaundice.

Acetaminophen use during pregnancy was ascertained from the Pharmaceutical Registry, which records every prescription filled in a pharmacy in Taiwan. We used Cox proportional hazard models to estimate effects, with adjustment for maternal age and maternal diabetes.

Results: When the mother had ≥6 prescriptions for acetaminophen across pregnancy with at least 2 in each trimester, the child had an increased risk of hepatocellular jaundice (HR=1.78, 95% CI 1.55-2.05).

Conclusions: This is among the first studies to investigate hepatic impacts of maternal acetaminophen use in pregnancy. Further research is needed to confirm results, examine potential confounding factors, and assess biologic mechanisms.

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Policy

Impact of the COVID-19 Public Health Emergency and Medicaid Postpartum Coverage Extension on Postpartum Blood Pressure Monitoring After Hypertensive Disorders of Pregnancy: A Comparative Interrupted Time Series Analysis *, Rong Rong, Man Tang, Yilu Lin, Kevin Callison, Bradley Martin, Daniel Fort, Xu Xiong, Nahed ElHassan, Abigail Gamble, Cheng Peng, Mahip Acharya, Janice Hall, Lizheng Shi,

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Policy

Impact of Universal Hepatitis C Screening Recommendations on Testing During Pregnancy

Anh Tran*, Anh Tran, Anh Tran, Krista F. Huybrechts, Joan Landon, Katelyn A. Pastick, Yanmin Zhu,

Hepatitis C virus (HCV) infection in pregnancy is associated with adverse maternal and perinatal outcomes. Prior to 2020, HCV screening in pregnancy was risk-based, targeting those with documented risk factors. In 2020, U.S. guidelines shifted to universal HCV antibody screening during each pregnancy; however, population-level uptake following this recommendation remains not well characterized.

Using the MarketScan 2017-2023, we identified 897,129 livebirth pregnancies. Maternal HCV antibody, HCV RNA, and hepatitis B surface antigen (HBsAg) testing were ascertained using procedure codes; HBsAg served as a negative control given longstanding universal screening recommendation. We estimated the proportions of pregnancies with testing in 6-month intervals overall and by substance use disorder (SUD) and HIV subgroups. Segmented regression with Prais-Winsten correction assessed screenings trends with January 2021 as the intervention point.

HCV antibody screening increased from 20.8% in early 2017 to 75.8% by late 2023. Screening increased by 1.7 percentage points (pp) every 6 months pre-2021 compared to 7.1 pp post-2021 (acceleration: +5.5 pp per period; 95% CI 4.8-6.2). In contrast, HBsAg screening remained stable at 90% from 2017-2023. HCV screening rate in early 2017 was higher in high-risk subgroups (26%) than the general population, which increased to 76.2% among those with SUD and 78.2% among those with HIV by late 2023. HCV RNA confirmatory testing after antibody screening doubled from 0.2% to 0.4% of all pregnancies.

Following the 2020 universal screening recommendations, prenatal HCV antibody testing increased substantially with increased RNA confirmatory testing indicating improvement in the identification of active infections. These findings demonstrate impactful real-world implementation of universal HCV screening guidelines in prenatal care and suggest policy recommendations that can effectively transform clinical practice when broadly disseminated.

Policy

The Impact of Public Health Emergency and Medicaid Postpartum Extension on Postpartum Glucose Monitoring Among Women with Gestational Diabetes: A Comparative Interrupted Time Series Analysis Man Tang*, Man Tang, Rong Rong, Yilu Lin, Kevin Callison, Bradley C. Martin, Daniel Fort, Xu Xiong, Nahed O. ElHassan, Abigail Gamble, Cheng Peng, Mahip Acharya, Janice L. Hall, Lizheng Shi,

Background: Postpartum glucose monitoring (PGM) is essential for early detection of persistent hyperglycemia and prevention of type 2 diabetes among women with gestational diabetes mellitus (GDM). However, PGM in the U.S. remains suboptimal and varies by insurance coverage. It is unclear how the COVID-19 Public Health Emergency (PHE) and Medicaid Postpartum Extension (MPE) policy reforms influence PGM rates.

Objective: To compare the PGM patterns during the PHE and MPE among women with GDM covered by Medicaid versus commercial insurance.

Methods: We conducted a comparative interrupted time series (ITS) analysis using EHR data (2016–2024) from a large Louisiana healthcare system. GDM was identified via a validated algorithm. PGM (OGTT, FPG, or HbA1c) was assessed at 2 and 12 months postpartum. We employed Poisson regression model with a log link function and offset for population size to estimate Rate Ratios (RR). Sensitivity analyses included a combined pre-gestational diabetes and GDM deliveries.

Results: Among women with GDM (Medicaid: n=3,293; Commercial: n=667), 12-month PGM rose from 15% to 21% in the Medicaid cohort while remaining stable (26–28%) in the commercial cohort. For Medicaid recipients, the MPE was associated with a significantly increasing trend (RR=1.02, p=0.001), while the PHE was associated with a significant declining trend (RR=0.99, p=0.02) in PGM. Compared to the commercial group, Medicaid recipients showed significantly higher 12-month PGM rates during the MPE period (3.4% higher; p=0.02) and lower during the PHE (-0.2%; p=0.002). Sensitivity analyses confirmed the robustness of these findings.

Conclusions: Extending Medicaid coverage (PHE during the pandemic, followed by MPE implementation) benefited the postpartum diabetes care for Medicaid patients in Louisiana. Future research is warranted to examine whether extended Medicaid postpartum coverage may mitigate disparities and improve care for high-risk populations.

Policy

Impact of Paid Family Leave Policies on Co-Sleeping in the US: A State-Level Policy Analysis Using PRAMS Data Laura Drew*, Laura Drew, Xueshi Wang, Claire Margerison,

Sudden unexpected infant death (SUID) is a leading cause of infant mortality in the United States, with rates increasing from 89.9 to 100.5 deaths per 100,000 live births from 2020-2022. Unsafe sleep practices that lead to accidental suffocation and strangulation in bed contribute to SUID. Paid family leave (PFL) policies may reduce the risk of SUID by giving parents greater capacity to follow recommended safe sleep practices, which include avoiding co-sleeping. While there is no federal requirement for private-sector employers to provide PFL, some states have implemented PFL policies. Therefore, we used 2012-2022 PRAMS data to test the hypothesis that PFL policies improve adherence to avoiding co-sleeping. We categorized four states with PFL policies into three cohorts based on PFL implementation year: New York (2018), Washington and D.C. (2020), and Massachusetts (2021), and created a series of control states based on complete data availability. We conducted heterogeneous difference-in-difference (HDID) analyses to examine the average treatment effect on the treated (ATET), which measures the effect of the policy on those who were treated (i.e., exposed to PFL policy). The HDID method extends the traditional DID framework by allowing the treatment effects to vary across different groups and time, which is crucial for studying the staggered rollout of PFL policies. Each additional year of PFL exposure (through the fourth year post-policy) was associated with an increase in the percentage of mothers reporting not co-sleeping, with statistically significant associations in years 3 and 4. PFL was associated with a significant 3 percentage point increase in not co-sleeping in NY and non-significant 2 percentage point increases in WA and DC. There was no association between PFL and co-sleeping in MA.

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Pregnancy outcomes

Clinical Preterm Delivery Phenotypes and Chronic Hypertension among Women in the Nurses' Health Study II Karolina Edlund*, Karolina Edlund, Xiaoyu Che, Holly Crowe, Kathryn Rexrode, Janet Rich Edwards,

Preterm delivery (PTD) has been linked to elevated maternal cardiovascular disease. Yet mechanisms, such as chronic hypertension, underlying observed associations remain unclear due to limited investigation of clinical PTD phenotypes.

Leveraging data from 69,273 parous women in the Nurses' Health Study II, we evaluated associations between lifetime PTD phenotype histories––spontaneous preterm labor (sPTL; n=1,775), preterm premature rupture of membranes (pPROM; n=1,037), medically indicated preterm delivery (miPTD; n=700), and/or nonphenotyped PTD (n=6,534)––and chronic hypertension up to 54 years since first birth. Cox proportional hazards models with time-varying exposures and covariates were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). We stratified estimates by time since first birth to identify potential periods of increased risk.

With a median follow-up of 29 years, we observed 27,376 (40%) cases of chronic hypertension. Lifetime histories of miPTD, sPTL, and nonphenotyped PTD were associated with 55% (HR 1.55; CI 1.39, 1.74), 12% (HR 1.12; CI 1.04, 1.21), and 13% (HR 1.13; CI 1.09, 1.18) increased rates of chronic hypertension, respectively, as compared to pregnancy histories uncomplicated by each phenotype. Adjustment for hypertensive disorders of pregnancy attenuated estimates for miPTD (HR 1.22; CI 1.09, 1.37), suggesting much of the risk associated with miPTD is driven by preeclampsia and gestational hypertension. Rates of chronic hypertension were highest in the first 10 years for miPTD (HR 2.33; CI 1.80, 3.01), sPTL (HR 1.61; CI 1.29, 2.01), and nonphenotyped PTD (HR 1.33; CI 1.18, 1.50). For pPROM, elevated risk of chronic hypertension emerged only after 40 years (HR 1.71; CI 1.09, 2.69).

Rates of chronic hypertension differed across clinical PTD phenotypes. Women with a lifetime history of miPTD were at greatest risk, especially during the first 10 years postpartum, indicating a critical window for screening and intervention.

Pregnancy outcomes

The relationship between prenatal care initiation and adverse birth outcomes by prior birth outcome in Michigan, 2013-2023 Caitlin Meyer*, Caitlin Meyer, Kristin Rankin, Garth Rauscher, Arden Handler,

Background: A prior adverse birth outcome increases risk of a subsequent adverse outcome; however, the effect of prenatal care (PNC) during the subsequent delivery on this relationship is largely unknown. This study assessed the relationship between first trimester PNC initiation and adverse birth outcomes among Michigan birthing individuals by prior birth outcome.
Methods: Data came from a maternally linked registry of live births and fetal deaths of Michigan residents, restricted to mothers whose first two deliveries occurred between 2013-2023 (n=200,391). The relationship between first trimester PNC initiation and adverse birth outcomes (i.e., fetal death, early neonatal death, small for gestational age, or preterm birth) in the second delivery was examined by prior birth outcome. Adjusted risk differences (aRD) and 95% CIs were estimated from multivariable modified ordinary least squares models adjusted for maternal age, race/ethnicity, payer, and interpregnancy interval and assessing effect modification by prior birth outcome.
Results: Only 73.8% of birthing individuals who had a prior adverse outcome (17.4%) initiated PNC in the first trimester of their subsequent pregnancy. Adverse outcomes in the second delivery were less likely among individuals with versus without first trimester PNC initiation among both those without a prior adverse birth outcome (9.1% vs. 10.9%, respectively; aRD= -1.8, 95% CI: -2.2, -1.4) and with a prior adverse birth outcome (28.8% vs. 34.0%, respectively; aRD= -5.2 95% CI: -6.4, -4.0). This relationship was more marked for those with a prior adverse outcome (interaction p-value <0.001).
Conclusion: First trimester PNC initiation reduces the risk of an adverse birth outcome for both those with and without a prior adverse outcome, with a greater effect among those with a prior adverse outcome. These findings suggest the importance of early PNC initiation, especially among those who have experienced adverse outcomes in prior deliveries.

Pregnancy outcomes

Individualized Growth Assessment Compared to Conventional Growth Charts for Detecting Growth-Related Morbidity Sarah Thornburgh*, Sarah Thornburgh, Madeline St. Ville, Elizabeth Williams, Zhen Chen, Jessica Gleason, Dian He, Roger Newman, Edward Chien, William Grobman, Angela Ranzini, Anthony Sciscione, Wesley Lee, Una Grewal, Fasil Tekola-Ayele, Katherine Grantz,

Individualized growth assessment (IGA) evaluates growth adequacy using each fetus as its own control. It is unclear whether IGA improves the ability to distinguish pathological fetal growth from constitutional small or large-for-gestational-age (SGA or LGA).

In a prospective cohort of 2,310 women with fetal measurements at up to 5 visits, we calculated estimated fetal weight (EFW) from 5,915 third trimester (3T) sonograms. EFW was categorized at each 3T scan by 2 methods: 1st as SGA, <10th; AGA, 10th-90th; or LGA, >90th percentile using NICHD unified growth charts; and 2nd by IGA which uses two second trimester scans and the Rossavik Growth Model to predict 3T growth potential and categorized each 3T scan as at, below, or above, expected growth potential. We compared categorization concordance, and predictive accuracy for composite neonatal morbidity/mortality. Logistic regression via GEE calculated odds of neonatal morbidity by discordant group (reference AGA-expected concordant group).

4,761 scans (80.5%) were categorized as AGA, 9.3% SGA, and 10.2% LGA using NICHD growth charts and 81.4%, 7.4%, and 11.2% at, below, or above expected using IGA. Among AGA, neonatal morbidity was 9.6% vs. 5.6% (p= 0.005) for above vs. expected by IGA, and 6.4% vs. 5.6% (p= 0.62) for below vs. expected. Among SGA, 9.2% vs. 6.6% (p= 0.26) for below vs. expected by IGA. Among LGA 8.8% vs. 10.3% (p= 0.54) for above vs. expected by IGA. Risk of composite neonatal morbidity/mortality was increased only for LGA-Expected, although LGA-Above had similar magnitude, but was statistically insignificant.

Evidence suggests IGA may improve detection of growth-related morbidity among smaller fetuses, but there was no improvement in our low-risk sample. Among larger fetuses, IGA may be less effective, as large size is an independent morbidity risk factor, e.g. birth injuries. Future comparisons should focus on high-risk pregnancies that may benefit most from improved detection.

Pregnancy outcomes

The Effects of Prenatal Care Initiation on Severe Maternal Morbidity Ava Holland*, Ava Holland, Ashley Longacre, Andrea Shields,

Background: Healthy People 2030 prioritizes increasing early and adequate prenatal care. Although prenatal care is considered essential for optimizing pregnancy outcomes, its association with severe maternal morbidity (SMM) remains uncertain. This study evaluated the relationship between timing of prenatal care initiation and SMM.

Methods: We conducted a population-based retrospective cohort study using National Vital Statistics System natality data of all US live births from 2019-2023. Prenatal care initiation was categorized as early (first trimester), late (second or third trimester), or no care. SMM was defined as maternal admission to an intensive care unit (ICU). Multivariable logistic regression estimated adjusted odds ratios (aORs) and 95% CIs for the association between prenatal care timing and SMM, controlling for maternal race and ethnicity, age, education, insurance type, and clinical factors (prepregnancy and gestational hypertension, prepregnancy and gestational diabetes, and eclampsia).

Results: Among 18,289,254 live births, 33,274 ICU admissions were reported (0.18%). Compared with early care initiation, late care was associated with higher odds of SMM (crude OR, 2.72 [95% CI 2.66-2.78]; aOR, 2.92 [95% CI, 2.86-2.99]). Absent prenatal care was similarly associated with an increased odds of SMM (crude OR 4.30 [95% CI 4.16-4.4]; aOR, 3.65 [95% CI, 3.53-3.78]).

Conclusions: Late or absent initiation of prenatal care was associated with significantly higher odds of SMM, as measured by ICU admission. These findings underscore the importance of timely engagement in prenatal care; however, causal inference is limited by residual confounding, the use of ICU admission as a surrogate for SMM, lack of data on prenatal care adequacy, and potential variation in ICU admission practices across hospitals. Further research using standardized SMM indicators is warranted.

Pregnancy outcomes

Long-Term Renal Consequences of Fetal Exposure to Maternal Diabetes – Results from the TEAM Study Shelley Ehrlich*, Shelley Ehrlich, Shelley Ehrlich,

While in utero exposure to maternal diabetes mellitus is associated with increased adverse health outcomes in offspring, including obesity, insulin resistance and diabetes, human evidence regarding in utero exposure to maternal diabetes and long-term renal disease risk in offspring is limited. The goal of this study was to determine 1) if there is a transgenerational effect of in utero exposure to dysglycemia on renal health outcomes in adult offspring of women with insulin dependent diabetes mellitus (IDDM); 2) to identify the gestational periods where glycemic dysregulation is most predictive of adverse renal outcomes in adulthood. The Transgenerational Effects on Adult Morbidity (TEAM) Study followed-up offspring of mothers with pre-pregnancy IDDM, who participated in a Program Project Grant (PPG). These women were closely monitored with detailed characterization of glycemic measures across pregnancy in addition to having obstetric and delivery data. Offspring participated in a complete clinical exam, which included markers of renal function (estimated glomerular filtration rate (eGFR), and urine albumin creatinine ratio (UACR)). Linear and logistic regression were used to identify associations between trimester-specific maternal glycohemoglobinA1 standard deviation (HbA1SD) and maternal glucose profiles (functional PCA) with offspring eGFR and UACR, adjusting for covariates (maternal history of microvascular disease, hypertensive disorders of pregnancy, BMI at LMP). In 161 offspring (mean age 32.3 years) increased HbA1SD and increased fluctuations in blood glucose levels in the third trimester were associated with lower eGFR, Also, increased HbA1SD in all 3 trimesters and higher fluctuations in trimester 2 were associated with increased UACR. Our findings indicate an association between maternal glycemia, as early as the first trimester of pregnancy, and decreased renal function in adult offspring.

Pregnancy outcomes

Ultrasound suspicion of fetal large for gestational age and maternal and neonatal outcomes Samantha Krueger*, Samantha Krueger, Giulia Muraca,

Objective: To compare maternal and neonatal outcomes among large-for-gestational-age (LGA) neonates with and without prenatal ultrasound suspicion of LGA.

Study Design: We conducted a population-based cohort study of term LGA births in Ontario, Canada (2012–2021) using linked health administrative data. LGA births with documented prenatal ultrasound suspicion of LGA were treated as exposed and compared with LGA births without such documentation. Outcomes included labor interventions, maternal complications, and neonatal outcomes. Propensity scores with overlap weights were applied in modified Poisson regression models. To explore potential mediating factors and misclassification bias, sensitivity analyses included 1) removing gestational hypertension variables from the propensity score and 2) including those without a documented complication of suspected LGA but a late third trimester ultrasound to the exposed group.

Results: Among 82,385 LGA births, 3,969 (4.8%) had prenatal ultrasound suspicion of LGA. After adjustment, suspected LGA had higher rates of labour induction (39.0% vs 64.0%; aIRR [adjusted incidence rate ratio] 1.48, 95% CI 1.44–1.52), planned cesarean delivery (4.3% vs 16.0%; 2.76, 2.54–3.00), unplanned cesarean delivery (15.9% vs 27.6%; 1.40, 1.33–1.48), postpartum hemorrhage (9.5% vs 11.4%; 1.16, 1.06–1.27), shoulder dystocia (15.4% vs 16.1%; 1.10, 1.02–1.19), and neonatal intensive care unit admission (12.1% vs 18.1%; 1.33, 1.23–1.43; Figure 1). Operative vaginal delivery and obstetric trauma rates were lower among deliveries with suspected LGA (8.2% vs 6.1%; 0.69, 0.61-0.79 and 5.7% vs 5.2%; 0.83, 0.72-0.96 respectively). Results from the two sensitivity analyses were similar to the main analysis.

Conclusion: Prenatal ultrasound suspicion of LGA is associated with increased interventions without improved maternal or neonatal outcomes other than a decrease in operative vaginal delivery and obstetric trauma.

Pregnancy outcomes

Associations between phthalate and replacement chemicals and indicators of placental development in the Human Placenta and Phthalates (HPP) study Andrea Chalem*, Andrea Chalem, Danielle Stevens, Elena Sinkovskaya, Anna Przybylska, Alfred Abuhamad, George Saade, Kelly Ferguson,

Background Abnormal placental development is a proposed mechanism underlying previously observed associations between phthalate exposure and adverse pregnancy and fetal health outcomes.

Objective Evaluate associations between early pregnancy biomarkers of phthalates and their replacements with early pregnancy placental volume and placental weight at delivery as indicators of placental development.

Methods The HPP study, a US prospective pregnancy cohort, measured biomarkers of phthalates and their replacements in urine collected at 2 visits between 12-16 weeks gestation, averaging repeat measures. Placental volume was measured at ~13 weeks via 3D ultrasound and placental weight was obtained at delivery. We used multivariable linear regression models to evaluate associations between biomarkers and placental measures, adjusting for prespecified covariates. We used quantile g-computation to estimate joint effects of low (LMW) and high-molecular weight phthalate mixtures and a replacement mixture.

Results We analyzed data from 165 participants with placental volume and 170 with placental weight. We found a significant association between increased MEP (LMW) and higher z-scored placental volume of 0.25 (95% confidence interval (CI) 0.003, 0.49). Other associations with placental volume were null. All LMW biomarkers, ∑DEHP, and the replacement ∑DEHTP were individually associated with lower placental weight, though CIs included the null. The LMW mixture was associated with a 0.16 (95% CI -0.55, 0.24) decrease in z-scored placental weight.

Conclusion We observed a significant association between early pregnancy MEP concentrations and 1st trimester placental development as measured by placental volume. We saw some associations between biomarker concentrations and decreased placental weight at birth. Studies with larger sample sizes are needed to further elucidate these associations and explore relationships between early pregnancy placental volume and placental weight at birth.

Pregnancy outcomes

Maternal occupational risks and adverse birth outcomes among emergency medical services workers, firefighters, and nurses Paulina Luna Ramirez*, Paulina Luna Ramirez, Michelle Valenti, Caitlin Clarkson Pereira, Lisa Woodson, Maia Brown, Stuart Sherman, Maria Koeppel, Jessica Rainbow, Jefferey Burgess, Melissa Furlong, Leslie Farland,

Emergency service and health care workers face hazardous conditions such as chemical exposure, shift work, stress, and physical strain which may negatively affect pregnancy. Few studies have investigated the impact of occupational exposure as a first responder and adverse pregnancy outcomes. With the use of birth certificates from the state of Arizona (2006-2013), we evaluated adverse birth outcomes among emergency medical services workers without fire exposure (N=414), firefighters(N=376), and nurses(N=13,737) compared to the general population. Using logistic regression, we estimated the association between maternal occupation and risk of low birth weight, preterm birth, cesarean section, low Apgar score, and neonatal intensive care unit (NICU) admission. Models were adjusted for mother’s education and age, as well as birth year. For the outcome of low birth weight, we additionally adjusted for gestational age. We observed higher odds of preterm birth for EMS workers (1.76, 95% CI: 1.34, 2.30), firefighters (1.40, 95% CI: 1.02, 1.88) and nurses (1.22, 95% CI:1.15, 1.30) compared to the general population. Increased odds of cesarean section were observed for EMS workers (1.41, 95% CI: 1.15, 1.72). NICU admission was elevated among emergency medical services workers (2.12, 95% CI: 1.56, 2.89) and firefighters (1.84, 95% CI: 1.30, 2.56) compared to the general population. None of the occupational groups had higher odds of low Apgar score and low birth weight when compared to the general population. These findings suggest associations between maternal occupation in emergency medical services, firefighting, and nursing and select adverse birth outcomes, highlighting the need for future research on implementing workplace protections for pregnant workers.

Pregnancy outcomes

Exploring Effects of PM2.5 and Neighborhood Stress on Inflammation in Pregnancy Teresa Janevic*, Teresa Janevic, Sarah Nowlin, Demina Williams, Rushna Tubassum, Anna Rommel, Alison Lee, Teresa Janevic,

Exposure to ambient fine particulate matter (PM2.5) during the first and second trimesters of pregnancy may increase inflammation in the third trimester measured through inflammatory indicator, HS-CRP. The relationship may be modified by stress due to neighborhood-based structural racism. We analyzed data from a New York City pregnancy cohort of individuals recruited between 2020-2022 who had an assayed sample of HS-CRP within the third trimester of pregnancy (> 196 days gestation), excluding samples taken a week within delivery and twin births. These analyses include 747 women with geocoded address data during pregnancy. We used the XIS-PM model of daily estimates of PM2.5 which we averaged by trimester. We used the Structural Racism Effect Index (SREI) to characterize neighborhood stress. To preserve temporality, we modeled first and second trimester-averages PM2.5 to estimate associations with percentage changes in third trimester log-transformed HS-CRP using linear regression. We included Race-ethnicity, Medicaid (yes/no), maternal age at enrollment, and gestational age at sample as covariates. We assessed effect modification by dividing SREI into quartiles where the fourth quartile represented the highest level of neighborhood stress. We excluded race-ethnicity from the interaction model with SREI. We found an association between first trimester PM2.5 and HS-CRP(adjusted percent change=4.67%, 95% CI=0.57%,8.88% per 1-unit increase in ug/m3).No association was observed between second trimester PM2.5 and HS-CRP(adjusted percent change=0.40%, 95% CI= -3.54%,4.34%). While no interaction was present, we observed a trend for second trimester PM2.5 in the fourth quartile supporting our hypothesis in highest SREI neighborhoods(adjusted percent change=7.6%, 95% CI= -0.06%,15.82%).This suggests that PM2.5 exposure in early gestation may be associated with higher inflammation in the third trimester and that women in highest-stress neighborhoods may be more susceptible.

Pregnancy outcomes

Discordant Smoking Patterns During Pregnancy and Adverse Infant Outcomes: A Sibling Analysis Jessica Swartz*, Jessica Swartz, Rebecca Baer, Gretchen Bandoli,

Background. Cigarette smoking during pregnancy (SDP) has consistently been associated with several adverse infant outcomes, most reliably low birthweight or small for gestational age (SGA) offspring. However, maternal and household level factors likely contribute to these results and are difficult to fully mitigate with conventional statistical adjustment. Sibling analyses can control for these often unmeasured factors. The objective of this study was to investigate the odds of preterm birth (PTB), neonatal intensive care unit (NICU) admission, and SGA infants among siblings exposed to SDP.

Methods. We utilized data from the Study of Mothers and Infants, a complete collection of California birth certificates from 2007 to 2021 linked to maternal/infant hospitalization records. We identified mothers with two consecutive live-birth deliveries and linked siblings for comparison. We used logistic regression in the full sample and conditional logistic regression in sibling pairs to estimate adjusted odds ratios (aOR) and 95% confidence intervals (CI). Models were adjusted for race/ethnicity, age, insurance source, body mass index, parity, hypertension, prenatal care, cannabis use, and other substance use.

Results. There were 6,429,186 singleton linked live births with 29,340 SDP discordant sibling pairs. In the full sample, SDP was associated with PTB (10.5% vs. 6.8%, aOR 1.38, 95%CI 1.35-1.41), NICU admission (9.6% vs. 5.7%, aOR 1.38, 95%CI 1.35-1.40) and SGA (12.4% vs. 8.5%, aOR 1.54, 95%CI 1.51-1.56). Among discordant sibling pairs, results attenuated but remained elevated: PTB (12.2% vs.10.3%, aOR 1.16, 95%CI 1.06-1.26), NICU admission (8.1% vs. 6.5%, aOR 1.19, 95%CI 1.09-1.29) and SGA (8.4% vs. 7.0%, aOR 1.23, 95%CI 1.15-1.32).

Conclusions. In a sibling sample, SDP was modestly but significantly associated with PTB, NICU admission, and SGA. Our findings highlight the utility of a sibling analysis in mitigating genetic and household level factors in observational data.

Pregnancy outcomes

Hyperemesis gravidarum and adverse pregnancy outcomes: A population-based cohort study of 2.5 million births in California Rebecca Gardner*, Rebecca Gardner, Jonathan Mayo, Virginia Winn, Gary Shaw, Julia Simard,

Background: Hyperemesis gravidarum (HG) affects 1-3% of pregnancies and is the leading cause of early pregnancy hospitalization. Maternal undernutrition in HG is hypothesized to lead to abnormal placental development and function, resulting in a higher risk for adverse pregnancy outcomes (APOs), specifically preeclampsia, preterm birth, and small for gestational age. A 2023 meta-analysis supported this association, but the majority of studies were European, and the only prior U.S. population-based study (from 1999) lacked adjustment for confounders.

Methods: In a California live birth cohort from 2007-2011 (~2.5 million singleton births), HG was defined based on primary diagnosis codes in prenatal hospitalization or emergency department encounter records (n=53,681). Poisson regression models were fitted to estimate the relative risk (RR) of HG on a given APO, adjusted for maternal age, insurance type, maternal education, cigarette use during pregnancy, and type 1 diabetes. Trimester of first hospitalization was considered as a source of effect heterogeneity and parity as an effect modifier.

Results: APOs were more common in the HG group: preeclampsia (4.0% vs 3.3%), preterm birth (9.0% vs 7.1%), and small for gestational age (10.6% vs 8.5%). Higher RRs for APOs persisted after adjusting for confounders, e.g., preeclampsia: adjusted RR 1.17 (95% CI 1.12-1.22). Women with HG first hospitalized in the second trimester had an even higher risk of APOs, e.g., preeclampsia: 4.8% vs 3.7% for first-trimester HG; 1.39, (1.29-1.51). Associations were stronger in multiparous women for multiple APOs, e.g., preterm birth, 1.34, (1.30-1.39) vs 1.14 (1.09-1.19) for nulliparous women.

Conclusion: In this first U.S. population-based study of HG and APOs with adjusted analyses, HG was associated with increased risk of APOs, particularly when first documented in the second trimester, suggesting it may be a risk factor for preeclampsia, preterm birth, and small for gestational age.

Pregnancy outcomes

Hospital costs of severe maternal morbidity across race/ethnicity and insurance status: a national serial cross-sectional study Amelia Srajer*, Amelia Srajer, Amity Quinn, Paul Ronksley, Erin Brennand, Amy Metcalfe,

Objective: Medicaid covers over 40% of United States births and disproportionately serves racial minority groups who already face elevated obstetrical risks. Coverage gaps relative to private insurance may further exacerbate these adverse outcomes and their associated healthcare costs. We assessed the odds and hospital costs of severe maternal morbidity (SMM) at the intersection of race/ethnicity and insurance status.

Methods: We analyzed 23.5 million weighted obstetric deliveries from 2015-2022 using the National Inpatient Sample. Ten interaction terms were created to compare Medicaid versus private insurance across White, Black, Hispanic, Asian, and Native American groups. The 21 SMM complications were defined using International Classification of Diseases codes. Multivariable logistic regression and generalized linear models, using 95% confidence intervals, assessed SMM odds and associated hospital costs respectively, adjusting for a validated obstetric comorbidity score, discharge year/quarter, mode of delivery, and hospital region.

Results: Medicaid insured 43.8% of deliveries, with higher coverage among Native American (67.6%), Black (66.7%), and Hispanic (66.6%) patients compared to White (32.3%) and Asian (27.9%) patients. Adjusted odds of composite SMM were higher among all intersectional groups compared to privately insured White patients ($p<0.001$). Within each racial category, Medicaid was associated with higher odds of SMM. SMM-related costs were higher among Black, Hispanic, and Asian patients across insurance types whereas Native American Medicaid patients demonstrated significantly lower costs.

Conclusion: Racial disparities in SMM risk are significantly amplified for those with Medicaid, yet race appears to be the primary driver of the disproportionate financial burden. Addressing these inequities requires policy reform that targets both insurance coverage gaps and the structural biases inherent to clinical care and resource allocation.

Pregnancy outcomes

Associations of prenatal acetaminophen use with birth outcomes Dorah Labatte*, Dorah Labatte, K.Joseph Hurt, Sheryl L. Rifas-Shiman, Marie-France Hivert, Emily Oken, Wei Perng,

Acetaminophen is a commonly used over-the-counter analgesic and antipyretic, yet potential risks for use during pregnancy remain uncertain. Here, we examined associations of prenatal acetaminophen use with preterm birth (PTB) and birth size among 2,049 pregnancies in the Project Viva cohort. During the 1st and 2nd trimesters, women reported medication use in the prior 3 months. We obtained fetal sex and birthweight from hospital records and determined gestational age at delivery using menstrual and prenatal ultrasound dating. We used logistic regression to evaluate associations of trimester-specific acetaminophen use (never, 1–9 times, ≥10 times) with PTB (<37 vs. ≤37 gestational weeks), and multinomial logistic regression for associations with small (SGA) and large-for-gestational-age vs. appropriate-for-gestational-age. Covariates included maternal age, parity, prepregnancy BMI, smoking, nativity, education, and prenatal antidepressant and antibiotic use. In sensitivity analyses, we reran models with prenatal ibuprofen use as a negative control exposure and again in a subsample of 1,691 women who were in the common support range for propensity to use acetaminophen based on 10 background characteristics. In the main analysis, 1st trimester acetaminophen use ≥10 times (vs. never) corresponded with 1.71 (95%CI 1.02, 2.78) odds of PTB. Additionally, 1st trimester use 1-9 times (vs. never) was associated with lower odds of SGA: OR 0.64 (0.41, 0.98), though no association was observed for ≥10 times. 2nd trimester use corresponded lower odds of SGA in a dose-response fashion: OR 0.75 (0.49, 1.14) and 0.54 (0.29, 1.00) for 1-9 and ≥10 times, respectively. The negative control exposure and the propensity-score restricted analyses suggest the existence of residual confounding by underlying conditions that are indications for acetaminophen use and risk factors for PTB. Associations of 2nd trimester use with lower risk of SGA may be causal and should be explored further.

Pregnancy outcomes

The Effects of Prenatal Care Initiation on Severe Maternal Morbidity Ava Holland*, Ava Holland, Ashley Longacre, Andrea Shields,

Background: Healthy People 2030 prioritizes increasing early and adequate prenatal care. Although prenatal care is considered essential for optimizing pregnancy outcomes, its association with severe maternal morbidity (SMM) remains uncertain. This study evaluated the relationship between timing of prenatal care initiation and SMM.

Methods: We conducted a population-based retrospective cohort study using National Vital Statistics System natality data of all US live births from 2019-2023. Prenatal care initiation was categorized as early (first trimester), late (second or third trimester), or no care. SMM was defined as maternal admission to an intensive care unit (ICU). Multivariable logistic regression estimated adjusted odds ratios (aORs) and 95% CIs for the association between prenatal care timing and SMM, controlling for maternal race and ethnicity, age, education, insurance type, and clinical factors (prepregnancy and gestational hypertension, prepregnancy and gestational diabetes, and eclampsia).

Results: Among 18,289,254 live births, 33,274 ICU admissions were reported (0.18%). Compared with early care initiation, late care was associated with higher odds of SMM (crude OR, 2.72 [95% CI 2.66-2.78]; aOR, 2.92 [95% CI, 2.86-2.99]). Absent prenatal care was similarly associated with an increased odds of SMM (crude OR 4.30 [95% CI 4.16-4.4]; aOR, 3.65 [95% CI, 3.53-3.78]).

Conclusions: Late or absent initiation of prenatal care was associated with significantly higher odds of SMM, as measured by ICU admission. These findings underscore the importance of timely engagement in prenatal care; however, causal inference is limited by residual confounding, the use of ICU admission as a surrogate for SMM, lack of data on prenatal care adequacy, and potential variation in ICU admission practices across hospitals. Further research using standardized SMM indicators is warranted.

Pregnancy outcomes

Ultrasound suspicion of fetal large for gestational age and maternal and neonatal outcomes Samantha Krueger*, Samantha Krueger, Giulia Muraca,

Objective: To compare maternal and neonatal outcomes among large-for-gestational-age (LGA) neonates with and without prenatal ultrasound suspicion of LGA.

Study Design: We conducted a population-based cohort study of term LGA births in Ontario, Canada (2012–2021) using linked health administrative data. LGA births with documented prenatal ultrasound suspicion of LGA were treated as exposed and compared with LGA births without such documentation. Outcomes included labor interventions, maternal complications, and neonatal outcomes. Propensity scores with overlap weights were applied in modified Poisson regression models. To explore potential mediating factors and misclassification bias, sensitivity analyses included 1) removing gestational hypertension variables from the propensity score and 2) including those without a documented complication of suspected LGA but a late third trimester ultrasound to the exposed group.

Results: Among 82,385 LGA births, 3,969 (4.8%) had prenatal ultrasound suspicion of LGA. After adjustment, suspected LGA had higher rates of labour induction (39.0% vs 64.0%; aIRR [adjusted incidence rate ratio] 1.48, 95% CI 1.44–1.52), planned cesarean delivery (4.3% vs 16.0%; 2.76, 2.54–3.00), unplanned cesarean delivery (15.9% vs 27.6%; 1.40, 1.33–1.48), postpartum hemorrhage (9.5% vs 11.4%; 1.16, 1.06–1.27), shoulder dystocia (15.4% vs 16.1%; 1.10, 1.02–1.19), and neonatal intensive care unit admission (12.1% vs 18.1%; 1.33, 1.23–1.43; Figure 1). Operative vaginal delivery and obstetric trauma rates were lower among deliveries with suspected LGA (8.2% vs 6.1%; 0.69, 0.61-0.79 and 5.7% vs 5.2%; 0.83, 0.72-0.96 respectively). Results from the two sensitivity analyses were similar to the main analysis.

Conclusion: Prenatal ultrasound suspicion of LGA is associated with increased interventions without improved maternal or neonatal outcomes other than a decrease in operative vaginal delivery and obstetric trauma.

Pregnancy outcomes

Clinical Preterm Delivery Phenotypes and Chronic Hypertension among Women in the Nurses' Health Study II Karolina Edlund*, Karolina Edlund, Xiaoyu Che, Holly Crowe, Kathryn Rexrode, Janet Rich Edwards,

Preterm delivery (PTD) has been linked to elevated maternal cardiovascular disease. Yet mechanisms, such as chronic hypertension, underlying observed associations remain unclear due to limited investigation of clinical PTD phenotypes.

Leveraging data from 69,273 parous women in the Nurses' Health Study II, we evaluated associations between lifetime PTD phenotype histories––spontaneous preterm labor (sPTL; n=1,775), preterm premature rupture of membranes (pPROM; n=1,037), medically indicated preterm delivery (miPTD; n=700), and/or nonphenotyped PTD (n=6,534)––and chronic hypertension up to 54 years since first birth. Cox proportional hazards models with time-varying exposures and covariates were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). We stratified estimates by time since first birth to identify potential periods of increased risk.

With a median follow-up of 29 years, we observed 27,376 (40%) cases of chronic hypertension. Lifetime histories of miPTD, sPTL, and nonphenotyped PTD were associated with 55% (HR 1.55; CI 1.39, 1.74), 12% (HR 1.12; CI 1.04, 1.21), and 13% (HR 1.13; CI 1.09, 1.18) increased rates of chronic hypertension, respectively, as compared to pregnancy histories uncomplicated by each phenotype. Adjustment for hypertensive disorders of pregnancy attenuated estimates for miPTD (HR 1.22; CI 1.09, 1.37), suggesting much of the risk associated with miPTD is driven by preeclampsia and gestational hypertension. Rates of chronic hypertension were highest in the first 10 years for miPTD (HR 2.33; CI 1.80, 3.01), sPTL (HR 1.61; CI 1.29, 2.01), and nonphenotyped PTD (HR 1.33; CI 1.18, 1.50). For pPROM, elevated risk of chronic hypertension emerged only after 40 years (HR 1.71; CI 1.09, 2.69).

Rates of chronic hypertension differed across clinical PTD phenotypes. Women with a lifetime history of miPTD were at greatest risk, especially during the first 10 years postpartum, indicating a critical window for screening and intervention.

Pregnancy outcomes

Long-Term Renal Consequences of Fetal Exposure to Maternal Diabetes – Results from the TEAM Study Shelley Ehrlich*, Shelley Ehrlich, Shelley Ehrlich,

While in utero exposure to maternal diabetes mellitus is associated with increased adverse health outcomes in offspring, including obesity, insulin resistance and diabetes, human evidence regarding in utero exposure to maternal diabetes and long-term renal disease risk in offspring is limited. The goal of this study was to determine 1) if there is a transgenerational effect of in utero exposure to dysglycemia on renal health outcomes in adult offspring of women with insulin dependent diabetes mellitus (IDDM); 2) to identify the gestational periods where glycemic dysregulation is most predictive of adverse renal outcomes in adulthood. The Transgenerational Effects on Adult Morbidity (TEAM) Study followed-up offspring of mothers with pre-pregnancy IDDM, who participated in a Program Project Grant (PPG). These women were closely monitored with detailed characterization of glycemic measures across pregnancy in addition to having obstetric and delivery data. Offspring participated in a complete clinical exam, which included markers of renal function (estimated glomerular filtration rate (eGFR), and urine albumin creatinine ratio (UACR)). Linear and logistic regression were used to identify associations between trimester-specific maternal glycohemoglobinA1 standard deviation (HbA1SD) and maternal glucose profiles (functional PCA) with offspring eGFR and UACR, adjusting for covariates (maternal history of microvascular disease, hypertensive disorders of pregnancy, BMI at LMP). In 161 offspring (mean age 32.3 years) increased HbA1SD and increased fluctuations in blood glucose levels in the third trimester were associated with lower eGFR, Also, increased HbA1SD in all 3 trimesters and higher fluctuations in trimester 2 were associated with increased UACR. Our findings indicate an association between maternal glycemia, as early as the first trimester of pregnancy, and decreased renal function in adult offspring.

Pregnancy outcomes

Hyperemesis gravidarum and adverse pregnancy outcomes: A population-based cohort study of 2.5 million births in California Rebecca Gardner*, Rebecca Gardner, Jonathan Mayo, Virginia Winn, Gary Shaw, Julia Simard,

Background: Hyperemesis gravidarum (HG) affects 1-3% of pregnancies and is the leading cause of early pregnancy hospitalization. Maternal undernutrition in HG is hypothesized to lead to abnormal placental development and function, resulting in a higher risk for adverse pregnancy outcomes (APOs), specifically preeclampsia, preterm birth, and small for gestational age. A 2023 meta-analysis supported this association, but the majority of studies were European, and the only prior U.S. population-based study (from 1999) lacked adjustment for confounders.

Methods: In a California live birth cohort from 2007-2011 (~2.5 million singleton births), HG was defined based on primary diagnosis codes in prenatal hospitalization or emergency department encounter records (n=53,681). Poisson regression models were fitted to estimate the relative risk (RR) of HG on a given APO, adjusted for maternal age, insurance type, maternal education, cigarette use during pregnancy, and type 1 diabetes. Trimester of first hospitalization was considered as a source of effect heterogeneity and parity as an effect modifier.

Results: APOs were more common in the HG group: preeclampsia (4.0% vs 3.3%), preterm birth (9.0% vs 7.1%), and small for gestational age (10.6% vs 8.5%). Higher RRs for APOs persisted after adjusting for confounders, e.g., preeclampsia: adjusted RR 1.17 (95% CI 1.12-1.22). Women with HG first hospitalized in the second trimester had an even higher risk of APOs, e.g., preeclampsia: 4.8% vs 3.7% for first-trimester HG; 1.39, (1.29-1.51). Associations were stronger in multiparous women for multiple APOs, e.g., preterm birth, 1.34, (1.30-1.39) vs 1.14 (1.09-1.19) for nulliparous women.

Conclusion: In this first U.S. population-based study of HG and APOs with adjusted analyses, HG was associated with increased risk of APOs, particularly when first documented in the second trimester, suggesting it may be a risk factor for preeclampsia, preterm birth, and small for gestational age.

Pregnancy outcomes

Exploring Effects of PM2.5 and Neighborhood Stress on Inflammation in Pregnancy Teresa Janevic*, Teresa Janevic, Sarah Nowlin, Demina Williams, Rushna Tubassum, Anna Rommel, Alison Lee, Teresa Janevic,

Exposure to ambient fine particulate matter (PM2.5) during the first and second trimesters of pregnancy may increase inflammation in the third trimester measured through inflammatory indicator, HS-CRP. The relationship may be modified by stress due to neighborhood-based structural racism. We analyzed data from a New York City pregnancy cohort of individuals recruited between 2020-2022 who had an assayed sample of HS-CRP within the third trimester of pregnancy (> 196 days gestation), excluding samples taken a week within delivery and twin births. These analyses include 747 women with geocoded address data during pregnancy. We used the XIS-PM model of daily estimates of PM2.5 which we averaged by trimester. We used the Structural Racism Effect Index (SREI) to characterize neighborhood stress. To preserve temporality, we modeled first and second trimester-averages PM2.5 to estimate associations with percentage changes in third trimester log-transformed HS-CRP using linear regression. We included Race-ethnicity, Medicaid (yes/no), maternal age at enrollment, and gestational age at sample as covariates. We assessed effect modification by dividing SREI into quartiles where the fourth quartile represented the highest level of neighborhood stress. We excluded race-ethnicity from the interaction model with SREI. We found an association between first trimester PM2.5 and HS-CRP(adjusted percent change=4.67%, 95% CI=0.57%,8.88% per 1-unit increase in ug/m3).No association was observed between second trimester PM2.5 and HS-CRP(adjusted percent change=0.40%, 95% CI= -3.54%,4.34%). While no interaction was present, we observed a trend for second trimester PM2.5 in the fourth quartile supporting our hypothesis in highest SREI neighborhoods(adjusted percent change=7.6%, 95% CI= -0.06%,15.82%).This suggests that PM2.5 exposure in early gestation may be associated with higher inflammation in the third trimester and that women in highest-stress neighborhoods may be more susceptible.

Pregnancy outcomes

Discordant Smoking Patterns During Pregnancy and Adverse Infant Outcomes: A Sibling Analysis Jessica Swartz*, Jessica Swartz, Rebecca Baer, Gretchen Bandoli,

Background. Cigarette smoking during pregnancy (SDP) has consistently been associated with several adverse infant outcomes, most reliably low birthweight or small for gestational age (SGA) offspring. However, maternal and household level factors likely contribute to these results and are difficult to fully mitigate with conventional statistical adjustment. Sibling analyses can control for these often unmeasured factors. The objective of this study was to investigate the odds of preterm birth (PTB), neonatal intensive care unit (NICU) admission, and SGA infants among siblings exposed to SDP.

Methods. We utilized data from the Study of Mothers and Infants, a complete collection of California birth certificates from 2007 to 2021 linked to maternal/infant hospitalization records. We identified mothers with two consecutive live-birth deliveries and linked siblings for comparison. We used logistic regression in the full sample and conditional logistic regression in sibling pairs to estimate adjusted odds ratios (aOR) and 95% confidence intervals (CI). Models were adjusted for race/ethnicity, age, insurance source, body mass index, parity, hypertension, prenatal care, cannabis use, and other substance use.

Results. There were 6,429,186 singleton linked live births with 29,340 SDP discordant sibling pairs. In the full sample, SDP was associated with PTB (10.5% vs. 6.8%, aOR 1.38, 95%CI 1.35-1.41), NICU admission (9.6% vs. 5.7%, aOR 1.38, 95%CI 1.35-1.40) and SGA (12.4% vs. 8.5%, aOR 1.54, 95%CI 1.51-1.56). Among discordant sibling pairs, results attenuated but remained elevated: PTB (12.2% vs.10.3%, aOR 1.16, 95%CI 1.06-1.26), NICU admission (8.1% vs. 6.5%, aOR 1.19, 95%CI 1.09-1.29) and SGA (8.4% vs. 7.0%, aOR 1.23, 95%CI 1.15-1.32).

Conclusions. In a sibling sample, SDP was modestly but significantly associated with PTB, NICU admission, and SGA. Our findings highlight the utility of a sibling analysis in mitigating genetic and household level factors in observational data.

Pregnancy outcomes

Individualized Growth Assessment Compared to Conventional Growth Charts for Detecting Growth-Related Morbidity Sarah Thornburgh*, Sarah Thornburgh, Madeline St. Ville, Elizabeth Williams, Zhen Chen, Jessica Gleason, Dian He, Roger Newman, Edward Chien, William Grobman, Angela Ranzini, Anthony Sciscione, Wesley Lee, Una Grewal, Fasil Tekola-Ayele, Katherine Grantz,

Individualized growth assessment (IGA) evaluates growth adequacy using each fetus as its own control. It is unclear whether IGA improves the ability to distinguish pathological fetal growth from constitutional small or large-for-gestational-age (SGA or LGA).

In a prospective cohort of 2,310 women with fetal measurements at up to 5 visits, we calculated estimated fetal weight (EFW) from 5,915 third trimester (3T) sonograms. EFW was categorized at each 3T scan by 2 methods: 1st as SGA, <10th; AGA, 10th-90th; or LGA, >90th percentile using NICHD unified growth charts; and 2nd by IGA which uses two second trimester scans and the Rossavik Growth Model to predict 3T growth potential and categorized each 3T scan as at, below, or above, expected growth potential. We compared categorization concordance, and predictive accuracy for composite neonatal morbidity/mortality. Logistic regression via GEE calculated odds of neonatal morbidity by discordant group (reference AGA-expected concordant group).

4,761 scans (80.5%) were categorized as AGA, 9.3% SGA, and 10.2% LGA using NICHD growth charts and 81.4%, 7.4%, and 11.2% at, below, or above expected using IGA. Among AGA, neonatal morbidity was 9.6% vs. 5.6% (p= 0.005) for above vs. expected by IGA, and 6.4% vs. 5.6% (p= 0.62) for below vs. expected. Among SGA, 9.2% vs. 6.6% (p= 0.26) for below vs. expected by IGA. Among LGA 8.8% vs. 10.3% (p= 0.54) for above vs. expected by IGA. Risk of composite neonatal morbidity/mortality was increased only for LGA-Expected, although LGA-Above had similar magnitude, but was statistically insignificant.

Evidence suggests IGA may improve detection of growth-related morbidity among smaller fetuses, but there was no improvement in our low-risk sample. Among larger fetuses, IGA may be less effective, as large size is an independent morbidity risk factor, e.g. birth injuries. Future comparisons should focus on high-risk pregnancies that may benefit most from improved detection.

Pregnancy outcomes

Associations between phthalate and replacement chemicals and indicators of placental development in the Human Placenta and Phthalates (HPP) study Andrea Chalem*, Andrea Chalem, Danielle Stevens, Elena Sinkovskaya, Anna Przybylska, Alfred Abuhamad, George Saade, Kelly Ferguson,

Background Abnormal placental development is a proposed mechanism underlying previously observed associations between phthalate exposure and adverse pregnancy and fetal health outcomes.

Objective Evaluate associations between early pregnancy biomarkers of phthalates and their replacements with early pregnancy placental volume and placental weight at delivery as indicators of placental development.

Methods The HPP study, a US prospective pregnancy cohort, measured biomarkers of phthalates and their replacements in urine collected at 2 visits between 12-16 weeks gestation, averaging repeat measures. Placental volume was measured at ~13 weeks via 3D ultrasound and placental weight was obtained at delivery. We used multivariable linear regression models to evaluate associations between biomarkers and placental measures, adjusting for prespecified covariates. We used quantile g-computation to estimate joint effects of low (LMW) and high-molecular weight phthalate mixtures and a replacement mixture.

Results We analyzed data from 165 participants with placental volume and 170 with placental weight. We found a significant association between increased MEP (LMW) and higher z-scored placental volume of 0.25 (95% confidence interval (CI) 0.003, 0.49). Other associations with placental volume were null. All LMW biomarkers, ∑DEHP, and the replacement ∑DEHTP were individually associated with lower placental weight, though CIs included the null. The LMW mixture was associated with a 0.16 (95% CI -0.55, 0.24) decrease in z-scored placental weight.

Conclusion We observed a significant association between early pregnancy MEP concentrations and 1st trimester placental development as measured by placental volume. We saw some associations between biomarker concentrations and decreased placental weight at birth. Studies with larger sample sizes are needed to further elucidate these associations and explore relationships between early pregnancy placental volume and placental weight at birth.

Pregnancy outcomes

Hospital costs of severe maternal morbidity across race/ethnicity and insurance status: a national serial cross-sectional study Amelia Srajer*, Amelia Srajer, Amity Quinn, Paul Ronksley, Erin Brennand, Amy Metcalfe,

Objective: Medicaid covers over 40% of United States births and disproportionately serves racial minority groups who already face elevated obstetrical risks. Coverage gaps relative to private insurance may further exacerbate these adverse outcomes and their associated healthcare costs. We assessed the odds and hospital costs of severe maternal morbidity (SMM) at the intersection of race/ethnicity and insurance status.

Methods: We analyzed 23.5 million weighted obstetric deliveries from 2015-2022 using the National Inpatient Sample. Ten interaction terms were created to compare Medicaid versus private insurance across White, Black, Hispanic, Asian, and Native American groups. The 21 SMM complications were defined using International Classification of Diseases codes. Multivariable logistic regression and generalized linear models, using 95% confidence intervals, assessed SMM odds and associated hospital costs respectively, adjusting for a validated obstetric comorbidity score, discharge year/quarter, mode of delivery, and hospital region.

Results: Medicaid insured 43.8% of deliveries, with higher coverage among Native American (67.6%), Black (66.7%), and Hispanic (66.6%) patients compared to White (32.3%) and Asian (27.9%) patients. Adjusted odds of composite SMM were higher among all intersectional groups compared to privately insured White patients ($p<0.001$). Within each racial category, Medicaid was associated with higher odds of SMM. SMM-related costs were higher among Black, Hispanic, and Asian patients across insurance types whereas Native American Medicaid patients demonstrated significantly lower costs.

Conclusion: Racial disparities in SMM risk are significantly amplified for those with Medicaid, yet race appears to be the primary driver of the disproportionate financial burden. Addressing these inequities requires policy reform that targets both insurance coverage gaps and the structural biases inherent to clinical care and resource allocation.

Pregnancy outcomes

The relationship between prenatal care initiation and adverse birth outcomes by prior birth outcome in Michigan, 2013-2023 Caitlin Meyer*, Caitlin Meyer, Kristin Rankin, Garth Rauscher, Arden Handler,

Background: A prior adverse birth outcome increases risk of a subsequent adverse outcome; however, the effect of prenatal care (PNC) during the subsequent delivery on this relationship is largely unknown. This study assessed the relationship between first trimester PNC initiation and adverse birth outcomes among Michigan birthing individuals by prior birth outcome.
Methods: Data came from a maternally linked registry of live births and fetal deaths of Michigan residents, restricted to mothers whose first two deliveries occurred between 2013-2023 (n=200,391). The relationship between first trimester PNC initiation and adverse birth outcomes (i.e., fetal death, early neonatal death, small for gestational age, or preterm birth) in the second delivery was examined by prior birth outcome. Adjusted risk differences (aRD) and 95% CIs were estimated from multivariable modified ordinary least squares models adjusted for maternal age, race/ethnicity, payer, and interpregnancy interval and assessing effect modification by prior birth outcome.
Results: Only 73.8% of birthing individuals who had a prior adverse outcome (17.4%) initiated PNC in the first trimester of their subsequent pregnancy. Adverse outcomes in the second delivery were less likely among individuals with versus without first trimester PNC initiation among both those without a prior adverse birth outcome (9.1% vs. 10.9%, respectively; aRD= -1.8, 95% CI: -2.2, -1.4) and with a prior adverse birth outcome (28.8% vs. 34.0%, respectively; aRD= -5.2 95% CI: -6.4, -4.0). This relationship was more marked for those with a prior adverse outcome (interaction p-value <0.001).
Conclusion: First trimester PNC initiation reduces the risk of an adverse birth outcome for both those with and without a prior adverse outcome, with a greater effect among those with a prior adverse outcome. These findings suggest the importance of early PNC initiation, especially among those who have experienced adverse outcomes in prior deliveries.

Pregnancy outcomes

Maternal occupational risks and adverse birth outcomes among emergency medical services workers, firefighters, and nurses Paulina Luna Ramirez*, Paulina Luna Ramirez, Michelle Valenti, Caitlin Clarkson Pereira, Lisa Woodson, Maia Brown, Stuart Sherman, Maria Koeppel, Jessica Rainbow, Jefferey Burgess, Melissa Furlong, Leslie Farland,

Emergency service and health care workers face hazardous conditions such as chemical exposure, shift work, stress, and physical strain which may negatively affect pregnancy. Few studies have investigated the impact of occupational exposure as a first responder and adverse pregnancy outcomes. With the use of birth certificates from the state of Arizona (2006-2013), we evaluated adverse birth outcomes among emergency medical services workers without fire exposure (N=414), firefighters(N=376), and nurses(N=13,737) compared to the general population. Using logistic regression, we estimated the association between maternal occupation and risk of low birth weight, preterm birth, cesarean section, low Apgar score, and neonatal intensive care unit (NICU) admission. Models were adjusted for mother’s education and age, as well as birth year. For the outcome of low birth weight, we additionally adjusted for gestational age. We observed higher odds of preterm birth for EMS workers (1.76, 95% CI: 1.34, 2.30), firefighters (1.40, 95% CI: 1.02, 1.88) and nurses (1.22, 95% CI:1.15, 1.30) compared to the general population. Increased odds of cesarean section were observed for EMS workers (1.41, 95% CI: 1.15, 1.72). NICU admission was elevated among emergency medical services workers (2.12, 95% CI: 1.56, 2.89) and firefighters (1.84, 95% CI: 1.30, 2.56) compared to the general population. None of the occupational groups had higher odds of low Apgar score and low birth weight when compared to the general population. These findings suggest associations between maternal occupation in emergency medical services, firefighting, and nursing and select adverse birth outcomes, highlighting the need for future research on implementing workplace protections for pregnant workers.

Pregnancy outcomes

Associations of prenatal acetaminophen use with birth outcomes Dorah Labatte*, Dorah Labatte, K.Joseph Hurt, Sheryl L. Rifas-Shiman, Marie-France Hivert, Emily Oken, Wei Perng,

Acetaminophen is a commonly used over-the-counter analgesic and antipyretic, yet potential risks for use during pregnancy remain uncertain. Here, we examined associations of prenatal acetaminophen use with preterm birth (PTB) and birth size among 2,049 pregnancies in the Project Viva cohort. During the 1st and 2nd trimesters, women reported medication use in the prior 3 months. We obtained fetal sex and birthweight from hospital records and determined gestational age at delivery using menstrual and prenatal ultrasound dating. We used logistic regression to evaluate associations of trimester-specific acetaminophen use (never, 1–9 times, ≥10 times) with PTB (<37 vs. ≤37 gestational weeks), and multinomial logistic regression for associations with small (SGA) and large-for-gestational-age vs. appropriate-for-gestational-age. Covariates included maternal age, parity, prepregnancy BMI, smoking, nativity, education, and prenatal antidepressant and antibiotic use. In sensitivity analyses, we reran models with prenatal ibuprofen use as a negative control exposure and again in a subsample of 1,691 women who were in the common support range for propensity to use acetaminophen based on 10 background characteristics. In the main analysis, 1st trimester acetaminophen use ≥10 times (vs. never) corresponded with 1.71 (95%CI 1.02, 2.78) odds of PTB. Additionally, 1st trimester use 1-9 times (vs. never) was associated with lower odds of SGA: OR 0.64 (0.41, 0.98), though no association was observed for ≥10 times. 2nd trimester use corresponded lower odds of SGA in a dose-response fashion: OR 0.75 (0.49, 1.14) and 0.54 (0.29, 1.00) for 1-9 and ≥10 times, respectively. The negative control exposure and the propensity-score restricted analyses suggest the existence of residual confounding by underlying conditions that are indications for acetaminophen use and risk factors for PTB. Associations of 2nd trimester use with lower risk of SGA may be causal and should be explored further.

Social determinants of health

Initiating but Not Sustaining: Adverse Childhood Experiences and Breastfeeding Outcomes in North Dakota Anna Kihlstrom*, Andrew Williams, Anna Khilstrom,

Background: Examining the role of Adverse Childhood Experiences (ACEs) in breastfeeding has implications to support women in meeting their breastfeeding goals. To date, few studies have examined rural or statewide samples. This study examines the association between ACEs and breastfeeding outcomes among a representative sample of women in North Dakota.

Methods: Data for 40,906 (weighted) women from 2017-2021 North Dakota Pregnancy Risk Assessment Monitoring Survey were used. Breastfeeding initiation was self-report to “Did you ever breastfeed or pump breast milk to feed your new baby, even for a short period of time?” (yes/no). Breastfeeding duration was self-reported, and 2- and 6-month duration variables were calculated. Participants reported(yes/no) to 10 ACEs and ≥2 ACEs was “High.” Logistic regression(adjusted for maternal factors) estimated odds ratios(OR) and 95% confidence intervals(95%CI) for the association between ACEs and breastfeeding outcomes. Regression models were fit for High ACEs and individual ACEs as exposures.

Results: High ACEs were reported by 37% of participants. For breastfeeding, 89% initiated breastfeeding, 70% breastfed at 2 months and 60% breastfed at 6 months. In regression analyses, High ACEs were not associated with breastfeeding initiation or breastfeeding at 2 months, yet High ACEs were associated with lower odds of breastfeeding at 6 months (OR:0.77, 95%CI:0.62,0.96). For Individual ACEs, exposure to household substance use was associated with lower odds of all outcomes, and parental divorce was associated with lower odds of 6-month breastfeeding.

Discussion: Results suggest High ACEs may not impede breastfeeding initiation, yet women with ACEs may have short breastfeeding duration, highlighting an intervention window. Associations between exposure to household substance use, parental divorce and reduced breastfeeding warrants further study. Women with ACEs may be an at-risk group to benefit from trauma-informed lactation support.

Social determinants of health

Where You Go to School Matters: Structural Determinants of Adolescent Cardiovascular Fitness Annabelle Ng*, Katharine McCarthy, Annabelle Ng, Ellerie Weber, Sophia Day, Kira Argenio, Kevin Konty, Maida Galvez, Teresa Janevic, Katharine McCarthy,

Understanding the relative influence of school- versus individual-level factors on adolescent cardiovascular fitness (CVF) is essential for guiding effective school-based policy. We fit multilevel generalized linear models to estimate associations of school- and individual-level attributes on adolescent CVF and the variance attributable to each level.

Data were from a New York City cross-sectional study of high school students aged ≥ 14 (2016-17 school year) using linked enrollment, automated school nurse record, and physical fitness surveillance data. We excluded students with diabetes, hypertension or asthma. Models were stratified by sex. CVF was assessed using sex- and age-adjusted physical fitness z-scores (FITNESSGRAM PACER, push-up, and curl-up tests) and by the number of Health Fitness Zones achieved (0-3). School measures included physical education (PE) resources per 1,000 students, PE teacher–student ratio, school based- health centers (SBHCs), salad bars, health education participation, bullying/harassment prevalence, school racial/ethnic segregation and school poverty. Individual-level covariates included grade, race/ethnicity, free/reduced lunch eligibility, and English language learner (ELL) status.

Among 177,688 students aged 14-19 nested in 406 schools, 14.7% of girls and 24.0% of boys achieved the Healthy Fitness Zone for all fitness components. Between-school differences accounted for 24% of CVF variance among girls and 17% among boys, attenuated after adjustment for school variables (girls 19%, boys 14%). Individual-level factors did not further reduce between-school variance. Within schools, higher bullying/harassment prevalence (β [95% CI]: girls −0.05 [−0.09, −0.02]; boys −0.04 [−0.07, −0.01]) and higher proportions of Black/Hispanic students (girls −0.04 [−0.06, −0.01]; boys −0.05 [−0.08, −0.03]) were negatively associated with CVF. SBHCs showed a positive, nonsignificant association among girls only (girls 0.07 [−0.02, 0.17]; boys (0.01 [−0.08, 0.09]). PE, salad bars, and health education were not associated with CVF.

School context emerged as a salient context for understanding differences in adolescent cardiovascular fitness, particularly among girls. Social climate emerged as a key modifiable factor for both sexes; school-based health centers were promising for girls.

Social determinants of health

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Substance Use

Fatal and non-fatal opioid overdose among pregnant and postpartum individuals in New Jersey Amanda Dorsey*, Amanda Dorsey, Hillary Samples, Elizabeth Suarez,

Background: Opioid overdose is a key contributor to the high maternal mortality rate in New Jersey (NJ). Yet the burden of fatal and non-fatal opioid overdose during pregnancy and 12 months postpartum in NJ has not been analyzed.

Methods: We used linked NJ resident birth, death, and discharge records from 2011-2020. Live births were included if a birth certificate and corresponding discharge record were identified. Pregnancies ending in non-live births were identified in discharge records. Opioid overdose events were identified with diagnosis codes in death certificates and discharge records. We estimated opioid overdose rates per 100,000 person-days pregnant or up to 12 months postpartum. The maternal mortality ratio was calculated with the number of live births as the denominator.

Results: Among 1,041,787 pregnancies, 848 non-fatal and 76 fatal opioid overdose events occurred in 808 pregnancies. Death certificates added 29 opioid overdose-related deaths during pregnancy. The opioid overdose maternal mortality ratio was 11.3 per 100,000 live births. Pregnancies with, versus without, an opioid overdose event were more likely to be among younger (12-24 years: 28.7 v. 18.6%), White (76.2 v. 62.1%), and publicly insured (39.1 v. 21.4%) individuals. The opioid overdose event rate was 0.15 (95% CI: 0.14, 0.16) per 100,000 pregnant or postpartum days and peaked during months 7-12 postpartum (0.21; 95% CI: 0.19-0.23). Postpartum overdose rates were higher following non-live birth outcomes: 0.77 (95% CI: 0.41-1.32) for stillbirths, 0.52 (95% CI: 0.44-0.60) for spontaneous abortions, and 0.53 (95% CI: 0.35-0.77) for terminations compared to 0.15 (95% CI: 0.14-0.16) for live births.

Conclusion: Opioid overdose remains a concern in NJ, particularly during late postpartum and following a non-live birth outcome.

Substance Use

Prenatal Substance Exposure and Neonatal Abstinence Syndrome in 4 Sites, 2020-2022

Mbabazi Kariisa*, Michaila Czarnik, Laura Pabst, Mbabazi Kariisa, James Small, Deborah Hinds, Sarah Powell, Janelle Wenstrup, Alyssa Pochkar, Mishka Terplan,

Women could use one or more substances during pregnancy. Yet, limited studies describe the types and combinations of substance exposures among infants with neonatal abstinence syndrome (NAS), including their exposure to medications for opioid use disorder (MOUD), the recommended treatment for opioid use disorder in pregnancy. This analysis describes substance exposure among infants meeting the 2019 CSTE Tier 1 NAS Standardized Surveillance Case Definition (SSCD). This analysis examined surveillance data of mother-infant dyads from four pilot sites; infants born January 2020-December 2022 meeting the SSCD were included. Substance exposure at any time in the prenatal period based on reported maternal history or maternal or infant toxicology testing was analyzed. Unique combinations of substance exposures were calculated. Percentages of cases experiencing single or multiple substance exposure and the most common combinations of substances stratified by MOUD exposure are reported. Of 6,745 cases, 61.3% had any documentation of MOUD. Among cases with MOUD (n=4137), 26.7% (n=1106) only had exposure to MOUD. Among cases with MOUD the most common substances included non-methadone opioids (38.1%), tobacco (35.9%), stimulants (27.5%), and cannabis (26.6%). Among cases without MOUD exposure (n=2465), the most common substance exposures included cannabis (52.9%), non-methadone opioids (49.0%), stimulants (42.6%), and tobacco (27.1%). Opioid, cannabis, and stimulant exposure was more common in the no-MOUD group compared to the MOUD group ($p<0.001$) while tobacco/nicotine was more common in the MOUD group ($p<0.001$). Clinicians and public health practitioners can use these findings to inform delivery of services for women and their infants, such as continued access to MOUD and cessation of other substances during pregnancy and beyond.

Substance Use

Fatal and non-fatal opioid overdose among pregnant and postpartum individuals in New Jersey Amanda Dorsey*, Amanda Dorsey, Hillary Samples, Elizabeth Suarez,

Background: Opioid overdose is a key contributor to the high maternal mortality rate in New Jersey (NJ). Yet the burden of fatal and non-fatal opioid overdose during pregnancy and 12 months postpartum in NJ has not been analyzed.

Methods: We used linked NJ resident birth, death, and discharge records from 2011-2020. Live births were included if a birth certificate and corresponding discharge record were identified. Pregnancies ending in non-live births were identified in discharge records. Opioid overdose events were identified with diagnosis codes in death certificates and discharge records. We estimated opioid overdose rates per 100,000 person-days pregnant or up to 12 months postpartum. The maternal mortality ratio was calculated with the number of live births as the denominator.

Results: Among 1,041,787 pregnancies, 848 non-fatal and 76 fatal opioid overdose events occurred in 808 pregnancies. Death certificates added 29 opioid overdose-related deaths during pregnancy. The opioid overdose maternal mortality ratio was 11.3 per 100,000 live births. Pregnancies with, versus without, an opioid overdose event were more likely to be among younger (12-24 years: 28.7 v. 18.6%), White (76.2 v. 62.1%), and publicly insured (39.1 v. 21.4%) individuals. The opioid overdose event rate was 0.15 (95% CI: 0.14, 0.16) per 100,000 pregnant or postpartum days and peaked during months 7-12 postpartum (0.21; 95% CI: 0.19-0.23). Postpartum overdose rates were higher following non-live birth outcomes: 0.77 (95% CI: 0.41-1.32) for stillbirths, 0.52 (95% CI: 0.44-0.60) for spontaneous abortions, and 0.53 (95% CI: 0.35-0.77) for terminations compared to 0.15 (95% CI: 0.14-0.16) for live births.

Conclusion: Opioid overdose remains a concern in NJ, particularly during late postpartum and following a non-live birth outcome.

Substance Use

Prenatal Substance Exposure and Neonatal Abstinence Syndrome in 4 Sites, 2020-2022

Mbabazi Kariisa*, Michaila Czarnik, Laura Pabst, Mbabazi Kariisa, James Small, Deborah Hinds, Sarah Powell, Janelle Wenstrup, Alyssa Pochkar, Mishka Terplan,

Women could use one or more substances during pregnancy. Yet, limited studies describe the types and combinations of substance exposures among infants with neonatal abstinence syndrome (NAS), including their exposure to medications for opioid use disorder (MOUD), the recommended treatment for opioid use disorder in pregnancy. This analysis describes substance exposure among infants meeting the 2019 CSTE Tier 1 NAS Standardized Surveillance Case Definition (SSCD). This analysis examined surveillance data of mother-infant dyads from four pilot sites; infants born January 2020-December 2022 meeting the SSCD were included. Substance exposure at any time in the prenatal period based on reported maternal history or maternal or infant toxicology testing was analyzed. Unique combinations of substance exposures were calculated. Percentages of cases experiencing single or multiple substance exposure and the most common combinations of substances stratified by MOUD exposure are reported. Of 6,745 cases, 61.3% had any documentation of MOUD. Among cases with MOUD (n=4137), 26.7% (n=1106) only had exposure to MOUD. Among cases with MOUD the most common substances included non-methadone opioids (38.1%), tobacco (35.9%), stimulants (27.5%), and cannabis (26.6%). Among cases without MOUD exposure (n=2465), the most common substance exposures included cannabis (52.9%), non-methadone opioids (49.0%), stimulants (42.6%), and tobacco (27.1%). Opioid, cannabis, and stimulant exposure was more common in the no-MOUD group compared to the MOUD group ($p<0.001$) while tobacco/nicotine was more common in the MOUD group ($p<0.001$). Clinicians and public health practitioners can use these findings to inform delivery of services for women and their infants, such as continued access to MOUD and cessation of other substances during pregnancy and beyond.

Violence or abuse victimization

Integrating Intimate Partner Violence into Maternal Health Research: Measurement and Design Considerations Jessica Williams*, Jessica Williams, Jessica Williams, Gabrielle Grant, Candace Burton, Abigail Hatcher, Natalia Villegas, Karen Sheffield-Abdullah,

Background: Intimate partner violence (IPV) is a significant threat to maternal health. IPV during pregnancy is associated with adverse maternal and perinatal outcomes, including hemorrhage, miscarriage, preterm birth, low birth weight, and intimate partner homicide. Despite its relevance to maternal morbidity and mortality, IPV is inadequately addressed in maternal and perinatal epidemiologic research.

Purpose: To identify key considerations for maternal health researchers incorporating IPV into pregnancy-related research, informed by an NIH-funded educational initiative (R25NR021325).

Methods: We synthesized insights from curriculum development, expert consultation, applied learning activities, our online toolkit (https://sparkipv.org), and participant feedback from four cohorts of maternal health researchers. Content focused on IPV conceptualization, measure selection and scoring, data collection, and ethical and safety considerations.

Results: Four critical considerations emerged: 1) aligning IPV measurement purpose (screening, assessment, or risk identification) with study aims; 2) selecting measures that capture IPV characteristics relevant to pregnancy, including type, timing, and relationship context; 3) choosing scoring approaches that appropriately reflect exposure severity and temporality; and 4) integrating trauma-informed procedures to ensure participant safety, confidentiality, and referral.

Conclusions: Rigorous and ethical incorporation of IPV into maternal and perinatal research is essential for advancing understanding of preventable contributors to maternal morbidity and mortality. Inadequate measurement or scoring may lead to exposure misclassification, biased estimates, and missed opportunities for intervention. This work provides practical guidance to support methodologically sound maternal health research that accounts for IPV as a critical contextual determinant of pregnancy outcomes.

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Women’s/Gynecologic Health

Vitamin D deficiency and the odds of bacterial vaginosis among US women: Results from NHANES 2001-2004 Yinglin Dai*, Yinglin Dai, Nicole Talge, Kristen Upson,

Bacterial Vaginosis (BV), a vaginal microbiome dysbiosis marked by depletion of protective Lactobacillus species and overgrowth of anerobic bacteria, affects about 30% of US premenopausal women. Vitamin D may support a healthy vaginal microbiome through glycogen synthesis used by Lactobacillus species to produce lactic acid, lower vaginal pH, and reduce BV risk. Thus, vitamin D deficiency could plausibly increase BV risk. However, studies among non-pregnant women have yielded discrepant results. We conducted a cross-sectional analysis using data from the National Health and Nutrition Examination Survey cycles 2001-2004. The study population comprised premenopausal, non-pregnant, non-breastfeeding women ages 20-49 years (unweighted N=1380). Serum 25-hydroxyvitamin D (25(OH)D) levels were categorized as <20, 20-30, and ≥30 ng/ml to define deficient, insufficient, and sufficient vitamin D status, respectively. Gram-stained slides of vaginal samples were examined by microscopy and scored using Nugent’s criteria for negative, intermediate, and positive BV. We conducted multinomial logistic regression to estimate the adjusted (aOR) and 95%CIs for the associations between vitamin D status and intermediate and positive BV. The weighted prevalence of intermediate and positive BV was 29% and 28%, respectively. Our data suggested that deficient (vs. sufficient) vitamin D was associated with increased odds of intermediate BV (aOR 1.31, 95%CI: 0.84-2.04) and positive BV (aOR 2.36 95%CI: 1.53-3.64). No association was observed with insufficient vitamin D. To explore the mechanism, we evaluated the outcome of higher vaginal pH (>4.5) using log-binomial regression. Deficient vitamin D was associated with higher vaginal pH (adjusted prevalence ratio 1.42, 95%CI: 1.39-1.45). In this US non-pregnant population, our results suggest that deficient vitamin D status is associated with BV. Further research is warranted in a prospective setting to understand the underlying mechanisms.

Women’s/Gynecologic Health

Trends, Outcomes, and Barriers to Integrating Midwifery into Hospital-Based Maternity Care in Louisiana: A Mixed-Methods Study Protocol Dovile Vilda*, Dovile Vilda, Julia Phillippi, Lillian Funke, Maeve Wallace,

Background: Childbirth in the United States has become increasingly medicalized, including among clinically low-risk pregnancies. Midwifery-led care is associated with fewer obstetric interventions and comparable or improved outcomes for low-risk births, yet midwives remain underrepresented in hospital-based maternity care in Louisiana. Population-based evidence describing trends in midwifery care, differences in maternal and birth outcomes by provider type, and barriers to integration is limited.

Methods: This sequential explanatory mixed-methods study includes two phases. Phase 1 is a retrospective cohort analysis of Louisiana Vital Records birth certificate data from 2012–2024, restricted to in-hospital births. We will examine temporal trends in the proportion of births attended by midwives overall and across sociodemographic and geographic subgroups. Among low-risk singleton, term pregnancies, we will compare maternal characteristics, obstetric intervention patterns, and selected birth outcomes between midwifery-attended and obstetrician-attended births. Outcomes include cesarean delivery, labor induction, epidural use where available, five-minute Apgar score, and birthweight categories. Log-binomial or Poisson regression models with robust variance will estimate adjusted relative risks, controlling for demographic and clinical covariates. Phase 2 consists of semi-structured interviews with midwives, obstetric clinicians, hospital administrators, and health system or policy stakeholders to explore barriers and facilitators to integrating midwifery care into hospital-based maternity care. Qualitative data will be analyzed using thematic analysis.

Conclusions: This study will provide the first statewide assessment of long-term trends in midwifery-attended hospital births and provider-type differences in low-risk pregnancies in Louisiana, complemented by stakeholder perspectives on integration. Findings will inform strategies to expand access to integrated, patient-centered maternity care in the Gulf South.

Women’s/Gynecologic Health

Endometriosis and Risk of Cardiovascular Disease among Women in the Utah Population Database Leslie V. Farland*, Leslie V. Farland, Maggie Fuzak, Bin Yan, Michael W. Varner, Jenna R. Krall, Kathryn Rexrode, Hediyeh Baradaran, Benjamin Brown, Jennifer J. Majersik, Jessica Page, Anna Z. Pollack, Karen C. Schliep,

Introduction: Emerging evidence suggests that women with endometriosis may have an increased risk of cardiovascular disease later in life, yet current research is limited by short follow-up (<10 years), small sample size, and cross-sectional designs. To overcome these limitations, we investigated the association between history of endometriosis and vascular diseases (hypertension, ischemic heart disease, peripheral vascular disease, acute myocardial infarction, atrial fibrillation, heart failure, and stroke) among women in the Utah Population Database (UPDB) between 1996-2021.

Methods: We assembled a cohort of over 2.9 million at-risk women (99,930 with endometriosis) within the UPDB. Endometriosis and vascular disease were identified via electronic health records. We used Cox proportional hazard models adjusted a priori for birth year, birth state, body mass index, race, and ethnicity to estimate hazard ratios (aHRs) and 95% confidence intervals (CIs) for vascular disease endpoints.

Results: With over 35 million person-years of follow-up, we observed that women with a history of endometriosis had increased risk of hypertension (aHR:1.42, 95% CI: 1.40-1.44), peripheral vascular disease (aHR:1.16, 95% CI:1.09-1.24), ischemic heart disease (aHR:1.13, 95% CI:1.09-1.17), and stroke (aHR:1.06, 95% CI:1.01-1.11) compared to women without a history of endometriosis in both age-adjusted and fully-adjusted models. However, we observed associations with atrial fibrillation (HR:1.16, 95% CI: 1.11-1.21), acute myocardial infarction (HR:1.07, 95%CI:1.00-1.14), and heart failure (HR:1.05, 95%CI: 1.01-1.10) in age-adjusted models, which attenuated and were no longer statistically significant in fully-adjusted models.

Conclusion: These results contribute to the growing evidence that endometriosis may contribute to increased risk of vascular disease; additional research is needed to understand the mechanisms of association and modifiable lifestyle factors for women with endometriosis.

Women’s/Gynecologic Health

Patterns of depot medroxyprogesterone acetate (DMPA) injectable contraceptive use and predictors of discontinuation in young Ugandan women ages 16-25 years Kristen Upson*, Kristen Upson, Juhee Lee, Renee Heffron, Andrew Mujugira, Flavia Matovu, Kenneth Mugwanya, Michael Yin, Chenxi Li, Robert Wright, Julio Landero, Quaker Harmon,

The injectable contraceptive depot medroxyprogesterone acetate (DMPA) is the leading hormonal contraceptive in Uganda. Yet, data on DMPA use patterns and predictors of discontinuation in Ugandan adolescent and young women are sparse. Thus, we used data from the Kampala Women’s Bone Study, a cohort of 499 young Ugandans ages 16-25 initiating DMPA or condom use. Participants were enrolled in years 2018-2020 and followed for 2 years with quarterly study visits. Among 268 DMPA initiators, we estimated the probability of DMPA continuation using Kaplan-Meier survival curves. We conducted Cox proportional hazard regression to estimate the adjusted hazard ratios (HR) and 95% CIs for associations between predictors and time to DMPA discontinuation. Predictors included baseline age, education, and travel time to study clinic and time varying factors of COVID-19 lockdown, vaginal sex frequency, menstrual bleeding, weight change (from baseline), and DMPA type (IM or SQ). Probability of DMPA continuation at 3-, 6-, 12-, and 24-months were 63%, 39%, 15%, and 2%, respectively. However, among those who discontinued, 32% restarted DMPA use. Factors associated with increased DMPA discontinuation risk included being age 20 (vs. age 19; HR 1.5, 95%CI: 1.0-2.3), COVID-19 lockdown (HR 2.9 95%CI: 1.9-4.2) and no vaginal sex in past 3 months (vs. 13-35 times; HR 1.6, 95%CI: 0.9-3.0). In contrast, vaginal sex >45 times in past 3 months was associated with decreased DMPA discontinuation risk (HR 0.7, 95%CI: 0.5-1.1) as well as having ≤7 years of education (vs. 12-16 years; HR 0.7, 95%CI:0.5-1.1), no menstrual bleeding (vs. regular bleeding; HR 0.6, 95%CI: 0.4-0.9) and only spotting (HR 0.4, 95%CI: 0.2-0.9). No associations were observed with travel time, weight change, or DMPA type. To our knowledge, this is the first study of DMPA use patterns and predictors of discontinuation in adolescent and young Ugandan women. Our results can inform efforts to reduce unintended pregnancy.

Women’s/Gynecologic Health

Declining contraception use among adolescents and young adults: a population-based cohort study Laura Schummers*, Laura Schummers, Wendy V Norman, Lucy Cheng, Andrea Stucchi, Sarah Munro, Elizabeth Nethery, Erin Brennand, Amy Metcalfe, Kim McGrail, Nathan Nickel, Fiona Clement, Michael R Law,

Introduction: Contraception access is essential to prevent unintended pregnancy. The sociopolitical climate surrounding contraception use is rapidly evolving, especially among adolescents and young adults. This population-based cohort study examined age-stratified contraception use trends from 2021-2024 and age-specific effects of a policy providing universal, no-cost contraception coverage on contraception use.

Methods: In population-based linked administrative data from British Columbia, Canada, we examined trends in the monthly proportion of the population using contraception by age stratum: <20, 20-29, 30-39, ≥40). Age-stratified interrupted time series analyses examined effects of universal coverage on contraception use.

Results: In January 2021, 18.2% of the cohort (n=1,162,018, age 15-49y) used prescription contraception, declining to 16.6% by December 2024. Adolescents (15-19y) and young adults (20-29y) were the most frequent contraception users, yet showed the steepest declines in use. The introduction of universal contraception coverage was associated with small immediate increases in contraception use for all age groups and attenuated declining trends among 15-29-year-olds. By 21-months post-policy, an additional 3.8% of 15-19-year-olds were using contraception than expected (12.9 expected vs. 16.7% observed; risk ratio (RR) 1.3 [95% CI 1.3-1.4]), while an additional 3.6% of 20-29-year-olds (18.4% expected vs. 22.2% observed; RR 1.2 [1.2-1.2]), 30-39-year-olds (15.7% vs 16.5%; RR 1.1 [1.0-1.1]) and 0.6% of 40-49-year-olds (11.5% vs 12.0%) were using contraception (RR 1.1 [1.0-1.1]).

Discussion: Contraception use was declining in this population-based cohort, driven by 15-29-year-olds. Universal contraception coverage increased contraception use for those under age 30, which offset declining pre-policy trends. We found that eliminating contraception cost contributes to, but is not sufficient, support contraception use for those younger than age 30.

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Birth defects

Association between pre-pregnancy physical activity and risk of congenital heart defects
Kaitlyn Long*, Kaitlyn Long, Kelly Evenson, John Cotton, Sanjida Mowla, Andrew Olshan, Gary Shaw, Tania Desrosiers,

Background: Though prenatal physical activity and reduced sitting time are associated with improved pregnancy outcomes, the relationship with birth defects is unclear. We examined whether pre-pregnancy physical activity/sitting is associated with congenital heart defects (CHDs).

Methods: We used data from two United States population-based, case-control studies: 2008-11 deliveries from the National Birth Defects Prevention Study (9 centers) and 2014-21 deliveries from the Birth Defects Study To Evaluate Pregnancy exposureS (7 centers). Case infants, stillbirths, and terminated pregnancies (n=1,553) diagnosed with one of 10 CHDs were identified through population-based registries. Control infants (n=3,461) without a major birth defect were randomly sampled using vital/hospital records. Mothers reported the type and duration of physical activity and sitting time in the three months before conception during telephone interviews after delivery. We used logistic regression to estimate associations between each type of CHD and five physical activity measures, time spent sitting, and a physical activity/sitting time index.

Results: Mothers reporting more moderate activity (tertile 3 [T3] vs. T1) and more total activity (T2/T3 vs. T1) had a lower odds of delivering an infant with total anomalous pulmonary vein return (TAPVR) and dextro-transposition of the great arteries. Mothers reporting more walking (T2/T3 vs. T1) and total activity (T3 vs. T1) had a higher odds of delivering an infant with aortic stenosis or hypoplastic left heart syndrome. Mothers reporting more sitting time (T2 vs T1) had a higher odds of delivering an infant with TAPVR.

Conclusion: Physical activity/sitting are potentially associated with some CHDs. The next steps include replication of these findings. Future studies may incorporate device-measured exposures and distinguish occupational from leisure-time physical activity.

Birth defects

Maternal race and ethnicity and the risk of preterm birth among infants with major structural birth defects in the National Birth Defects Prevention Study and Birth Defects Study To Evaluate Pregnancy exposureS Katherine L. Ludorf*, Katherine L. Ludorf, Renata H. Benjamin, Peichun Han, Rachel P. Allred, Jenil R. Patel, Wendy N. Nembhard, Gary M. Shaw, Suzan L. Carmichael, Tania A. Desrosiers, Eirini Nestoridi, Eva M. Williford, Michael D. Swartz, Zeynep Coban Akdemir, Courtney Byrd-Williams, A.J. Agopian, The National Birth Defects Prevention Study , The Birth Defects Study to Evaluate Pregnancy Exposures ,

Background: Preterm birth (PTB) affects 1 in 10 U.S. infants, is >50% more frequent among non-Hispanic Black (NHB) women, and is a major contributor to morbidity and mortality. These risks are increased among infants with, compared to without, structural birth defects. Although racial and ethnic differences in PTB risk are well-documented in the general population, associations between race and ethnicity and PTB among infants with birth defects are not.

Methods: We analyzed liveborn infants with major structural birth defects and gestational ages 24–44 weeks from two national, population-based studies: the National Birth Defects Prevention Study (1997–2011) and the Birth Defects Study to Evaluate Pregnancy exposureS (2014–2021). PTB (<37 weeks) was examined overall and by early (<32 weeks) and moderate (32–36 weeks) PTB. Poisson regression models with robust errors were computed across 37 birth defect categories to estimate unadjusted risk ratios (RRs) and adjusted risk ratios (aRRs) for PTB and maternal race and ethnicity, categorized as non-Hispanic White (NHW; reference group), NHB, and Hispanic. Other maternal race and ethnicity categories were not considered due to small counts.

Results: Among 31,898 infants with birth defects, 24.1% were born preterm. As expected, PTB prevalence was highest among infants of NHB mothers (33.0%), followed by Hispanic (24.6%) and NHW mothers (22.3%). Compared with infants of NHW mothers, PTB risk was elevated (RR >1.5) for infants of NHB mothers in 14/37 defect groups and for infants of Hispanic mothers in 3/37 groups. Associations for birth defect groups were also observed following adjustment for covariates (maternal age at delivery, education level, pre-pregnancy body mass index, alcohol consumption, smoking, and previous live births). For example, among infants with Tetralogy of Fallot, PTB risk remained elevated for NHB (RR 1.34 to aRR 1.25) and Hispanic mothers (RR 1.40 to aRR 1.31). Associations were generally stronger for early PTB than for moderate PTB.

Conclusion: In this large, multi-state study, infants with several types of birth defects born to NHB mothers, and to a lesser degree Hispanic mothers, were at elevated risk of PTB. These findings highlight maternal race and ethnicity groups as important factors to better understand PTB risk among this population.

Birth defects

Maternal Dietary Intakes and Gastroschisis in Offspring Julie Petersen*, Julie Petersen, Yiqun Jiang, Rashida Smith-Webb, Kathleen Angell, Deepanjali Bhale, Muskan Ahuja, Corrine Hanson, Martha Werler,

Gastroschisis is a serious congenital abdominal wall defect in which the intestines herniate outside the body. While young maternal age is a strong risk factor, few modifiable factors are known. We examined associations between maternal dietary intake and gastroschisis using the Slone Birth Defects Study, a North American case–control design (1998–2015). Cases included 273 pregnancies affected by isolated gastroschisis. Controls were 2,591 live borns without major anomalies, frequency-matched by center. Mothers completed standardized interviews within 6 months postpartum. Diet for the 6 months before pregnancy (proxy for early prenatal intake) was assessed with a modified Willett food frequency questionnaire. Quartiles for 28 macro- and micronutrients were derived based on the control distribution and energy-adjusted using the residual method. Gastroschisis associations with each nutrient were estimated using LASSO logistic regression, adjusting for age, race, education, income, parental relationship status, BMI, pregnancy intention, smoking, alcohol consumption, oral contraceptive use, nonsteroidal anti-inflammatory drug use, folic acid supplementation, parity, and the other nutrients. Nutrients were identified as relevant based on adjusted odds ratios (aORs), permutation-based changes in AUC, and Shapley values. Compared with the lowest quartile, moderate glutamic acid (aOR 0.57, 95% CI 0.34–0.97), vitamin E (0.72, 0.49–1.0), and polyunsaturated fat (0.80, 0.53–1.0), and high magnesium (0.60, 0.33–1.0) and calcium (0.76, 0.47–1.0), were associated with reduced odds of gastroschisis. Higher cryptoxanthin intake was associated with increased odds (1.29, 1.0–1.9). These results suggest a potential nutritional mechanism. While most nutrients showed protective benefits, finding high cryptoxanthin (in yellow/orange fruits/vegetables) was associated with increased odds was surprising. Replication and clarification of clinically relevant intake thresholds are needed.

Birth defects

Association between Environmental Quality Index and Congenital Heart Defects in Arkansas Jenil Patel*, Lydia Famuyide, Jenil Patel, Wendy Nembhard,

Introduction: Congenital heart defects (CHDs) occur in 1% of live births in the United States (US) and are the leading cause of death from birth defects. While prior studies have largely focused on isolated environmental exposures, fewer have examined the cumulative influence of multiple environmental domains. This study evaluated whether county-level cumulative environmental quality is associated with the prevalence of CHDs in Arkansas.

Methods: We conducted a retrospective cohort study using births occurring from 2006-2010, linking CHD cases identified through the Arkansas Reproductive Health Monitoring System to county-level Environmental Quality Index (EQI) measures. The overall EQI and five domain-specific indices (air, water, land, sociodemographic, and built environment) were categorized into quartiles. Crude and adjusted prevalence ratios (PR) and 95% Cis were estimated using Poisson regression with cluster-robust standard errors, adjusting for maternal age, smoking during pregnancy, race/ethnicity, rural-urban continuum codes, and maternal education.

Results: Overall environmental quality was not significant associated with CHD prevalence after adjustment (Adjusted PR: 0.85; 95% CI: 0.71, 1.01). No significant associations were observed for the air, land, water, built and sociodemographic domains in the adjusted models. In crude analyses, worse land domain environmental quality was associated with a lower prevalence of CHDs (Crude PR: 0.81; 95% CI: 0.68, 0.97), though this association was attenuated after adjustment.

Conclusion: County-level cumulative environmental quality, as measured by the EQI, was not independently associated with overall CHD prevalence in Arkansas after appropriate adjustment for key maternal and contextual factors. Ongoing analyses will examine associations between EQI domains and specific CHD phenotypes, which may be differentially sensitive to environmental conditions and could be obscured in analyses of CHDs as a heterogenous group.

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Birth defects

Maternal race and ethnicity and the risk of preterm birth among infants with major structural birth defects in the National Birth Defects Prevention Study and Birth Defects Study To Evaluate Pregnancy exposureS Katherine L. Ludorf*, Katherine L. Ludorf, Renata H. Benjamin, Peichun Han, Rachel P. Allred, Jenil R. Patel, Wendy N. Nembhard, Gary M. Shaw, Suzan L. Carmichael, Tania A. Desrosiers, Eirini Nestoridi, Eva M. Williford, Michael D. Swartz, Zeynep Coban Akdemir, Courtney Byrd-Williams, A.J. Agopian, The National Birth Defects Prevention Study , The Birth Defects Study to Evaluate Pregnancy Exposures ,

Background: Preterm birth (PTB) affects 1 in 10 U.S. infants, is >50% more frequent among non-Hispanic Black (NHB) women, and is a major contributor to morbidity and mortality. These risks are increased among infants with, compared to without, structural birth defects. Although racial and ethnic differences in PTB risk are well-documented in the general population, associations between race and ethnicity and PTB among infants with birth defects are not.

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Conclusion: In this large, multi-state study, infants with several types of birth defects born to NHB mothers, and to a lesser degree Hispanic mothers, were at elevated risk of PTB. These findings highlight maternal race and ethnicity groups as important factors to better understand PTB risk among this population.

Birth defects

Association between pre-pregnancy physical activity and risk of congenital heart defects
Kaitlyn Long*, Kaitlyn Long, Kelly Evenson, John Cotton, Sanjida Mowla, Andrew Olshan, Gary Shaw, Tania Desrosiers,

Background: Though prenatal physical activity and reduced sitting time are associated with improved pregnancy outcomes, the relationship with birth defects is unclear. We examined whether pre-pregnancy physical activity/sitting is associated with congenital heart defects (CHDs).

Methods: We used data from two United States population-based, case-control studies: 2008-11 deliveries from the National Birth Defects Prevention Study (9 centers) and 2014-21 deliveries from the Birth Defects Study To Evaluate Pregnancy exposureS (7 centers). Case infants, stillbirths, and terminated pregnancies (n=1,553) diagnosed with one of 10 CHDs were identified through population-based registries. Control infants (n=3,461) without a major birth defect were randomly sampled using vital/hospital records. Mothers reported the type and duration of physical activity and sitting time in the three months before conception during telephone interviews after delivery. We used logistic regression to estimate associations between each type of CHD and five physical activity measures, time spent sitting, and a physical activity/sitting time index.

Results: Mothers reporting more moderate activity (tertile 3 [T3] vs. T1) and more total activity (T2/T3 vs. T1) had a lower odds of delivering an infant with total anomalous pulmonary vein return (TAPVR) and dextro-transposition of the great arteries. Mothers reporting more walking (T2/T3 vs. T1) and total activity (T3 vs. T1) had a higher odds of delivering an infant with aortic stenosis or hypoplastic left heart syndrome. Mothers reporting more sitting time (T2 vs T1) had a higher odds of delivering an infant with TAPVR.

Conclusion: Physical activity/sitting are potentially associated with some CHDs. The next steps include replication of these findings. Future studies may incorporate device-measured exposures and distinguish occupational from leisure-time physical activity.

Birth defects

Maternal Dietary Intakes and Gastroschisis in Offspring Julie Petersen*, Julie Petersen, Yiqun Jiang, Rashida Smith-Webb, Kathleen Angell, Deepanjali Bhale, Muskan Ahuja, Corrine Hanson, Martha Werler,

Gastroschisis is a serious congenital abdominal wall defect in which the intestines herniate outside the body. While young maternal age is a strong risk factor, few modifiable factors are known. We examined associations between maternal dietary intake and gastroschisis using the Slone Birth Defects Study, a North American case–control design (1998–2015). Cases included 273 pregnancies affected by isolated gastroschisis. Controls were 2,591 live borns without major anomalies, frequency-matched by center. Mothers completed standardized interviews within 6 months postpartum. Diet for the 6 months before pregnancy (proxy for early prenatal intake) was assessed with a modified Willett food frequency questionnaire. Quartiles for 28 macro- and micronutrients were derived based on the control distribution and energy-adjusted using the residual method. Gastroschisis associations with each nutrient were estimated using LASSO logistic regression, adjusting for age, race, education, income, parental relationship status, BMI, pregnancy intention, smoking, alcohol consumption, oral contraceptive use, nonsteroidal anti-inflammatory drug use, folic acid supplementation, parity, and the other nutrients. Nutrients were identified as relevant based on adjusted odds ratios (aORs), permutation-based changes in AUC, and Shapley values. Compared with the lowest quartile, moderate glutamic acid (aOR 0.57, 95% CI 0.34–0.97), vitamin E (0.72, 0.49–1.0), and polyunsaturated fat (0.80, 0.53–1.0), and high magnesium (0.60, 0.33–1.0) and calcium (0.76, 0.47–1.0), were associated with reduced odds of gastroschisis. Higher cryptoxanthin intake was associated with increased odds (1.29, 1.0–1.9). These results suggest a potential nutritional mechanism. While most nutrients showed protective benefits, finding high cryptoxanthin (in yellow/orange fruits/vegetables) was associated with increased odds was surprising. Replication and clarification of clinically relevant intake thresholds are needed.

Child health and development

Perinatal exposure to meteorological-air pollutant mixture and autism spectrum disorders

Wanyu Huang*, Wanyu Huang, Krista Huybrechts, Sonia Hernandez-Diaz, Matthew Shupler, Xinye Qiu, Michael Leung, Hayon Michelle Choi, Yaguang Wei, Joel Schwartz, Brent Coull, Christopher McDougle, Antonella Zanobetti, Marc Weisskopf, Stefania Papatheodorou,

Objective: The prenatal period is critical for brain formation and neurodevelopment. Prenatal exposures to, for example, PM2.5 and extreme weather may increase the risk of neurodevelopmental disorders. Yet few studies have examined the joint effect of air pollutants and meteorological factors with autism spectrum disorder (ASD) in children.

Methods: Daily levels of temperature, relative humidity and fine particulate matter (PM2.5) from spatiotemporal models were linked to a longitudinal cohort of mothers/infants from the Medicaid Analytic eXtract (MAX) database. ASD was identified based on ICD-9/10 codes and modeled as a time-to-event outcome. Weekly levels of each exposure were assigned based on residential zip codes for mothers, then averaged into levels during each trimester. Quantile g-computation models were applied to assess the joint effects of the mixture, adjusting for maternal age, race/ethnicity, socioeconomic factors (area-level), as well as season of delivery.

Results: We included a total of 1,543,129 term births from 2001 to 2013; and observed a cumulative hazard ratio (HR) of 1.05 (95% CI: 0.95 – 1.15) for the mixture per interquartile range (IQR) increase in exposure. Of the factors that were associated with increased ASD, third-trimester PM2.5 contributed the largest share of the positive effect (42%), followed by first- and second trimester relative humidity. Some factors (e.g., 3rd trimester temperature) had an inverse association with ASD (**Fig. 1**).

Conclusion: PM2.5, especially during the third trimester, contributed the most to the increased risk of ASD, with relative humidity in the 1st and 2nd trimesters also contributing to the association. Continuing to mitigate ambient PM2.5 levels is important in potentially alleviating childhood ASD risk among the socioeconomically disadvantaged US population.

Child health and development

Childhood hearing difficulty and injury DaShaunda Taylor*, DaShaunda Taylor, MyNgoc Nguyen,

Background: Hearing loss is a common disability in children with implications for social, emotional, and educational milestones. The American Academy of Pediatrics (AAP) has provided recommendations for hearing screening throughout childhood to improve overall health. Although pediatric hearing loss has been linked to educational, social, and developmental outcomes, less is known about its relationship with unintentional injury risk in children. One possible consequence may be physical injury, as hearing difficulty can limit a child's ability to effectively respond to auditory warning cues and detect environmental hazards. **Objectives:** This study sought to determine the prevalence of parent or guardian-reported hearing difficulty and injury in children and whether there was an association between hearing difficulty and injury, after accounting for demographic characteristics in a nationally-representative sample of children. **Methods:** Data from the 2020-2021 and 2023-2024 National Health Interview Survey (NHIS) were utilized to assess the relationship between hearing difficulty and injury in children. Chi-squared analyses and multivariable logistic regression of the weighted sample were conducted. **Results:** Among 26,610 children, the prevalence of injury in the past three months was 9.16%, and 2.24% had difficulty hearing sounds. Children with difficulty hearing had significantly higher odds of injury versus those with no difficulty hearing (odds ratio [OR] = 1.63, 95% confidence interval [95% CI]: 1.23-2.16). This association persisted after adjusting for age, sex, race/ethnicity, and health insurance status (OR=1.61, 95% CI: 1.22-2.13). **Conclusions:** This study indicates that hearing loss may be an important factor to consider when evaluating a child's potential injury risk. These results highlight the need for further research to determine whether adherence to AAP pediatric hearing screening recommendations may be associated with improved child safety outcomes.

Child health and development

Maternal Residential Exposure to Agricultural Neonicotinoid Insecticides and Risk of Cerebral Palsy in California Yunyue Shi*, Yunyue Shi, Haoran Zhuo, Alan Cao, Myles Cockburn, Beate Ritz, Zeyan Liew,

Background: Neonicotinoids (NEOs) are insecticides increasingly used that target the central nervous systems of insects and cause paralysis. Developmental neurotoxicity from NEOs exposure has been suggested in human studies, but it has not been studied whether they are associated with cerebral palsy (CP), the most common neuromotor disorder in childhood.

Methods: We conducted a nested case-cohort study in California that included 4,958 cases ascertained from the Department of Developmental Services, and 925,683 controls selected at random from California live births during 2007–2015. We geocoded maternal residential addresses at delivery and estimated ambient pesticide exposure to five most common NEOs applied during pregnancy (within a 500 m buffer) using an advanced geographic information system model that combines the California Pesticide Use Reporting (PUR) and land use data. We estimated the odds ratio (OR) and 95% confidence interval (CI) for CP according to prenatal exposure to any or each of five NEOs, adjusting for confounding factors. We also restricted analyses to mothers who lived in proximity (within 500 m) to any agricultural pesticide applications recorded in the PUR to rule out confounding from other exposures associated with home location.

Results: Approximately 11.2% of live births in California were exposed to any NEOs during pregnancy, increasing from 9.5% in 2007 to 14.1% in 2015. Maternal residential exposure to any NEOs during pregnancy was associated with CP (OR=1.11, 95% CI: 0.98, 1.26), with a 29–33% increase in the odds for CP observed for dinotefuran (OR=1.33, 95% CI: 1.12, 1.58) and thiamethoxam (OR=1.29, 95% CI: 1.06, 1.57). The results remained robust in the restricted study population of mothers who lived in proximity (within 500 m) to agricultural pesticide applications in California.

Conclusion: Maternal residential exposure to certain agricultural NEOs, including dinotefuran and thiamethoxam, was associated with an increased risk of CP. Future studies examining the biological mechanisms by which NEO exposure may affect CP etiology are warranted to inform causality.

Child health and development

Developmental Heterogeneity in Infant Brain Development Associated with Prenatal and Early Life Lead Exposure Da-Yea Song*, Da-Yea Song, Rui Chen, Jason Feinberg, Ashley Song, Christine Austin, Paul Curtin, Stephen Dager, Annette Estes, Alan Evans, Daniele Fallin, Jessica Girault, Heather Hazlett, Mauro Martinez, Natasha Marrus, Juhi Pandey, Robert Schultz, Young Truong, Joseph Piven, Manish Arora, Heather Volk,

Background: Lead is a neurotoxicant with wide-ranging effects on brain development. However, less is understood about how prenatal and early-life lead exposure relate to both the trajectory and variability of structural brain development. The aim of this study was to examine associations between early-life lead exposure and longitudinal measures of brain development.

Methods: Data were drawn from the Infant Brain Imaging Study. Prenatal and postnatal lead exposure were each quantified using laser ablation-inductively coupled plasma mass spectrometry of shed deciduous teeth. Structural brain measures, including total brain volume (TV), surface area (SA), and cortical thickness (CT), were derived from T1-weighted MRI scans acquired at 6, 12, and 24 months of age. Linear mixed-effects models evaluated associations between lead exposure and mean brain measures. Developmental heterogeneity was assessed by modeling squared residuals from subject-specific mean estimates using generalized linear models as a function of lead exposure and visit.

Results: A total of 142 infants at high or low familial likelihood for autism, none of whom met autism diagnostic criteria, were included in the analysis. Higher prenatal lead exposure was associated with lower SA (=-39,280, t=-2.23), whereas no associations were observed with mean TV or CT. Associations between lead exposure and SA variability were modest (prenatal lead: p=0.055; postnatal lead: p=0.044), and no associations were observed for TV variability. In contrast, prenatal and postnatal lead exposure showed strong associations with CT variability. Higher lead exposure was associated with reduced variability at baseline (prenatal lead: p<0.001; postnatal lead: p=0.013), but significant lead-by-visit interactions showed greater variability at 24 months (prenatal lead: p=0.002; postnatal lead: p=0.012).

Conclusion: Prenatal and early infancy are critical windows for the impact of lead exposure on structural brain development.

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Environment/climate change

Wildfire Smoke Exposure Increases Risk for Gestational Hypertension Samantha Piekos*, Samantha Piekos, Qi Wei, Michael Strasser, Jennifer Hadlock,

Wildfire smoke exposure is a growing environmental threat during pregnancy, yet its effects remain poorly characterized. In a retrospective cohort study, we examined associations between wildfire smoke exposure and pregnancy complications among 287,612 singleton deliveries (2015–2020) across five western US states (CA, ID, MT, OR, and WA) through partnership with Providence St. Joseph Health. Daily wildfire-attributable $PM_{2.5}$ exposure was estimated using the Childs et al. (2020) model mapped to residential census tracts. Overall, 194,918 (67.8%) pregnancies experienced smoke exposure, with higher exposure among rural residents, middle socioeconomic and second-lowest area deprivation quintiles, younger individuals, those conceiving in the first half of the year, and non-Hispanic Native American, Pacific Islander, or White populations (all $p<0.0001$ except Pacific Islander, $p<0.05$).

Primary outcomes were gestational hypertension, preeclampsia, and preterm birth. We identified 21 confounding variables by taking a union of features in directed acyclic graphs for each primary outcome and top 10 most important features for an XGBoost classifier for smoke exposure during pregnancy (PR-AUC=0.998). We adjusted for these using propensity score matching. We identified gestational week susceptibility windows by comparing exposure levels between cases and controls. There was an increased risk of gestational hypertension during two periods: gestational weeks 3-7 (aOR=1.09, 95% CI: 1.03–1.15, $p<0.01$) and weeks 22-25 (aOR=1.07, 95% CI: 1.01–1.13, $p<0.05$). There was no difference in rates of preeclampsia or preterm birth in people exposed to smoke during these periods of pregnancy.

These findings demonstrate that smoke exposure during early first trimester or late second trimester elevates the risk for gestational hypertension. Understanding this temporal vulnerability is essential for developing targeted public health interventions and mitigation strategies to protect pregnant people in wildfire-prone regions.

Environment/climate change

Prenatal exposure to wildfire smoke and neurodevelopmental delays in children among Medicaid recipients: a national cohort study Stefania Papatheodorou*, Stefania Papatheodorou, Hayon Michele Choi, Krista Huybrechts, Yang Liu, Danlu Zhang, Xinye Qiu, Sonia Hernandez-Diaz, Wanyu Huang, Matthew Shupler, Michael Leung, Brent Coull, Yaguang Wei, Joel Schwartz, Marc Weisskopf, Antonella Zanobetti,

Objective: Wildfires pose a threat to human health. Although past studies have shown that wildfire smoke (WFS) exposure may be associated with adverse birth outcomes, its association with children ‘s neurodevelopment has been understudied. We examined the association between prenatal WFS exposure and neurodevelopmental outcomes in a national birth cohort of Medicaid enrollees from 2007 to 2014.

Methods: We assigned WFS pregnancy average concentrations from a daily spatiotemporal model at the residential zip code of mother-infant pairs in a longitudinal cohort from the Medicaid Analytic eXtract (MAX) dataset from 2007 to 2014. Identification of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) were based on ICD-9 codes and validated algorithms. We applied stratified Cox models (by year and county), adjusting for non-wildfire PM2.5, temperature, relative humidity, maternal age, race/ethnicity, behavioral risk factors (e.g., smoking, alcohol, drug use), and socioeconomic status (area-level). We examined effect modification by sex.

Results: We included 1,010,197 births from 2007 to 2014. The overall R2 of the WFS model was 0.75, and the pregnancy average wildfire PM2.5 ranged from 0 to 19 µg/m3. A 1-µg/m3 increase in prenatal exposure to WFS was associated with an increased risk of ASD (Overall HR:1.07, 95% CI: 1.01, 1.15, Males: HR:1.05, 95% CI: 1.00, 1.08, Females: HR:1.12, 95% CI: 1.03, 1.26) and ADHD (Overall: HR:1.13, 95% CI: 1.09, 1.17, Males: HR:1.11, 95% CI: 1.07, 1.15, Females: HR:1.18, 95% CI: 1.13, 1.23).

Conclusion: Our findings suggest that prenatal exposure to wildfire smoke is associated with an increased risk of ASD and ADHD among children. If causal, these results highlight the need for targeted public health interventions and policies to protect pregnant women and young children from wildfire-related air pollution. Further research is needed to explore the underlying biological mechanisms of sex differences and their long-term impacts, as well as the sensitive windows of exposure.

Environment/climate change

Wildfire Smoke Exposure Increases Risk for Gestational Hypertension Samantha Piekos*, Samantha Piekos, Qi Wei, Michael Strasser, Jennifer Hadlock,

Wildfire smoke exposure is a growing environmental threat during pregnancy, yet its effects remain poorly characterized. In a retrospective cohort study, we examined associations between wildfire smoke exposure and pregnancy complications among 287,612 singleton deliveries (2015–2020) across five western US states (CA, ID, MT, OR, and WA) through partnership with Providence St. Joseph Health. Daily wildfire-attributable $PM_{2.5}$ exposure was estimated using the Childs et al. (2020) model mapped to residential census tracts. Overall, 194,918 (67.8%) pregnancies experienced smoke exposure, with higher exposure among rural residents, middle socioeconomic and second-lowest area deprivation quintiles, younger individuals, those conceiving in the first half of the year, and non-Hispanic Native American, Pacific Islander, or White populations (all $p<0.0001$ except Pacific Islander, $p<0.05$).

Primary outcomes were gestational hypertension, preeclampsia, and preterm birth. We identified 21 confounding variables by taking a union of features in directed acyclic graphs for each primary outcome and top 10 most important features for an XGBoost classifier for smoke exposure during pregnancy (PR-AUC=0.998). We adjusted for these using propensity score matching. We identified gestational week susceptibility windows by comparing exposure levels between cases and controls. There was an increased risk of gestational hypertension during two periods: gestational weeks 3-7 (aOR=1.09, 95% CI: 1.03–1.15, $p<0.01$) and weeks 22-25 (aOR=1.07, 95% CI: 1.01–1.13, $p<0.05$). There was no difference in rates of preeclampsia or preterm birth in people exposed to smoke during these periods of pregnancy.

These findings demonstrate that smoke exposure during early first trimester or late second trimester elevates the risk for gestational hypertension. Understanding this temporal vulnerability is essential for developing targeted public health interventions and mitigation strategies to protect pregnant people in wildfire-prone regions.

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Environment/climate change

Exploring Oxylipins as Metabolic Mediators in Pathway Linking Prenatal Per- and Poly-Fluoroalkyl Substances (PFAS) and Prenatal Depression in the Maternal and Developmental Risks from Environmental and Social Stressors (MADRES) Cohort *, Himal Suthar, Helen Foley, Tingyu Yang, Sandrah Eckel, Rima Habre, Shohreh Farzan, Xinci Chen, Subramaniam Pennathur, Lixia Zeng, Stephanie Eick, Jesse Goodrich, Andrea Aguiar, Carrie Breton, Theresa Bastain, Max Aung,

Up to 20% of individuals in the US experience depression during pregnancy. Growing evidence links prenatal exposure to per- and polyfluoroalkyl substances (PFAS), persistent organic pollutants ubiquitous in the environment, to prenatal depression. Oxylipins are endogenous metabolites with myriad functions including inflammation and oxidative stress – processes implicated with prenatal depression and PFAS exposure. In this analysis, we sought to uncover shared oxylipin signatures associated with PFAS exposure and prenatal depression in 100 pregnant individuals in the Maternal and Developmental Risks from Environmental and Social Stressors (MADRES) cohort. We measured fourteen serum PFAS, of which four were highly-detected (detection rate ≥70%) and included in analysis (PFHxS, PFNA, PFOA, PFOS; median gestational age (GA) 19 weeks), a panel of 45 plasma oxylipins and five parent compounds (median GA 31 weeks), and clinically-relevant third trimester depressive symptoms (scores ≥ 16) using the Center for Epidemiological Studies Depression Scale. Using pairwise regressions, we quantified associations between PFAS congeners and plasma oxylipins, and prenatal depression, respectively; and plasma oxylipins and prenatal depression, adjusting for age, pre-pregnancy BMI, education, GA at visit, and parity. We found one significant association between PFHxS and prenatal depression, 41 between PFAS and oxylipin levels, and 12 between oxylipin levels and prenatal depression. A doubling in PFHxS was associated with increased odds of prenatal depression (Odds Ratio (OR) = 3.3, 95% CI: 1.1, 9.7), and decreased log arachidonic acid (AA; -40.0%, 95% CI: -51.6, -25.6%) and increased 20-carboxy arachidonic acid (CAA; 17.0%, 95% CI: 4.3, 31.1%) levels. Prenatal depression was associated with a 1-SD increase in CAA (OR = 2.4, 95% CI: 1.2, 4.5) and AA (OR = 0.5, 95% CI: 0.2, 0.9). Findings suggest CAA and AA as potential mechanistic links between PFAS exposure and prenatal depression.

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Fertility and fecundity

Endometriosis Typology and Infertility Rachel Myrer*, Rachel Myrer, Bin Yang, Joseph Stanford, Christy Porucznik, Leslie Farland, Anna Pollack, C. Matthew Peterson, Karen Schliep,

Background: Endometriosis affects approximately 11% of women of reproductive age and is a significant cause of female factor infertility. Current classification systems inadequately predict infertility diagnoses, highlighting the need for improved classification approaches. **Objective:** The main objective is to evaluate the relationship between endometriosis subtypes and infertility risk using a large population-based cohort. **Methods:** We used a retrospective cohort from the Utah Population Database (1996–2020) including 461,684 women, with 79,600 diagnosed with endometriosis. Endometriosis subtypes were classified as superficial endometriosis (SE), ovarian endometriomas (OE), deep infiltrating endometriosis (DE), and other endometriosis. The primary analysis used Cox proportional hazards models to assess the hazard ratio of infertility diagnosis across endometriosis subtypes. **Results:** Women with endometriosis had a significantly higher risk of infertility compared to women without endometriosis (adjusted Hazard Ratio [aHR] 6.07, 95% CI 5.77-6.40). Infertility risk differed by endometriosis subtype, with the highest risk among those with deep infiltrating disease and/or ovarian endometriomas (aHR 9.01; 95% CI: 8.45–9.60), followed by other endometriosis (aHR 5.35; 95% CI: 4.94–5.79) and superficial endometriosis (aHR 4.36; 95% CI: 4.04–4.71). **Conclusion:** Endometriosis subtypes demonstrate different infertility risks, with deep infiltrating and ovarian endometriomas associated with the highest risk. These findings suggest the importance of considering endometriosis typology in clinical practice and research, potentially offering a more nuanced approach to patient care and fertility management.

Fertility and fecundity

Long-term exposure to ambient air pollution concentrations and fecundability among U.S. Black women Sydney Carolan*, Sydney Carolan, Yvette Cozier, Mary Willis, Jacqueline Hicks, Junenette Peters, Stephanie Grady, Jean Costello, Wendy Kuohung, Julie Palmer, Lauren Wise, Amelia Wesselink,

Previous research shows associations between air pollution and infertility. However, few studies have included large numbers of Black women, despite documented inequitable exposures to air pollution in the United States. Using data from the Black Women's Health Study, a prospective cohort study of 59,000 U.S. Black women, we examined the association of long-term exposure to ambient air pollution with fecundability, the per-cycle probability of conception. Participants enrolled in 1995 and are followed by biennial questionnaires. In 2011, participants were asked about time-to pregnancy for planned pregnancies that resulted in a birth and unsuccessful pregnancy attempts. Our analysis included 2,199 pregnancy attempts from 1,716 participants during 1995-2011. We used annual average ambient concentrations of particulate matter ≤2.5 µm (PM2.5), nitrogen dioxide (NO2), and ozone (O3) estimated using spatiotemporal models and linked to geocoded participant addresses. We fit proportional probabilities regression models with generalized estimating equations to estimate fecundability ratios (FR) and 95% confidence intervals for each pollutant adjusting for age, calendar year, geographic region, educational attainment, neighborhood SES, and co-pollutants. We fit adjusted generalized additive models (GAM) with smooth terms to assess joint effects and non-linear associations between pairs of pollutants. Residential concentrations of NO2 and O3 were associated with decreased fecundability: FRs for a 5-ppb increase in exposure were 0.93 [95% CI: 0.88-1.00] and 0.92 [95% CI 0.85-1.00], respectively. In contrast, PM2.5 exposure was associated with greater fecundability (FR=1.26 per 5-µg/m3 increase, 95% CI: 1.09-1.46). GAM results indicated little evidence of non-linear associations or interactions between pollutants. Our findings add to the body of evidence for federal air quality standards aimed at mitigating the impact of air pollution on adverse reproductive health outcomes.

Fertility and fecundity

A prospective preconception cohort study of the association between prior miscarriage and fecundability in Kenyan women trying to conceive Hanna Shephard*, Hanna Shephard, Erica Lokken, Marianne Mureithi, Walter Jaoko, Kishor Mandaliya, R. Scott McClelland,

Background: Evidence suggests prior miscarriage might impair subsequent fecundability. However, existing data are from high-income settings, leaving an evidence gap from low- and middle-income countries. The Microbiota and Pre-term Birth (MPTB) Study is a prospective, preconception cohort of Kenyan women trying to conceive.

Objective: To examine whether prior miscarriage is associated with reduced fecundability among women in the MPTB Study.

Methods: At enrollment, participants reported prior pregnancy outcomes (miscarriage, termination, stillbirth, live birth). To identify incident pregnancies, participants underwent monthly pregnancy testing for up to six months. The exposure was self-reported prior miscarriage, defined as spontaneous abortion <20 weeks' gestation. We fit proportional probability models to estimate fecundability ratios (FRs) and 95% confidence intervals (CI) comparing women with and without prior miscarriage. We also estimated associations for women with 1 prior miscarriage and >1 prior miscarriages, separately.

Results: Among 423 gravid participants, 22.5% had prior miscarriage; 18.8% had 1 prior miscarriage and 4.1% had >1 prior miscarriages. In unadjusted analysis, prior miscarriage was associated with lower fecundability (FR 0.88, 95% CI: 0.66, 1.17), but confidence intervals were wide. After adjustment for age, study site, education, body mass index, menstrual regularity, vaginal washing, and sexually transmitted infections, the association was attenuated (aFR 0.93, 95% CI: 0.69, 1.25). When compared to those without prior miscarriage, fecundability was slightly lower for those with 1 miscarriage (aFR 0.94: 95% CI: 0.68, 1.30) and even lower for those with >1 prior miscarriages (aFR 0.87, 95% CI: 0.46, 1.64), but confidence intervals remained wide.

Conclusions: Prior miscarriage, especially >1 prior miscarriage, may be associated with slightly lower fecundability, but confidence intervals encompassed the null, limiting interpretability.

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Fetal loss/stillbirth/infant mortality

Residing in a Neighborhood with Historical redlining and stillbirth occurrence in Arkansas
*, Olabowale Olola, Scott Alsbrook, Wendy Nembhard, Kari Weber,

Background: Historical redlining has been associated with disparities in birth outcomes. However, the specific relationship between historical redlining and stillbirth has not been studied, especially in Arkansas, a state with both a history of residential segregation and significant racial health disparities. This study examined the relationship between living in historically redlined neighborhoods and stillbirth occurrence in Arkansas.

Methods: Data were births January 1997 to December 2013 from the Arkansas Reproductive Health Monitoring System. The Homeowners' Loan Corporation (HOLC) Security Maps, developed in the 1930s, assigned neighborhoods one of four grades: green (grade A) "Best," blue (grade B) "Still Desirable," yellow (grade C) "Definitely Declining," and red (grade D) "Hazardous," (redlined). Grade A served as the reference category. Geocoded maternal residential addresses at the time of birth were linked to the HOLC map to assign each address a grade. Logistic regression models were used to estimate unadjusted and adjusted odds ratios and 95% confidence intervals (CIs) for stillbirth outcomes, with grades B, C, and D (redlined) evaluated separately.

Results: This study included 642 stillbirths (cases) and 601 livebirths (controls). Compared with participants residing in grade A neighborhoods, those living in grade B (OR = 5.66; 95% CI: 3.58–8.94), grade C (OR = 4.85; 95% CI: 3.08–7.66), and grade D "redlined" (OR = 5.42; 95% CI: 3.74–7.85) neighborhoods had significantly higher odds of stillbirth.

Conclusion: This study reveals a strong and consistent pattern, indicating that historical redlining is associated with significantly increased odds of having a stillbirth.

KEYWORDS: Historical redlining, stillbirth, HOLC

Fetal loss/stillbirth/infant mortality

Pattern of maternal chronic conditions among stillbirth pregnancies Anne Marie Darling*, Anne Marie Darling, Steven Kerr, Martha Werler, Julie Petersen, Meredith Howley, Sarah Fisher, Wendy Nembhard, Mahsa Yazdy, Eirino Nestoridi,

Background: Several maternal chronic conditions have been linked to stillbirth, but most research has examined them individually. Patterns of co-occurrence may reflect distinct etiologic pathways, yet they remain poorly characterized. Identifying chronic condition clusters may help guide future etiologic research on stillbirth and clinical care.

Objective: To estimate the prevalence of maternal chronic conditions among women with pregnancies ending in stillbirth enrolled in the Birth Defects Study to Evaluate Pregnancy exposureS (BD-STEPS), and to identify distinct chronic condition profiles.

Methods: We estimated the prevalence of 23 chronic conditions, as well as the occurrence of multiple chronic conditions (≥2 conditions) and complex multimorbidity (≥3 conditions across ≥3 body systems), among 366 BD-STEPS participants whose pregnancies ended in a stillbirth and were unaffected by birth defects. We used latent class analysis (LCA) to identify chronic condition profiles among those reporting ≥2 conditions. We selected the final model based on statistical fit criteria and clinical interpretability.

Results: A majority of women (58.2%, 95% CI 53.1-63.2) reported multiple chronic conditions. Nearly one third (31.1%, 95% CI 26.4, 35.9) met the criteria for complex multimorbidity. Among those reporting ≥2 conditions (n=213), LCA identified two distinct classes of chronic conditions based on modal posterior assignment. The larger class (69%) was characterized by a moderate burden of cardiometabolic conditions and a lower burden of mental health conditions while the smaller class (31%) was characterized by a high burden of mental health conditions and a relatively lower burden of cardiometabolic conditions.

Conclusion: Maternal chronic conditions appear to commonly co-occur among women with pregnancies ending in stillbirth. LCA identified subgroups reflecting differing frequencies of cardiometabolic and mental health conditions. Future research could help determine whether these chronic condition phenotypes are associated with stillbirth risk.

Fetal loss/stillbirth/infant mortality

Identifying Gaps in Stillbirth Support in the Hospital: Lessons from the Utah SOARS Survey Danielle Larson*, Danielle Larson,

Introduction: Families experiencing stillbirth require specialized bereavement care in the hospital to mourn the loss of their child. Inadequate or unsupportive care from healthcare providers following a stillbirth may create additional trauma that can influence future health behaviors.

Methods: The purpose of this analysis was to identify aspects of stillbirth care in the hospital that are associated with feeling supported by a provider using data from the Utah Study of Associated Risks of Stillbirth (SOARS) survey from 2018 to 2023. Odds ratios and 95% confidence intervals were calculated using complex survey procedures in SAS 9.4.

Results: A total of 770 surveys were included in the analysis. The odds of feeling supported by a provider were 3.0 times higher for mothers who received information on lactation following their stillbirth compared to those who did not (95% CI 1.9-5.0). Those who had a conversation with their doctor about what may have happened to their baby had 4.2 times the odds of feeling supported compared to those who did not have a discussion (95% CI 2.5-7.0), and those who were offered the opportunity to share a hospital room with their baby had 3.3 times the odds of feeling supported compared to those who did not receive the same offer (95% CI 1.8-6.0).

Conclusion: Following the initial analysis, resources about lactation after loss and autopsy fact sheets were developed by SOARS staff and community partners. Additionally, SOARS staff assisted in the adaptation of an Australian stillbirth resource booklet for parents titled “Guiding Conversations”. These materials will be disseminated to hospital systems, peer support organizations, and funeral homes. The goal of these materials is to improve communication, build trust, and prevent additional trauma for families experiencing these losses. Hospitals and providers should also consider assessing current practices to ensure that families are receiving adequate support.

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Conclusion: Following the initial analysis, resources about lactation after loss and autopsy fact sheets were developed by SOARS staff and community partners. Additionally, SOARS staff assisted in the adaptation of an Australian stillbirth resource booklet for parents titled “Guiding Conversations”. These materials will be disseminated to hospital systems, peer support organizations, and funeral homes. The goal of these materials is to improve communication, build trust, and prevent additional trauma for families experiencing these losses. Hospitals and providers should also consider assessing current practices to ensure that families are receiving adequate support.

Fetal loss/stillbirth/infant mortality

Pattern of maternal chronic conditions among stillbirth pregnancies Anne Marie Darling*, Anne Marie Darling, Steven Kerr, Martha Werler, Julie Petersen, Meredith Howley, Sarah Fisher, Wendy Nembhard, Mahsa Yazdy, Eirino Nestoridi,

Background: Several maternal chronic conditions have been linked to stillbirth, but most research has examined them individually. Patterns of co-occurrence may reflect distinct etiologic pathways, yet they remain poorly characterized. Identifying chronic condition clusters may help guide future etiologic research on stillbirth and clinical care.

Objective: To estimate the prevalence of maternal chronic conditions among women with pregnancies ending in stillbirth enrolled in the Birth Defects Study to Evaluate Pregnancy exposureS (BD-STEPS), and to identify distinct chronic condition profiles.

Methods: We estimated the prevalence of 23 chronic conditions, as well as the occurrence of multiple chronic conditions (≥2 conditions) and complex multimorbidity (≥3 conditions across ≥3 body systems), among 366 BD-STEPS participants whose pregnancies ended in a stillbirth and were unaffected by birth defects. We used latent class analysis (LCA) to identify chronic condition profiles among those reporting ≥2 conditions. We selected the final model based on statistical fit criteria and clinical interpretability.

Results: A majority of women (58.2%, 95% CI 53.1-63.2) reported multiple chronic conditions. Nearly one third (31.1%, 95% CI 26.4, 35.9) met the criteria for complex multimorbidity. Among those reporting ≥2 conditions (n=213), LCA identified two distinct classes of chronic conditions based on modal posterior assignment. The larger class (69%) was characterized by a moderate burden of cardiometabolic conditions and a lower burden of mental health conditions while the smaller class (31%) was characterized by a high burden of mental health conditions and a relatively lower burden of cardiometabolic conditions.

Conclusion: Maternal chronic conditions appear to commonly co-occur among women with pregnancies ending in stillbirth. LCA identified subgroups reflecting differing frequencies of cardiometabolic and mental health conditions. Future research could help determine whether these chronic condition phenotypes are associated with stillbirth risk.

Genetics/Molecular/Omics

Michigan Newborn Screening Metabolite Patterns and SIDS Avery Armstrong*, Avery Armstrong, Jean Kerver, Xiaoyu Liang, Nicole Talge, Yeyi Zhu,

Some portion of mortality due to Sudden Infant Death Syndrome (SIDS) may be preventable. Prior work using California data reported associations between newborn screening metabolites, maternal factors, and SIDS. We aimed to test and extend these findings using the recent data from Michigan.

We conducted a matched a case-control study using Vital Records data from infants born in the state of Michigan between 2005-2011 and 2016-2022. SIDS cases were matched 1:4 to controls by gestational age and birth weight z-score. We did not include data from 2012-2015 to investigate whether findings are robust to changes in SIDS definitions that took place across this timeframe. We analyzed the 2005-2011 and 2016-2022 data separately, splitting each into model training (2/3rd) and testing (1/3rd) subsets.

The study included 309 cases from 2005-2011 and 240 cases from 2016-2022. We then used a modified version with 12 metabolites and risk factors from a previous California-based SIDS model (JAMA Pediatr. 2024;178(11):1183) as Michigan does not collect alanine. In the 2005-2011 dataset, inadequate prenatal care, <18 year maternal age at birth, 35+ year maternal age at birth, and carnitine 12:1 were significant predictors of SIDS risk. In the 2016-2022 data set, inadequate prenatal care, intermediate prenatal care, Black maternal race, and 35+ year maternal age at birth were significant factors. This is similar to previous results. The area under the curve for the different time frames were 0.68 (95% CI: 0.62-0.75) and 0.73 (0.67-0.80), respectively, which is similar to performance of the model using California data which was 0.70 (0.65-0.75).

These results replicate and expand previous results which show an association of newborn screening metabolites and SIDS. Further directions will include building our own model of SIDS risk to potentially refine and triangulate common predictors of this currently unpredictable outcome.

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Health equity

Hypertensive Disorders of Pregnancy and Black–White Racial Disparities in Severe Maternal Morbidity Rashida S. Smith-Webb*, Rashida S. Smith-Webb, Samantha E. Parker, Martha M. Werler, Christina D. Yarrington, M. Maria Glymour, Collette N. Ncube,

Background: Limited research has examined the contribution of hypertensive disorders of pregnancy (HDP) to racial disparities in severe maternal morbidity (SMM); however, quantifying the role of HDP more precisely could help prioritize strategies to reduce disparities in SMM. We used mediation analysis to estimate the contribution of HDP to Black–White racial disparities in SMM.

Methods: We identified Black and White birthing people aged 12–55 years with deliveries in Massachusetts from 1998 to 2021 using the Pregnancy to Early Life Longitudinal Data System (N = 1,242,574). We estimated the total absolute effect of maternal race, as a proxy for exposure to racism, on SMM using generalized linear models, and applied G-estimation of a structural nested mean model to estimate the counterfactual disparity measure for the direct effect. We then calculated the proportion of the Black–White racial disparity in SMM that could be eliminated by preventing all HDP and severe HDP, separately.

Results: Black birthing people had a higher rate of SMM than White birthing people (114.0 vs. 50.4 per 10,000 in-hospital deliveries), corresponding to an excess of 63.6 events per 10,000 in-hospital deliveries (95% confidence interval [CI]: 57.9, 69.3). Under complete prevention of all HDP, the SMM disparity was reduced to 38.4 events per 10,000 in-hospital deliveries (95% CI: 33.4, 44.8), suggesting that 39.7% of the absolute Black–White racial disparity in SMM could be eliminated. Preventing severe HDP reduced the SMM disparity to an excess of 45.8 events per 10,000 in-hospital deliveries (95% CI: 40.2, 51.5), representing elimination of 27.9% of the disparity.

Conclusion: Preventing HDP could reduce Black–White racial disparities in SMM. These findings highlight the need for further research on preventive strategies among Black birthing people, with specific attention to effective messaging and adherence to prenatal aspirin, which has been shown to reduce the incidence of preeclampsia.

Health equity

Poor housing conditions, home tenure, and their estimated joint effects on preterm birth, stillbirth and neonatal death in Canada: a population-based study Azar Mehrabadi*, Azar Mehrabadi, Gabriel Shapiro, Nichole Austin, Michelle Dimitris, Jay Kaufman, Seungmi Yang,

Background. Socioeconomic risk factors are important determinants of adverse birth outcomes, and housing is a key social determinant of health.

Objectives. To estimate the combined effects of housing conditions and home tenure (i.e., renting versus owning) on preterm birth and other adverse birth outcomes.

Methods. This population-based study used 2014-2016 Canadian birth registration data linked with the 2016 long-form census and included singleton births among homeowners and renters. Outcomes were preterm birth, infant death, and stillbirth. Log-binomial regression estimated the combined association between the need for repairs and home tenure and outcomes adjusting for sociodemographic risk factors and parity. We explored the additional contributions of single parenthood to adverse outcomes.

Results. Compared to being a homeowner without the need for repairs, being a renter in need of major repairs was associated with preterm birth (8.8% vs 6.1%, aRR 1.30, 95% CI 1.21-1.40) and infant death (5.6 vs 2.8 per 1000 deliveries, aRR 2.33, 95% CI 1.45-3.72), followed by a weaker association between being a renter without the need for repairs and preterm birth (aRR 1.12, 95% CI 1.07-1.18). No association was observed between being an owner in need of major repairs and preterm birth (aRR 1.04, 95% CI 0.95-1.14). Although attenuated, renting without reported need for any repairs remained associated with infant mortality (3.9 vs 2.8 per 1000 deliveries, aRR 1.57, 95% CI 1.25-1.98). No clear association was found between poor housing conditions and risk of stillbirth. Single parenthood and needing major repairs were associated with an increased risk of preterm birth among both home renters and owners.

Conclusions. Poor housing conditions in combination with renting one’s home are associated with an increased risk of preterm birth and infant death. If these associations are causal, then addressing poor housing conditions among renters may improve birth outcomes.

Health equity

Intersectional inequities in maternal cardiometabolic health: the role of weathering, racial marginalization, and socioeconomic deprivation Elleni Hailu*, Elleni Hailu, Mahasin Mujahid, Safyer McKenzie-Sampson, Audrey Lyndon, Suzan Carmichael,

Compared to White women, Black women have higher risk of adverse perinatal cardiovascular conditions—leading causes of maternal mortality. Yet, how accelerated physiologic decline i.e., “weathering” and intersecting sources of social adversity jointly shape these disparities is understudied. We used hospital discharge data from California births occurring at ≥20 weeks’ gestation between 2007-2019 among Black and White women (N=1,880,400) to quantify perinatal cardiometabolic risk at the intersection of racial marginalization, weathering, and socioeconomic deprivation. We examined hypertensive disorders of pregnancy (HDP; chronic hypertension, gestational hypertension/preeclampsia, or eclampsia) and HDP subtypes. We also examined non-optimal cardiovascular health before and during pregnancy using a metric evaluating hypertension, diabetes, smoking, body mass index, and gestational weight-gain. We used modified Poisson regression models with robust standard errors, adjusting for pregnancy-related factors and year fixed-effects, to estimate increases in age-related risk of adverse outcomes and corresponding average predicted probabilities across combinations of race and socioeconomic status (SES; education or insurance). Across SES levels, age-related increases in perinatal cardiometabolic risk were higher among Black women than White women in similar or more deprived SES categories. Disparities widened with age. Moreover, Black women with high SES had more pronounced or equivalent age-related risk increases as low SES White women. For example, among college-educated Black women, each 5-year increase in age was associated with a 27% higher risk of HDP (95% Confidence Interval (CI): 1.24-1.29), while a similar increase in age was associated with a 23% higher risk among White women with a high school degree or less (95% CI: 1.22-1.24). Findings highlight the need to address structural forces and unique chronic stressors among Black women earlier in the life-course.

Health equity

Assessing mediation of sexual orientation disparities in miscarriage by age at pregnancy

Payal Chakraborty*, Payal Chakraborty, Colleen Reynolds, Isa Berzansky, Brittany Charlton,

Background: Existing studies show sexual orientation-related disparities in miscarriage. Because age is strongly associated with miscarriage and may lie on the causal pathway (e.g., higher rates of both teen and later-life pregnancies among sexual minority people), conventional age adjustment fails to produce direct effect estimates. To address this, we used formal mediation methods to evaluate the role of age at pregnancy in sexual orientation disparities in miscarriage.

Methods: We used pregnancy data from the Nurses' Health Study 2, randomly selecting one pregnancy per person as pregnancy outcomes within a person are correlated. Because exposure induced mediator-outcome confounding was likely present, we estimated interventional mediated effects (interventional pure natural direct effect [iPNDE] and total natural indirect effect [iTNIE]). Our outcome was miscarriage (yes vs. no). We treated age as multinomial (pregnancies at age <20 or ≥35 vs. 20–34 years). We examined sexual orientation dichotomously (sexual minority vs. heterosexual) and with sexual minority groups disaggregated (heterosexual with same-sex experience, mostly heterosexual, bisexual, and lesbian/gay). Baseline covariates included measures of social origin and mediator-outcome confounders included a variety of demographic and health factors.

Results: Among 64,713 participants, 12% had a miscarriage. About 3% of pregnancies occurred at age <20 and 16% at age ≥35 years. We found some evidence of mediation by age comparing sexual minority groups combined to heterosexual participants (iPNDE: 1.17; 95% CI: 1.00–1.37; iTNIE: 1.02; 95% CI: 1.01–1.04; proportion mediated: 12%). Results varied for sexual orientation subgroups.

Conclusions: Age at pregnancy may contribute to a small portion of sexual orientation disparities in miscarriage. Analyses of other clinically relevant pregnancy characteristics, such as use of medically assisted reproduction, are ongoing.

Health equity

Barriers to Oral health care access and utilization among American Indian pregnant women in North Dakota (PRAMS DATA 2017-2021) Nishat Sultana*, Andrew Williams, Nishat Sultana,

Background: In the United States, dental care is largely separate from prenatal care, creating significant challenges for women seeking prenatal oral health care. Barriers include high costs, limited dental insurance coverage, provider shortages, and transportation difficulties. These barriers are even more pronounced among American Indian (AI) women in North Dakota (ND), who already experience disproportionate access to healthcare. To better understand these disparities, this study examines the most barriers to oral health care access among AI women in ND.

Methods: A sample of AI, White, and other race women from the 2017–2021 ND Pregnancy Risk Assessment Monitoring System (PRAMS) data was analyzed (weighted n=40023). Receiving dental cleaning during pregnancy and reported barriers to care (e.g., lack of dental insurance, difficulty finding providers who accept Medicaid, cost of care, and transportation challenges) were self-reported. Descriptive statistics (overall and by race) were obtained, and logistic regression models odds of obtaining a dental cleaning in pregnancy by race, adjusted for maternal sociodemographic and health behavior factors.

Results: Only 26.6% of AI women received a dental cleaning during pregnancy, compared with 56.3% of White women. AI mothers reported higher prevalence of every barrier measured (all $p<.001$). After adjusting for maternal demographic and health factors, Indigenous women had significantly lower odds of receiving a dental cleaning (OR=0.28, 95%CI:0.15–0.52). After accounting for all barriers to dental care, AI women remained significantly less likely to receive dental care (OR=0.24, 95%CI:0.12–0.46).

Conclusion: In ND, racial disparities in prenatal oral health treatment persist after accounting for barriers to oral healthcare, indicating deeper systemic inequalities. To improve oral health outcomes for AI women, targeted, culturally informed interventions are warranted.

Health equity

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Objectives. To estimate the combined effects of housing conditions and home tenure (i.e., renting versus owning) on preterm birth and other adverse birth outcomes.

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Conclusions. Poor housing conditions in combination with renting one’s home are associated with an increased risk of preterm birth and infant death. If these associations are causal, then addressing poor housing conditions among renters may improve birth outcomes.

Infectious disease/COVID 19

Measles outbreak across the United States: estimating vaccine coverage by HHS regions

Anne Bischops*, Anne Bischops, Erin N. Hulland, Mia Patzakis, Ella Madsen, Mikkel Nagorsen, Rosemary A. Martoma, Maimuna Majumder,

Objective

The United States (US) currently faces its largest measles epidemic since its elimination in 2000, with cases now reported in 45 states. The latest available vaccine coverage data, from the 2023-2024 school year, are limited to kindergarteners. Assessing current regional measles vaccine coverage is therefore essential to identify gaps in population immunity and inform public health response.

Methods

We used daily measles incidence counts as reported routinely by state departments of health from January 23 until December 12, 2025. We estimated the early-phase vaccine coverage by Health and Human Services (HHS) region by comparing the basic reproduction number ($R0$) (average number of infections caused by an individual in a fully susceptible population) to the current effective reproduction number (Rt) using the R packages EpiEstim and VaxEstim. We focused on the early-phase using the initial *Rt* value, when we can assume that immunity was primarily conferred by pre-outbreak vaccination. We used literature-based measles estimates for the serial interval (SI) (14.5 days, SD 3.3), prior distribution of *Rt* (15.3, SD 5) and vaccine effectiveness (95%). HHS regions were included when they reported more than 50 cases.

Results

The initial *Rt* for all seven regions was above the propagation threshold of 1, ranging from 1.57 (95% CI 1.02-2.28) in Kansas City to 7.73 (4.03-13.22) in Atlanta. Four HHS regions showed vaccination coverage below the herd immunity threshold of 93% in all scenarios, while three regions were below the threshold except in the most conservative scenarios. The largest immunity gap was found in the Atlanta region (61.74%). Further analyses of vaccine coverage by state, and for different SI and *Rt* are ongoing.

Conclusions

We find substantial measles immunity gaps across HHS regions, leading to high vulnerability of the US population to measles. Extensive vaccination efforts are needed to limit further transmission and prevent further outbreaks.

Infectious disease/COVID 19

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Mental health

Perinatal depression and breastfeeding practices Healthy Start participants, 2019-2024

Jihong Liu*, Jihong Liu, Peyton Mosher, Xingpei Zhao, S.M Rokonuzzman, Kimberly Alston, Bo Cai, Anwar Merchant,

Few studies have examined associations between perinatal depression and breastfeeding duration among predominantly low-income Black populations, a group with persistently low breastfeeding rates.

We examined associations between prenatal and postnatal depression with breastfeeding initiation and duration in a prospective cohort of women in the Midlands Healthy Start program (2019-2024). Depressive symptoms were assessed during pregnancy and postpartum using the Center for Epidemiologic Studies-Depression Scale (CES-D) or Edinburgh Postpartum Depression Scale (EPDS). Standardized depressive symptom scores were calculated, and depression was defined by established cut-offs (EPDS ≥ 10; CES-D ≥ 16). Breastfeeding practices were assessed repeatedly during follow-up. Linear and logistic regression models were used.

Among 644 participants, 88% were Black and 93.8% were Medicaid insured. Overall, 15.9% had prenatal and 8.1% had postnatal depression; 74.4% initiated breastfeeding, 31.4% breastfed ≥2 months, and 14.5% ≥6 months. Standardized prenatal and postnatal depression scores were lower among women with longer breastfeeding duration, but differences were not significant. Postnatal depression was associated with reduced odds of breastfeeding at 2 months (adjusted odds ratio [AOR] 0.44, 95% CI 0.21-0.92) and 6 months (AOR 0.48, 95% CI 0.17-1.36). Receipt of ≥6 Healthy Start services was associated with higher odds of breastfeeding initiation (AOR: 2.08, 95% CI: 1.24-3.49). Higher education and being married were associated with better breastfeeding practices.

In this underserved cohort, breastfeeding initiation matched national averages for Black women, yet duration remained suboptimal. Postnatal depression was associated with shorter breastfeeding duration, while greater engagement with Healthy Start services and sociodemographic advantages were linked to improved outcomes, underscoring the importance of integrated community-based mental health and breastfeeding support.

Mental health

Perinatal mental illness following antepartum, intrapartum, and postpartum severe maternal morbidity Maya Rajasingham*, Maya Rajasingham, Priya Premranjith, Aaron Jones, Hilary K. Brown, Daniel J. Atkinson, Rohan D'Souza, Benicio N. Frey, Sheryl M. Green, Susan M. Jack, Giulia M. Muraca,

Background

We assessed the association between severe maternal morbidity (SMM) and perinatal mental illness (PMI) by period of SMM occurrence.

Methods

We conducted a population-based cohort study using health administrative data on primiparas who gave birth ≥20 weeks' gestation in Ontario, Canada (2012-2021). SMM was defined using the Canadian Perinatal Surveillance System definition and categorized based on period of occurrence [antepartum, intrapartum, and postpartum (delivery discharge to six weeks postpartum)]. PMI was identified using inpatient/outpatient diagnoses and billing codes from conception to 1-year postpartum. Analyses were stratified into two cohorts: individuals with and without preexisting mental illness. Within each cohort, we further stratified by period of SMM occurrence and fit Cox proportional hazard models with propensity score overlap weights to quantify the association between SMM and PMI.

Results

There were 459,422 primiparas, of whom 71,457 (15.6%) had a preexisting mental illness. Overall, the PMI rate was higher among individuals with versus without SMM (without preexisting mental illness: 13.0% vs. 9.3%; with preexisting mental illness: 49.9% vs. 44.2%). Across strata, the highest PMI rate was following antepartum SMM, and the most common PMI was mood and anxiety disorders. Among individuals without preexisting mental illness, the risk of PMI was 2-fold higher with versus without antepartum SMM (131.2 vs. 55.0 per 1,000 person-years, adjusted hazard ratio 2.26, 95% confidence interval 1.99-2.58). This varied by month of SMM occurrence during pregnancy, from 2-fold higher in Month 2 to 6-fold higher in Month 9. Similar patterns were found in the cohort with preexisting mental illness. No association was observed in either cohort with intrapartum SMM, while postpartum SMM was associated with a 2-fold higher risk of PMI.

Conclusion

This study underscores the importance of PMI assessment and supports for individuals with SMM.

Mental health

Association between Maternal Nativity and Treatment Engagement Kendria Kelly-Taylor*, Kendria Kelly-Taylor, Sara Aghaee, Joshua Nugent, Nina Oberman, Ai Kubo, Charles Quesenberry Jr, Kathryn Erickson-Ridout, Mibhali Bhalala, Lyndsay Avalos,

Racial/ethnic disparities in prenatal depression diagnosis and treatment engagement are well-documented; less is known how maternal nativity (US-born vs. non-US-born) is associated with treatment initiation and type. This study examines differences in treatment initiation and type by maternal nativity among a cohort of pregnant individuals universally screened for depression. We conducted a retrospective cross-sectional analysis (2013-2019) of Kaiser Permanente Northern California members newly diagnosed with depression between the first day of LMP to the day before a live birth (n=27,044). Nativity, determined from birth records, and treatment initiation (any vs. none), type (antidepressant medication vs. psychotherapy), and covariates (e.g., maternal age, Medicaid, anxiety, parity, substance use, depression severity via Patient Health Questionarrie-9) ascertained from electronic health records. Logistic regression models estimated the adjusted odds ratio (aOR) and 95% CIs. In models excluding depression severity, non-US-born individuals had 22% higher odds of initiating treatment compared with US-born (aOR:1.22;95%CI:1.12-1.34), yet the associated attenuated after adjusting for severity. Of those who initiated treatment, non-US-born individuals had greater odds of engaging in psychotherapy (vs. medication), persisting after adjustment for depression severity (aOR:1.29;95%CI:1.05-1.58). Findings suggest differences in treatment engagement by maternal nativity may hinge on the severity of depression symptoms, which could mediate the pathway between nativity and treatment initiation. Prior research among KPNC pregnant individuals showed non-US -born individuals presented equivalent or higher depression severity than US-born counterparts. Nativity differences vanish after adjusting for severity, underscoring severity’s possible mediating effect. Further, findings offer clinical insight for tailoring depression treatment options during pregnancy based on nativity.

Mental health

Metabolomic markers associated with antenatal depression Priscilla Clayton*, Priscilla Clayton, Kathy Trang, Sixto Sanchez, Guisong Wang, Marta Rondon, Michelle Williams, Zhen Chen, Amy Deik, Clary Clish, Bizu Gelaye,

Background: Maternal depression affects up to 20% of pregnancies and is associated with adverse maternal and offspring outcomes. Several studies link antenatal depression to alterations in metabolites such as amino acids, lipids, and energy metabolism. However, few studies have examined these patterns during pregnancy.

Methods: We leveraged samples from the Pregnancy Outcomes, Maternal and Infant Study (PrOMIS) to examine metabolomic differences in 298 pregnant women. We assessed depression using the Patient Health Questionnaire-9 (score ≥10) and conducted targeted metabolomic profiling using liquid chromatography–mass spectrometry. We randomly partitioned the dataset into a training set (n=198) and an independent testing set (n=100). In the training set, we screened candidate metabolites using univariate logistic regression ($p<0.05$), followed by Elastic Net regularized logistic regression for the best model. We constructed receiver operating characteristic (ROC) curves to evaluate predictive performance.

Results: A total of 43 metabolites were significantly associated with depression ($p<0.05$), of which 17 were retained in the final model. Five metabolites were negatively associated (alloisoleucine, glutathione, pyruvic acid, PC P-34:0, palmitoyl-EA), while 12 were positively associated (R-3-hydroxy myristic acid, carnosine, PC O-38:5, glutamine, tridecylic acid, threonine, CAR 8:0; OH, N1,N8-diacetylspermidine, methionine, 3R-hydroxypalmitic acid, 2-aminoheptanoic acid, CAR DC6:0). ROC analyses yielded area under the curve (AUC) values of 0.81 (training), 0.73 (testing), and 0.78 (overall), adjusting for maternal age, pre-pregnancy BMI, gestational age, parity, and access to basic needs.

Conclusion: We identified metabolic signatures associated with antenatal depression, highlighting potential biomarkers and pathways such as amino acid, nitrogen, and anabolic metabolism. Future research should validate these findings in larger samples to establish clinical utility and potential for risk stratification.

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Conclusion

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Mental health

Perinatal depression and breastfeeding practices Healthy Start participants, 2019-2024

Jihong Liu*, Jihong Liu, Peyton Mosher, Xingpei Zhao, S.M Rokonuzzman, Kimberly Alston, Bo Cai, Anwar Merchant,

Few studies have examined associations between perinatal depression and breastfeeding duration among predominantly low-income Black populations, a group with persistently low breastfeeding rates.

We examined associations between prenatal and postnatal depression with breastfeeding initiation and duration in a prospective cohort of women in the Midlands Healthy Start program (2019-2024). Depressive symptoms were assessed during pregnancy and postpartum using the Center for Epidemiologic Studies-Depression Scale (CES-D) or Edinburgh Postpartum Depression Scale (EPDS). Standardized depressive symptom scores were calculated, and depression was defined by established cut-offs (EPDS ≥ 10; CES-D ≥ 16). Breastfeeding practices were assessed repeatedly during follow-up. Linear and logistic regression models were used.

Among 644 participants, 88% were Black and 93.8% were Medicaid insured. Overall, 15.9% had prenatal and 8.1% had postnatal depression; 74.4% initiated breastfeeding, 31.4% breastfed ≥2 months, and 14.5% ≥6 months. Standardized prenatal and postnatal depression scores were lower among women with longer breastfeeding duration, but differences were not significant. Postnatal depression was associated with reduced odds of breastfeeding at 2 months (adjusted odds ratio [AOR] 0.44, 95% CI 0.21-0.92) and 6 months (AOR 0.48, 95% CI 0.17-1.36). Receipt of ≥6 Healthy Start services was associated with higher odds of breastfeeding initiation (AOR: 2.08, 95% CI: 1.24-3.49). Higher education and being married were associated with better breastfeeding practices.

In this underserved cohort, breastfeeding initiation matched national averages for Black women, yet duration remained suboptimal. Postnatal depression was associated with shorter breastfeeding duration, while greater engagement with Healthy Start services and sociodemographic advantages were linked to improved outcomes, underscoring the importance of integrated community-based mental health and breastfeeding support.

Methods

Multilevel Analyses of Child Welfare Agency Effects on Youth Sexual Initiation Syeda Naqvi*, Syeda Naqvi,

This study demonstrates that child welfare agencies can significantly influence the sexual risk trajectories of child welfare system (CWS) involved youth. While prior research has focused on the effect of child welfare agency characteristics on child outcomes such as mental health, no study has examined the relationship between agency characteristics and sexual health outcomes. As such, this study draws from existing neighborhood effects methodologies to examine child welfare agency effects on youth sexual initiation.

Hierarchical regression, using the zero-variance method, was used to perform a weighted subpopulation multilevel analysis of data from the National Survey of Child and Adolescent Well-Being (NSCAWII), focusing on youth sexual initiation between Wave 1 and Wave 3 of the survey. Factor, cluster, and discriminant analyses were also used to further explore sexual initiation by agency type.

This study found that sexual initiation was 2.7 times higher among youth served by agencies that did not make referrals for tutoring services (OR=2.71, CI [1.18-6.18]). Youth served by Type 1 agencies (n=460) also had three times higher odds of becoming sexually active compared to youth served by Type 3 agencies (n=400, OR=3.23, CI [1.05-9.92]). Type 1 agencies were more rigid, less collaborative, and had a higher turnover than Type 3 agencies. Type 3 agencies were more decentralized and collaborative and engaged more with biological parents.

This study makes an original contribution to the fields of child welfare and public health by identifying the presence of child welfare agency effects on youth sexual initiation. Child welfare policy makers and public health practitioners are encouraged to work together to co-design sexual risk prevention strategies for CWS youth. Child welfare leaders are also further urged to invest in trauma-informed sexual risk prevention training for their workers to help position them as the frontline defense against sexual risk-taking among these vulnerable youth.

Methods

Development of an Electronic Health Records (EHR)-Based Algorithm for Identification of Gestational Diabetes Mellitus Man Tang*, Man Tang, Yilu Lin, Rong Rong, Bradley C Martin, Cheng Peng, Xu Xiong, Kevin Callison, Nahed O. ElHassan, Daniel Fort, Mahip Acharya, Abigail Gamble, Brian D Christman, William B. Hillegass, Lizheng Shi,

Background: Accurate identification of gestational diabetes mellitus (GDM) from electronic health records (EHRs) is critical for research and quality assessment, yet validated EHR-based approaches remain limited compared with claims-based algorithms. This study developed an EHR-based GDM identification algorithm.

Methods: Using EHR data (August 2016–June 2024) from a large Louisiana healthcare system, we identified women with pregnancy episodes using a published delivery-identification algorithm. We developed a GDM algorithm integrating ICD-10-CM diagnosis codes, CPT codes, LOINC-mapped laboratory results, and antidiabetic medication prescriptions. GDM was defined by: (1) ≥2 GDM diagnosis codes on different dates during pregnancy, excluding preexisting diabetes; (2) ≥1 CPT code for glucose challenge or oral glucose tolerance testing at ≥20 weeks' gestation; (3) laboratory evidence of abnormal glucose values using ADA thresholds; or (4) ≥1 antidiabetic medication prescription during gestation. We compared our algorithm to an adapted claims-based framework. Agreement was assessed at the individual and episode levels using Cohen's κ.

Results: Among 72,349 women and 92,714 pregnancy episodes, the EHR-based algorithm identified 8,521 women (11.78%) and 9,150 pregnancy episodes (9.87%) with GDM. Annual GDM prevalence ranged from 7.74% to 13.65%. The adapted claims-based algorithm identified 8,724 women (12.06%) and 9,333 pregnancy episodes (10.07%), with annual prevalence ranging from 7.83% to 13.42%. The two approaches demonstrated near-perfect agreement at the episode (κ = 0.92) and individual level (k=0.93).

Conclusions: This multidimensional EHR-based algorithm demonstrated high agreement with a claims-based algorithm. By leveraging clinical details often absent from administrative claims, this approach provides a robust foundation for identifying GDM among pregnant mothers to support epidemiologic research and policy evaluations using EHR systems.

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Nutrition/obesity

The role of maternal bean consumption in child bean consumption Xiaozhong Wen*, Xiaozhong Wen, Awnish Shankar, Farah Malik, Sinkera Ya, Sri Ijjapureddy, Mohammed Haque, Anna Nezha, Todd Rideout,

Background: Early-life nutrition is highly influential in establishing lifelong health.

Objectives: To examine how maternal bean consumption during pregnancy and postpartum may influence child bean consumption.

Methods: We analyzed data from a U.S. cohort of 537 mother-infant dyads in the Infant Feeding Practices Study II and its six-year follow-up. In late pregnancy and early postpartum, mothers reported the frequency of consumption and portion size of dried beans, chili, and bean soup over the previous month. They also reported their child's consumption of bean foods at 6 years of age.

Results: There was a moderate Spearman correlation between maternal consumption of dried beans (r=0.279, P-value<0.001) or bean soup (r=0.263, P-value<0.001) during pregnancy and child bean consumption. The corresponding correlation was smaller for maternal chili consumption (r=0.134, P-value=0.002) during pregnancy. In the multivariable linear regression model, a 1-cup/week increment of maternal dried bean consumption was associated with a 0.09 times/day (95% CI, 0.05-0.13; P-value<0.001) higher child bean consumption after adjusting for socio-demographic confounders and overall dietary quality. The corresponding number was similar for maternal bean soup consumption (mean difference, 0.09 times/day [95% CI, 0.03, 0.15]; P-value=0.002), but much smaller and non-significant for maternal chili consumption (mean difference, 0.02 times/day [95% CI, -0.04, 0.08]; P-value=0.469). Overall, the corresponding results for maternal bean consumption during postpartum were similar to those during pregnancy.

Conclusion: Maternal bean consumption during pregnancy and postpartum was positively associated with offspring's bean consumption in middle childhood. This association appeared stronger for dried bean and bean soup than for chili consumption.

Nutrition/obesity

Maternal egg consumption during pregnancy and risk of small-for-gestational-age birth

Xiaozhong Wen*, Xiaozhong Wen, Fatima Mohammed, Akashpreet Grewal, Khadija Nadeem, Keith Bannerman, Todd Rideout,

Objectives: To examine the associations of overall egg intake during pregnancy and different components of eggs/different preparation methods with fetal growth.

Methods: Data from a U.S. cohort of 1,119 mother-infant dyads in the Infant Feeding Practices Study II were analyzed. In late pregnancy, mothers reported the frequency and portion size of their consumption of egg-related products in the past month, including total eggs, whole eggs, egg whites, egg substitutes, eggs with fat, and egg salads. We used multivariable logistic and linear regression models to examine associations of egg consumption with small-for-gestational-age [SGA], adjusting for socio-demographics, pregnancy-related characteristics, and the Healthy Eating Index.

Results: Maternal total egg consumption was marginally associated with a lower risk of SGA birth. Pregnant individuals who consumed eggs 1-2 times per week tended to have a lower risk of SGA (6.6% vs 13.4%; confounder-adjusted odds ratio or aOR, 0.50 [95% confidence interval or CI, 0.25-1.02]; P-value=0.056), compared to those who never consumed eggs. One egg/week increment in total egg consumption corresponded to 0.93 (95% CI, 0.86-1.00) times lower risk of SGA birth. When examining specific egg foods, the results for whole egg consumption were similar to those for total egg consumption. Pregnant individuals who consumed eggs with fat 2+ times per week had a significantly lower risk of SGA (7.3% vs 10.0%; aOR, 0.46 [95% CI, 0.23-0.91]; P-value=0.025), compared to those who never consumed eggs with fat. The risk of SGA birth decreased with consuming eggs with fat, and aOR was 0.90 (95% CI, 0.82-0.99; P-value = 0.038) per one egg/week increment in consumption of eggs with fat.

Conclusions: High consumption of eggs with fat, possibly total eggs and whole eggs, was associated with a lower risk of SGA birth. No such associations were found for egg whites, egg substitutes, or egg salad.

Nutrition/obesity

Is maternal obesity in early pregnancy associated with offspring infection-related hospital admissions, from birth to 10 years? Preliminary findings from a longitudinal study using linked, national data from Scotland, UK Victoria Coathup*, Victoria Coathup, Claire Carson, Maria Quigley,

Introduction
There is growing evidence to support a link between maternal obesity in pregnancy and increased risk of adverse long-term outcomes for offspring. A number of studies have reported associations between maternal body mass index (BMI) and childhood infection. The primary objective of this study is to explore associations between maternal BMI and infection-related hospital admissions throughout childhood. The secondary objective is to explore whether breastfeeding, child obesity, early antibiotic exposure and mode of birth are potential mediators.

Methods
Birth registration, death registration and hospital admission data were linked for all births in Scotland between 2011 and 2019. All live, singleton births with maternal BMI data were included in this analysis. Height and weight were recorded during their first antenatal appointment. The primary outcome was an infection-related hospital admission. Poisson generalized estimating equation models were fitted to estimate rate ratios (RR) with 95% confidence intervals (CI) for overall infections and by infection type. Models were adjusted for socio-economic and pregnancy related factors.

Results
379,283 children were included in the analysis. Approximately 28%, 14%, 6% and 3% of mothers were classed as overweight, obese grade 1, obese grade 2 and obese grade 3, respectively. Almost one third (27%) of children experienced at least one infection-related hospital admission between birth and 10 years. Upper and lower respiratory tract infections were the most common cause of an infection-related hospital admission, especially within the first two years of life. Compared to those with a healthy BMI, children born to women with grade 1, 2 and 3 obesity had adjusted RRs of 1.17 (95%CI:1.12-1.21), 1.23 (95%CI:1.17-1.30) and 1.39 (95%CI:1.30-1.48), respectively.

Conclusions
Preliminary findings indicate a modest but consistent association between maternal overweight and obesity in early pregnancy and childhood infections.

Nutrition/obesity

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Conclusion: Maternal bean consumption during pregnancy and postpartum was positively associated with offspring's bean consumption in middle childhood. This association appeared stronger for dried bean and bean soup than for chili consumption.

Obstetric health

Revisiting racial disparities in hypertensive disorders of pregnancy: missed opportunities for prevention Candice Johnson*, Candice Johnson, Yinbo Wang, Evan Myers, Danielle Gartner, Prudence Kunyangna, Sarahn Wheeler,

Background. Clinical algorithms guiding the use of low-dose aspirin to prevent preeclampsia and other hypertensive disorders of pregnancy (HDP) are race-based, despite race being a social construct whose use in clinical algorithms is increasingly questioned. Because of well-documented Black-White disparities in HDP, the guidance advises that Black patients need fewer medical risk factors before aspirin prophylaxis is recommended. However, rates of HDP in other historically marginalized racial-ethnic groups are poorly described. As a result, current race-based guidance may omit other groups who might also merit special consideration for aspirin prophylaxis.

Methods. We analyzed 6.5 million U.S. live birth certificates (2022-2023), categorizing participants into 264 mutually exclusive Hispanic ethnicity-racial groups. We calculated the prevalence of HDP in each group and reported estimates for the 140 groups with ≥50 births.

Results. HDP prevalence was 10.2% overall, ranging from 3.1% to 16.9% across racial-ethnic groups. 31 groups had higher HDP prevalence than the non-Hispanic Black population (prevalence > 11.7%), 26 of which were American Indian or Alaska Native (AIAN) or Native Hawaiian or Pacific Islander (NHPI) populations. 93 groups had lower HDP prevalence than the non-Hispanic White population (prevalence < 10.7%), a group typically considered low-risk and recommended no specific HDP prevention.

Conclusions. If the aspirin prophylaxis algorithm continues to be race-based, current guidance focusing solely on Black race is likely incomplete. Our results question if AIAN and NHPI populations should also be given special consideration and if the current guidance inappropriately treats non-Hispanic White populations as low risk. A more inclusive approach may be necessary if guidance for low-dose aspirin prophylaxis—one of the only effective methods for HDP prevention—continues to be based on race.

Obstetric health

Cardiovascular Disease in the Offspring Following Placental Abruption: The Role of Preterm Delivery Subtypes Cande Ananth*, Cande Ananth, Cande Ananth, Wen Wei Loh, Rachel Lee, Sonia Grandi, Linda Valeri, William Kostis,

Background: Placental abruption confers increased CVD risks in the offspring. Regarded as an acute and devastating complication, abruption often warrants an emergent clinical intervention, leading to early delivery; some of these pregnancies also deliver preterm spontaneously. In turn, preterm delivery is a risk marker for CVD.

Objective: To evaluate the extent to which clinician-initiated (PTDIND) and spontaneous (PTDSPT) preterm delivery shapes the singleton offspring's risks of CVD associated with abruption.

Methods: We used the Placental Abruption and Cardiovascular Event Risk (PACER) cohort, comprising births linked to deliveries, all subsequent hospitalizations, and mortality in NJ (1993-2020). We examined CVD events as the primary outcome and non-CVD-related deaths as a competing event. We evaluated PTDIND and PTDSPT (<37 weeks) as competing causal mediators of the association between abruption and offspring CVD. We fit cause-specific Cox proportional hazards models with abruption, preterm delivery subtypes, and their interactions. All associations were adjusted for potential confounders.

Results: The prevalence of abruption was 1.0% (n = 28,641) among 2,949,992 singleton births. Over the 28-year follow-up, offspring CVD event rates were 622 and 184 per 100,000 person-years in the abruption and non-abruption groups, respectively. Singleton offspring born of abruption pregnancies were at a 2.69-fold (95% confidence interval [CI] 2.47, 2.69) increased risk of CVD. The risk ratios for the indirect effects operating through PTDIND and PTDSPT were 1.63 (95% CI 1.57, 1.68) and 1.13 (95% CI 1.12, 1.18), respectively. These translate the mediated proportions of 50% and 13% (combined 63%). The direct effect explained 37% of the total effect.

Conclusions: Despite the increased offspring CVD risks associated with abruption, this study suggests that clinician-initiated and, to a lesser extent, spontaneous preterm delivery are important pathways in shaping CVD risks.

Obstetric health

Anemia on Admission for Childbirth and Perinatal Mood and Anxiety Disorders –Modification by Intravenous Iron Katharine E. Bruce*, Katharine E. Bruce, Kimiko Van Wickle, Alison M. Stuebe, Stephanie M. Engel,

Background: Perinatal anemia is common and may increase risk of Perinatal Mood and Anxiety Disorders (PMADs). Prior association studies have been mixed, and none have examined the role of IV iron in modifying this association.

Methods: This retrospective cohort study evaluated the relationship between hemoglobin (Hb) on admission for childbirth and PMADs within 3 months postpartum using medical records data from UNC Health System. Participants gave birth at ≥20 weeks gestation from April 1, 2016 to June 12, 2024. Hb, collected from complete blood count labs, was categorized as severe (<9 g/dL), moderate (9-<11 g/dL), or none (≥11 g/dL). Patients were considered to have PMAD symptoms if they screened positive on the Edinburgh Postnatal Depression Scale (cutoff: 10), Patient Health Questionnaire 9 (cutoff: 5), and/or General Anxiety Disorder 7 (cutoff: 5). Generalized Estimated Equations calculated risk ratios, adjusting for age, race/ethnicity, insurance, parity, multifetal gestation, comorbidities, and Area Deprivation Index of home address.

Results: Among 26,186 participants, 24% met criteria for 3rd trimester anemia, 3% received IV iron before discharge, and 16% had PMADs. Compared to those without anemia, those with severe anemia had 1.24 times the risk of PMADs (95% Confidence Interval (CI): 1.02-1.52), and those with moderate anemia had 1.10 times the risk of PMADs (CI: 1.03-1.17). The relationship between anemia and PMADs persisted in those who did not receive IV iron (Severe: relative risk (RR): 1.21, CI: 0.97-1.52; Moderate: RR: 1.08, CI: 1.01-1.16), but there was less evidence of an association in those who did (Severe: RR: 1.05, CI: 0.60-1.87; Moderate: RR: 1.14, CI: 0.77-1.70).

Conclusion: Anemia on admission for childbirth was associated with an increased risk of PMADs. The stronger relationship between anemia and PMADs among those who did not receive IV iron compared to those who did suggests that treating anemia before discharge may mitigate this risk.

Obstetric health

Early-Life Trauma, Minority Stress, and Hypertensive Disorders of Pregnancy: Evidence from a Large Prospective Cohort Michelle Tam*, Michelle Tam, Isa Berzansky, Colleen Reynolds, Payal Chakraborty, Sarah McKetta, Cindy Veldhuis, Brittany Charlton,

Background: Early-life trauma, such as childhood physical and sexual abuse, is linked to hypertensive disorders of pregnancy (HDP) in adulthood. Sexual minority (SM) individuals experience higher rates of childhood abuse and HDP. It is unclear whether sexual orientation modifies the association between early-life trauma and HDP.

Methods: The Nurses' Health Study 3 is a longitudinal cohort of nurses born on or after January 1, 1965, living in the US or Canada (N=36,834 pregnancies from 13,854 participants). We assessed type (i.e., physical and sexual abuse) and severity of early-life trauma and prevalence of HDP (i.e., gestational hypertension, preeclampsia) across sexual orientation groups (completely heterosexual, heterosexual with same-sex experiences/mostly heterosexual, and bisexual/lesbian). We used modified Poisson models to estimate risk ratios (RR) and 95% confidence intervals (CI).

Results: Compared to completely heterosexual individuals, all SM groups had higher prevalence of childhood physical abuse (ranging from 49–52% vs. 40%) and childhood sexual abuse (37–49% vs. 28%). Prevalence of HDP was higher in all SM groups (9–11% vs. 7%). Compared to completely heterosexual individuals who had no childhood physical abuse, risk of HDP was higher amongst heterosexual with same-sex experience/mostly heterosexual individuals who had mild/moderate physical abuse (RR, 1.18, 95% CI, 1.02–1.37) and severe physical abuse (1.34, 1.05–1.69). Compared to completely heterosexual individuals who had no childhood sexual abuse, risk of HDP was higher amongst heterosexual with same-sex experience/mostly heterosexual (1.25, 1.08–1.44) and bisexual/lesbian (1.47, 1.09–1.98) individuals who had sexual abuse. Multiplicative and additive interaction terms showed modest evidence of effect modification by sexual orientation.

Conclusion: Both childhood abuse and sexual minority status increase HDP risk underscoring the impact of socially patterned trauma on pregnancy health.

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Occupational

Workplace stressors and maternal depressive and anxiety symptoms in pregnancy: early findings from the Healthy Brain and Child Development Study Diana Pacyga*, Diana Pacyga, Ashley Acheson, Heather H. Burris, Stephanie M. Engel, Yong Zhu, Leigh-Anne Cioffredi,

Background/objective: Pregnant women are exposed to circadian, physical, and chemical stressors in the workplace that are linked with poor pregnancy outcomes. We investigated the association of workplace stressors with maternal mental health in pregnancy, which remains poorly understood.

Methods: Employed pregnant women from the Healthy Brain and Child Development Study reported their workplace exposure to circadian (e.g., regular vs. shift work), physical (e.g., strenuous physical activity, heat exposure) and chemical (e.g., janitorial cleaners, laboratory chemicals) stressors. We calculated depression and anxiety scores from the Patient-Reported Outcomes Measurement Information System (PROMIS) Depression and Anxiety Short Forms. Using mixed models with Poisson distribution, we estimated relative risks (RRs) and 95% confidence intervals (CIs) for moderate and high vs. low anxiety symptoms (tertiles) and high vs. low depressive symptoms (1 standard deviation ≥ or < population norm). Models accounted for site as a random effect and age, pre-pregnancy body mass index, educational attainment, pregnancy intention, marital status, alcohol intake, and substance use as fixed effects.

Results: Almost 70% of employed women (n=925) had a college education and annual household incomes ≥$75,000, while 6% had high depressive symptoms. Around 22% engaged in shift work, while 60% and 39% were exposed to workplace physical and chemical stressors, respectively. Exposure to physical stressors was associated with higher depressive and anxiety symptoms. Compared to unexposed workers, those exposed to workplace physical stressors had an elevated risk of high depressive (RR: 2.11; 95% CI: 0.98, 4.55) and high anxiety (RR: 1.33; 95% CI: 1.02, 1.75) symptoms. Associations with circadian and chemical stressors were weaker and less precise.

Conclusion: Physically demanding work in pregnancy may contribute to higher depressive and anxiety symptoms with implications for maternal and child health.

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Pharmacoepidemiology

Descriptive analysis to assess changes in antidiabetic medication use at first prenatal care visit for patients with preexisting Type 2 diabetes Andrea Chalem*, Andrea Chalem, Andrea Chalem, Elizabeth Simmons, Chase Latour, Baijun Zhou, Shakia Hardy, Stephanie Engel, Lauren Kucirka, Mollie Wood,

Background Treatment of type 2 diabetes mellitus (T2DM) in pregnancy differs from treatment in the non-pregnant population, due to physiologic changes and possible fetal risks. Early pregnancy patterns of medication change are not well understood, but entry into prenatal care (PNC) could be a critical window for these changes

Objective Describe changes in antidiabetic medications following first PNC claim for patients with T2DM.

Methods We used to identify pregnancies with an estimated start date between 8/1/2016 and 2/1/2023. Eligibility criteria were preexisting T2DM and continuous antidiabetic before first PNC. We defined first PNC as the first prenatal claim with a code for ongoing pregnancy and continuous use as repeated prescription fills with ≤30 day gaps between end of dispensed supply and next prescription fill. Antidiabetics were grouped as: pregnancy-preferred (insulin only), acceptable in pregnancy (metformin or glyburide only; insulin combinations), or not pregnancy-preferred (all others). We evaluated regimen changes in the 45 days after first PNC.

Results Among 1459 eligible pregnancies, median gestational age at PNC was 8.6 weeks (IQR: 6.3-9.0) and was similar across baseline regimens. Prior to PNC, 248 (17%) were using insulin only, 624 (43%) were on an acceptable regimen, and Of the 624 on an acceptable regimen, 284 (46%) continued and 13 (2%) switched to insulin only in the 45 days after PNC. Of the 587 on a not preferred regimen, 37 (6%) switched regimen and 120 (n=20%) filled a prescription. Overall, 39% (n=567) filled a prescription after PNC.

Conclusion Most patients did not fill a prescription for any antidiabetic, including insulin, in the 45 days after PNC. Regimen changes were uncommon, even for not pregnancy-preferred medications. Early pregnancy-specific clinical guidance for T2DM medication is needed to help mitigate risks to maternal and fetal health.

Pharmacoepidemiology

Dispensations of prescription pain medications and opioids during the first year postpartum among TRICARE beneficiaries, 2013-2022 Celeste Romano*, Celeste Romano, Jackielyn Lanning, Clinton Hall, Ava Marie Conlin, Marissa Seamans,

Objective: To describe person-time with any prescription pain medication and prescription opioids during the first year postpartum.

Methods: Birth and Infant Health Research program data were used to identify patients with a live birth while enrolled in TRICARE, the health insurance program for US military families, 2013–2022. Live births were identified using diagnostic and procedure codes in administrative medical records and confirmed via linkage to enrollment data. Patients were followed until 1-year postpartum, with loss to care and return to care accounted for in estimation of person-time. Dispensed pain medications, excluding those for opioid use disorder treatment, were identified in outpatient pharmacy records. The mean number of days on 1) any pain medication and 2) opioid medications were calculated overall and by military status. Mean differences comparing military vs non-military patients were estimated and bootstrap resampling was used to obtain estimates of precision.

Results: Overall, 1,037,793 live deliveries were identified, with 59% of postpartum patients filling a pain medication prescription and 41% filling an opioid prescription. Across 10.4 million person-months, 3% of person-time was spent on any prescription pain medication (mean ± SD: 10.3 ± 29.0 days) and 1% was spent on an opioid medication (mean ± SD: 3.7 ± 15.5 days). Approximately one-third of time spent on pain medications occurred within the first 2 weeks postpartum (34%). Compared to non-military patients, postpartum military service members, who comprised 17% of the sample, spent an additional 3.7 days, on average, on any pain medication (95% CI: 3.6-3.9), although time on opioid medications was comparable (mean difference: 0.4 days; 95% CI: 0.3-0.4).

Conclusions: Pain medications were frequently dispensed during the first year postpartum, particularly among military service members. Although opioid dispensations were also common, time on opioids was low, indicating good stewardship.

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Policy

The Impact of NY Paid Family Leave on Postpartum A1C after Gestational Diabetes: A controlled interrupted time series analysis Natalie Boychuk*, Natalie Boychuk, Natalie A. Boychuk,

Paid family leave (PFL) is linked with improved infant health, breastfeeding, and postpartum healthcare use, but potential benefits for postpartum physical health are underexplored. Hemoglobin A1C may signal future cardiometabolic risk and is mandatorily reported in New York City (NYC), providing a marker of postpartum health. We examined the impact of New York PFL on A1C 4-12 months postpartum in privately insured women with gestational diabetes using a controlled interrupted time series of linked NYC birth, hospital discharge, and A1C registry data, 2014-2019 (n=3,371). Deliveries were classified as pre- (January 2014-December 2018) or post- (January 2018-March 2019) PFL. We estimated policy effects in women who were employed during pregnancy, with women who were unemployed as a control series. We used log binomial, linear, and quantile segmented regression to assess level/slope changes in 1) risk of prediabetic postpartum A1C (≥5.7%), 2) A1C z-score, and 3) median A1C, adjusting for race, education, parity, and nativity. Almost 80% (78.5%) of women were employed. Median A1C was 5.5 (IQR: 0.5). When A1C was binarized, no immediate post- vs. pre-PFL differences or sustained changes by employment were present (post vs. pre, treatment vs. controls, adjusted risk ratio (aRR): 1.00, 95% CI: 0.85, 1.17), post-PFL slope treatment vs. controls aRR: 1.00, 95% CI: 0.96, 1.05). In models of A1C z-score, we found an adjusted post vs. pre difference between treatment and control groups of -1.01 standard deviations (95% CI: -1.96, -0.07); however, a positive post-policy difference in slope by treatment was present (β: 0.28, 95% CI: 0.03, 0.52). In quantile regression, we similarly found an immediate -0.09 percentage point reduction in median A1C post- vs. pre-PFL in treatment vs. controls (95% CI: -0.25, 0.02) but no sustained changes by employment. Results suggest that PFL may have improved postpartum A1C among privately insured women immediately after policy implementation.

Policy

Quasi-Experimental Evaluation of Michigan’s Prenatal Syphilis Screening Mandate Expansion Meredith Cahill*, Meredith Cahill, Claire Margerison,

Michigan’s congenital syphilis incidence increased by over 1000% from 2012-2023, mirroring national trends. Because testing and treatment during pregnancy can prevent most cases of congenital syphilis, prenatal screening is a key prevention strategy. In 2019, Michigan expanded its prenatal syphilis screening mandate (MCL §333.5123), adding a 3rd trimester screening requirement to the existing 1st prenatal visit requirement. We evaluated the impact of this expansion on Michigan’s congenital syphilis incidence using a synthetic control design. We constructed a state-year panel (2012–2023) using congenital syphilis incidence data from the CDC and natality data for Michigan and 18 U.S. states that maintained the same screening requirement as Michigan’s pre-expansion requirement across the study period. We fit a synthetic Michigan using pre-expansion log-transformed congenital syphilis incidence and the percentages of Medicaid-covered births and births receiving first-trimester prenatal care. We estimated post-expansion effects as differences in log incidence and reported them as percent change beginning in 2020 to account for gestational timing. The synthetic control closely approximated Michigan’s pre-expansion trends (root mean squared prediction error [RMSPE]=0.19). Post-expansion divergence modestly exceeded pre-period error (post/pre RMSPE ratio=1.23). Initially, Michigan’s mandate expansion appeared to increase congenital syphilis incidence by 19% (2020) and 20% (2021) relative to the synthetic control, but in 2022 the trend reversed and incidence was 32% lower. Augmented synthetic control models and placebo tests supported the robustness of these findings. Our study provides one of the first quasi-experimental evaluations of state prenatal syphilis screening mandates and offers initial evidence of the population-level effects of expanded state screening requirements amid the current congenital syphilis epidemic.

Policy

The Impact of NY Paid Family Leave on Postpartum A1C after Gestational Diabetes: A controlled interrupted time series analysis Natalie Boychuk*, Natalie Boychuk, Natalie A. Boychuk,

Paid family leave (PFL) is linked with improved infant health, breastfeeding, and postpartum healthcare use, but potential benefits for postpartum physical health are underexplored. Hemoglobin A1C may signal future cardiometabolic risk and is mandatorily reported in New York City (NYC), providing a marker of postpartum health. We examined the impact of New York PFL on A1C 4-12 months postpartum in privately insured women with gestational diabetes using a controlled interrupted time series of linked NYC birth, hospital discharge, and A1C registry data, 2014-2019 (n=3,371). Deliveries were classified as pre- (January 2014-December 2018) or post- (January 2018-March 2019) PFL. We estimated policy effects in women who were employed during pregnancy, with women who were unemployed as a control series. We used log binomial, linear, and quantile segmented regression to assess level/slope changes in 1) risk of prediabetic postpartum A1C (≥5.7%), 2) A1C z-score, and 3) median A1C, adjusting for race, education, parity, and nativity. Almost 80% (78.5%) of women were employed. Median A1C was 5.5 (IQR: 0.5). When A1C was binarized, no immediate post- vs. pre-PFL differences or sustained changes by employment were present (post vs. pre, treatment vs. controls, adjusted risk ratio (aRR): 1.00, 95% CI: 0.85, 1.17), post-PFL slope treatment vs. controls aRR: 1.00, 95% CI: 0.96, 1.05). In models of A1C z-score, we found an adjusted post vs. pre difference between treatment and control groups of -1.01 standard deviations (95% CI: -1.96, -0.07); however, a positive post-policy difference in slope by treatment was present (β: 0.28, 95% CI: 0.03, 0.52). In quantile regression, we similarly found an immediate -0.09 percentage point reduction in median A1C post- vs. pre-PFL in treatment vs. controls (95% CI: -0.25, 0.02) but no sustained changes by employment. Results suggest that PFL may have improved postpartum A1C among privately insured women immediately after policy implementation.

Policy

Quasi-Experimental Evaluation of Michigan’s Prenatal Syphilis Screening Mandate Expansion Meredith Cahill*, Meredith Cahill, Claire Margerison,

Michigan’s congenital syphilis incidence increased by over 1000% from 2012-2023, mirroring national trends. Because testing and treatment during pregnancy can prevent most cases of congenital syphilis, prenatal screening is a key prevention strategy. In 2019, Michigan expanded its prenatal syphilis screening mandate (MCL §333.5123), adding a 3rd trimester screening requirement to the existing 1st prenatal visit requirement. We evaluated the impact of this expansion on Michigan’s congenital syphilis incidence using a synthetic control design. We constructed a state-year panel (2012–2023) using congenital syphilis incidence data from the CDC and natality data for Michigan and 18 U.S. states that maintained the same screening requirement as Michigan’s pre-expansion requirement across the study period. We fit a synthetic Michigan using pre-expansion log-transformed congenital syphilis incidence and the percentages of Medicaid-covered births and births receiving first-trimester prenatal care. We estimated post-expansion effects as differences in log incidence and reported them as percent change beginning in 2020 to account for gestational timing. The synthetic control closely approximated Michigan’s pre-expansion trends (root mean squared prediction error [RMSPE]=0.19). Post-expansion divergence modestly exceeded pre-period error (post/pre RMSPE ratio=1.23). Initially, Michigan’s mandate expansion appeared to increase congenital syphilis incidence by 19% (2020) and 20% (2021) relative to the synthetic control, but in 2022 the trend reversed and incidence was 32% lower. Augmented synthetic control models and placebo tests supported the robustness of these findings. Our study provides one of the first quasi-experimental evaluations of state prenatal syphilis screening mandates and offers initial evidence of the population-level effects of expanded state screening requirements amid the current congenital syphilis epidemic.

Policy

Effect of universal, no-cost contraception coverage on gynecological procedure volume: a population-based interrupted time series analysis Andrea Stucchi*, Andrea Stucchi, Lucy Cheng, Wendy Norman, Erin Brennand, Regina-Maria Renner, Michael Law, Laura Schummers,

Background: Long-acting reversible contraception (LARC, e.g., intrauterine devices), may reduce the need for gynecological procedures for abnormal uterine bleeding or permanent contraception. In Canada, physician visits and procedures are covered through public insurance; prescription medications/devices are generally covered through a mix of public and private insurance or out-of-pocket by patients. In 2023, British Columbia introduced universal no-cost prescription contraception coverage. This policy substantially increased LARC use, though impacts on gynecological procedure volumes remain unknown.

Methods: Using population-based linked health administrative data, we used physician billing, hospitalization, and emergency department records to identify endometrial ablation, hysterectomy, salpingectomy, and tubal ligation procedures in a cohort of provincially insured female BC residents from 2017-2024. We excluded events with a recent cancer or uterine prolapse diagnosis. We used an interrupted time-series analysis to estimate level and trend changes in monthly procedure rates (per 10,000 females) and compared observed to expected (counterfactual) rates as of December 2024.

Results: We identified 101,686 gynecological procedures from 2017-2024. Pre-policy, there were 8 (CI 7, 9) procedures per 10,000 females/month, increasing by 0.08 (CI 0.03, 0.12) per month. After the policy change, there was an immediate nonsignificant reduction in the procedure rate (-0.41; CI −0.83, 0.02), followed by a significant decline in the trend (-0.06; CI -0.11, -0.02 per 10,000 females/month). By December 2024, there were 1.6 fewer procedures per 10,000 females/month than expected without the policy change, amounting to an 18% volume reduction.

Conclusion: Universal no-cost contraception coverage reduced gynecological procedure volume. Expanded contraceptive access may reduce downstream demand for resource-intensive procedures for permanent contraception or abnormal uterine bleeding.

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Pregnancy outcomes

Investigating the relationship between long-term, stable partnership and pregnancy outcomes among women in the Mombasa Reproductive and Perinatal Health Study Hanna Shephard*, Hanna Shephard, Kishor Mandaliya, John Kinuthia, Walter Jaoko, Scott McClelland,

Background: Women engaged in sex work face intersecting social and health vulnerabilities that may shape their perinatal outcomes. While marriage and long-term partnership have been associated with lower risks of stillbirth and child mortality in general populations, evidence among women engaged in sex work is limited. The Mombasa Reproductive & Perinatal Health (MRPH) Study was designed to generate data on reproductive and perinatal health in this population.

Objective: To assess whether stable, long-term partnership or marriage during pregnancy is associated with live birth among MRPH Study participants.

Methods: At enrollment, participants reported partnership status and outcomes for up to ten prior pregnancies. The exposure of this study was stable, long-term partnership or marriage during pregnancy (yes/no). The outcome was live birth versus other all other pregnancy outcomes (miscarriage, termination, stillbirth, and ectopic pregnancy). Relative risks (RR) and 95% confidence intervals (CI) were estimated using modified Poisson regression with cluster-robust standard errors, adjusting for maternal age and education.

Results: Among 641 participants contributing 2,124 pregnancies (≈3 per participant), 81.2% of pregnancies resulted in live birth, 10.9% miscarriage, 5.6% termination, and 2.3% stillbirth. The proportion of pregnancies resulting in live birth was higher among pregnancies with a stable partnership (88.3%) compared to those without (74.5%). In unadjusted analyses, stable partnership was associated with an 18% higher probability of live birth (RR 1.18, 95% CI 1.13, 1.25). After adjustment for age and education, the association was slightly attenuated (RR 1.15, 95% CI 1.10, 1.21).

Conclusions: Among MRPH study participants, stable, long-term partnership during pregnancy was associated with a modest but meaningful increase in the probability of live birth. Findings suggest that relationship stability may be protective for perinatal health within this group.

Pregnancy outcomes

Maternal Mortality among Black/ African American Women in Arizona, 2016-2020

Samantha Davidson*, Samantha Davidson, Glenda M. Ramirez, Aubrianna Perez, Mary Glidden, Vivienne Rubio, Devina Wadhera, Martin Celaya,

At the national and Arizona levels, Black women experience disproportionately high rates of maternal mortality compared to other racial/ ethnic groups, except American Indian or Alaska Native women in Arizona, prompting a population-specific analysis. The goal of this study was to disseminate, for the first time, maternal mortality data specific to Black women in Arizona to inform the design of targeted interventions for improving maternal health in this population.

The Arizona Maternal Mortality Review Committee (MMRC) reviews deaths in Arizona of women ages 10-60 with a pregnancy in the past year and offers recommendations to prevent future deaths and improve maternal health. Results focused on Black/ African American women (2016-2020) whose deaths were Pregnancy-Related (resulting from a pregnancy complication, a chain of events initiated by pregnancy, or the aggravation of an unrelated condition by the physiologic effects of pregnancy). Descriptive statistics and Pregnancy-Related Mortality Ratios (PRMR)– the number of pregnancy-related deaths (PRD) compared to live births– were reported.

The MMRC identified 12 PRDs among Black women; 92% were preventable, 89% involved discrimination, and 58% were linked to inadequate mental health and substance use support. The most common cause of death was cardiovascular conditions. Over half of the preventable deaths occurred 43 days to 1 year postpartum. The PRMR for Black women was over double that of all Arizona women (52.8 vs. 24.4 deaths per 100,000 live births).

These findings highlight systemic issues such as limited access to financial resources, care coordination gaps, and the effects of discrimination and structural racism. Coordinated action from healthcare systems and community organizations is crucial for improving maternal health and supporting Black women in Arizona. This is the first race-specific analysis of maternal deaths in Arizona; future studies may address other disproportionately affected populations.

Pregnancy outcomes

Association of maternal physical activity domains, intensities and duration with neonatal anthropometry in the NICHD Fetal Growth Studies – Singletons Kathryn Wagner*, Kathryn Wagner, Zhen Chen, Jessica Gleason, Madison Ouellette, Dian He, Susanna Mitro, Roger Newman, William Grobman, Daniel Skupski, Stefanie Hinkle, Cuilin Zhang, Jagteshwar Grewal, Katherine Grantz,

Prior studies have focused on total or exercise physical activity (PA) and birthweight (BW), potentially missing nuanced relationships between PA domains, intensities and duration with neonatal size, including fat measures.

In a prospective cohort (n=2441), self-reported first trimester PA (type, intensity and duration) were categorized as tertiles and whether they met ACOG guidelines. Neonatal anthropometrics (BW, g; birth length (BL, cm); circumferences (cm) – head (HC), mid-upper arm (MUAC), chest (CC), abdominal (AC), and mid-upper thigh (MUTC); and skinfold thicknesses (mm) –tricep (TSF), subscapular (SSF), abdominal (ASF), and anterior thigh (ATSF)) were measured after delivery or abstracted from medical records. Generalized linear regressions evaluated the associations, adjusted for covariates.

Home, work, light, moderate, and duration of PA and meeting ACOG guidelines were associated with smaller neonatal anthropometrics. Specifically, 3rd tertile home PA was associated with smaller MUAC (β=-0.15;SE=0.08), TSF (β=-0.19;SE=0.09), CC (β=-0.24;SE=0.12), ASF (β=-0.18;SE=0.09) and ATSF (β=-0.24;SE=0.12), compared to the 1st tertile. 2nd tertile work PA, but not 3rd, was associated with smaller BW (β=-89.6;SE=29.7). 2nd and/or 3rd tertile light PA was associated with smaller TSF (2nd: β=-0.17, SE=0.08; 3rd: β=-0.19;SE=0.08) and CC (3rd: β=-0.24;SE=0.11). 2nd tertile moderate PA was associated with several smaller measures (BW: β=-71.4,SE=26.8; HC: β=-0.19,SE=0.08; MUAC: β=-0.15,SE=0.07; CC: β=-0.22,SE=0.11; AC: β=-0.30,SE=0.011; ASF: β=-0.19,SE=0.08). 3rd tertile PA duration was associated with a smaller SSF (β=-0.16,SE=0.08). Meeting ACOG guidelines was associated with smaller BL (β=-0.21;SE=0.11), compared to not. Transportation, exercise, sedentary and vigorous PA were not associated with neonatal measures.

These findings highlight non-monotonic relationships of PA and neonatal anthropometry, as well as the importance of assessing PA domains beyond exercise.

Pregnancy outcomes

C-reactive protein levels during pregnancy and its association with tobacco product exposure in the United States population: A cross-sectional study using the NHANES database *, Brook Gebremariam, Chukwudike Igwe, Erik Parker, Stephanie Dickinson, Robert Pepin, Hsien-Chang Lin, Wei-Chung Su, Alexandra Noël, Patricia Silveyra, Sarah Commodore,

C-reactive protein (CRP) is a marker for low-grade systemic inflammation linked to adverse pregnancy outcomes. This study evaluates whether tobacco exposure modifies serum high-sensitivity CRP (hs-CRP) levels among pregnant women in the United States using the National Health and Nutrition Examination Survey (NHANES) database. This cross-sectional study analyzed data from 9,015 participants between 2021 and 2023. Measurements of hs-CRP, in milligrams per liter (mg/L), were obtained from the serum of the NHANES participants, with 0.15 mg/L as the lower limit of detection. Pregnancy was verified with a positive urine pregnancy test result, and tobacco exposure status was obtained from a self-reported questionnaire. Participants were grouped by pregnancy status and tobacco exposure. Mean ± standard deviation hs-CRP values were compared with independent samples t-tests; significance was set at $p < 0.05$. Among 41 pregnant participants, 10 (24%) reported tobacco exposure. The exposed subgroup had a higher mean hs-CRP concentration (5.2 ± 5.4 mg/L) than the unexposed subgroup (3.6 ± 7.4 mg/L), and this difference was statistically significant ($p = 0.036$). The median hs-CRP level for the exposed group was 3.7 mg/L. No significant differences were observed in demographic or clinical covariates between the two groups, but the modest sample size limited the ability to conduct subgroup analyses. Tobacco exposure during pregnancy is associated with elevated hs-CRP levels, indicating increased inflammatory risk and highlighting the need for targeted tobacco cessation interventions and follow-up research in this population.

Pregnancy outcomes

The Role of Gravity and Informative Censoring in Explaining the Association Between Pregnancy Loss and Subsequent Hypertension Sabrina Chiodo*, Sabrina Chiodo, Kristian B. Filion, Sonia M. Grandi,

Background: Pregnancy loss is linked to hypertension risk, but prior studies have not accounted for the potential influence of reproductive history or informative censoring. We examined how accounting for gravidity and informative censoring impacts the association between pregnancy loss and the five-year incident hypertension risk.

Methods: This population-based retrospective cohort study used administrative health data from British Columbia, Canada (1994–2016). Participants were nulliparous women (15–49 years) with a recorded pregnancy and no prior hypertension. Pregnancy loss (miscarriage/stillbirth) was identified via ICD codes. We used inverse probability of treatment and censoring weights to account for confounding and informative censoring. Time to incident hypertension was estimated using Weibull accelerated failure time models under three analytic strategies: (1) gravidity excluded from weighting/outcome models; (2) gravidity in the treatment weighting model only; and (3) gravidity in both the weighting and outcome models.

Results: Among 309,608 pregnancies (27,044 losses), losses were linked to older age, higher BMI, and higher gravidity. Without accounting for gravidity, pregnancy loss was associated with a 15% shorter time to hypertension (Time Ratio [TR] 0.85, 95% CI 0.80, 0.90). When gravidity was included in the treatment weighting model only, pregnancy loss remained associated with earlier hypertension onset (TR 0.91, 95% CI 0.86, 0.97), though this association was attenuated after additionally accounting for informative censoring (TR 0.96, 95% CI 0.90, 1.03). When gravidity was included in both the weighting and outcome models, pregnancy loss was no longer associated with hypertension (TR 0.95, 95% CI 0.90, 1.02).

Conclusion: The observed association between pregnancy loss and earlier hypertension may largely be driven by reproductive history and informative censoring. Future studies must explicitly account for these factors to avoid biased inference.

Pregnancy outcomes

HIV Status And Cardiometabolic Health During Pregnancy: A Cross-Sectional Analysis From A Prospective Southeast US Based Cohort Danielle Carson*, Danielle Carson, Lauren Collins, Christina Mehta, Seble Kassaye, Aadia Rana, Daniel Westreich, Elizabeth Topper, Maria Alcaide, Anandi Sheth, Angela Bengtson,

Cardiometabolic complications during pregnancy have increased in the past decade and pose heightened risks for women with HIV (WWH), who face compounded vulnerabilities from chronic inflammation, antiretroviral therapy (ART) exposure, and intersecting health disparities. We conducted a cross-sectional analysis of baseline data from pregnant participants at enrollment into STAR. We assessed associations between HIV status and cardiometabolic indicators (blood pressure, glucose, HbA1c, lipids) using linear regression and prevalent conditions (chronic hypertension (BP ≥140 or ≥90, medication use, or self-report diagnosis <20 weeks), hypertension in pregnancy (BP ≥140 or ≥90, medication use, or self-report diagnosis ≥20 weeks), type 2 diabetes (HgbA1c ≥6.5% or FBG ≥126 mg/dL, medication use, or self-report diagnosis < 24 weeks), and gestational diabetes (self-report diagnosis or study ascertainment)) using log-binomial regression. Prevalence was also examined overall and stratified by race and age group. Among 119 pregnant participants (80 WWH, 39 women without HIV (WWoH)), characteristics were: 73% identified as Non-Hispanic Black, median age 30.6 years, and 55% were obese, and most participants were multiparous, with 68% reporting two or more prior pregnancies. WWH vs WWoH had higher mean systolic blood pressure (112.6 vs 112.5 mmHg), diastolic blood pressure (70.3 vs 63.0 mmHg) and glucose levels (83.0 vs 75.8 mg/dL) but lower total (209.0 vs 231.0 mg/dL), HDL (68.0 vs 69.7 mg/dL), and LDL cholesterol (12.6 vs 131.7 mg/dL). Chronic hypertension was more prevalent among WWH (20% vs 8%, PR: 2.60, 95% CI: 0.81, 8.40), as was hypertension in pregnancy (15% vs 8%, PR: 1.95, 95% CI: 0.58, 6.51) and type 2 diabetes (13% vs 8%, PR: 1.65, 95% CI: 0.47, 5.57), while gestational diabetes was more prevalent among WWoH (4% vs 10%, PR: 0.37, 95% CI: 0.09, 1.55). Although overall prevalence ratios were higher among WWH, stratified analyses showed heterogeneity by age and race, with some older strata exhibiting high prevalence regardless of HIV status. These findings highlight substantial cardiometabolic vulnerability during pregnancy and the need for longitudinal follow up to assess age and race specific impacts of HIV.

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Pregnancy outcomes

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Background: Pregnancy loss is linked to hypertension risk, but prior studies have not accounted for the potential influence of reproductive history or informative censoring. We examined how accounting for gravidity and informative censoring impacts the association between pregnancy loss and the five-year incident hypertension risk.

Methods: This population-based retrospective cohort study used administrative health data from British Columbia, Canada (1994–2016). Participants were nulliparous women (15–49 years) with a recorded pregnancy and no prior hypertension. Pregnancy loss (miscarriage/stillbirth) was identified via ICD codes. We used inverse probability of treatment and censoring weights to account for confounding and informative censoring. Time to incident hypertension was estimated using Weibull accelerated failure time models under three analytic strategies: (1) gravidity excluded from weighting/outcome models; (2) gravidity in the treatment weighting model only; and (3) gravidity in both the weighting and outcome models.

Results: Among 309,608 pregnancies (27,044 losses), losses were linked to older age, higher BMI, and higher gravidity. Without accounting for gravidity, pregnancy loss was associated with a 15% shorter time to hypertension (Time Ratio [TR] 0.85, 95% CI 0.80, 0.90). When gravidity was included in the treatment weighting model only, pregnancy loss remained associated with earlier hypertension onset (TR 0.91, 95% CI 0.86, 0.97), though this association was attenuated after additionally accounting for informative censoring (TR 0.96, 95% CI 0.90, 1.03). When gravidity was included in both the weighting and outcome models, pregnancy loss was no longer associated with hypertension (TR 0.95, 95% CI 0.90, 1.02).

Conclusion: The observed association between pregnancy loss and earlier hypertension may largely be driven by reproductive history and informative censoring. Future studies must explicitly account for these factors to avoid biased inference.

Social determinants of health

Access to Maternal Care, Broadband Infrastructure, and Prenatal Care: A County-level Analysis in the United States Andrew Williams*, Andrew Williams, Rylee Bergeron, Maggie Thorsen, Corey Smith,

Background: Many regions in the United States lack access to maternity care services. Internet access may help overcome barriers to prenatal care (PNC). This ecologic analysis examines the association between maternal care availability and PNC, and the potential effect modification of internet infrastructure and rurality.

Methods: We used county-level data (n=3140) from the Federal Communications Commission's Connect2Health. Early PNC was the percent of births with first trimester PNC in a county (continuous). Maternal care availability was categorized into 4 access levels: full, moderate, low, and no access. County-level broadband investment in U.S. dollars and percentage of residents with broadband access were categorized into sample-based quartiles. Rurality was the percent population residing in a rural block group within a county (sample-based tertiles; urban, moderate rural, rural). Linear regression models estimated the association between Maternal Care Availability and Early PNC, adjusted for county-level sociodemographic variables, rurality, and broadband factors. Models were fit overall, and by rurality to examine potential effect modification.

Results: In overall analyses, broadband reduced gaps in early PNC rates. Prior to adjusting for broadband, compared to areas with full access, counties with no access had 1.2% (95% CI: -1.77, -0.58) lower rates of early PNC. After adjusting for broadband, counties with no access had a 0.7% (95% CI: -1.34, -0.12) lower rate of early PNC. Stratified by rurality, there was no difference in early PNC among no access counties for any rurality strata, or among the most rural counties. Yet low access counties had 2-4% lower early PNC rates in the more urban counties.

Discussion: Further investment in broadband internet in areas with limited access to healthcare may reduce barriers to PNC. However, technological advancements cannot fully address the lack of clinic space to obtain PNC in both urban and rural communities.

Social determinants of health

Life-course Trajectories of Neighborhood Deprivation and Cognitive Consequences in Midlife: The Bogalusa Heart Study Eunsun Gill*, Eunsun Gill, Jeanette Gustat, Katherine Theall, Dohyeong Kim, Owen Carmichael, Soo Jung Kang, Ileana De Anda-Duran, Lydia Bazzano, Camilo Fernandez, Richard MacLehose, David Libon, Emily Harville,

Introduction: Neighborhood socioeconomic deprivation contributes to cognitive function (CF) in middle-aged and older adults, yet life-course and longitudinal patterns remain understudied. We examined associations of cumulative and trajectory-based Area Deprivation Index (ADI) with midlife CF in the Bogalusa Heart Study.

Methods: We analyzed 1,052 adults (61% White, 39% Black; mean age at CF: 48±5.3). Residential addresses (1974–2016) were geocoded and linked to 17 census-based indicators. ADI was derived using weighted principal component analysis, with census/American Community Survey data (1990, 2000, 2006–2010, and 2013–2017) matched to address and year. Latent class growth curve models identified ADI trajectories, and cumulative ADI was estimated using the trapezoidal method. CF domains were age- and sex-standardized. Linear regression models estimated associations of cumulative and trajectory-based ADI with CF, adjusting for race, sex, parental education, adult education, and income. Multiple imputation was used to adjust for bias due to missing at random variables.

Results: Three ADI trajectories were identified: high-steady, middle-steady, and low-to-moderate increasing deprivation. Compared with the low-to-moderate increasing deprivation, high- and middle-steady deprivation had lower global CF (β= –0.36 [95% CI: –0.54, –0.18] and –0.23 [–0.41, –0.05]) and poorer verbal episodic memory and attention. The largest differences were observed in working memory (high: –0.47 [–0.71, –0.23]; middle: –0.30 [–0.50, –0.10]). No associations were found for processing speed. Cumulative ADI was inversely associated with global CF (–0.06 [–0.02, –0.10]), working memory (–0.07 [–0.13, –0.01]), and processing speed (–0.12 [–0.20, –0.04]), but not with verbal episodic memory.

Conclusions: Persistent high neighborhood deprivation and greater cumulative exposure across the life course were associated with poorer midlife CF, particularly working memory.

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Substance Use

Polysubstance use during pregnancy and preterm birth Xiaozhong Wen*, Xiaozhong Wen, Aye Moe, Hanchen Jiang, Porsche Lee,

Objective: We aimed to examine 1) the prevalence of polysubstance use during pregnancy, and 2) the association between polysubstance use during pregnancy and the risk of preterm birth.

Methods: We used data from 237,288 mothers enrolled in the U.S. Pregnancy Risk Assessment Monitoring System from 2016-2021. Postpartum mothers reported the status of their use of combustible cigarettes, electronic cigarettes (e-cigarettes), marijuana, alcohol, and drugs (e.g., amphetamines, methadone, Adderall, heroin, cocaine, tranquilizers, hallucinogens, sniffing gas) in the last 3 months of pregnancy. We created a correlation matrix to explore the patterns of polysubstances. We used multivariable logistic regression models to estimate the associations between the different polysubstance use groups during pregnancy with preterm birth, adjusting for socio-demographic and pregnancy-related confounders.

Results: The three most prevalent substances used during pregnancy were alcohol (9.35%), cigarettes (7.11%), and marijuana (4.84%). The highly correlated substance combinations were cigarettes and e-cigarettes (correlation coefficient r=0.600), cigarettes and marijuana (r=0.553), cigarettes and amphetamines (r=0.595), cigarettes and methadone (r=0.620), e-cigarettes and methadone (r=.518), marijuana and amphetamines (r=0.635), Adderall and amphetamines (r=.636), and amphetamines and methadone (r=.689). The use of cigarettes and marijuana (confounder-adjusted odds ratio or aOR=1.59 [95% confidence intervention or CI, 1.29-1.95]; p-value <0.001) as well as the use of cigarettes and amphetamines (aOR=1.71 [95% CI, 1.18-2.48]; p-value=0.005) was associated with increased odds of preterm birth compared to non-users. Furthermore, the use of all three cigarettes, marijuana, and amphetamines was also significantly linked to preterm birth (aOR=1.73 [95% CI, 1.06-2.84]; p-value=0.029).

Conclusion: Co-use of cigarettes/marijuana and cigarettes/amphetamines is associated with preterm birth.

Substance Use

Prenatal cannabis use and birth outcomes: Evidence from a statewide population-based pregnancy cohort Ban Al-Sahab*, Ban Al-Sahab, Harish Neelam, Jean Kerver, Omayma Alshaarawy, Kipling Bohnert, Nigel Paneth,

Background: Evidence on prenatal cannabis effects based on biomarker-validated exposure in legalized settings is limited. We examined associations between prenatal cannabis use (PCU) and birth outcomes using objective toxicology measures in a representative pregnancy cohort in Michigan, a state with legalized recreational cannabis. **Methods**: Data are from singleton births in the Michigan Archive for Research in Child Health (MARCH) cohort that recruited pregnant women at first prenatal visit from 20 clinics (2017-2022). PCU was measured via self-reports and urine toxicology testing. Birth outcomes included birthweight (BW, grams), gestational age (GA, weeks), low birthweight (LBW<2500 grams), preterm birth (PTB<37 weeks) and small for gestational age (SGA<10th percentile). Poisson and linear regression models with robust standard errors estimated adjusted risk ratios (RR) and beta coefficients (β) along with 95% confidence intervals (CI), adjusting for sociodemographic factors, other prenatal substance use, and pre-pregnancy complications. **Results:** Among 839 participants, the weighted prevalence of PCU was 15.5%. PCU was negatively associated with all birth outcomes, except PTB, in crude analysis. After adjustment, associations were attenuated and no longer statistically significant (BW: β=-117.16, 95% CI: -241.77, 7.45; GA: β=-0.24, 95% CI: -0.66, 0.17; LBW: RR=1.53, 95%: 0.79, 2.96; PTB: RR=1.22, 95% CI: 0.69, 2.17; SGA: RR=1.74, 95% CI: 0.80, 3.78). When concurrent tobacco smoking and PCU were considered as the main exposures, women who used both substances had significantly higher risk of SGA (RR=3.13, 95% CI: 1.16-8.49) and lower BW (β =-207.07, 95% CI: -399.27, -14.87). **Conclusion:** While independent associations between PCU and adverse birth outcomes were attenuated after adjustment, the risk was significantly elevated for women who used both cannabis and tobacco during pregnancy. Findings underscore the need to screen for and address co-use in prenatal care.

Substance Use

Associations between maternal e-cigarette use during pregnancy and infant mortality in the first 6 months of life Xiaozhong Wen*, Xiaozhong Wen, Chan Li, Jennifer Chen, Alexia Pezzino, Aaron Fanti, Bhavika Garg,

Background: Electronic cigarettes (e-cigarettes) have been increasingly used, while combustible cigarettes have been decreasingly used among pregnant people, partially due to the harm reduction perception.

Objectives: We aimed to investigate the impact of maternal e-cigarette use on infant mortality.

Methods: We analyzed secondary data from the U.S. Pregnancy Risk Assessment Monitoring System (PRAMS, 2016-2021, N=233,642). Mothers were stratified into 4 groups based on self-reported e-cigarette and cigarette use status during the last 3 months of pregnancy: (exclusive) e-cigarette users, (exclusive) combustible cigarette users, dual-users of e-cigarettes and cigarettes, and non-users. Infant deaths up to 6 months of age were obtained from questionnaire surveys. We used multivariable logistic regression to examine the associations between maternal e-cigarette/cigarette use and infant mortality, as well as the mediation roles of two adverse birth outcomes (small-for-gestational-age [SGA] birth and preterm birth).

Results: The majority of mothers were non-users (91.1%) during late pregnancy, followed by cigarette users (7.4%), dual users (0.8%), and e-cigarette users (0.7%). Cigarette users (0.87%; confounder-adjusted odds ratio [aOR]=1.85 [95% confidence interval, 1.39-2.45]; p-value<0.001), but not e-cigarette users (0.54%; 1.38 [0.57-3.34]; p-value=0.482) or dual users (0.40%; 1.02 [0.39-2.68]; p-value=0.962), had a significantly higher infant mortality, compared with non-users (0.42%). The association between maternal cigarette use and infant mortality was partially mediated by SGA (aOR attenuated to 1.76 [1.28-2.41]; p-value<0.001) or preterm birth (aOR attenuated to 1.55 [1.15-2.08]; p-value=0.003).

Conclusion: In this U.S. cohort, exclusive cigarette use during late pregnancy is a risk factor for infant mortality, which is partially explained by smoking-related SGA and preterm birth. Exclusive e-cigarette use or dual use is less likely to play a critical role in infant mortality.

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Women’s/Gynecologic Health

Racial and ethnic disparities in new-onset postpartum diabetes risk after varying glycemia levels during pregnancy: a population-based longitudinal cohort study Mounika Parimi*, Mounika Parimi, Cassondra Marshall, Amani Nuru-Jeter, Amanda Ngo, Mara Greenberg, Assiamira Ferrara, Yeyi Zhu,

Individuals with gestational diabetes mellitus (GDM) have 8-10 times higher risk of diabetes compared to those without GDM. Gestational glucose intolerance (GGI) – intermediate glycemia levels not meeting the GDM diagnostic threshold at oral glucose tolerance test (OGTT) – may also increase diabetes risk. How these associations vary by race and ethnicity and disaggregated subgroups remain unknown.

Leveraging a population-based cohort of 374,486 pregnancies in an integrated healthcare system in Northern California, we assessed associations of varying pregnancy glycemia levels with risk of postpartum diabetes, overall and by racial and ethnic groups, and disaggregated subgroups, using covariates-adjusted Cox regression models. Glycemia was categorized as normoglycemia, GGI with zero (GGI-0) or one (GGI-1) abnormal OGTT value, and GDM without (GDM-0) or with (GDM-1) abnormal fasting OGTT values.

With 2,026,810 person-years of follow-up, increasing pregnancy glycemia levels were associated with higher diabetes risk compared to normoglycemia [average adjusted HR (95% CI): 1.84 (1.54, 2.19), 4.46 (3.72, 5.34), 7.77 (6.65, 9.06), 13.30(11.59, 15.26)) for GGI-0, GGI-1, GDM-0, and GDM-1, respectively]. All racial and ethnic groups had a statistically significant elevated risk of diabetes after GGI-0, GGI-1, GDM-0, and GDM-1 compared to NGT. Black individuals had the highest risk of diabetes after GGI [GGI-0 and GGI-1 vs. NGT] 3.73 (2.87-4.85)], while White individuals had the highest risk after GDM [GDM-0 and GDM-1 vs. NGT] 15.35 (12.61,18.68)] compared to other racial and ethnic counterparts. While Asians overall did not have the highest diabetes risk after GDM or GGI, disaggregation revealed that Vietnamese had the highest risk for both compared to all other racial and ethnic groups and subgroups.

GGI is currently not clinically managed but confers significant postpartum diabetes risk. Variations in diabetes risk after GGI and GDM by race and ethnicity group and disaggregated subgroups highlight the need for tailored surveillance and intervention strategies.

Women’s/Gynecologic Health

Menstrual bleeding intensity as a determinant of PFAS concentrations in blood serum and endometrial tissue Joanna M. Marroquin*, Joanna M. Marroquin, Helen B. Chin, Jenna R. Krall, Karen Schliep, Leslie V. Farland, Morgan Reynolds, Kannan Kurunthachalam, Anna Z Pollack,

Background
Menstruation may be a pathway of per- and polyfluoroalkyl substances (PFAS) elimination. Studies show mixed results but have relied on serum measurements, which may not reflect levels at the uterus, as PFAS concentrations can vary by matrix.

Objectives

To evaluate associations between a daily diary-based measure of weighted menstrual bleeding intensity and PFAS concentrations measured in blood serum and eutopic endometrial tissue.

Methods
This analysis included 609 participants with blood and a subset of 425 with endometrial PFAS data from a prospective cohort evaluating incidence of endometriosis. They completed a daily menstrual diary for one menstrual cycle, reporting bleeding intensity as spotting, light, moderate, or heavy. A weighted mean bleeding intensity score was calculated based on that one cycle. Concentrations were quantified by high performance liquid chromatography-tandem mass spectrometry for PFDA, PFHxS, PFNA, PFOA, PFDoDA, PFHpA, PFOSA, and PFUnDA. PFAS were analyzed as log transformed continuous outcomes. Linear regression models were used to estimate associations between weighted bleeding intensity quartiles and individual PFAS, adjusting for age, body mass index, race and ethnicity, smoking, gravidity, and hormonal contraceptive use information collected at baseline.

Results
Mean bleeding days was 6.2 ± SD 4. Nearly 75% reported at least one heavy day of bleeding. Higher weighted bleeding intensity quartiles were associated with lower PFDA, PFHxS, PFNA, PFOA, and PFOS concentrations in blood and with lower PFHxS, PFNA, and PFOS concentrations in eutopic endometrial tissue.

Conclusions
Higher weighted mean bleeding intensity was associated with lower PFAS concentrations in serum and endometrial tissue. Measuring PFAS in endometrial tissue may address limitations of prior studies that focused on blood serum.

Women’s/Gynecologic Health

Beyond Adverse Pregnancy Outcomes: Capturing Subclinical Cardiometabolic Risk with Life’s Essential 8 Ellen Francis*, Ellen Francis, Shalin Patel, Anushka Pande, Alexa Freedman, Lauren Keenan-Devlin, Emily Barrett, Ann Borders, Gregory Miller, Shristi Rawal, Linda Ernst, Amy Crockett,

Importance: Cardiovascular health (CVH) during pregnancy may unmask latent metabolic vulnerability and provide an early indicator of long-term cardiometabolic disease risk. However, the prognostic value of the American Heart Association’s Life’s Essential 8 (LE8) framework during pregnancy remains uncertain.

Objective: To evaluate whether CVH measured during pregnancy using a modified Life’s Essential 8 (mLE8) score is associated with time to incident postpartum cardiometabolic disease.

Design: Prospective cohort study with electronic medical record (EMR) surveillance for 7 years postpartum (2017–2025). Adjusted accelerated time-to-failure models estimated the association of mLE8 with incident cardiometabolic conditions.

Setting: A single-center, population-based prenatal cohort recruited from a large academic medical system in South Carolina.

Participants: Singleton pregnancies among individuals aged 18 to 44 years without pre-existing diabetes or cardiovascular disease. Participants were predominantly low-income and racially and ethnically diverse.

Exposures: A 7-component mLE8 score assessed during pregnancy, incorporating hypertensive disorders of pregnancy (HDP), 50-g glucose tolerance test results, pre-pregnancy body mass index, smoking status, sleep adequacy, diet quality, and physical activity. Scores ranged from 0 to 100, with higher scores indicating more favorable CVH.

Main Outcomes and Measures: Incident postpartum cardiometabolic conditions captured through EMRs and classified as obesity, chronic hypertensive conditions, chronic metabolic conditions (e.g., dyslipidemia, impaired glucose regulation), and cardiovascular disease (CVD). Time to incident diagnosis was measured in days from delivery.

Results: Among 1,256 pregnancies (mean age, 25.0 [5.3] years), 310 incident cardiometabolic events occurred over a mean follow-up of 7.0 (1.7) years. Each 10-point higher mLE8 score was associated with a longer time to incident chronic hypertensive conditions (time ratio [TR], 1.36; 95% CI, 1.07–1.72) and chronic metabolic conditions (TR, 1.29; 95% CI, 1.11–1.49). Healthier HDP, glucose, BMI, and sleep scores were most strongly associated with delayed onset of cardiometabolic disease. Results were robust to sensitivity analyses excluding individuals who developed gestational diabetes or HDP.

Conclusions and Relevance: Better CVH during pregnancy was associated with a longer time to incident postpartum cardiometabolic conditions. Pregnancy-based CVH assessment may help identify individuals with elevated and emerging cardiometabolic risk who could benefit from early, targeted intervention and enhanced postpartum surveillance.

Women’s/Gynecologic Health

Infertility history and rate of mortality among Mexican women Leslie V. Farland*, Leslie V. Farland, William J. Degnan, Marion Brochier, Liliana Gomez-Flores-Ramos, Jorge E. Chavarro, Gregory Talavera, John M. Ruiz, Ellen C. Caniglia, Britton Trabert, Martin Lajous, Dalia Stern,

Background: Evidence suggests that infertility may serve as an early-life marker for mortality, however most research is among high-income non-Hispanic White women (NHWW). Therefore, our goal was to estimate the relationship of infertility to mortality among Hispanic women, who are 70% more likely to experience infertility compared NHWW.

Methods: We followed 90,561 women in the Mexican Teachers Cohort study from 2008-2019, who were 44y at baseline. Women with infertility were compared to parous women without infertility. Infertility diagnoses (fallopian tube, polycystic ovary syndrome (PCOS), ovulatory, endometriosis, uterine factor, or male factor) were analyzed separately. Mortality was ascertained via cross-linkage with national registries. Cox proportional hazard models adjusted for a priori confounders were used to estimate hazard ratios and 95% confidence intervals for all-cause and cause-specific mortality (cardiometabolic [CM], breast cancer [BC], gynecologic cancer [GC; ovarian, endometrial]).

Results: At baseline, 22% reported infertility. Over 10.6 years of follow-up, there were 1,541 deaths (377 CM, 139 BC, and 65 GC). Women with infertility had a 17% higher rate of all-cause mortality compared to parous women without infertility (95% CI: 1.04-1.32). Infertility was associated with a 46% increased rate of CM mortality (95% CI: 1.16-1.83) and a 2.66-fold increased rate of GC mortality (1.61-4.41). There was no association with BC mortality (HR 0.67, 95% CI: 0.42-1.08). Infertility attributed to PCOS (HR 1.45, 95% CI: 1.06-1.98), fallopian tube (HR 1.26, 95% CI: 0.94-1.67), ovulatory (HR 1.19, 95% CI: 0.89-1.59), and endometriosis (HR 1.19, 95% CI: 0.78-1.82) were positively associated with all-cause mortality, but some estimates were imprecise.

Conclusions: Infertility was associated with an increased rate of all-cause, CM, and GC mortality. PCOS, fallopian tube, ovulatory, and endometriosis-related infertility may individually confer an elevated rate of death.

Women’s/Gynecologic Health

Symptom Frequency and Patterns across the Menstrual Cycle: Insights from Mobile Logging Data in a U.S. Digital Cohort Sophia Werdin*, Sophia Werdin, Zifan Wang, Gowtham Asokan, Erin Dracup, Paola Bojorquez-Ramirez, Anne Marie Jukic, Jukka-Pekka Onnela, Michelle Williams, Russ Hauser, Brent Coull, Shruthi Mahalingaiah,

Background: Menstrual symptoms affect multiple body systems, can impact quality of life, and may signal underlying pathology. We analyzed mobile menstrual symptom logging data to assess symptom frequency and patterns across the menstrual cycle (MC) in a diverse U.S. cohort.

Methods: We analyzed data from 25,033 participants in the Apple Women’s Health Study enrolled between 11/2019 and 06/2025 who consented, completed relevant surveys, and logged at least one menstrual symptom. Restricting to cycles with matched monthly survey data, we examined symptom frequency and MC-related patterns by age, gynecologic condition, and hormone use, including latent class analysis to identify symptom clusters. Mixed-effects linear regression, adjusted for age and race/ethnicity, was used to assess associations of hormone use and gynecologic conditions with symptom frequency per cycle.

Results: Participants had a mean age of 32.7 years (standard deviation [SD] = 8.1), were predominantly non-Hispanic White (72.3%), and logged a mean of 6.8 cycles (SD = 8.8) and 25.7 symptoms (SD = 63.3). The most commonly logged symptoms were abdominal cramps (65%), fatigue (42%), and bloating (39%). The frequency of logging acne and nausea decreased with age, while logging of fatigue, headache, and night sweats increased. Symptom density followed a double-peak cyclic pattern, with the highest frequency during bleeding days and a smaller secondary peak in the late luteal phase. Gynecologic conditions such as endometriosis were associated with higher symptom frequency per cycle ($\beta = 0.32$, 95% confidence interval [CI] = 0.16-0.48), while hormonal contraceptive use showed no significant association.

Conclusion: Menstrual symptom logging data reveal distinct cyclic patterns and variation in symptom frequency and composition by age and gynecologic condition. Mobile application-based logging offers new opportunities to advance our understanding of menstrual physiology and health across the lifespan.

Women’s/Gynecologic Health

SARS-CoV-2 Infection and Asthma Exacerbations Among Pregnant Women with Asthma in South Carolina, 2020-2021 Aisha Alkandari*, Aisha Alkandari, Aisha Alkandari,

Background: The association between SARS-CoV-2 infection and asthma exacerbations among women with asthma during pregnancy is unclear. We evaluated this association and examined heterogeneity by race/ethnicity and residence.

Methods: We conducted a cohort study of 6,005 pregnancies (5,876 women) using the South Carolina COVID-19 Cohort Pregnancy Database (March 2020-December 2021). Asthma exacerbation was defined as an emergency department visit, intensive care unit admission, or inpatient hospitalization with an ICD-10 asthma diagnosis during pregnancy. We fit a trimester piecewise Cox model with race/ethnicity-specific baseline hazards, adjusting for maternal age, modified obstetric comorbidity index, education, pre-pregnancy body mass index, insurance, and calendar time, using a natural cubic spline to capture COVID-19 pandemic changes. Robust standard errors were used to account for multiple pregnancies per woman.

Results: Overall, 1,818 (30.3%) experienced asthma exacerbation. SARS-CoV-2 infection was not associated with asthma exacerbation overall (adjusted hazard ratio [aHR] 1.19, 95% CI 0.91-1.55), but the association varied by trimester (p=0.042). First trimester infection was associated with higher risk (aHR 2.57, 95% CI 1.09-6.05) compared with no infection, with no associations in later trimesters. Race/ethnicity modified the association (p=0.065), with higher risk among White infected in the first trimester (aHR 3.30, 95% CI 1.37-7.84) and Hispanic infected in the first (aHR 5.38, 95% CI 1.83-15.84) and second trimester (aHR 2.91, 95% CI 1.12-7.54), compared to uninfected pregnancies within the same trimester and race/ethnicity group.

Conclusion: Among pregnancies with asthma, SARS-CoV-2 infection early in gestation was associated with increased hazard of asthma exacerbation, with evidence of heterogeneity by race/ethnicity. Results may inform risk assessment during respiratory virus surges and point to early gestation as a key vulnerable window.

Women’s/Gynecologic Health

Menarche to Menopause: The impact of the reproductive lifespan on gynecological health

Iridian Guzman*, Mary Ingle, Iridian Guzman,

Background: A woman’s reproductive lifespan (age at menopause-age at menarche) is anchored within two significant physiological shifts. On average, women spend half their life in this phase and are susceptible to gynecological diseases. It remains unclear if reproductive lifespan length exacerbates the prevalence of these diseases. The aim of the menarche to menopause (M2M) study is to understand the impact of the reproductive lifespan on women’s health over time.

Methods: The M2M study included women (10-90 yrs.) with a documented age at menarche and 1> annual encounter between 2014-2024 within a large Midwestern Health System (n=341,216). Demographics, gynecological conditions, and comorbidities were extracted from electronic health records. Descriptive statistics for continuous variables are presented as means and standard deviations and counts and percentages are used to describe categorical and dichotomous variables. Ages were stratified in quartiles by birth year: Q1(1924-1959), Q2 (1960-1972), Q3 (1973-1985), and Q4 (1986-2013). Unadjusted logistic models (Odds ratio (OR), 95% confidence internals (CI)) determined associations between reproductive lifespan (>40, 38-40, 33-37, and <33 yrs.) with health outcomes.

Results: Women were mostly Non-Hispanic White (72%), never smokers (53%), with an average age of 45 yrs. Average age at menarche was 13 yrs., 55 yrs. for menopause, while the average reproductive lifespan was 43 yrs. Age at menarche was lower (12 yrs.) for women born between 1986-2013 (Q4) compared to others (p<.0001). Age at menopause decreased by 24 years from Q1 (1924-1959) to Q4 (p<.0001). Reproductive lifespan was shorter for younger women (Q4, 22 yrs.) compared to older women (Q1, 47 yrs.) (p<.0001). Most prevalent gynecological conditions were polycystic ovary syndrome (PCOS) (21%), amenorrhea (9%) & uterine fibroids (7%). Endometriosis (OR=11, 95%CI: 10,12), PCOS (OR=16, 95%CI:14,16) % adenomyosis (OR=15, 95%CI:12,18) were associated with shorter reproductive lifespans (p<.0001).

Conclusion: Age at menarche, menopause, and the reproductive lifespan have decreased significantly over time. M2M preliminary results suggest associations with gynecological outcomes. Further modeling is warranted to understand the impact of reduced reproductive lifespan on women’s health.

Women’s/Gynecologic Health

Beyond Adverse Pregnancy Outcomes: Capturing Subclinical Cardiometabolic Risk with Life’s Essential 8 Ellen Francis*, Ellen Francis, Shalin Patel, Anushka Pande, Alexa Freedman, Lauren Keenan-Devlin, Emily Barrett, Ann Borders, Gregory Miller, Shristi Rawal, Linda Ernst, Amy Crockett,

Importance: Cardiovascular health (CVH) during pregnancy may unmask latent metabolic vulnerability and provide an early indicator of long-term cardiometabolic disease risk. However, the prognostic value of the American Heart Association’s Life’s Essential 8 (LE8) framework during pregnancy remains uncertain.

Objective: To evaluate whether CVH measured during pregnancy using a modified Life’s Essential 8 (mLE8) score is associated with time to incident postpartum cardiometabolic disease.

Design: Prospective cohort study with electronic medical record (EMR) surveillance for 7 years postpartum (2017–2025). Adjusted accelerated time-to-failure models estimated the association of mLE8 with incident cardiometabolic conditions.

Setting: A single-center, population-based prenatal cohort recruited from a large academic medical system in South Carolina.

Participants: Singleton pregnancies among individuals aged 18 to 44 years without pre-existing diabetes or cardiovascular disease. Participants were predominantly low-income and racially and ethnically diverse.

Exposures: A 7-component mLE8 score assessed during pregnancy, incorporating hypertensive disorders of pregnancy (HDP), 50-g glucose tolerance test results, pre-pregnancy body mass index, smoking status, sleep adequacy, diet quality, and physical activity. Scores ranged from 0 to 100, with higher scores indicating more favorable CVH.

Main Outcomes and Measures: Incident postpartum cardiometabolic conditions captured through EMRs and classified as obesity, chronic hypertensive conditions, chronic metabolic conditions (e.g., dyslipidemia, impaired glucose regulation), and cardiovascular disease (CVD). Time to incident diagnosis was measured in days from delivery.

Results: Among 1,256 pregnancies (mean age, 25.0 [5.3] years), 310 incident cardiometabolic events occurred over a mean follow-up of 7.0 (1.7) years. Each 10-point higher mLE8 score was associated with a longer time to incident chronic hypertensive conditions (time ratio [TR], 1.36; 95% CI, 1.07–1.72) and chronic metabolic conditions (TR, 1.29; 95% CI, 1.11–1.49). Healthier HDP, glucose, BMI, and sleep scores were most strongly associated with delayed onset of cardiometabolic disease. Results were robust to sensitivity analyses excluding individuals who developed gestational diabetes or HDP.

Conclusions and Relevance: Better CVH during pregnancy was associated with a longer time to incident postpartum cardiometabolic conditions. Pregnancy-based CVH assessment may help identify individuals with elevated and emerging cardiometabolic risk who could benefit from early, targeted intervention and enhanced postpartum surveillance.

Women’s/Gynecologic Health

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Women’s/Gynecologic Health

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Conclusion: Age at menarche, menopause, and the reproductive lifespan have decreased significantly over time. M2M preliminary results suggest associations with gynecological outcomes. Further modeling is warranted to understand the impact of reduced reproductive lifespan on women’s health.

Women’s/Gynecologic Health

Infertility history and rate of mortality among Mexican women Leslie V. Farland*, Leslie V. Farland, William J. Degnan, Marion Brochier, Liliana Gomez-Flores-Ramos, Jorge E. Chavarro, Gregory Talavera, John M. Ruiz, Ellen C. Caniglia, Britton Trabert, Martin Lajous, Dalia Stern,

Background: Evidence suggests that infertility may serve as an early-life marker for mortality, however most research is among high-income non-Hispanic White women (NHWW). Therefore, our goal was to estimate the relationship of infertility to mortality among Hispanic women, who are 70% more likely to experience infertility compared NHWW.

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Conclusions: Infertility was associated with an increased rate of all-cause, CM, and GC mortality. PCOS, fallopian tube, ovulatory, and endometriosis-related infertility may individually confer an elevated rate of death.

Women’s/Gynecologic Health

Racial and ethnic disparities in new-onset postpartum diabetes risk after varying glycemia levels during pregnancy: a population-based longitudinal cohort study Mounika Parimi*, Mounika Parimi, Cassondra Marshall, Amani Nuru-Jeter, Amanda Ngo, Mara Greenberg, Assiamira Ferrara, Yeyi Zhu,

Individuals with gestational diabetes mellitus (GDM) have 8-10 times higher risk of diabetes compared to those without GDM. Gestational glucose intolerance (GGI) – intermediate glycemia levels not meeting the GDM diagnostic threshold at oral glucose tolerance test (OGTT) – may also increase diabetes risk. How these associations vary by race and ethnicity and disaggregated subgroups remain unknown.

Leveraging a population-based cohort of 374,486 pregnancies in an integrated healthcare system in Northern California, we assessed associations of varying pregnancy glycemia levels with risk of postpartum diabetes, overall and by racial and ethnic groups, and disaggregated subgroups, using covariates-adjusted Cox regression models. Glycemia was categorized as normoglycemia, GGI with zero (GGI-0) or one (GGI-1) abnormal OGTT value, and GDM without (GDM-0) or with (GDM-1) abnormal fasting OGTT values.

With 2,026,810 person-years of follow-up, increasing pregnancy glycemia levels were associated with higher diabetes risk compared to normoglycemia [average adjusted HR (95% CI): 1.84 (1.54, 2.19), 4.46 (3.72, 5.34), 7.77 (6.65, 9.06), 13.30(11.59, 15.26)) for GGI-0, GGI-1, GDM-0, and GDM-1, respectively]. All racial and ethnic groups had a statistically significant elevated risk of diabetes after GGI-0, GGI-1, GDM-0, and GDM-1 compared to NGT. Black individuals had the highest risk of diabetes after GGI [GGI-0 and GGI-1 vs. NGT] 3.73 (2.87-4.85)], while White individuals had the highest risk after GDM [GDM-0 and GDM-1 vs. NGT] 15.35 (12.61,18.68)] compared to other racial and ethnic counterparts. While Asians overall did not have the highest diabetes risk after GDM or GGI, disaggregation revealed that Vietnamese had the highest risk for both compared to all other racial and ethnic groups and subgroups.

GGI is currently not clinically managed but confers significant postpartum diabetes risk. Variations in diabetes risk after GGI and GDM by race and ethnicity group and disaggregated subgroups highlight the need for tailored surveillance and intervention strategies.

Women’s/Gynecologic Health

Menstrual bleeding intensity as a determinant of PFAS concentrations in blood serum and endometrial tissue Joanna M. Marroquin*, Joanna M. Marroquin, Helen B. Chin, Jenna R. Krall, Karen Schliep, Leslie V. Farland, Morgan Reynolds, Kannan Kurunthachalam, Anna Z Pollack,

Background
Menstruation may be a pathway of per- and polyfluoroalkyl substances (PFAS) elimination. Studies show mixed results but have relied on serum measurements, which may not reflect levels at the uterus, as PFAS concentrations can vary by matrix.

Objectives

To evaluate associations between a daily diary-based measure of weighted menstrual bleeding intensity and PFAS concentrations measured in blood serum and eutopic endometrial tissue.

Methods
This analysis included 609 participants with blood and a subset of 425 with endometrial PFAS data from a prospective cohort evaluating incidence of endometriosis. They completed a daily menstrual diary for one menstrual cycle, reporting bleeding intensity as spotting, light, moderate, or heavy. A weighted mean bleeding intensity score was calculated based on that one cycle. Concentrations were quantified by high performance liquid chromatography-tandem mass spectrometry for PFDA, PFHxS, PFNA, PFOA, PFDoDA, PFHpA, PFOSA, and PFUnDA. PFAS were analyzed as log transformed continuous outcomes. Linear regression models were used to estimate associations between weighted bleeding intensity quartiles and individual PFAS, adjusting for age, body mass index, race and ethnicity, smoking, gravidity, and hormonal contraceptive use information collected at baseline.

Results
Mean bleeding days was 6.2 ± SD 4. Nearly 75% reported at least one heavy day of bleeding. Higher weighted bleeding intensity quartiles were associated with lower PFDA, PFHxS, PFNA, PFOA, and PFOS concentrations in blood and with lower PFHxS, PFNA, and PFOS concentrations in eutopic endometrial tissue.

Conclusions
Higher weighted mean bleeding intensity was associated with lower PFAS concentrations in serum and endometrial tissue. Measuring PFAS in endometrial tissue may address limitations of prior studies that focused on blood serum.