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Women’s health

Maternal history of fibroids and uterine fibroid development in offspring in a prospective ultrasound study of Black/African American women Christine Langton* Quaker Harmon Dona Baird

Uterine fibroids are highly prevalent benign tumors of the uterine muscle. Fibroids are the leading indication for hysterectomy, and Black/African American women are disproportionally burdened. Family history of fibroids may be a risk factor for fibroid development, but results from prior studies have been mixed, and none utilized ultrasounds to prospectively assess fibroid incidence and growth.

We evaluated the association between maternal history of fibroids and fibroid development among self-identified Black/African American women aged 23-35 years in the Study of Environment, Lifestyle & Fibroids. For most participants, maternal fibroid history was gathered directly from their mothers (89%). A standardized ultrasound examination was conducted during 4 clinic visits over 5 years to detect fibroids ≥0.5 cm in diameter. We used Cox regression models to estimate hazard ratios (HRs) and 95% CIs for the association between maternal history of fibroids (any history as well as early onset – diagnosed before age 35) and incident fibroids. Fibroid growth was calculated as change in log-volume per 18 months for fibroids matched at successive visits. Both incidence and growth models were adjusted for maternal and participant factors.

Of 1,187 fibroid-free participants at enrollment, 424 participants (36%) had mothers with fibroids, 38% of whom had early onset. Over the study, 285 participants (24%) developed incident fibroids. Participants with maternal history of fibroids had higher risk of incident fibroids compared with those without (aHR=1.21; 95% CI: 0.96, 1.52), but the elevated risk was limited to those whose mothers had early onset (aHR=1.46; 95% CI: 1.07, 1.99 vs. aHR=1.03; 95% CI: 0.78, 1.36). Average fibroid growth differed little by maternal history of fibroids.

Results from this first ultrasound-based, prospective fibroid study support maternal history of fibroids as a risk factor for incident fibroids, particularly when the mother is diagnosed at an early age.

Gynecological health

Disordered Eating Behaviors during Childhood and Adolescence and Risk of Endometriosis: A Prospective Cohort Study Sarah Thornburgh* Ariella Tabaac Leslie Farland Holly Harris Kendrin Sonneville Alison Field Jorge Chavarro Stacey Missmer Audrey Gaskins

Objective: Disordered eating behaviors may impact the gynecologic health of adolescents; however, few studies have evaluated these associations. We examined the association between a history of engaging in disordered eating behaviors in childhood and adolescence and risk of endometriosis.

Methods: We included 12,617 female participants (aged 9-15 years at enrollment) from the prospective Growing Up Today Study (1996-2016). Physician diagnosed endometriosis and frequency of binge eating, laxative use, and vomiting over the past year were self-reported on repeated questionnaires during follow-up. Multivariable logistic regression models with generalized estimating equations were used to calculate adjusted odds ratios (aORs) and 95% confidence intervals (CIs) adjusting for smoking status, height, birth year, age at menarche, race, childhood body size, menstrual cycle characteristics, and other disordered eating behaviors while accounting for sibling clusters.

Results: Over 20 years of follow-up, we identified 306 incident cases of endometriosis (2.4%). A total of 7646 girls (61%) reported ever binge eating, 1722 (14%) reported ever vomiting to lose weight, and 1159 (9%) reported ever using laxatives to lose weight. The odds of endometriosis was 1.15 (95% CI 0.78, 1.70) times greater for girls who reported vomiting less than monthly and 2.36 (95% CI 1.30, 4.26) times greater for girls who reported vomiting at least monthly during follow-up, compared to girls who never reported vomiting. Binge eating and laxative use were not statistically significantly associated with endometriosis, although estimates were imprecise (aOR: 1.31 95% CI 0.44, 3.91 for girls with at least weekly binging and aOR: 0.68, 95% CI: 0.25, 1.90 for girls with at least monthly laxative use compared to girls never displaying those behaviors).

Conclusions: Girls with a history of vomiting to lose weight during childhood and adolescence may be at increased risk of endometriosis.

Women’s health

Agreement of preoperative diagnoses of endometriosis and adenomyosis for hysterectomy with the corresponding post-operative pathology report in a diverse U.S. population Joacy Gerard Mathias* Lauren G Anderson Natalie A Rivadeneira Michael J Green Whitney R Robinson

Introduction Endometriosis and adenomyosis are chronic, often painful, gynecological conditions. Despite improvements in diagnostic accuracy, these conditions can be difficult to diagnose without surgery. Among a diverse set of hysterectomy patients, we compared surgical findings from hysterectomy with pre-surgical indications for the surgery.

Methods Using electronic health record (EHR) data from 1,753 premenopausal hysterectomy patients (aged 18-44 years) treated in a large healthcare system between 2014 and 2017, we calculated agreement between the main indications for surgery noted in pre-surgical EHR notes versus surgical findings noted in the pathology report. We used chi-square tests to assess variation by race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic).

Results Among 132 patients with pre-surgical endometriosis indications, most (60.6%) did not have endometriosis findings in the pathology report (p=0.61 for racial/ethnic differences). Among 41 patients with pre-surgical adenomyosis indications, 31.7% did not have adenomyosis in the pathology report (p=0.01 for racial/ethnic differences). Of 242 cases with surgical findings of endometriosis, only 21.5% had it as a main indication before surgery (p=0.03 for racial/ethnic differences). Among 548 with adenomyosis findings, only 5.1% had adenomyosis as a main indication for their hysterectomies (p=0.27 for racial/ethnic differences).

Conclusion When using hysterectomy pathology reports as a gold standard, pre-surgical diagnoses of endometriosis and adenomyosis were frequently inaccurate.

Women’s health

Menstrual cycle characteristics throughout the reproductive lifespan and cognitive function in middle-aged women Diana Soria-Contreras* Jiaxuan Liu Rebecca Lawn Jan Shifren Alexandra Purdue-Smithe Francine Grodstein Karestan Koenen Jorge Chavarro Emily Oken

Menstrual cycle irregularities reflect alterations in the hypothalamic-pituitary-ovarian axis and signal an unbalanced hormonal milieu that may contribute to a later risk of cognitive impairment. We evaluated the associations between menstrual cycle characteristics during the reproductive years and cognitive function around midlife in the Nurses’ Health Study II.

We studied 13,751 nurses with data on cognitive function and menstrual cycle characteristics. We evaluated cognitive function in 2014-2019 with the Cogstate Brief Battery (composite z-scores capturing global cognition, psychomotor speed and attention, and learning and working memory). Cycle regularity (very regular [ref.], regular, irregular/no period) and length (≤25, 26-31 [ref.], ≥32 days/too irregular to estimate) were self-reported at baseline in 1989 for ages 14-17 and 18-22 and again in 1993 when the nurses were 28-48 y. We used linear regression models adjusted for age at the assessment of cycle characteristics, age at cognitive assessment, race and ethnicity, childhood and adulthood socioeconomic status, education, age at menarche, body fat and lifestyle factors at ages 14-17, 18-22 or 28-48, depending on the exposure.

Mean (SD) age at cognitive assessment was 60.8 (4.6) y. Women with irregular cycles at 28-48 y, vs. those with very regular cycles, had a lower z-score in the learning and working memory composite (β -0.04 [95% CI -0.08, 0.00]). We did not observe differences in cognitive function by cycle regularity at 14-17 or 18-22 y or by cycle length at 28-48 y. However, women with cycles ≤25 days at 18-22 y had a lower score in the learning and working memory composite (β -0.09 [-0.16, -0.03]).

Women with irregular cycles at 28-48 y and with cycles ≤25 days at 18-22 y had a lower performance in learning and working memory cognitive tasks. The associations were inconsistent across the lifespan but may support a role for reproductive hormones on cognition seen in other studies.

Gynecological health

Investigation of intrauterine exposures and adenomyosis risk using a population-based case-control study employing two control groups Mandy S. Hall* Holly R. Harris Sawsan As-Sanie Kristen Upson

Adenomyosis is characterized by the presence of endometrial tissue within the myometrium. As the gold standard for diagnosis requires hysterectomy, control selection for a case-control study is challenging. Adenomyosis risk may increase with disruption during fetal development. Yet, few studies have investigated this critical developmental window. We investigated intrauterine exposure to indicators of maternal stress including age, stillbirth history, and participant birth order and maternal cigarette smoking on adenomyosis risk. Among enrollees ages 18-59 of an integrated healthcare system in Washington, cases (n=386) had incident, pathology-confirmed adenomyosis diagnosed between 2001-2006. Two control groups were employed: hysterectomy controls (n=233) and randomly selected age-matched enrollees with an intact uterus (“population controls”, n=323). A family history questionnaire was mailed to collect data on early-life factors. We estimated ORs and 95% CIs using logistic regression, adjusting for age, reference year, maternal smoking, birthweight, and first-born status. Comparing cases to population controls, participants whose mothers were ages ≤19 (vs. ages 25-29) at participant’s birth had 80% increased adenomyosis risk (OR 1.8, 95% CI: 0.9, 3.5). Participants who were the fourth or later live birth (vs. first-born) had 40% increased adenomyosis risk (OR 1.4, 95% CI: 0.8, 2.3). In analyses using hysterectomy controls, these associations were attenuated. However, maternal stillbirth history before the participant’s birth was associated with twice the risk of adenomyosis (OR 2.1, 95% CI: 1.1, 3.8). Among never-smoking participants, we observed intrauterine exposure to cigarette smoking was associated with 30-40% increased adenomyosis risk (hysterectomy controls: OR 1.3, 95% CI: 0.7, 2.2; population controls: OR 1.4, 95% CI: 0.9, 2.3). Our findings suggest an altered intrauterine milieu may increase adenomyosis risk in adulthood and warrant further investigation.

Gender and sexual identity

Sexual orientation-related disparities in fetal and neonatal outcomes Payal Chakraborty* Colleen A. Reynolds Sarah McKetta Kodiak Soled Aimee K. Huang Brent Monseur Jae Downing Juno Obedin-Maliver A. Heather Eliassen Jorge E. Chavarro S. Bryn Austin Bethany Everett Sebastien Haneuse Brittany M. Charlton

Background: Sexual minority women (SMW; i.e., those with same-sex attractions/partners or identify as lesbian/gay/bisexual) experience structural inequities that result in adverse perinatal health. Compared to heterosexual women, SMW have less healthcare access, lower social support during pregnancy, and higher maternal stress. Thus, SMW may be at risk for adverse obstetrical outcomes.

Methods: We used data from the Nurses' Health Study II—a cohort of nurses across the US—restricted to those who had live births (N=63,001). Participants were asked about sexual orientation identity (current/past) and past same-sex attractions/partners. We examined disparities in self-reported preterm birth (PTB), low birthweight (LBW), and macrosomia among seven groups: (1) completely heterosexual (reference), (2) heterosexual, had past same-sex attractions/partners or identified previously as SMW, (3) heterosexual, missing data on past attractions/partners/self-identification (due to non-response), (4) heterosexual, missing data on past attractions/partners/self-identification (due to not receiving questions), (5) mostly heterosexual, (6) bisexual, and (7) lesbian. We used log-binomial models to estimate risk ratios (RRs) for each outcome and used weighted generalized estimating equations to account for multiple pregnancies per person over time and informative cluster sizes.

Results: Compared to completely heterosexual women, offspring born to parents in all SMW groups (groups 2, 5-7) had higher risks of PTB and LBW, but not macrosomia. RRs were statistically significant for lesbian women (RR[95%CI] for PTB: 1.47[1.03–2.09] and LBW: 1.56[1.01–2.41]), heterosexual women with past same-sex attractions/partners or SMW identification (PTB: 1.25[1.13–1.38], LBW: 1.35[1.21–1.52]), and both heterosexual missing data groups.

Conclusions: These findings highlight the need to examine health risks among SMW due to heterogeneity in identity and behavior, which meaningfully influences PTB/LBW risk.

Obstetric health

Rural residency, pregnancy complications, and acute healthcare utilization in the first 24 months' postpartum Katherine Ahrens* Kristin Palmsten Charlie Grantham Heather Lipkind Christina Ackerman-Banks

Objective: To estimate the rate of acute healthcare use among postpartum women in Maine by rurality of residence and pregnancy complications.

Methods: We used the Maine Health Data Organization's All Payer Claims Data to identify deliveries during 2007-2019 (n=123,125). We estimated the rate of hospitalizations and emergency department (ED) visits, separately, overall and by rurality of residence (based on ZIP code) and pregnancy complication for the first 24 months' postpartum. Pregnancy complications were prenatal depression, hypertensive disorders of pregnancy (HDP), and gestational diabetes (GDM). We used Poisson regression models and adjusted for potential confounders. Data were weighted to account for censoring before 24 months' postpartum.

Results: Approximately 4% of women had at least one hospitalization within 24 months' postpartum (mean monthly rate per 100 deliveries= 0.35). Adjusted rates were not different between rural and urban women; however, women with prenatal depression (adjusted rate ratio [aRR]=1.9; 95%CI 1.5, 2.5), HDP (aRR=1.4; 1.0, 2.0), and GDM (aRR=1.4; 0.9, 2.0) had higher rates than those without these conditions. Approximately 45% of women had at least one ED visit (treat and release) within 24 months' postpartum (mean monthly rate per 100 deliveries= 5.6). Adjusted ED rates were similar by rurality of residence; however, adjusted rates were higher for women living in small rural as compared with urban areas (aRR=1.3; 1.2, 1.4). Women with prenatal depression (aRR=1.8; 1.7, 1.9), HDP (aRR=1.1; 1.0, 1.2), and GDM (aRR=1.3; 1.2, 1.4) had higher ED rates than those without these conditions. Within each pregnancy condition, ED rates were highest among those living in small rural areas.

Conclusion: Measures may be needed to prevent acute health care encounters postpartum for women with common pregnancy conditions. In addition, efforts to identify why women living in small rural areas have higher rates of ED visits postpartum appear warranted.

Social determinants of health

Family Cash Transfers in Childhood and Maternal and Perinatal Outcomes later in life on an American Indian Reservation Brenda Bustos* Marcela Lopez Tim Bruckner

Background: In 1996, the introduction of a casino on a rural American Indian (AI) reservation led to large cash transfers to all AI members. Previous work finds adolescent health benefits within AI families after the cash transfer. Less is known about whether AI children in 1996, who were exposed to the cash transfer for longer durations of their childhood, show relatively improved maternal and perinatal outcomes once they reach childbearing age.

Objective: We used a "difference in difference" approach to compare maternal and perinatal outcomes among AI to non-AI mothers (who did not receive the cash transfer) as well as to AI mothers who were relatively older in 1996 and therefore were less exposed to the family cash transfer in childhood. We expected that a longer duration of cash transfer exposure during childhood would precede improved maternal and perinatal outcomes.

Method: We obtained birth records for three counties on this AI reservation, from the North Carolina Birth file, for 1997 to 2018 (n=6,368). We applied linear (for continuous outcomes) and logistic (binary outcomes) regression analysis to examine age and educational attainment at childbearing, maternal pre-pregnancy body mass index (BMI), birthweight, and preterm.

Results: Mean childbearing age (coef.= .13 years, 95% confidence interval [CI]: .05, .21) and educational attainment at childbearing are greater than expected among AI mothers more exposed to the cash transfer payments during their childhood. By contrast, maternal pre-pregnancy BMI (coef.= -.42 kg/m^2, 95%CI: -.69, -.15) and birthweight among normal weight births (coef.= -10.2 grams, 95%CI: -18.9, -1.4) are relatively lower. We observe no relation with preterm.

Discussion: In this rural setting, AI exposure to family cash transfers in childhood precede, older age of childbearing and increased educational attainment among mothers, lower pre-pregnancy BMI, and relatively lighter (i.e., closer to mean birthweight) infants.

Obstetric health

Disparities in Severe Maternal Morbidity and Maternal Mortality among Women at the Intersection of Physical Disability and Race or Ethnicity in the United States: Results from Nationally Representative Hospital Data Ilhom Akobirshoev* Anne Valentine Mike Vetter Willi Horner-Johnson Maytal Bach Monika Mitra

Introduction:

Previous research has found that both disabled women and women from minoritized racial and ethnic groups are at greater risk for severe maternal morbidity (SMM) and maternal mortality. Risks for SMM and maternal mortality could be greater in women who have both a disability and belong to a minoritized racial or ethnic group. Therefore, this study examined SMM and maternal mortality risk at the intersection of physical disability and race or ethnicity.

Methods:

We conducted a retrospective cohort study of Nationwide Inpatient Sample delivery hospitalizations from 2004-2019 in Healthcare Cost and Utilization Project data. We identified physical disability using ICD-9/10 codes established in previous studies. We used modified Poisson regressions to obtain covariate-adjusted risk ratios (RR) and 95% confidence intervals (CI) for SMM and maternal mortality in non-Latinx (NL) White women with physical disabilities, in NL Black women with and without physical disabilities, and in Latinas with and without physical disabilities compared to a reference group of NL White women without physical disabilities.

Population Studied:

The final analytical sample included 9,688,710 women who gave birth during the study period, including 5,721,674 NL White women with no physical disabilities (reference group), 20,073 NL White women with physical disabilities (cohort 1), 1,520,434 NL Black women with no physical disabilities (cohort 2), 4,354 NL Black women with physical disability (cohort 3), 2,418,058 Latina with no physical disabilities (cohort 4), and 4,117 Latina with physical disabilities (cohort 5).

Results:

After adjusting for sociodemographic and hospital characteristics, the risk for SMM and maternal mortality for women with physical disabilities who were Black or Latina was compounded, with adjusted risk ratios (SMM: RR=6.28: 95%CI=5.79-6.82 for Black, 6.14: 5.60-6.73 for Latina; Maternal mortality: 76.4: 57.8-100.9 for Black, 84.3: 63.7-111.5 for Latina) more than the sum of the risk ratios for disability alone (SMM: 4.26: 4.04-4.49, maternal mortality: 62.1: 51.5-74.8) and, respectively, Black race (SMM: 1.70: 1.66-1.73, maternal mortality: 1.74: 1.52-2.00), and Latinx ethnicity (SMM: 1.20: 1.17-1.23, maternal mortality: 0.79: 0.67-0.93), alone.

Conclusions:

Women with physical disabilities, especially Black and Latinx women are at extremely high risk for SMM and especially for Maternal Mortality. The risk of SMM and Maternal Mortality associated with both having a physical disability and belonging to a minoritized racial or ethnic community is compounded. It is critical to understand what pathways/mechanism contribute to these disparities among women with physical disabilities from communities of color. For example, by looking at the

role of structural ablism and structural racism such as the explicit/implicit biases towards disability community and towards minoritized populations. There is also an urgent need to understand the cumulative burden of a lifetime experience of ableism and racism, including stressful life events, and other social determinants of health to help develop policies and practices to eliminate them.

Implications for Policy or Practice:

Policy actions might include: designate people with disabilities as Special Medically Underserved Population (SMUP) or “Health Disparity Population; incorporate standardized indicators of disability and types of disabilities, and needed accommodations into EHRS (e.g. Medicaid, Insurance); increase ratio of OB/GYNs of color; address bias among health professionals; introduce disability curricula in medical education.

Mental health

Neighborhood Racial Residential Segregation and Mental Health during Pregnancy Sylvia Badon* Wendy Dyer Alex Asera Huyun Dong Tess Baker Nerissa Nance Kiarri Kershaw Charles Quesenberry Kelly Young-Wolff Mibhali Bhalala Kathryn Erickson-Ridout Lyndsay Avalos

The impact of social, physical, and socioeconomic contexts of residing in segregated neighborhoods on mental health is unclear. This study assessed the influence of racial residential segregation on prenatal mental health among Asian/Pacific Islander, Black, and Hispanic individuals. We used data for 125,341 pregnancies in the Kaiser Permanente Northern California healthcare system (2014-2019). Race and ethnicity (self-reported), address, and prenatal depression and anxiety diagnoses were extracted from electronic health records. We used the local Getis-Ord Gi* statistic in each race and ethnicity group as a measure of neighborhood racial residential segregation [low (1.96)] and regression models stratified by race and ethnicity to estimate associations. Depression and anxiety diagnoses were highest in Black (18%) and Hispanic (13-14%) groups, and lower in Asian/Pacific Islanders (6-7%). Asian/Pacific Islander (40% vs 32%) and Black individuals (43% vs 23%) were more likely to live in neighborhoods with high vs low segregation, while Hispanic individuals were equally likely (35% vs 34%). In Black individuals, high segregation was associated with greater odds of depression (aOR=1.25; 95%CI: 1.10,1.42) and anxiety (aOR=1.14; 95%CI: 1.00,1.29) during pregnancy. In Asian/Pacific Islander and Hispanic individuals, high segregation was associated with lower odds of depression (aOR=0.76; 95%CI: 0.70,0.84 and aOR=0.88; 95%CI: 0.82,0.94, respectively) and anxiety (aOR=0.81; 95%CI: 0.74,0.88 and aOR=0.88; 95%CI: 0.82,0.93, respectively) during pregnancy. The demonstrated associations between racial residential segregation and worse prenatal mental health for Black individuals, but better mental health for Asian/Pacific Islander and Hispanic individuals may reflect different drivers of segregation by race and ethnicity. Further, findings suggest policies reducing segregation and its impacts may improve mental health in pregnant Black individuals.

Child health and development

Autism and Attention Deficit Hyperactivity Disorder in children born after subfertility and fertility treatment in England: evidence from linked primary care and fertility register records Claire Carson* Brooke Hewitson Yangmei Li Chun Hei Kwok Maria A Quigley Jennifer J Kurinczuk

Background: Around 1 in 6 couples experience difficulty conceiving, and the use of Assisted Reproductive Technologies (ART) such as In Vitro Fertilisation (IVF) and Intracytoplasmic Sperm Injection (ICSI) continues to increase globally. While ART babies are generally healthy, concerns persist about adverse outcomes including neurodevelopmental conditions such as Autism and Attention Deficit Hyperactivity Disorder (ADHD).

Methods: A linked dataset combined family doctor and hospital records from the Clinical Practice Research Datalink and details of ART cycles from the Human Fertilisation and Embryology Authority (HFEA) register. Singletons born in England between 1992 and 2017 were grouped by conception history, based on mother's records. Autism and ADHD were identified from the children's diagnosis and prescription records. Cox proportional hazard models were used to estimate hazard ratios (HRs), adjusted for sociodemographic factors.

Results: 410,810 mother-baby pairs were included: 93% of the children were born to mothers with no recorded fertility problems (reference), 4.8% after untreated subfertility, and 2.2% following fertility treatments, including 1.3% after IVF/ICSI. For Autism, adjusted HRs were 1.20 (95% confidence interval: 1.05, 1.37) in the subfertile group, 1.21 (95%CI: 0.94, 1.56) for any fertility treatment and 1.21 (95%CI: 0.92, 1.58) in IVF/ICSI. For ADHD, there was no evidence of an increase in the subfertile group (adj HR 1.07 (0.92, 1.25), but treatment groups displayed increased HRs (adj HR 1.42 (1.07, 1.87) for any treatment and 1.35 (0.98, 1.85) for IVF/ICSI specifically).

Conclusions: Children born after subfertility were more likely to have an Autism diagnosis than those born to women with no recorded fertility problems, while IVF/ICSI babies had a similar but not statistically significant risk. ADHD was higher in those born after any ART, suggesting an association with treatment not explained by underlying parental subfertility.

Substance Use

Impact of perinatal opioid exposure on childhood depression in a matched cohort analysis

Monique Hedderson* Sam Pimental Michael Kuzniewicz Cynthia Campbell Lena Sun Sandra Comer

Opioid use is at epidemic proportions but the long-term impact of prenatal opioid exposure (POE) on pediatric mental health is largely unknown. It is critical to disentangle confounding factors such as neighborhood deprivation and maternal mental health when examining the long-term effects on prenatal exposure on child health. We measured the impact of POE on risk of depression during childhood accounting for confounding factors and differential follow-up time.

We conducted a matched cohort study using infants born between 2010-2019 in the Kaiser Permanente Northern California integrated health care delivery system with a median follow up time of 7.0 years. POE was identified via pharmacy records, urine drug screens, and chart review. Child depression diagnosis was based on ICD codes. A 15% sample of the unexposed cohort was used for risk modeling, leaving 85% for matching. Each infant with POE was matched to 5 unexposed infants using cardinality matching. Risk differences and Cox coefficients were computed. Stratified multivariate models adjusted for indicators for maternal history of ADHD and depression, child sex, gestational hypertension, and placenta previa.

A total of 3,266 matched sets were constructed, each with one exposed subject and five unexposed subjects chosen from an initial pool of 293,309. Matching balanced all baseline variables within 0.1 standard deviations, and balance tests failed to detect difference in 97% of variables. 0.3% of exposed infants had a depression diagnosis, versus 0.1% in the matched unexposed. The POE risk difference (p=0.001) and the hazard ratio [HR] were significant [HR 17.8 [95% CI: 2.1- 152.7]].

While our sample size was limited, after matching on risk factors for developmental and behavioral problems, infants with POE were at higher risk for developing depression in childhood. Infants exposed to opioids prenatally may need to be screened for depression in early childhood.

Child health and development

Pediatric migraine and risk of young adult depression and anxiety in the Growing Up Today Study Holly Crowe* Alexandra Purdue-Smith Kathryn Rexrode Janet Rich-Edwards

Migraine is the fifth most prevalent childhood chronic condition (8%) and is linked to impaired social functioning, absenteeism, and reduced quality of life. Migraine and anxiety/depression share common risk factors (e.g., genetics) and are highly co-morbid in adults. However, no longitudinal studies have examined pediatric migraine and risk of anxiety/depression in young adulthood. We examined the association between physician-diagnosed migraine before 20 years of age and 5-year risk of incident physician-diagnosed anxiety and depression in the prospective Growing Up Today Study participants aged 19-25 (n=3,357). We ascertained migraine diagnosis prior to 2011 and depression and anxiety diagnosis between 2011 and 2016 from the GUTS 2016 questionnaire, excluding individuals with a prior history of depression or anxiety. We used log-binomial regression to compute risk ratios (RR) and 95% confidence intervals to estimate the association between pediatric migraine and risk of incident mental health conditions. The overall prevalence of migraine in the cohort was 8% (males: 3%, females: 12%). Nine percent of participants reported incident anxiety (males: 5%, females 11%) and 7% reported incident depression (males: 5%, females: 8%). After adjusting for age and sex, individuals with a diagnosis of migraine prior to 20 years of age had nearly double the risk of developing depression (RR: 1.9, 95% CI 1.3-2.8) and 60% greater risk of developing anxiety (RR: 1.6, 95% CI 1.1-2.3) compared to children and young adults who were not diagnosed with migraine. We were unable to stratify these findings by sex due to the relative rarity of migraines among males. Our findings suggest that young migraineurs are more likely to develop depression or anxiety in early adulthood than young people who do not experience migraine. Young adults with a history of pediatric migraine may benefit from increased screening for depression and anxiety.

Mental health

Delayed high school start times impact depression symptoms: heterogeneous effects in a natural experiment Ekaterina Sadikova* Rachel Widome Elise Robinson Izzuddin Aris Henning Tiemeier

Background

Initiatives to delay high school start times prolong weekday sleep. However, it is not clear if longer sleep alleviates depression symptoms and if the impact is homogeneous across adolescents.

Methods

Leveraging a natural experiment design, we examined the effect of a start time delay policy on the Kandel-Davies depression symptom scores in 2134 high school students (mean age 15.15 ± 0.35 years) from the Minneapolis metro area. Using the policy as an instrument, we estimated the impact of a sustained gain in weekday sleep on depressed mood. We used SuperLearner prediction and hierarchical *tmle* to detect if the policy's effect is heterogeneous and to evaluate if optimizing the delay's implementation to subgroups that benefit most results in lower depression symptoms relative to random or universal implementation.

Results

The delay policy reduced overall depression symptoms at 1 year (-1.98 points, 95%CI [-3.43,-0.53]) but not 2 years (-0.12 points, 95%CI [-0.27,0.03]) of follow-up. A sustained 1-hour gain in weekday sleep decreased overall depression symptoms by 1.18, 95%CI [-1.19,-1.16] points over 2 years. Motivation and sleep-related symptoms were most strongly affected. The impact of the delay was heterogeneous for low mood, hopelessness, and worry symptoms, with an expected reduction of 1.26 points, 95%CI [-1.93,-0.59] under optimal vs random delay implementation. Allowance for longer weekday morning sleep was particularly efficacious for older students with higher BMI and greater daily screen use, but optimization did not yield benefit relative to universal implementation (-0.13 points, 95%CI [-0.79,0.53]).

Conclusion

High school start time delay is likely to universally decrease motivation and sleep-related symptoms of depression in adolescents. Students who benefit most with respect to low mood, hopelessness, and worry are older, heavier, and spend more time on screens.

Environment/climate change

Exposure to high ambient temperatures across spermatogenesis and semen quality Carrie Nobles* Timothy Canty Lindsey Russo Neil Perkins Pauline Mendola Enrique Schisterman Sunni Mumford Richard Pilsner

Introduction: Spermatogenesis is uniquely susceptible to heat stress, including decrements in sperm count, morphologic differentiation, and acquisition of motility. Despite the anticipated global increase in high-temperature exposures, few clinical studies have evaluated the relationship of ambient temperatures with semen quality.

Methods: The Folic Acid and Zinc Supplementation Trial (FAZST) enrolled 2,015 men from couples seeking infertility treatment near Salt Lake City, Utah (2013-2017). Semen samples were collected at enrollment and at 2-, 4-, and 6-months and evaluated for sperm concentration, morphology, and motility. Ambient temperature was abstracted from weather stations and averaged across spermatogenesis and four susceptible windows of spermatogenesis: spermiation (0-10 days prior to ejaculation), spermiogenesis (11-32 days), meiosis I+II (33-58 days), and mitosis (59-74 days). Linear mixed models estimated differences in semen quality parameters during the warm (Apr. 1–Sept. 30) vs. cold (Oct. 1–Mar. 31) seasons. Sperm concentration and morphology were log-transformed and models adjusted for fine particulate matter and participant characteristics.

Results: Median (IQR) daily ambient temperature was 22.7 (16.0, 26.8)°C in the warm season and 4.6 (-0.2, 10.0)°C in the cold season. A 2°C increase in ambient temperature during spermatogenesis was associated with lower sperm concentration during the warm season (% difference -0.87, 95% CI -1.74, 0.02) and lower percent morphologically normal sperm in both the warm (% difference -0.99, 95% CI -2.40, -0.36) and cold (% difference -1.10, 95% CI -2.36, 0.17) seasons. Associations with sperm concentration were greatest in the warm season during spermiogenesis (% difference -1.04, 95% CI -1.96, -0.12) and meiosis (% difference -0.85, 95% CI -1.64, -0.04).

Discussion: Associations of high temperatures with decrements in semen quality may have important implications for men’s fertility in a changing climate.

Gynecological health

Blood lead concentrations and uterine fibroid incidence: A prospective study Mandy Hall*, Kristen Upson Mandy S. Hall Quaker E. Harmon Robert O. Wright Lauren A. Wise Ganesa Wegienka Ruth J. Geller Amelia K. Wesselink Birgit Claus Henn Janet E. Hall Erik J. Tokar Donna D. Baird Mandy Hall

Toxic metal lead exhibits mutagenic and hormonal properties that may contribute to the development of uterine fibroids (smooth muscle neoplasms). Prior human studies of lead and fibroids have yielded discrepant results. However, none were prospective, screened for fibroids by ultrasound, or accounted for progestin-only injectable contraceptive use and recent birth, factors associated with increased blood lead concentrations and decreased fibroid incidence. We investigated the association between blood lead concentrations and fibroid incidence in the Study of Environment, Lifestyle & Fibroids, a prospective cohort study of 1,693 Black women ages 23-35 years in the Detroit, Michigan area. Participants underwent transvaginal ultrasound at baseline and every 20 months for 5 years to detect fibroids ≥0.5cm in diameter. Baseline whole blood lead concentrations were measured using inductively coupled plasma-mass spectrometry-triple quadrupole. Among 1,215 fibroid-free participants, we conducted Cox regression to estimate adjusted hazard ratios (aHRs) and 95%CIs for the association between quartiles of lead and fibroid incidence, adjusting for time-varying factors of parity, years since last birth, years since last depot medroxyprogesterone acetate (DMPA) use, body mass index, smoking, education, and blood cadmium concentrations. Median blood lead concentration was 0.47 µg/dl (IQR: 0.36-0.65). Select blood lead quartiles (Q2 and Q3) were associated with decreased fibroid incidence (vs. Q1) (Q2: aHR 0.87, 95%CI: 0.63-1.19; Q3: aHR 0.68, 95%CI: 0.48-0.97; Q4: aHR 0.94, 95%CI: 0.65-1.35). Sensitivity analyses excluding smokers, DMPA use in past 2 years, and birth in past 3 years, and restricting follow-up to the first 20-month visit yielded similar results. Our data suggest a possible non-linear association between blood lead concentrations and fibroid incidence. This work is a vital first step in a larger research program to evaluate metal mixtures and fibroid incidence.

Men’s health

Pre- and postnatal dioxin exposure and semen quality in young adulthood Deborah Kurz* Josef Lehner Katharina Hancke Raphael Peter Cornelia Weickert Katharina Penczynski Jon Genuneit Martin Wabitsch Stephanie Brandt Hermann Brenner Dietrich Rothenbacher Klaus Abraham

Introduction: Dioxin exposure in fetal life and early infancy may be harmful for the male reproductive system. We investigated the associations between early dioxin exposure and semen quality in young adulthood.

Methods: The Ulm Birth Cohort Study is a population based longitudinal birth-cohort study (recruited 11/2000-11/2001). Human milk was collected from lactating mothers 6 weeks postpartum and stored at -80 ^{0}C. Concentrations of polychlorinated dibenzo-p-dioxins (PCDDs), dibenzofurans (PCDFs), and biphenyls (PCBs) were measured by gas chromatography/mass spectrometry (GC-MS/MS). Semen provided by male offspring in 2021/22 was analyzed according to the 2010 WHO manual. Multivariable linear regression adjusted for covariates was used to analyze the associations of (1) dioxin concentrations in human milk (mainly reflecting prenatal exposure) and of (2) cumulative dioxin dose (concentration x duration of breastfeeding, mainly reflecting the exposure in infancy) with semen quality.

Results: Semen was available for n=98 males (age 20.4 ± 0.4 years; 86% were breastfed at 6 weeks). Median WHO_{2005}-PCDD/F+PCB-TEQ concentration was 0.516 pg/g milk (n=77 samples, IQR 0.296-0.715). In adjusted analyses, we found no associations of dioxin concentration or of cumulative dioxin dose with total sperm count, sperm concentration, and total progressive sperm count. Lower mean %-progressive motility was observed for higher dioxin concentrations: -11.8 in mean percentage points (95% confidence interval -20.3; -3.3), -0.2 (-8.6; 8.2), and -8.8 (-17.2; -0.5) for Q2, Q3, and Q4 vs Q1, respectively; for cumulative dioxin dose, the results are -11.2 (-20.0; -2.4), -4.3 (-13.1; 4.6) and -5.4 (-13.9; 3.2) for Q2, Q3 and Q4 vs Q1, respectively.

Conclusion: We found no consistent patterns between early dioxin exposure and relevant sperm quality parameters in adulthood.

Gynecological health

Menstrual bleeding heaviness and PFAS concentrations in endometrial tissue Joanna Marroquin* Jenna R. Krall Cherie Marfori Kristen Upson Vimailkumar Krishnamoorthi Kurunthachalam Kannan Anna Z Pollack

Background: Menstrual bleeding may be an excretion route for per-and polyfluoroalkyl substances (PFAS). We examined the association between menstrual bleeding heaviness and PFAS concentrations in eutopic endometrial tissue.

Methods: In the Investigating Mixtures of Pollutants and Endometriosis in Tissue Study, eutopic endometrial tissue was examined for PFAS concentrations by tandem mass spectrometry in 495 women aged 18-44 years who had gynecologic surgery from 2007-2009. Participants were asked if they experienced changes in menstrual bleeding (heaviness) in the past 12 months via questionnaire and at the last menstrual period (LMP) before surgery by menstrual diary. Heavy menses at LMP was defined as having greater than 3 days of heavy menstrual bleeding based on menstrual product pictogram diary. We conducted linear regression to evaluate the association between log PFAS concentrations and heavy menstrual bleeding at LMP and experiencing heavier menstrual bleeding within the past 12 months (yes or no) and corresponding 95% confidence intervals (CI), adjusting for age, body mass index and hormonal contraception.

Results: Median eutopic concentrations of PFOSA (0.12ng/g), PFHxS (0.65ng/g), PFOS (6.58ng/g), PFOA (1.93ng/g), and PFNA (0.58ng/g) were obtained. Heavy menstrual bleeding in the last 12 months was associated with a lower PFHxS (-26.58%, CI –44.51, -2.87%) and PFNA (-35.73%, CI –58.56, -0.28%). No association was seen for PFOSA, PFOA, and PFOS nor between heavy menstrual bleeding at LMP and PFAS concentrations.

Conclusion: These findings support chronic heavy menstrual bleeding as a route of PFAS excretion. However, an association was not observed when menstrual bleeding heaviness at LMP was characterized. Improved tools are needed to measure long-term menstrual bleeding heaviness.

Women’s health

Female orgasm frequency and time to pregnancy in pregnancy planners Julia Bond* Katharine White Amelia Wesselink Lauren Wise

Introduction: The evolutionary origin of the female orgasm has been a subject of intense scientific debate. One hypothesis is that female orgasm facilitates conception, though no research has directly evaluated the relationship between female orgasm and time to conception.

Methods: We used data from Pregnancy Study Online (PRESTO), a North American preconception cohort study of pregnancy planners (2013-2022). Self-identified female participants completed questionnaires at enrollment and were followed up every eight weeks for pregnancy status. Beginning in March 2021, we invited female PRESTO participants to complete an optional survey related to sexual health that included a question about orgasm frequency during sexual intercourse in the past 4 weeks. Participants in our analysis were residents of the United States or Canada, aged 21-45, attempting pregnancy without the use of fertility treatment, in a relationship with a male partner, had <2 menstrual cycles of pregnancy attempts at enrollment, and completed the sexual health questionnaire within 2 months of enrollment (N=575). We used fully conditional specification methods to impute missing data on exposures and covariates. We used proportional probabilities regression to calculate fecundability ratios (FRs) and 95% confidence intervals (CIs) comparing orgasm frequency and time to pregnancy, adjusting for prespecified confounders.

Results: Twelve percent of the sample reported that they rarely or never orgasmed, 13% reported <half the time, 16% reported half the time, 23% reported >half the time, and 37% reported almost always or always with corresponding FRs and 95% CIs, compared to those who reported never/rarely orgasming, of 0.88 (0.61, 1.25), 0.81 (0.58, 1.14), 0.88 (0.64, 1.20), and 1.07 (0.80, 1.42), respectively, after adjustment for confounders.

Conclusions: There was no consistent pattern between orgasm frequency and time to pregnancy.

COVID-19 Pandemic

Racial/Ethnic Differences in Correlates of Missed Pediatric Preventive Care due to the COVID-19 Pandemic: Results from the 2021 National Survey of Children's Health Maya Tabet* Russell Kirby Pamela Xaverius

Background: The COVID-19 pandemic has resulted in disruptions in medical care. Yet, information on the frequency and correlates of missed pediatric preventive care in the US is lacking.

Objectives: To examine the prevalence and correlates of missed preventive care due to the COVID-9 pandemic among US children (0-17 years), by race/ethnicity, and to examine whether missed preventive care was associated with hospital emergency room visits.

Methods: This cross-sectional study included 39,736 children from the 2021 National Survey of Children's Health, a nationally representative survey of children 0-17 years of age. Multivariable Poisson regression was conducted to ascertain weighted adjusted relative risks (RR) and 95% confidence intervals (CI) for associations under study. Predisposing, enabling, and need factors were examined, as guided by the Andersen behavioral model of health services use.

Results: More than one-fourth of children in the US (28.3%) have missed preventive check-ups due to the COVID-19 pandemic, the highest rates being among children (30.8%) and children of other racial groups (30.6%). Multivariable Poisson regression revealed that financial difficulty was associated with 34%-71% increased risk of missed preventive care among different racial/ethnic groups. Other factors associated with missed pediatric preventive care differed by racial/ethnic groups.

Conclusions: Findings of this study revealed racial/ethnic differences in missed pediatric preventive care among US children, the highest rates being among Hispanic children and children of other racial groups. Our findings are of concern, given the potential deleterious impacts of missed pediatric preventive care, and highlight predisposing, enabling, and need factors that may guide the design of targeted interventions to enhance pediatric preventive care among different racial/ethnic groups.

Child health and development

Assessing interruption of infant well-child visits and vaccination during the COVID-19 Pandemic – Pregnancy Risk Assessment Monitoring System, 2020 Ayeesha Sayyad* Regina Simeone Reena Oza-Frank Beatriz Salvesen von Essen Jessica Meeker Lauren Zapata Romeo Galang Sascha Ellington

The COVID-19 pandemic disrupted healthcare delivery, including routine infant health care such as vaccinations. We used data from the 2020 Pregnancy Risk Assessment Monitoring System to describe interruptions in infant well-child visits and vaccinations.

Our analysis included 11,879 women with a live birth during April to December 2020 who responded to a yes/no question that assessed cancellation or delay of well-child visits, and postponement of vaccination due to COVID-19. Weighted percentages were calculated for these infant care experiences. Adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) estimated associations of maternal race and ethnicity and income levels (percent federal poverty line (FPL)) with infant care experiences. Models were adjusted for maternal characteristics and infant low birth weight.

Overall, 7.3% of women reported having infant well-child visits canceled/delayed and 5.4% reported having infant vaccines postponed. Compared to non-Hispanic white women, American Indian/Alaska Native (aPR=1.8, CI: 1.1-3.0) and non-Hispanic Black (aPR=1.8, CI: 1.3-2.5) women were more likely to report having their infants' immunizations postponed. Compared to women with household incomes greater than twice the federal poverty line (FPL), women with household incomes at or below FPL and those at 101-200% FPL were more likely to report their infants' visits canceled/delayed (aPR=1.9, CI: 1.4-2.6 and aPR=1.4, CI: 1.1-2.0, respectively) and their infants' vaccines postponed (aPR=2.3, CI: 1.7-3.2 and aPR=1.6, CI: 1.1-2.4, respectively).

American Indian/Alaska Native women, non-Hispanic Black women, and those with lower income were more likely to report disruptions to their infant's routine healthcare during the early part of the COVID-19 pandemic. Efforts are needed to maintain essential, preventive infant health care services during public health emergencies and prevent inequitable disruptions in healthcare delivery.

Social determinants of health

Child Opportunity Index at birth and risk for developmental delay up to age 3 Diane Putnick* Erin Bell Jordan Tyris Akhgar Ghassabian Pauline Mendola Rajeshwari Sundaram Edwina Yeung

The Child Opportunity Index (COI) includes 29 social determinants of health, selected and weighted relative to adult life expectancy, mental and physical health, and social mobility. The COI has demonstrated ability to predict child hospitalizations and cardiometabolic health but remains to be explored with respect to child development.

This study prospectively explored how COI at birth related to children's developmental delays in 5,875 children from the Upstate KIDS cohort across New York state. Home addresses were extracted from birth certificates and linked to the COI 2.0 at the census tract level. The COI has three subdomains–education, health/environment, and social/economic–and was state-normed from 1-100. Mothers completed the Ages and Stages Questionnaire (ASQ) to measure probable developmental delays in 6 domains (total, fine and gross motor, communication, personal-social, and problem-solving skills) up to 7 times from 4-36 months of age.

On average, families lived in tracts with COI=64.27 (*SD*=24.16; range=1-100). Fewer than 10% of children had a probable delay. Unadjusted linear mixed models with logit link and repeated effect of child age suggested that 10-point higher COI and subdomains at birth was associated with a 2-9% reduction in the odds of developmental delay from 4-36 months (OR for total COI and total ASQ=.945, 95% CI=.922, .969). However, the total ASQ, fine motor, and gross motor models had stronger effects in children 18-36 months than younger. Associations weakened slightly when adjusting for child sex, fertility treatment, parity, plurality, insurance status, and maternal age, race/ethnicity, education, and employment status during pregnancy (adjusted OR for total COI and total ASQ=.962, 95% CI=.935, .991).

This study supports the Child Opportunity Index as a measure of social determinants of healthy child development, but this cohort was skewed toward higher COI and therefore results should be replicated in a more diverse sample.

Child health and development

Associations of Neighborhood Opportunity and Vulnerability with Incident Asthma Among U.S. Children in the ECHO cohorts Izzuddin Aris* Izzuddin Aris Wei Perng Dana Dabelea Amy Padula Akram Alshawabkeh Carmen Vélez-Vega Judy Aschner Carlos Camargo Tamara Sussman Anne Dunlop Amy Elliott Assiamira Ferrara Christine Joseph Anne Singh Carrie Breton Tina Hartert Ferdinand Cacho Margaret Karagas Barry Lester Nichole Kelly Jody Ganiban Su Chu Thomas O'Connor Rebecca Fry Gwendolyn Norman Leonardo Trasande Bibiana Restrepo Diane Gold Peter James Emily Oken

Background: Physical and social attributes of neighborhoods may promote or inhibit healthy child development. The extent to which these attributes play a role in the development of childhood asthma remains understudied.

Objective: To examine associations of neighborhood-level measures of opportunity and social vulnerability with asthma incidence rates in childhood.

Methods: We used residential address and parental report of physician-diagnosed asthma data obtained from 10,516 children participating in the nationwide Environmental influences on Child Health Outcomes (ECHO) program. We linked geocoded residential addresses at birth, infancy (median 1.4 years), and early childhood (median 4.7 years) to census-tract level Child Opportunity Index (ChOI) and Social Vulnerability Index (SVI). We followed children to the date of asthma diagnosis, date of last visit or loss to follow-up, or age 20 years. We used multilevel Poisson regression to estimate asthma incidence rate ratios (IRR) associated with ChOI or SVI, adjusting for family sociodemographic factors, parental asthma history, and prenatal characteristics.

Results: Overall, 23.4% of ECHO children lived in neighborhoods with very high (≥80th percentile, based on nationwide distributions) ChOI or very low (<20th percentile) SVI. We identified 2,452 incident asthma cases in 105,073 child-years of follow-up; median age at asthma diagnosis was 6.6 years. Compared with very low ChOI, high (60th–<80th percentile) and very high ChOI in infancy was associated with lower asthma incidence: adjusted IRR 0.82 (95% CI 0.71, 0.96) and 0.84 (95% CI 0.72, 0.98), respectively. Higher ChOI at birth and early childhood were also associated with lower asthma incidence but estimates were nonsignificant. However, SVI was not associated with asthma incidence.

Conclusion: Access to high levels of neighborhood opportunities in infancy, compared with very low neighborhood opportunities, are associated with lower asthma incidence in childhood.

Child health and development

Perinatal Correlates of Cardiovascular Health During Early Childhood: The Healthy Start Study Wei Perng* Izzuddin Aris Natalie Slopen Nolan Younoszai Valerie Swanson Noel Mueller Katherine Sauder Dana Dabelea

Background: The American Heart Association recently put forth an updated cardiovascular health (CVH), Life's Essential 8 (LE8), comprising 4 health factors (BMI, glucose, non-HDL cholesterol, blood pressure) and 4 behavioral factors (nicotine exposure, diet quality, physical activity, sleep duration). Few studies have applied LE8 in pediatric populations.

Objectives: To assess CVH among 305 participants aged 4-7 years in the Healthy Start cohort and identify perinatal correlates of early-life CVH.

Methods: First, we estimated prevalence of low, moderate, high, and optimal CVH based on LE8 criteria. Next, we used multivariable logistic regression to identify perinatal correlates of high or optimal CVH, followed by multivariable linear regression to examine associations of perinatal characteristics with continuous scores for overall CVH and the behavioral and health factors. Perinatal characteristics of interest included maternal sociodemographic factors (age, household income, education level, parity, race/ethnicity), prenatal behaviors (smoking, Healthy Eating Index [HEI] score, physical activity), metabolic traits (pre-pregnancy BMI, gestational weight gain, gestational diabetes), preterm delivery, birth size, and breastfeeding duration.

Results: No children had low or optimal CVH; 43.9% had high and 56.1% had moderate CVH. In multivariable analyses, maternal diet quality was the primary correlate of high CVH: $OR_{HEI > vs. \leq 57}$ =1.90 (1.12, 3.21). When CVH was assessed as a continuous score, key correlates were maternal education ($\beta_{college\ vs.\ high\ school}$=3.24 [0.71, 5.77]; $\beta_{graduate\ school\ vs.\ high\ school}$=3.10 [0.36, 5.84]) and diet quality ($\beta_{HEI > vs. \leq 57}$=2.26 [0.81, 3.72]); these findings were driven by associations of the perinatal characteristics with the behavioral factors.

Conclusions: At 4-7 years of age, no children had optimal CVH and less than half had high CVH. Prenatal diet quality is a potentially modifiable target to promote CVH during early childhood.

Pharmacoepidemiology

Association Between Benzodiazepine or Z-Hypnotic Use in Early Pregnancy and the Risk of Stillbirth, Preterm Birth, and Small for Gestational Age Lin-Chieh Meng* Chih-Wan Lin Yi-Chin Lin Shih-Tsung Huang Yi-Yung Chen Chi-Yung Shang Chia-Yi Wu K Arnold Chan Fei-Yuan Hsiao

Introduction: Maternal benzodiazepines (BZDs) and z-hypnotics use has been linked to adverse neonatal outcomes, including stillbirth, preterm birth, and small for gestational age (SGA), but most existing studies did not adequately control for potential confounders. This study thus aims to evaluate these associations using various methods to address potential confounders.

Methods: We conducted a nationwide cohort study using Taiwan's healthcare and birth certificate databases. Logistic regression models with propensity score (PS) fine stratification to control for potential confounders were used to examine the association between BZDs/z-hypnotics use during early (the first 20 weeks of) pregnancy and risk of stillbirth, preterm birth, and SGA. Odds ratios (ORs) and 95% confidence intervals (CIs) for these outcomes were reported. We also adopted confounding by indication control analyses, a sibling control study, and a paternal negative control design to further account for unmeasured confounders.

Results: The cohort included 2,882,292 pregnancies, with 2.6% (75,655) exposed to BZDs/z-hypnotics during early pregnancy. BZDs/z-hypnotics use was associated with increased risks of stillbirth, preterm birth, and SGA, with PS-weighted ORs of 1.19 [95% CI 1.10-1.28], 1.19 [1.16-1.23], and 1.16 [1.13-1.19], respectively. However, in models controlling for confounding by indication, these associations were attenuated. In the sibling controls study, BZDs/z-hypnotics use was associated with a small increase in the risk of SGA (aOR 1.13, 95% CI 1.06-1.20), but not with stillbirth or preterm birth. Similar findings were found in the paternal negative control design.

Conclusions: Our findings suggest that BZD/z-hypnotic use in early pregnancy was not significantly associated with increased risks of stillbirth and preterm birth when controlling for confounders. However, clinicians should be aware of the potential increased risk of SGA associated with maternal BZD/z-hypnotic use.

Birth defects

Metformin use in the first trimester and risk of congenital anomalies: emulating a target trial using real-world data Yu-Han Chiu* Krista Huybrechts Elisabetta Patorno Carolyn Cesta Brian Bateman Ellen Seely Miguel Hernán Sonia Hernández-Díaz

Background: Metformin is the first-line pharmacotherapy for type 2 diabetes, but the safety of metformin use in early pregnancy for women with type 2 diabetes is uncertain. We aimed to evaluate the teratogenic potential of metformin use in the first trimester in women with type 2 diabetes.

Methods: Using real-world data from a US healthcare claims database (2011-2020), we emulated a target trial of two antidiabetic strategies: 1) discontinue metformin and initiate insulin within 90 days of last menstrual period (LMP) (insulin monotherapy) or 2) continue metformin and initiate insulin within 90 days of LMP (insulin plus metformin) in women with type 2 diabetes on metformin monotherapy in the 180 days before their LMP. The outcomes were live birth and live birth with congenital anomalies. We estimated the absolute risk and risk ratio using standardization to account for potential confounders and selection bias.

Results: Of 4019 eligible women, 196 used insulin monotherapy and 574 used insulin plus metformin. The groups had similar characteristics, including age, diabetic complications, and glycemic control. The estimated probability of live birth was similar under both strategies: 75.3% vs 74.8%, with a risk ratio of 0.99 (95%CI: 0.96, 1.06). The estimated risk of live birth with congenital anomalies was 5.1% (95%CI: 1.1%, 12.2%) for the insulin monotherapy group and 3.8% (95%CI: 1.8%, 9.1%) for the insulin plus metformin group; the risk ratio was 0.74 (95%CI: 0.30, 3.34). Results were similar for the conditional risk ratio of congenital anomalies among live birth (risk ratio: 0.73; 95%CI: 0.30, 3.17).

Conclusions: Our findings suggest that metformin continuation in early pregnancy does not substantially increase the risk of congenital anomalies. Emulating a clinically plausible target trial minimized confounding by indication (population restricted to women with type 2 diabetes) and channeling bias (compared groups used insulin, a marker for diabetes progression).

Methods

The Impact of Differential Exposure Misclassification in a Study of Maternal Genitourinary Infections and the Risk of Gastroschisis Rashida S. Smith-Webb* Martha M. Werler Mahsa M. Yazdy Matthew P Fox

Background: Maternal genitourinary infections (GUIs) have been shown to increase the risk for gastroschisis, a severe abdominal wall defect. However, retrospective assessment of GUIs might be prone to reporting inaccuracies potentially resulting in recall bias. We conducted quantitative bias analyses to quantify the direction and magnitude of the potential impact of differential exposure misclassification in a study of maternal GUIs and the risk of gastroschisis.

Methods: Using data from two external validation studies which compared self-reported GUIs to medical records and serology tests, we parameterized sensitivity as 50% among controls, and based on expert judgement, specificity as 96% among controls. Assuming that cases more accurately recalled their exposures than controls, we modeled the difference in sensitivity for cases as 10% and 15% greater than controls whereas specificity was 2% greater than controls. We conducted summary-level probabilistic bias analyses (PBA), using 1,000,000 Monte Carlo simulations and used a beta distribution to model probability density functions for the selected bias parameters. To account for greater uncertainty in the chosen values, we divided the bias parameters by 1.2 to the widen distribution.

Results: The conventional OR for maternal report of any GUI in the first trimester compared to no GUI on the risk of gastroschisis was 1.80 (95% CI: 1.30, 2.40) adjusted for maternal age. After adjusting for differential misclassification of GUIs, assuming a 10% and 15% difference in sensitivity and 2% difference in specificity, the OR was 1.95 (95% Simulation Interval [SI]: 1.27, 3.04) and 1.67 (95% SI: 1.10, 2.55), respectively.

Conclusion: Our findings suggest that adjusting for differential exposure misclassification does not lead to changes in the interpretation for the impact of GUIs on gastroschisis, assuming specificity is high, and sensitivity is 50% among controls and 60% or 65% among cases.

Environment/climate change

Tropical cyclones and risk of preterm birth: a distributed-lag non-linear model approach in a time-to-event framework. Andreas Neophytou* Nathan Ryder Brooke Anderson Kayleigh Keller Jacob Hochard

Tropical cyclone (TC) related exposures are a severe and recurring threat, causing infrastructure and property damage, as well as directly threatening human health. Much of the health impacts of TCs, including the potential increased risk of perinatal outcomes associated with these exposures is not well characterized. In this study we examine the relationship between TC-related wind exposure assessed at the county level and risk of preterm birth in over 760,000 singleton live births recorded in North Carolina between 2011 and 2017. We fit distributed-lag non-linear Cox models to examine the exposure-lag-response between tropical cyclone-related wind exposures and risk of preterm birth while adjusting for month and year of birth and several pre-pregnancy risk factors. The approach allows for a flexible relationship between timing and intensity of exposure and the outcome. Exposure to a TC event with winds greater than 17.5 meters per second (lower bound of gale-force winds on the Beaufort scale) at any point during pregnancy was associated with a hazard ratio (HR) of 1.04 (95% confidence interval (CI) 1.01 – 1.06) for risk of preterm birth. Results from a quantitative exposure-lag-response analysis indicated that exposure around the 20^{th} week of gestation was potentially more influential than in other periods. Exposure to TC related winds at 17.5 meters per second during the 20^{th} week was associated with a HR of 1.09 (95% CI: 1.06 – 1.12) for risk of preterm birth when compared to no TC-related wind exposure. Our findings suggest an association between TCs and risk of preterm birth, as well as some potentially influential windows of exposure during gestation. A better understanding of the pathways of effect as well as identification of potential intervention variables on these pathways may help mitigate this potential health burden of an increasingly prevalent exposure.

Health equity

Investigating the potential perinatal health implications of reparations payments to Black American descendants of the enslaved Collette Ncube* Jonathan Huang Ka Kei Sum

Background: Racial disparities in the US are striking and persistent. They have been documented for a plethora of health outcomes, with perinatal health being no exception. The centrality of structural determinants in explaining the disproportionately worse outcomes of Black individuals in America has been part of scholarly discourse as early as 1899 when Du Bois published *The Philadelphia Negro: A Social Study*). In epidemiology, the critical examination of fundamental causes of health inequities (such as wealth) has recently come into view. Our objective was to investigate whether reparations, a debt owed to Black American descendants of enslaved persons in the US, might narrow racial disparities in preterm delivery (PTD) risk.

Methods: We designed a retrospective cohort study using data from the Panel Study of Income Dynamics (PSID), a multigenerational panel study. We identified 2,926 individuals who delivered a liveborn infant in 2013-2019 PSID waves and were born to parents of self-reported non-Hispanic Black or non-Hispanic White race. Using a probabilistic model, we simulated the likely impact of reparations on Black-White disparities in PTD. Reparations payments were estimated using a land-based (William Darity, 2008) and wage-based (Thomas Craemer, 2020) approach.

Results: The absolute mean difference in PTD prevalence was 4.9% (9.1% vs 14.0% among White and Black individuals, respectively). Under Darity's land-based approach to reparations estimation, the remaining disparity was 3.7% (95%CI: 1.3%-6.1%) or 4.0% (95%CI: 1.4%-6.4%) based upon 100% versus 50% of Black Americans being eligible for reparations payments. Under Craemer's wage-based approach, the remaining disparity was 3.5% (95%CI: 1.1%-5.9%) or 3.7% (95%CI: 1.4%-6.2%) based on the different eligibility criteria.

Conclusion: These preliminary data suggest Black-White disparities in PTD may be reduced by 24-30% in the presence of reparations payments to Black American descendants of slaves.

Environment/climate change

Personal care product use and perfluoroalkyl substances in pregnant and postpartum women and adolescents: The MIREC and HOME studies Amber Hall* Jillian Ashley-Martin

Background: Perfluoroalkyl substances (PFAS) are ubiquitous toxic chemicals routinely detected in personal care products (PCPs). Few studies have quantified the contribution of PCP use on PFAS concentrations. This study evaluates PCP use and PFAS in maternal plasma, human milk, and adolescent serum.

Methods: We used data from 2 pregnancy cohorts. MIREC (2008-2011) enrolled women from 10 Canadian cities and HOME (2003-2006) enrolled women from Cincinnati Ohio. Participants reported frequency of use for 8 PCP categories in MIREC and past 24-hour use for 15 PCPs in HOME. In MIREC, we quantified PFAS in maternal plasma (6–13 weeks' gestation; N=1,940) and human milk (2–10 weeks postpartum; N=664). In HOME, we measured PFAS in adolescent serum (11-14 years; N=193). Using linear regression, we estimated percent differences in PFAS concentrations with PCP use, adjusted for sociodemographic factors.

Results/Conclusions: In MIREC, higher use of nail care products, fragrances, hair dyes, sprays and gels, and makeup was associated with greater maternal plasma perfluorooctane sulfonic acid (PFOA) and/or perfluorooctane sulfonic acid (PFOS) concentrations. Greater use of hair dyes, partial highlights, nail care products, makeup, and nail polish were associated with higher PFOS or PFOA in human milk. Higher use of hair dyes, hair styling products, and makeup was associated with greater human milk perfluorononanoic acid. Additionally, greater use of nail care products and polish, and full highlights without bleach were associated with higher human milk perfluorohexane sulfonic acid concentrations. No PCP-PFAS associations were observed in HOME; the lack of associations may be explained by the smaller sample size or narrower window of PCP use (past 24-hour vs. general use). Our results suggest that some PCPs contribute to maternal plasma and human milk PFAS. Future studies could examine if associations depend on country and age, timing and frequency of use, or product formulation.

Birth defects

Validity of diagnosis codes for major genitourinary birth defects in Military Health System administrative data, 2006–2014 Sandra Magallon* Celeste Romano Clinton Hall Anna Bukowinski Gia Gumbs Ava Marie Conlin

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Objective: To assess the validity of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes for selected genitourinary birth defects in the Military Health System.

Methods: Among infants captured in Department of Defense Birth and Infant Health Research program data from 2006 to 2014, we selected a random sample of ICD-9-CM screen-positive cases of each of six major genitourinary birth defects, selected in order of increasing prevalence in the population, and a random sample of non-cases for chart review. To increase the likelihood of capturing false negatives, non-cases were additionally stratified and sampled by record of small for gestational age and preterm birth. Positive predictive value (PPV) and negative predictive value (NPV) were calculated for individual genitourinary birth defects and any included birth defect and weighted by the inverse probability of being sampled to permit extrapolation to the full population.

Results: Of 461,557 infants, 686 were sampled for chart review. Bladder exstrophy was accurately reported, with PPV exceeding 90%, while the accuracy of renal dysplasia, renal agenesis/hypoplasia, and hypospadias was moderate (PPV range = 66%–68%). Posterior urethral valve and/or prune belly and congenital hydronephrosis had low accuracy (PPV = 49% and 20%, respectively). NPVs always exceeded 98%. The PPV for any included genitourinary birth defect was 50%; however, excluding congenital hydronephrosis screen-positive cases, which comprised the majority of false positives (45%), resulted in a PPV of 69%.

Conclusion: The validity of major genitourinary birth defect codes in Military Health System administrative data varies, with high accuracy for some codes but poor accuracy for others. Assessment of overall genitourinary birth defects should omit congenital hydronephrosis due to its low PPV and frequent co-occurrence with other genitourinary birth defects.

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The study protocol was approved by the Naval Health Research Center Institutional Review Board in compliance with all applicable Federal regulations governing the protection of human subjects. Research data were derived from approved Naval Health Research Center Institutional Review Board protocols, numbers NHRC.1999.0003 and NHRC.2015.0035.

Birth defects

Investigation of a Transient Increase in Omphalocele Prevalence in a U.S. Military Birth Cohort Jackie Lanning* Clinton Hall Sandra M. Magallon Anna T. Bukowinski Gia R. Gumbs Ava Marie S. Conlin

Background: The Department of Defense Birth and Infant Health Research (BIHR) program conducts ongoing surveillance of birth defects among infants born to military families. Omphalocele is a major abdominal wall defect with a yearly prevalence of ~2 per 10,000 births in BIHR data, but an unexpected increase was observed from 2017 to 2019, peaking at 6.4 per 10,000 births in 2018; rates returned to baseline in 2020. To investigate this transient increase in prevalence, this study aimed to validate all omphalocele cases in BIHR data from 2016 to 2021.

Methods: Using the BIHR birth cohort and associated medical encounter data, omphalocele cases were identified by the presence of International Classification of Diseases, Tenth Revision (ICD-10) code Q79.2 on one inpatient or two outpatient infant encounter records in the first year of life. Cases were validated using available maternal and infant electronic health records. Characteristics of true and false positive cases were assessed using bivariate analyses and compared over time.

Results: Of 638,905 live births 2016-2021, 230 met the ICD-10 case definition for omphalocele; 138 (60.0%) of these cases had available electronic health records, of which 68 (49.3%) were true positives. Among the 70 false positives, 36 (51.4%) were cases of misdiagnosed umbilical hernia. The mean time from birth to first ICD-10 omphalocele diagnosis was 0.4 (standard deviation [SD]): 2.4) days for true positives and 57.5 (SD: 83.2) days for false positives ($p<0.0001$). Rates of misdiagnosed umbilical hernia and delayed omphalocele diagnosis (i.e., >7 days after birth) were elevated during the 2017-2019 period. No temporal trends in maternal, hospital, or geographic characteristics were noted.

Conclusions: Higher misuse of ICD-10 code Q79.2 during 2017-2019 likely explained the associated increase in omphalocele prevalence. Timing of first diagnosis should be considered for omphalocele case definitions based on medical encounter data.

Birth defects

School-recorded special educational needs among children with major congenital anomalies born in England: A population-based study Ania Zylbersztejn*, Kate Lewis Maria Peppa Bianca De Stavola Ruth Gilbert Ania Zylbersztejn

We provide a national overview of recorded special educational needs (SEN) provision among children with hospital identified major congenital anomalies (MCAs) who attended state-funded schools in England. We also report changes before and after government reform of SEN in 2014.

Using linked administrative health and education data, we followed singleton children born in England between 1 September 2003 and 31 August 2013 up to school year 6 (age 10/11 years), death, or 31 August 2019, whichever was earliest. MCAs were identified by the presence of 'European Network of Population-based Registries for Congenital Malformations' (EUROCAT)-defined diagnostic codes in hospital admission records during infancy. We used at least one record of SEN in the education data as a proxy for SEN provision, grouped by lower level (Action Plan, Action Plan Plus or SEN Support) and higher level (SEN Statement or Education, Health and Care Plan and/or special school attendance) SEN.

Among 5,043,209 children in the birth cohort who were enrolled in state-funded primary school, 170,817 (3.4%) were identified as having any MCA. 70,049 (41.0%) of children with MCAs had at least one SEN record during primary school (of which, 67.7% had lower and 32.4% higher level SEN) compared with 1,246,923 (25.6%) of children without MCAs (88.4% lower and 11.6% higher level SEN). Children with chromosomal, nervous system and eye anomalies had the highest proportion of SEN recorded (92.9%, 73.2% and 65.6%, respectively). The proportion of children with at least one SEN record in Year 1 (age 5/6 years) was lower for those attending school from 2014/15 onward (29.9%) compared with before 2014/15 (34.5%) for all but the chromosomal and ear, face and neck anomaly subgroups.

Recorded SEN among children with hospital identified MCAs was markedly higher than for those without MCAs, however more than half had no recorded SEN. Our findings suggest government reform in 2014 reduced SEN provision for children with MCAs.

Birth defects

Bullying among children with heart conditions, National Survey of Children's Health, 2018-2020 Brittany Wright* Karrie Downing Michael Fundora Jill Glidewell Kevin Vagi Sherry Farr

Introduction: Children with chronic illnesses often report bullying by peers, yet little is known about bullying among children with heart conditions (HCs). We examined the prevalence of being bullied among children with and without HCs and associated demographic and health characteristics.

Methods*:* Using 2018-2020 parent-reported National Survey of Children's Health data, prevalence and frequency of being bullied among children 6-17y were compared by HC status (congenital/acquired HC vs. none). Among children with HCs, associations between demographic and health characteristics and being bullied, and prevalence of anxiety or depression diagnoses by bullying status were examined. Differences were assessed using chi square tests and multivariable logistic regression using predicted marginals to produce adjusted prevalence ratios (aPR) and 95% confidence intervals (CI). Weights yielded national estimates.

Results: Of 69,218 children, 2.2% had HCs. Being bullied was more common among children with HCs (56.3%) than without (43.3%; aPR=1.3, 95% CI [1.2, 1.4]). Children with HCs were bullied more frequently than their peers [almost every day (4.7% vs 4.2%), 1-2x/week (15.4% vs 8.1%) ($p<0.05$)]. Among children with HCs, being bullied was more common for those ages 6-8y, 9-11y, and 12-14y than 15-17y (56.2%, 68.8%, 58.7% vs 42.9%; aPR=1.3 [1.0, 1.7]; 1.5 [1.3, 1.9] and 1.3 [1.1, 1.7]) and for children with genetic conditions than without (66.1% vs 54.6%; aPR=1.2 [1.0, 1.4]). Being bullied was less common for non-Hispanic black than non-Hispanic white children (42.2% vs 59.9%; aPR=0.7 [0.6, 1.0]). Among children with HCs, those bullied more commonly had a diagnosis of anxiety (28.8% vs 12.8%) or depression (11.0% vs 4.6%) than those not bullied, respectively ($p<0.05$).

Conclusions: Children with HCs were more likely to be bullied, and bullied more often, than peers, which may affect mental health. Findings highlight social and psychosocial needs of children with HCs.

Birth defects

Birth Prevalence of Penoscrotal Transposition in the Texas Birth Defects Registry by Maternal Characteristics, 1999-2018 Rachel Allred* Joanne Nguyen Mark Canfield Charles Shumate

Penoscrotal transposition (PST) is a rare congenital defect in which the penis is positioned inferior to the scrotum. The purpose of this study was to describe PST prevalence recorded in the Texas Birth Defects Registry (TBDR) by maternal characteristics. PST cases recorded in the TBDR, an active surveillance system, between 1999-2018 were identified. Birth prevalence (PR) was calculated by dividing total count of PST by the sum of male live births per 10,000. Nonoverlapping confidence intervals (CI) were used as a means for determining statistically significant differences between levels of maternal characteristics including age, education, and race/ethnicity. Overall PR was 0.60/10,000 live male births (95% CI: 0.53-0.68). Birth prevalence was significantly higher among those whose mothers had greater than high school education (PR: 0.75; 95% CI: 0.62-0.88) compared to those whose mothers had less than high school education (PR: 0.32; 95% CI: 0.21-0.43) and among those whose mothers were 35 and older (PR: 1.03; 95% CI: 0.75-1.32) compared to those whose mothers were 25-34 (PR: 0.62; 95% CI: 0.51-0.73) and less than 25 years of age (PR: 0.45; 95% CI: 0.34-0.56). Hypospadias, chordee, and cryptorchidism affected 70%, 56%, and 20% of cases, respectively. Atrial septal defect and stenosis/atresia of the large intestine (both 8% of cases) were the most common co-occurring defects outside of the genitourinary system. To our knowledge this is the first investigation exploring PST prevalence in a birth defects registry, and the largest to date. In Texas, between 1999-2018, PST prevalence was significantly higher among those whose mothers were older and more educated. Consistent with the literature, PST co-occurred with other genital anomalies including hypospadias, chordee, and cryptorchidism. These data provide insight into prevalence of a rare urogenital malformation syndrome present at birth.

Birth defects

Non-chromosomal birth defects and childhood cancer: a systematic review with meta-analysis Eugene Wong* Charles Poole Tania A. Desrosiers Erin Sley Philip J. Lupo Hazel B. Nichols Susan M. Smith Andrew F. Olshan

Background: Infants born with certain birth defects (BDs) are 2-30 times as likely to develop certain childhood cancers (CCs). While this relationship has been established for certain chromosomal anomalies and CCs, producing precise estimates of the association for non-chromosomal BDs has been hindered by small study sizes. To address this limitation, we conducted a systematic review with meta-analysis to summarize the evidence on associations between non-chromosomal BDs and CCs.

Methods: We conducted a systematic search for original articles reporting associations between individual or “any” non-chromosomal structural BD and individual or “any” CC published through November 2022 within PubMed, Embase, and SCOPUS. Two authors conducted a title/abstract review to identify eligible articles. We evaluated results for publication bias, combined into summary estimates when indicated, and examined the impact of study characteristics on summary estimates.

Results: 19 of 7,155 articles met the inclusion criteria. In general, many of the associations we examined had an increased rate of CCs. For example, the rate of any CC was increased in children born with any BD [random-effects summary incidence rate ratio (IRR): 1.8; 95% prediction interval (PI): 1.0, 3.3; n=9]. The rate of any CC was also increased in children born with nervous system defects (random-effects summary IRR: 4.8, 95% PI: 1.4, 16.0; n=9). In our analyses, there was some evidence of publication bias and study characteristic associations.

Conclusions: By combining the results of individual studies, our systematic review with meta-analysis yielded more precise estimates of the association between non-chromosomal BDs and CCs. We found an increased incidence of CC among children born with any BD, as well as among specific BDs. Our results could be used to inform cancer screening guidelines for children with BDs and future investigations of the shared genetic profile between these phenotypes.

Birth defects

Associations between birth defects with neural crest cell developmental origins and pediatric embryonal tumors Eugene Wong* Philip J. Lupo Tania A. Desrosiers Hazel B. Nichols Susan M. Smith Charles Poole Andrew F. Olshan

Background: While having a birth defect is one of the strongest risk factors for developing childhood cancer, there have been few assessments to evaluate associations between BDs with neural crest cell developmental origins (BDNCO) and embryonal tumors, which are characterized by undifferentiated cells similar to neural crest cells. Thus, investigating the overlap between these phenotypes may reveal insights into shared etiologic pathways and genetic origins.

Methods: Using a multi-state, population-based registry linkage cohort study of over 10 million births, we evaluated BDNCO-embryonal tumor associations by generating hazard ratios (HR) and 95% confidence intervals (CI) with Cox regression models. BDNCOs included defects of the ear, face, neck, Hirschsprung's disease, and a selection of congenital heart defects. Embryonal tumors included neuroblastoma, nephroblastoma, and hepatoblastoma. We also investigated potential effect measure modification (EMM) by infant sex, maternal race/ethnicity, maternal age, and maternal education.

Results: Overall, 105 participants were diagnosed with both a BDNCO and pediatric embryonal tumor. The cumulative incidence of embryonal tumors among those with BDNCOs was 0.09%. Children with BDNCOs were 4.2 times (95% CI: 3.5, 5.1) as likely to be diagnosed with an embryonal tumor before 18 years of age compared to children born without BDs. BDNCOs were most strongly associated with hepatoblastoma (HR: 16.1, 95% CI: 11.3, 22.9), and the HRs for neuroblastoma (3.1, 95% CI: 2.3, 4.2) and nephroblastoma (2.9, 95% CI: 1.9, 4.4) were also elevated. There was no notable EMM by the aforementioned factors.

Conclusions: Overall, children with BDNCOs were more likely to develop embryonal tumors compared to children without BDs. We hypothesize that disrupted developmental pathways could lead to both phenotypes, which could inform future genomic assessments of these conditions, as well as cancer surveillance strategies for children with BDNCOS.

Birth defects

Parental characteristics associated with orofacial clefts by infant sex: A latent class analysis approach Sanjida Mowla*, Sanjida Mowla Sanjida Mowla Tania Desrosiers Daniela Sotres-Alvarez Eva Williford A.J. Agopian Natalie Archer Marilyn Browne Sarah Fisher Gary Shaw Andrew Olshan National Birth Defects Prevention Study Sanjida Mowla

Orofacial clefts (OFCs), including cleft palate (CP) and cleft lip and palate (CLP), are birth defects that vary in prevalence by infant sex. We aimed to identify sex differences in associations between parental risk factors and OFCs.

We analyzed data from the National Birth Defects Prevention Study (NBDPS; 1997-2011) for a sample of 2585 males/1871 females with cleft lip or cleft palate (cases) and 5764 male/5526 female infants without a birth defect (controls). Maternal (age, education, income, substance use) and paternal characteristics (age, substance use) were reported after delivery. We used latent class analysis to identify distinct groups of parental characteristics among cases and controls. Multivariable logistic regression was used to estimate adjusted odds ratios (aORs) and 95% confidence intervals (CIs) for the association between each latent class and OFCs, stratified by sex, adjusted for study site and birth year.

Five latent classes were identified. Of the participants, 18% were in Class 1 (≤24 years, 12 years education), 23% were in Class 2 (mother ≤24 years, father 24-34 years, 0-11 years education), 10% were in Class 3 (24-34 years, >12 years education, 10-50k income), 41% were in Class 4 (24-34 years old, >12 years education, >50k income; referent) and 8% were in Class 5 (≤24 years old, 12 years education, substance use in both parents). For male infants, Class 5 was associated with CP (aOR: 1.44; 95% CI: 1.10, 1.87) and CLP (aOR: 1.44; 95% CI: 1.18, 1.76) compared with Class 4. Among female infants, Class 5 was strongly associated with CLP (aOR: 2.45; 95% CI: 1.56, 3.85) compared with those in Class 4. The risk of CLP did not differ significantly by sex, p-value=0.10.

This study provides insights into etiologic heterogeneity by sex for OFCs when considering parental characteristics. Of those with both parents who reported a higher frequency of substance use, increased risks were observed for CP and CLP among males but only for CLP among females.

Child health and development

Urinary phenol concentrations and breast bud diameter during minipuberty in female infants: the Infant Feeding and Early Development Study Mandy Goldberg* Danielle R. Stevens Margaret A. Adgent Helen B. Chin Kelly K. Ferguson Donna D. Baird Virginia A. Stallings Dale P. Sandler David M. Umbach

Evidence from animal and epidemiologic studies suggests that endocrine-disrupting chemicals (EDCs) can alter breast development across the lifecourse. Phenols are suspected EDCs that are highly prevalent in personal care and consumer products. Whether exposure to phenols is associated with breast bud size in girls during minipuberty, a period of endocrine activity in infancy, is unknown. We examined associations of urinary concentrations of 7 phenols with breast bud diameter assessed via ultrasound at ages 16, 24, and 32 weeks in 83 girls from a prospective cohort of term infants (enrolled 2010-2013 in the Philadelphia area). We measured total phenol concentrations at ages 6-8 weeks and/or 12 weeks, then we averaged natural log (ln)-transformed creatinine-adjusted concentrations across weeks after imputing values below the limit of detection (LOD) as LOD/√2. For each phenol, we estimated age-adjusted differences (β [95% confidence interval]) in ln-transformed breast bud diameter corresponding to a concentration increase of one interquartile range using linear mixed-effects models with a subject-specific random intercept. Most infants were Black (64%) and exclusively fed cow’s milk formula (63%). Median breast bud diameter (mm) was 10.9 at 16 weeks, 12.4 at 24 weeks, and 13 at 32 weeks. Detection rates were >90% for bisphenol A, benzophenone-3, 2,4 dichlorophenol (DCP), methyl (mPB) and propyl (pPB) paraben, 88% for 2,5 DCP and 64% for triclosan. Despite median paraben concentrations (mPB: 2846.6 ng/mg Cr, pPB: 79.8 ng/mg Cr) considerably higher than relevant published estimates, neither parabens (β: -0.03 [-0.13, 0.06] for mPB, β: -0.04 [-0.17, -0.09] for pPB) nor other phenols were associated with breast bud diameter. Our results suggest that urinary phenols are not associated with breast bud diameter during minipuberty. Investigation of other endocrine-sensitive outcomes during infancy are warranted considering widespread phenol exposure.

Child health and development

Sleep duration in middle childhood and age at menarche Mia Zhu* Mercedes Mora-Plazas Constanza Marin Eduardo Villamor

Puberty is characterized by shortened sleep phases. However, it is unclear if sleep duration earlier in childhood could influence the timing of pubertal events. We aimed to assess the association between middle childhood nighttime sleep duration and age at menarche (AAM) in a cohort of 819 premenarcheal Colombian girls who were followed through adolescence. We estimated adjusted hazard ratios (HR) with 95% confidence intervals (CI) for menarche by sleep duration categories using Cox models. Analyses were stratified by age at sleep assessment. Among girls aged 9 to <11 y, compared with girls who slept within recommendations, sleeping above recommendations was related to an adjusted 76% (95% CI: 4%, 198%; $P = 0.04$) higher probability of experiencing menarche during follow up. In girls aged ≥11 y, compared with girls who slept within recommendations, sleeping under recommendations was related to an adjusted 42% (95% CI: 5%, 93%; $P = 0.03$) higher probability of experiencing menarche during follow-up. Sleep duration was not associated with AAM in girls aged <9 y at the time of sleep assessment. In conclusion, sleeping above recommendations in girls 9 to <11 y-old and sleeping under recommendations in girls ≥11 y-old is associated with earlier menarche. Further studies on sleep duration and timing of pubertal events involving assessments prior to puberty onset are warranted.

Child health and development

Association between gestational weight gain and three-dimensional fetal body composition in the NICHD Fetal 3D Study Kathryn Wagner* Zhen Chen Stefanie Hinkle Jessica Gleason Wesley Lee William Grobman Roger Newman John Owen Daniel Skupski Daniel He Robert Gore-Langton Seth Sherman Cuilin Zhang Jagteshwar Grewal Katherine Grantz

Excessive gestational weight gain (GWG) has been associated with increased fetal growth, birthweight, and risk of future offspring adiposity. However, it remains unclear whether these changes reflect a global increase or are due to differential lean and fat tissue growth and at what timepoint in gestation changes in fetal body composition occur. We evaluated the relationship between GWG and fetal body composition in a diverse, prospective US pregnancy cohort.

Maternal pre-pregnancy weight was self-reported and subsequent weight was measured at each study visit and abstracted from prenatal records (median=19 measures). Up to five 3D ultrasounds were completed across gestation, from which fetal body composition was obtained. Among pregnancies with at least one GWG and ultrasound measure (n=2158), linear mixed models were used to separately estimate fetal body composition and maternal weight trajectories across gestation. Linear regression examined associations between trimester-specific GWG and fetal body composition at 14-, 28-, and 39-weeks' gestation, adjusted for prior GWG and known confounders.

For each kg increase in first trimester GWG, there was an increase in fractional fat arm volume (β=0.001 cm^3, 95% CI: 0.0004, 0.002), lean thigh volume (β=0.0006 cm^3, 95% CI: 0.0000, 0.001), fat thigh volume (β=0.0006 cm^3, 95% CI: 0.0002, 0.001), abdominal area (β=1.69 mm^2, 95% CI: 0.85, 2.54) and maximum abdominal subcutaneous tissue thickness (β=0.004 mm, 95% CI: 0.0003, 0.007). In the second trimester, there was an increase in abdominal area (β=26.17 mm^2, 95% CI: 13.77, 38.56). There were no associations with third trimester GWG and fetal body composition.

The positive association between GWG and fetal size began in early pregnancy and manifested as increases in both lean and fat measures that did not persist through the third trimester. Understanding the relationship between GWG and fetal fat deposition is important given potential implication for future offspring health.

Child health and development

Maternal stress, depression, and fetal organ volumes in the National Institute of Child Health and Human Development (NICHD) Fetal Growth 3D Study Alexandra Jean-Louis* Jessica Gleason Zhen Chen Kathryn Wagner William Grobman Roger Newman Wesley Lee Robert Gore-Langton Seth Sherman John Owen Deborah Wing Daniel Skupski Jagteshwar Grewal Katherine Grantz

Background: Maternal stress and depression are associated with increased risk of adverse perinatal outcomes including low birthweight in some studies. Maternal stress and anxiety have also been found to be associated with smaller fetal hippocampal volumes and accelerated frontal lobe cortical folding. However, the relationship between stress and depression with fetal organs other than the brain have not been studied.

Methods: This study utilizes data from the prospective NICHD Fetal 3D study (2009-2013) with three-dimensional (3D) ultrasound scans from low risk, non-smoking singleton pregnancies (n=2,455) at enrollment (10-13 weeks). Based on prior literature, stress was defined as: a Perceived Stress Scale (PSS) score of 15 or higher and depression as a score of 10 or higher on the Edinburgh Postnatal Depression Scale (EPDS). Fetal cerebellar, lung, liver, and kidney volumes were measured longitudinally up to five times between 14-39 weeks using 3D ultrasound. We evaluated associations between stress and depression with organ volume across pregnancy using linear models to calculate mean differences and 95% confidence intervals (CI) adjusted for maternal sociodemographic characteristics.

Results: Continuous PSS and EPDS scores were moderately correlated (r=0.67). Fetuses of women with PSS ≥15 compared to <15 had larger lung volumes at 14 weeks (mean differences 0.05 cm^3, 95% CI: -0.002, 0.10), 21 weeks (0.31 cm^3, CI: -0.001, 0.61), 28 weeks (0.89 cm^3, CI: 0.04, 1.74), 34 weeks (1.37 cm^3, CI: 0.15, 2.60), and 39 weeks (1.46 cm^3, CI: 0.12, 2.80). There were no associations between depression and organ volumes.

Conclusion: Maternal stress early in pregnancy may be associated with enhanced lung growth. Implications for larger lung volume are currently unclear, but further investigation is warranted since offspring respiratory morbidities, such as asthma, have been observed after increased prenatal stress exposure.

Child health and development

Neurodevelopmental outcomes of young children exposed to general anaesthesia in early life: a population-based study Diana Bond* Francisco Schneuer Samantha Lain Justin Skowno Andrew Martin Adam Guastella Natasha Nassar

Background: Studies examining the long-term effect of general anaesthesia (GA) on the developing brain have shown inconsistent results due to differences in study methodology and outcome measures. The aim of this study was to evaluate neurodevelopmental outcomes of children exposed to GA in early life.

Methods: This population-based record-linkage study included all term births in New South Wales (NSW), Australia from 2001-2007 with follow-up to end-2017. Data were ascertained from the NSW Perinatal, Admitted Hospital and Disability Services Data Collections. Association between exposure to GA <3 years and two neurodevelopmental outcomes: autism spectrum disorder and attention deficit/hyperactivity disorder (ADHD) were assessed using multivariable Cox regression models, overall and stratified by number (1,2,3+) and age of GA (<1, ≥1 year) with sensitivity analyses conducted using discordant sibling design and inverse probability weighting with propensity scores.

Results: Of 695,246 birth records, 57,867 (8.3%) children had GA exposure. Compared to unexposed children, any GA exposure was associated with 1.5-fold increased risk of neurodevelopmental outcomes: autism (1.2% vs 2%, adjusted Hazard ratio (aHR) 1.45; 95%CI 1.36, 1.54), ADHD (0.5% vs 0.9%, aHR 1.53; 95%CI 1.39-1.68). The majority (75%) of children had one GA, with risk of neurodevelopmental outcomes increasing with greater GA exposure (eg for autism: aHR 1.33 (1.24, 1.42), 2.13 (1.84, 2.46), 2.49 (1.92, 3.22) for 1,2,3+ GA exposure, respectively) and for children with GA exposure aged <1 year compared to ≥1 year. Results were similar for sensitivity analyses.

Conclusions: Although the absolute risk is low, increasing number and GA exposure at younger ages was associated with greater risk of adverse neurodevelopmental outcomes. While mechanisms of causality remain unclear, results help identify developmental domains that may require ongoing monitoring and follow-up of children with early exposure to GA.

Child health and development

EARLY SKIN-TO-SKIN CONTACT AND NEURODEVELOPMENTAL OUTCOME AT 51/2 YEARS IN VERY PRETERM INFANTS: THE EPIPAGE-2 COHORTveronique pierrat*, Ayoub Mitha laetitia marchand Jean-Christophe Roze pierre kuhn isabelle le ray monique kaminski veronique pierrat veronique pierrat

Aim of the study

Long-term effects of Skin-to-Skin Contact (SSC) on neurodevelopmental outcome of children born very preterm are still debated. This study aims to evaluate associations between early SSC, cognition and behavior at $5^{1/2}$ years among children born very preterm.

Methods

The population was derived from the French national population-based cohort EPIPAGE-2 of very preterm infants born in 2011. Early SSC was defined as SSC performed during the first week of life. To adjust for confounding and control for the nonrandom assignment of children in treatment groups, exposition to SSC was analyzed by a propensity score analysis based on individual and unit characteristics with inverse probability of treatment weighting approach. Outcomes were full-scale-intelligence-quotient (Wechsler Preschool and Primary Scale of Intelligence, 4th edition) and behavioral scores (Strengths and Difficulties Questionnaire) among 2 561 children born between 24 and 31 weeks and survivors at $5^{1/2}$ years.

Results

Among survivors, 1 581 (61.7%) were exposed to early SSC with large variability among neonatal units (range 15%-75%). At $5^{1/2}$ years, early SSC was associated with increased proportions of children with full-scale-intelligence-quotient $\geq$ – 1 standard deviation (adjusted odd ratio 1.27, 95% confidence interval (1.01;1.59), p=0.042). In a subgroup analysis by gestational age, differences in full-scale-intelligence-quotient were statistically significant in children born at 28-31 weeks but not in those born at 24-27 weeks. SDQ scores for behavioral difficulties were not different between groups exposed/not exposed to early SSC.

Conclusion

Early SSC among very preterm infants was associated with increased full-scale-intelligence-quotient at $5^{1/2}$ years. Variability of practices among units deserves attention. Further evaluation of the dose-effect is needed.

Child health and development

Neurodevelopment at 5 years according to Ages and Stages questionnaire at 2 years corrected age in children born preterm: The EPIPAGE-2 cohort studyveronique pierrat*, marie-laure charkaluk gildas kana valerie benhammou isabelle guellec mathilde letouzey andrei scott morgan alexandra nuytten heloise torchin sabrina twilhaar stephane marret pierre-yves ancel veronique pierrat veronique pierrat

Objectives To report neurodevelopment at 5 ½ years according to the Ages and Stages Questionnaire (ASQ) results at 2 years corrected age in preterm-born children

Methods Population-based cohort EPIPAGE-2, France, 2011 to 2017. Inclusion of children born at 24-26, 27-31 and 32-34 weeks, free of cerebral palsy, deafness or blindness at 2 years corrected age. Neurodevelopmental disabilities defined as moderate/severe, mild or absent at 5 ½ years using gross and fine motor, sensory, cognitive, and behavioural evaluations. [1] ASQ completed between 22-26 months corrected age described as scores below or above threshold.

Results Among 2504 participants, 2060 responded at 5 ½ years (82.3%); among them, 823 (38.5%) had an ASQ below threshold. Risks of moderate/severe or mild disability were higher in children with an ASQ below threshold compared to children with an ASQ above threshold: respectively 15.2% versus 7.3%, adjusted odd ratio (OR) = 2.9, 95% confidence interval (CI) (1.9 to 3.4), and 40.2% versus 31.0%, adjusted OR = 2.8, 95% CI (2.0 to 3.8). In children with an ASQ below threshold, the number of domains below threshold, very low gestational age and severe neonatal morbidities increased the risk of disabilities at 5 ½ years. In those with an ASQ above threshold this risk was increased for boys and children born small-for-gestational age. In both groups maternal level of education was strongly associated with outcomes.

Conclusion In this French population of preterm-born children, ASQ results at 2 years corrected age were associated with neurodevelopmental disabilities at 5 ½ years. The ASQ could be used as a first line screening tool for enhanced developmental surveillance of this high-risk population. Its interpretation needs to consider children characteristics at birth, neonatal complications, and social environment.

1. Pierrat V, et al. 2021 Apr 28;373:n741. doi: 10.1136/bmj.n741.

Child health and development

Adolescent dietary patterns and age at menarche in a prospective study of US girls Colette Davis* Kara Cushing-Haugen Jorge Chavarro Holly Harris

Objective: The objective of this study was to evaluate the association between adolescent dietary patterns and age at menarche, taking into account the impact of body size.

Methods: The Growing up Today Study (GUTS) is a prospective cohort study of children ages 9-15 at study enrollment. In this analysis we included 15,044 premenarchal GUTS participants who completed food frequency questionnaire(s) (FFQ) and self-reported age at menarche. Cox proportional hazards models were used to calculate the hazard ratios (HRs) and 95% confidence intervals (CI) for the associations between two dietary patterns, the Alternative Healthy Eating Index (AHEI) and the Empirical Dietary Inflammatory Pattern (EDIP), and age at menarche. As BMI or height could mediate the association between dietary intake and age at menarche we examined models with and without adjustment for these variables and considered these variables as mediators.

Results: 13,977 participants (93%) reported menarche during the study period. Participants with the highest quintile of AHEI diet score (indicating a healthier diet) were 8% less likely to attain menarche within the next month compared to those with in the lowest quintile (95% CI=0.85-0.98; p_{trend}=0.02). This association remained after adjustment for body mass index (BMI) and height (corresponding HR=0.92; 95% CI=0.86-1.00; p_{trend}=0.02). Participants in the highest quintile of EDIP score (i.e., most inflammatory diet), were 15% more likely to attain menarche in the next month relative to those in lowest quintile (HR=1.15; 95% CI=1.06-1.25; p_{trend}=0.0004) with the association remained following adjustment for BMI and height (corresponding HR=1.14; 95% CI=1.05-1.24; p_{trend}=0.0008). No significant mediation by BMI or height was observed.

Conclusion: Our findings of an association between both the AHEI and EDIP and age at menarche indicate that dietary habits may play a role in age at menarche independent of the impacts of BMI or height.

Child health and development

Routine vaccine uptake in school-aged autistic and non-autistic youth: A linked database study Linda Dodds* Christopher Filliter Leslie Anne Campbell Noni MacDonald Sarah Shea Eve Dubé Isabel Smith Jillian Filliter

Background: School-based vaccination programs are employed in much of Canada, including in Nova Scotia (NS), but vaccine uptake in autistic youth has not been studied in the context of school-based delivery models. This study was conducted to determine whether school-aged autistic youth received routine vaccines at a lower rate than their non-autistic peers.

Methods: In NS, Canada, vaccines routinely delivered in early adolescence are administered to Grade 7 students through a school-based Public Health vaccination program. NS youth eligible to receive Grade 7 vaccinations between 2011 and 2017 were included in this study. Autism spectrum disorder (ASD) diagnoses were determined from administrative health data. Rates of receipt of any Grade 7 vaccine and of individual vaccines were compared between autistic and non-autistic youth. Subgroup analyses included comparing Grade 7 vaccine receipt between autistic youth and their non-autistic siblings and early childhood vaccine receipt between autistic and non-autistic cohorts.

Results: The rate of receipt of any vaccine was 73% among 916 autistic youth and 82% among 49,599 non-autistic youth (relative risk = 0.90; 95% confidence interval = 0.86-0.94). Similar results were found for individual vaccines. Subgroup analyses revealed lower rates of Grade 7 vaccine receipt among autistic youth compared to their non-autistic siblings. Rates of early childhood vaccine receipt did not differ between those later identified as autistic and non-autistic.

Conclusions: Autistic youth were under-vaccinated compared to their non-autistic peers for Grade 7 vaccinations. Lower vaccination rates in autistic youth compared to their non-autistic siblings suggest that vaccine delivery-related factors may contribute more to the under-vaccination of autistic youth than parental vaccine hesitancy. Barriers to vaccine uptake for school-aged autistic youth, including those unique to school-based vaccination programs, must be explored and addressed.

Child health and development

Age and ethnic variations in the association between maternal infection and childhood leukemia risk: results from an international meta-analysis of individual participant data

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Introduction: Maternal infections during pregnancy may affect fetal development making offspring immunologically vulnerable to diseases such as childhood acute leukemia (AL). Previous studies suggested that contribution of maternal infections in AL might vary by subtype (lymphoblastic, ALL; myeloid, AML), ethnicity and/or age at diagnosis of the child. We examined the overall association, as well as its potential variation across these characteristics.

Method: Individual participant data (IPD) from 17 case-control studies within the Childhood Cancer and Leukemia International Consortium (CLIC) were analyzed. We used a two-stage random-effects IPD meta-analysis to assess the association between maternal infection and the risk of leukemia in the offspring. We then stratified analyses by ethnicity groups (Hispanics, Non-Hispanic whites, Others) and age at diagnosis/recruitment (0-1 years, 2-6 years, 7-15 years).

Results: Overall, 18.4% of mothers reported at least one infection during pregnancy. A non-significant association was observed for leukemia risk overall (odds ratio (OR)=1.13, 95% confidence interval (CI): 0.91-1.40), with similar estimates for ALL and AML. However, ethnic variations in ALL risk were observed between Hispanics (OR=0.88, 95% CI=0.57-1.37) and non-Hispanic whites (OR=1.23, 95% CI=0.99-1.52) with prominent associations in children age 6 years or less (≤1 year: OR=1.32, 95% CI=1.04-1.69; 2-6 years: OR=1.29, 95% CI=1.03-1.61), but not in older children (OR=1.02, 95% CI=0.76-1.36). In these non-Hispanic white children, associations were specifically observed for viral infections, respiratory infections and genital infections with higher magnitudes before the age of 2.

Conclusion: Although maternal recall bias, ethnicity classification and design heterogeneity cannot be ruled out, this analysis suggests that some maternal infections during pregnancy may be a risk factor for childhood ALL in non-Hispanic whites, but not in Hispanic children.

Child health and development

Excess mortality in childhood-onset Type 1 diabetes: population-based study Samantha Lain* Lindsay Stevens Kim Donaghue Maria Craig Alison Pryke Natasha Nassar

Background: People with childhood-onset type 1 diabetes (T1D) have higher mortality rates than the general population, but impact of age at diagnosis has not been examined. This study aims to assess the risk of mortality for T1D and examine the impact of sex and age of diagnosis.

Methods: The study population were identified from the Australasian Paediatric Endocrinology Group diabetes register, diagnosed with T1D <16 years in New South Wales (NSW), Australia from 1990-2010. The register was linked to NSW Death registrations to ascertain timing and cause of death up to December 31, 2019. Risk factors for mortality were assessed using multivariable Cox regression models and observed mortality rate compared to 'expected' rates in the Australian general population using indirect-standardised mortality ratios (SMR), overall and by sex & age at diagnosis (<8, 8-15 years).

Results: Of 5,412 children diagnosed with T1D, 113 died with all-cause mortality of 1.15/1,000 person-years. Most common causes of death were acute complication (DKA) (29%), diabetes without complication (17%), accident/misadventure (12%), cancer (11%) and chronic complications of T1D (10%). Older age at diagnosis (adjusted Hazards Ratio (aHR) 1.75, 95%CI 1.16, 2.70) & living in most disadvantaged areas (aHR 2.24 95%CI 1.20, 4.23) were associated with increased risk of mortality. Overall SMR was 1.74 (95%CI 1.44, 2.11) with females having higher SMR than males (3.05 vs 1.21) and females 30-39 years having highest SMR of 5.34 (3.27, 8.72). Older age at diagnosis had double the SMR 2.00 (1.62, 2.49) compared with younger ages (SMR 1.22; 0.82, 1.82).

Discussion: Compared to the general population, people with childhood-onset T1D had higher risk of mortality, particularly for females, those diagnosed at older ages and SMR increased with age. Given increased insulin resistance with age, targeted strategies to reduce diabetes-fatigue, improve glycaemic control and prevention of chronic diseases are required.

COVID-19 Pandemic

Incidents of domestic violence, loneliness and suicidal ideation among perinatal Japanese women during the COVID-19 pandemic Midori Matsushima* Naoki Kondo Hiroyuki Yamada Takahiro Tabuchi Kaho Hisamatsu

Suicide rates increased among Japanese women during the COVID-19 pandemic; however, the reasons are unknown. Particularly, perinatal women were at increased risk as they were more prone to psychosocial issues that emerged during the pandemic, such as domestic violence (DV) and loneliness. Using a nationwide web survey, panel data over two time periods (July-August 2021 and January-February 2022) was used to determine the association between the onset of DV and loneliness and the onset of suicidal ideation. Multinomial regression models were run using a sample of 3101 women, excluding those with psychiatric history. Four different groups were set as outcome variables: never had suicidal ideation during their entire life (*Resilient* group), had suicidal ideation throughout the two time periods of the surveys (*Persistent* group), did not have suicidal ideation in the first survey but onset during the second survey (*Onset* group), and was recovered by the second survey (*Recovered* group). Exposure variables were DV and moderate-to-severe loneliness, and they were measured as: never experienced, experienced throughout the two surveys, not experienced in the first but onset during the second survey and experienced in the first but resolved by the second survey. By adjusting the possible confounders including physical health status, demographic and economic characteristics, results showed that the onset of DV raised the risk of becoming the *Onset group (*Odds ratio (OR) 3.0 and 95% Confidence Interval (CI) [1.7-5.3]). The onset of loneliness also raised the risk of the onset of suicidal ideation with OR 9.2 [95% CI (4.5-18.8)]. Those who experienced DV in the first survey but for whom it had ended by the second survey were more likely to be recovered from suicidal ideation. Similar results were obtained for loneliness. Targeting DV and loneliness could be important points of intervention for pandemic-related suicide prevention.

COVID-19 Pandemic

Pandemic-related changes in stillbirth rates in Canada K.S. Joseph* Sophie Simon Sid John Amelie Boutin Giulia Muraca Neda Razaz Sarka Lisonkova

Introduction: There is conflicting evidence on whether Canadian stillbirth rates were adversely impacted by obstetric service disruptions due to the Covid-19 pandemic. Reasons for study differences include the data source, methods, unit of analysis (month vs quarter), and region examined. We carried out an interrupted time series analysis to determine if the pandemic had an effect on stillbirth rates in Canada.

Methods: The study included all live births and stillbirths >=20 weeks' gestation in Canada, 2015-2020, with data obtained from the live birth and stillbirth files of Statistics Canada. Stillbirths were analyzed by month, with Jan 2015-Feb 2020 and Mar 2020-Dec 2020 considered to be the pre-pandemic and pandemic periods, respectively. Interrupted time series analyses were used to determine pandemic effects after addressing seasonality.

Results: The study population included 18,475 stillbirths and 2,244,240 live births (stillbirth rate >=20 weeks' gestation 8.2 per 1,000 total births; >=28 weeks 2.8 per 1,000 total births). Stillbirths >=20 weeks increased marginally in the pre-pandemic period (0.009 per 1,000 total births/month, 95% CI 0.003 to 0.015), by 1.01 per 1,000 total births (95% CI 0.56 to 1.46) with pandemic onset, and declined substantially in the pandemic period (-0.247 per 1,000 total births/month, 95% CI -0.335 to -0.159). Stillbirths >=28 weeks showed no change in the pre-pandemic period (0.001 per 1,000 total births/month, 95% CI -0.002 to 0.004), a pandemic onset increase of 0.35 per 1,000 total births (95% CI 0.16-0.54), and a pandemic period change of -0.069 per 1,000 total births/month (95% CI -0.100 to -0.037). There was a pandemic-related excess of 90 stillbirths >=20 weeks and 19 stillbirths >=28 weeks gestation between March and May 2020.

Interpretation: The Covid-19 pandemic was associated with a transitory increase in stillbirths in Canada, followed by a rapid return to pre-pandemic stillbirth rates.

COVID-19 Pandemic

Injury-related pediatric emergency department visits during the first 2 years of the COVID-19 pandemic Francesca del Giorgio* Emilie Groulx-Boivin Jocelyn Gravel Olivier Drouin

Background: The long-term impact of the COVID-19 pandemic on pediatric injuries remains largely unknown.

Objective: To quantify changes in monthly incidence and severity of pediatric injury-related emergency department (ED) visits in Quebec during the first two years of the COVID-19 pandemic.

Methods: This retrospective longitudinal study was conducted at a large tertiary care center in Montréal, Quebec. Segmented negative binomial regression was used to estimate the change in monthly incidence of injury-related pediatric ED visits during the first (March 2020-Feb 2021) and second (March 2021-Feb 2022) year of pandemic, overall and by age categories (0-4, 5-11, and 12-17 years). In secondary analysis, logistic regression was used to estimate the change in seasonal risk of hospitalization during the first two years of the pandemic. A 4-year historical control period (April 2016-Feb 2020) was used to account for secular time-trends and seasonality.

Results: There was evidence of a 49% reduction in visits at the onset of the pandemic (Incidence Rate Ratio (IRR)=0.51, 95% CI=0.43-0.61), followed by a surplus of cases starting in the winter of 2020 and peaking in January of 2020 by 52% (IRR 1.52, 95% CI=1.34-1.72), returning to the expected incidence by the end of Spring 2021. This trend was held for children 5-11 and 12-17 years of age but not for pre-schoolers (0-4 years), for which there was no change in incidence of ED visits. The risk of hospitalization due to injury increased at the onset of the pandemic by 71% (risk Ratio (RR) 1.71, 95% CI 1.11-2.56), but was reduced in the fall (-58%, RR 0.42, 95% CI 0.24-0.74) and winter of the first year of the pandemic (-57%, RR 0.43, 95% CI 0.24-0.76) relative to expected risk.

Conclusion: Seasonal patterns in injury-related pediatric ED visits were disrupted in the two years proceeding the onset of the COVID-19 pandemic. Understanding these changes in incidence may assist in future development of injury prevention strategies.

COVID-19 Pandemic

Stressful COVID-19 experiences and the association with postpartum depression Stefanie Hinkle*, Eliza Kinsey Stefanie Hinkle Shimrit Keddem Stefanie Hinkle

Background: The COVID-19 pandemic was a major disruptor to domestic and economic life and numerous studies have documented the adverse impact of the pandemic on mental health outcomes. We evaluated the relationship between stressful pandemic experiences during pregnancy with postpartum depression.

Methods: This cross-sectional, population-based study used data from 26 states (plus DC, New York City and Puerto Rico) that participated in the CDC's Pregnancy Risk Assessment Monitoring System (PRAMS) and implemented a retrospective COVID experiences survey starting in October 2020 (n=14,474 births). Survey weighted regression models were used to assess the association between stressful experiences due to COVID and the risk of postpartum depression. All models were adjusted for individual-level sociodemographic characteristics as well as for self-report of depression prior to pregnancy and gestational timing at the start of the pandemic (i.e., preconception, 0-20, 20+ weeks).

Results: Among the eligible 13,016 participants (weighted N=762,397), there was a high prevalence of stressful experiences due to COVID including problems paying bills (17%), loss of childcare (19%), food insecurity (13%), losing work (26%), becoming homeless (1%), and increasing intimate partner violence (2%). The prevalence of postpartum depression was 13%. Becoming homeless was most strongly associated with postpartum depression (aOR=2.1; 95% CI 1.2-3.5) while other stressors including increased intimate partner violence (aOR=1.8; 1.1-2.7), difficulty paying bills (aOR=1.4; 1.1-1.7), food insecurity (aOR=1.3; 1.0-1.7), and losing work (aOR=1.3; 1.1-1.6) were also associated with postpartum depression. Losing childcare and spending more time caring for children were not associated with postpartum depression.

Discussion: The COVID pandemic added additional stressors to birthing people that may have contributed to an excess number of individuals experiencing postpartum depression.

COVID-19 Pandemic

Changes in Gestational Weight Gain in Louisiana during the COVID-19 Pandemic Nicole Cohen*, Emily Harville Chelsea Kracht Nicole Cohen Elizabeth Sutton Maryam Kebbe Leanne Redman Nicole Cohen

Objectives: To examine how gestational weight gain (GWG) changed during the COVID-19 pandemic and explore differences by race.

Methods: A retrospective review of medical records from March 2019 – March 2022 (23,553 total deliveries) at a major delivery hospital, Woman's in Baton Rouge, LA. GWG was evaluated as total GWG and adherence to the 2009 IOM recommendations. Deliveries (cross-sectionally) and conception cohorts prior to the pandemic were compared to those occurring later, using linear, log-linear, and polynomial regression with control for covariates.

Results: Between March 2019 and March 2022), around 30% of women met GWG recommendations, regardless of time frame From March 2019 to February 2020, 41.9% exceeded the recommended weight gain; from March 2020-March 2021, 45.3%; and from March 2021-March 2022, 43.8%. Women had higher average GWG if they delivered peak (adjusted beta 0.39 kg, SE 0.32) or late (0.82, 0.30) pandemic compared to those who delivered pre-pandemic (p=0.02), with a tendency for this increase to be larger for Black women. When cohorts were defined by conception date, women who conceived before the pandemic but delivered after it started had higher GWG compared to those whose entire pregnancy occurred before the pandemic started (adjusted beta 0.52 kg, SE 0.17). This declined somewhat in the pregnancies conceived after the pandemic started (0.30, 0.13) and the late pandemic (0.17, 0.16) (p=0.01) There was a similar pattern towards exceeding the GWG recommendations (adjusted risk ratio 1.07, 1.03-1.11 for delivery during the peak and 1.04, 1.00-1.08 for late). Examining mean weight gain month by month suggested a small dip in GWG for March 2020, followed by raised average GWG for the following year.

Conclusions: Women who spent critical timepoints of their pregnancy during the COVID-19 pandemic gained more weight compared to previous years. This increase leveled off as the pandemic progressed.

COVID-19 Pandemic

Perinatal health and healthcare utilization during the COVID-19 pandemic: an interrupted time series analysis using the Pregnancy Risk Assessment Monitoring System Alison Gemmill*, Deborah Karasek Daniel Collin Kaitlyn Jackson Rita Hamad Alison Gemmill Alison Gemmill

Background: Research evaluating the impact of the COVID-19 pandemic on perinatal health in the US has largely focused on birth outcomes. It is unclear how the pandemic affected other outcomes, including maternal health and healthcare utilization, as well as inequities.

Methods: Using population-based data from the Pregnancy Risk Assessment Monitoring System 2016-2020, we employed a Bayesian structural time-series approach using the *CausalImpact* R package. Prenatal and postnatal outcomes following the onset of the COVID-19 pandemic in March 2020 included prenatal care initiation and utilization, depression during pregnancy, gestational diabetes mellitus (GDM), hypertensive disorders of pregnancy (HDP), gestational weight gain (GWG), postpartum care utilization, and postpartum depression. We specified a univariate model consisting of the outcomes without covariates. A second model included month of birth, and aggregated covariates for maternal age, education, race/ethnicity, and insurer. We also examined heterogeneity by race/ethnicity and income.

Results: The univariate models showed evidence of reduced relative effect for prenatal care utilization (-4.3%;95% CI: -5.6, -3.1) and postpartum visit utilization (-2.8%;95%CI: -3.6, -2.0), and an increased relative effect for HDP (13.4%;95%CI: 5.1, 21.3), GDM (24.4%, 95% CI: 14.6, 34.1), and depression during pregnancy (18.7%;95%CI: 9.4, 28.0). Models did not indicate a change in prenatal care initiation, GWG, or postpartum depression. Results were similar in adjusted models. Stratified models revealed differences by race/ethnicity and income.

Discussion: Using a rigorous interrupted time series design, we found that stress or healthcare changes of the pandemic may have reduced prenatal and postpartum care utilization and adversely impacted maternal morbidities. As maternal health imparts enduring impacts for birthing people and infants, our result provide insight into the population health effects of the pandemic.

Disability status

Differences in Preconception Health Risks by Type of Disability Willi Horner-Johnson* Ilhom Akobirshoev Anne Valentine Robyn Powell Monika Mitra

Background: An estimated 18% of reproductive age women in the U.S. have a disability. Previous studies have found worse preconception health among disabled women overall, which may contribute to adverse perinatal outcomes in this population. However, little is known about how preconception health differs by disability type.

Methods: We analyzed 2016-2019 national-level data from the Behavioral Risk Factor Surveillance System. Our sample included non-pregnant women ages 18-44 who had not had a hysterectomy. Data were available on 18 indicators of preconception health identified by the Core State Preconception Health Indicators Working Group. We compared the prevalence of each preconception health risk among women with physical, cognitive, sensory, or multiple disabilities to non-disabled women.

Results: Women with multiple disabilities were the most likely to experience poor general health, unmet needs for dental care and Pap testing, frequent mental distress, inadequate social support, and current asthma, and to have less than a high school education and be current smokers. Women with cognitive disabilities were the most likely to engage in heavy drinking and binge drinking. Physically disabled women were the most likely to experience diabetes, obesity, and lack of exercise. Women with vision disability had the highest proportions with no health coverage, no checkup in the past year, and no flu vaccination in the past year. Women with hearing disability had significantly more health risks than non-disabled women but fewer risks than women with other disabilities.

Conclusions: Many of the health risks we observed among disabled women are potentially modifiable. Our findings emphasize the need for increased attention to the preconception health of disabled women and highlight areas of need for women with different types of disabilities. Given the diversity of disabled women, measures to address the unique preconception health needs of each disability group are critical.

Disability status

Pregnancy complications and adverse maternal outcomes among Black and Hispanic women with physical disabilities Willi Horner-Johnson* Bharti Garg Aaron Caughey Ilhom Akobirshoev Monika Mitra

Background: Women with physical disabilities have increased risk of adverse perinatal outcomes. Risks may be even greater for disabled women in minoritized racial or ethnic groups. To assess these potentially cumulative risks, we examined perinatal outcomes at the intersection of physical disability and race or ethnicity.

Methods: We used linked hospital discharge and vital records data from California, 2000-2012. We identified women with physical disabilities using ICD-9 codes for major injuries, congenital anomalies, musculoskeletal disorders, or nervous system disorders. We excluded multiple gestations and gestational ages <23 weeks or >42 weeks. We compared women in 5 groups (Black and Hispanic with and without physical disabilities, White with physical disabilities) to a reference group of non-Hispanic White women without disabilities. We used multivariable logistic regression to assess associations with gestational hypertension, preeclampsia, gestational diabetes, cesarean delivery, preterm delivery, and severe maternal morbidity (SMM), while controlling for sociodemographic and clinical confounders.

Results: For most outcomes, odds ratios (OR) were largest for Black disabled women, followed by Hispanic disabled women. In particular, Black and Hispanic disabled women had more than four times the odds of SMM as the reference group (Black disabled OR=4.98, 95% confidence interval (CI): 3.57, 6.96; Hispanic disabled OR=4.37, 95% CI: 3.74, 5.09), while non-disabled Black (OR=2.03, 95% CI: 1.90, 2.16), non-disabled Hispanic (OR=1.34, 95% CI: 1.28, 1.39), and disabled White women (OR=1.89, 95% CI: 1.51, 2.38) had markedly lower odds of SMM.

Conclusions: Black and Hispanic women with physical disabilities are especially likely to experience SMM. Efforts are needed to understand underlying causes of these disparities and develop policies and practices to eliminate them.

Environment/climate change

PFAS Concentrations in Early and Mid-Pregnancy and Risk of Gestational Diabetes Mellitus within the Ethnically Diverse PETALS Cohort Alicia Peterson* Yeyi Zhu Sophia Fuller Juanran Feng Stacey Alexeeff Susanna Mitro Kurunthachalam Kannan Morgan Robinson Amy Padula Assiamira Ferrara

Background

Per- and polyfluoroalkyl substances (PFAS) are persistent synthetic chemicals and have been linked to disrupting glucose homeostasis but results remain inconclusive for their role in risk of gestational diabetes mellitus (GDM). We examined prospective associations of PFAS concentrations measured in early and mid-pregnancy with GDM risk.

Methods

In the PETALS pregnancy cohort, a nested case-control study included 41 GDM cases and 87 controls. PFAS analytes were measured at first and second trimesters, with cumulative concentrations estimated by the area-under-the-curve (AUC). Individual adjusted weighted unconditional logistic regression models examined seven PFAS in association with GDM risk. P-values were corrected using the false-discovery-rate (FDR). We examined effect modification by Asian/Pacific Islander (A/PI) or non-A/PI, given the higher GDM risk in A/PI. Mixture models were analyzed with Bayesian kernel machine regression.

Results

First trimester levels of the following PFAS were individually associated with higher GDM odds per interquartile range (IQR): PFOA (Odds Ratio; 95% CI =1.15; 1.04, 1.27), PFNA (1.40; 1.24, 1.58), and PFDA (1.23; 1.09, 1.38). PFHxS and PFUnDA were associated with lower GDM odds (0.48; 0.38, 0.60; and 0.79; 0.64, 0.98, respectively). Results were consistent for the second trimester and for the AUC with the addition of PFOS and PFUnDA being associated with increased GDM odds (Trimester Two: 1.41; 1.17, 1.71 and 1.49; 1.18, 1.89, respectively). Compared to non-A/PI, A/PI had higher PFAS levels and stronger associations of PFAS with higher GDM odds, and PFHxS was associated with higher GDM odds. Mixture analyses showed similar suggestive effects, although overall mixtures were not significant.

Conclusions

Overall, PFAS concentrations were associated with higher odds of GDM, especially among A/PI, suggesting corroboration in larger sample sizes and that people at high risk of GDM should potentially avoid known sources of PFAS.

Environment/climate change

Association between prenatal exposure to particulate matter and birth size Ian Trees* Ian Trees Diane Putnick Priscilla Clayton Rajeshwari Sundaram Pauline Mendola Erin Bell Edwina Yeung

Background: Perinatal exposure to air pollution is associated with adverse birth outcomes. This study explores how prenatal exposure to particulate matter (PM) at different time windows during pregnancy impacts risk of being born at extremes in birth size.

Methods: We included participants from the Upstate KIDS birth cohort in New York State. Census tract level air pollution data came from the EPA's Community Multiscale Air Quality model matched to home addresses at birth. Birthweight and gestational age from vital records were used to define newborns as large (LGA, >90th percentile), small (SGA, <10th percentile), or appropriate for gestational age among singletons using a population reference (n=3881); as well as low birthweight (LBW, <2500g) and macrosomia (>4000g) among all infants (n=4959). We ran multiple logistic regressions adjusting for maternal age, race, education, smoking status, private insurance status, traffic-related pollutants (O_3, NO, and SO_2), infant sex, plurality (as applicable), and seasonality.

Results: Participants were exposed to PM concentrations below EPA standards (median $PM_{2.5}$: 5.89 µg/m^3, median PM_{10}: 8.14 µg/m^3). No associations were found for 1st trimester PM exposure. However, $PM_{2.5}$ exposure in the 2nd trimester was associated with macrosomia in fully-adjusted models (Odds Ratio: 1.48, 95% CI: 1.15, 1.92). PM_{10} exposure in the 3rd trimester was negatively associated with LGA and macrosomia, but these associations were attenuated after adjusting for covariates. Finally, higher mean levels of $PM_{2.5}$ across pregnancy were associated with increased odds of macrosomia (OR: 1.37, 95% CI: 1.00, 1.87) after adjustment for traffic pollutants, but not in unadjusted models (OR: 0.92, 95% CI: 0.79, 1.05). No associations were found between PM exposure at any time point and SGA or LBW.

Conclusion: Prenatal exposure to particulate matter may impact birth size depending on the pollutant mixture and specific windows of exposure.

Environment/climate change

Toxic Metals and Pediatric Immune Dysfunction: A Scoping Review Krystin Sinclair* Krystin Sinclair Sonia Habel Nitzana Spiegel Olivia Castello Erin Kulick Marina Feiler

Objective: To understand and summarize the existing literature on the association between toxic metals (lead, mercury, arsenic, and cadmium) and pediatric immune dysfunction.

Materials and methods: Seven databases (PubMed (NLM), Embase (Elsevier), CINAHL (Ebsco), Web of Science (Clarivate Analytics), ProQuest Public Health Database, and ProQuest Environmental Science Collection) were searched following PRISMA guidelines for search reporting based on a combination of keywords and subject headings. Rayaan software was used to identify duplicates and screen by title and abstract in blinded (two reviewers per article) and independently reviewed records from databases, a third reviewer was used if a tiebreaker was needed. The remaining full texts were reviewed for content and summarized.

Results: The above search criteria produced 7,111 search results; 2,406 articles were removed due to duplication. Among the remaining 4,705 articles, 4,603 articles were excluded during the title, abstract, and full-text reviews for the following exclusion reasons: 1) not original research, 2) not epidemiology, 3) did not include toxic metals, 4) did not examine an immune health outcome, or 5) not pediatric (<18 years). The final review included 102 studies evaluating the association between toxic metals (lead, mercury, arsenic, and cadmium) and outcomes indicative of pediatric immune dysregulation. The most common immune outcomes evaluated included antibody levels, immune cell levels (T cells, B cells, etc.), asthma diagnosis, eczema, and wheezing.

Conclusions: The existing literature suggests an association between toxic metals and pediatric immune dysregulation. However, results are not consistent across regions, and clinical versus biomarker outcomes. The existing evidence still lacks a clear relationship between the impact of these toxic metals on biomarkers of immune function and how these translate to clinically meaningful outcomes.

Environment/climate change

Effects of Prenatal Chemical Exposures on Early Menarche: A Scoping Review of Prospective Studies Melanie Sandquist* Somdat Mahabir

Age at menarche is an important risk factor for health and disease, including breast cancer. While emerging evidence indicates that prenatal exposures to certain chemicals in the environment result in increased risk of early menarche, much remains unknown. Many of the environmental chemicals that children are exposed to prenatally are known endocrine disruptors. Since prenatal environmental exposures are an important public health concern, potentially modifiable, and offer opportunities for disease prevention, we conducted a scoping review to assess the state of the published literature. This scoping review assesses the state of epidemiologic research on prenatal chemical exposure and age at menarche. Searches conducted in PubMed, SCOPUS and Embase returned 149 papers. Based on established exclusion/inclusion criteria, we included twenty-two prospective studies in our analysis. The literature search assessed several chemical categories, such as agricultural chemicals, metals, phthalates, phenols, biphenyls, per-/polyfluoroalkyl (PFAS) substances, medications, and tobacco smoke in relation to age at menarche. Relevant information was then extracted from each study, tabulated, and synthesized. Several chemical exposures impacted age at menarche. Contraceptives, smoking, atrazine, several phenols, phenyls and PFAS were associated with early menarche. This scoping review shows that prenatal chemical exposures may have potentially harmful health effects later in life by pathways that affect age at menarche. There are large gaps in knowledge that must be filled to improve understanding of prenatal environmental chemicals as well as the mechanisms by which they affect menarche. Many of the published prospective analyses of prenatal chemical exposures and menarche are based on ancillary studies to parent cohorts. There is a need for diverse prospective pregnancy cohorts with a priori aims that address prenatal chemical exposures and their effects on the age of menarche.

Environment/climate change

Prenatal exposure to ambient fine particulate matter and child lung function in the CANDLE cohort Allison Sherris* Adam Szpiro Marnie Hazlehurst Logan Dearborn Margaret Adgent Kecia Carroll Drew Day Kaja Lewinn Christine Loftus Yu Ni Qui Zhao Catherine Karr Paul Moore

Background: Ambient fine particulate matter ($PM_{2.5}$) adversely impacts airway health in childhood, yet research on prenatal $PM_{2.5}$ exposure and child lung function is limited. We investigated these associations in the ECHO-PATHWAYS Consortium, focusing on the role of exposure during different stages of fetal lung development.

Methods: We included 725 children in the CANDLE cohort born from 2007-2011 in Shelby County (Memphis), TN. Prenatal exposure to ambient $PM_{2.5}$ was estimated using a spatiotemporal model based on maternal residential address and averaged over established prenatal periods of lung development: pseudoglandular (5–16 weeks of gestation), canalicular (16–24 weeks), and saccular (24–36 weeks). Forced expiratory volume in the first second (FEV1) and forced vital capacity (FVC) were measured by spirometry at age 8-10 years. We used linear regression to estimate associations between mutually adjusted exposure periods and lung function z-scores, adjusting for maternal/child characteristics, prenatal/postnatal smoke exposure, and birth year/season. As a confirmatory analysis, we used Bayesian Distributed Lag Interaction Models (BDLIM) to flexibly explore critical windows of exposure.

Results: The average ambient concentration of $PM_{2.5}$ during pregnancy was 10.7 $\mu g/m^3$. Lower FEV1 z-scores were observed in association with $PM_{2.5}$ exposure during weeks 5-16 of gestation (-0.11 standard deviations per $\mu g/m^3$, 95% CI: -0.21, -0.01) and weeks 25-36 of gestation (-0.10, 95% CI: -0.18, -0.01). Results were qualitatively similar for FVC z-scores, while the ratio of FEV1/FVC was not associated with $PM_{2.5}$ in any exposure window. BDLIM analyses also identified potential critical exposure windows in early and late pregnancy for FEV1 and FVC.

Conclusions: In a diverse U.S. cohort, prenatal $PM_{2.5}$ exposure was associated with lower lung function at age 8-10 (FEV1 and FVC). Exposure during the pseudoglandular and saccular periods of lung development may be particularly detrimental.

Environment/climate change

Associations between built food environment and adverse birth outcomes in a North Carolina birth cohort Maxwell Hatala*, Nichole Kulikowski Thomas Luben Archana Lamichhane Maxwell Hatala Maxwell Hatala

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Neighborhood characteristics, including the built food environment, can influence accessibility to and availability of healthy food options and are associated with dietary intake and health outcomes. We examine whether there is an association between the built food environment, using supermarket accessibility as an indicator, and adverse birth outcomes in a North Carolina birth cohort (n = 1,260,919) from 2003-2013. For adverse birth outcomes, we identified cases of low birth weight (<2500 g), preterm birth (<37 weeks gestation), and term low birth weight (birth weight <2500 g and ≥ 37 weeks gestation). We identified specific food-related industries (i.e., supermarkets) using the North American Industry Classification (NAICS) codes reported in the Dun & Bradstreet's (D&B) business dataset and based on prior knowledge of literature. We used the geocoded supermarket addresses and participants' residential locations to calculate distance to the nearest supermarket from the residential locations and number of supermarkets with the various buffers of residential locations using Euclidian and Network distance in ArcGIS Pro. Preliminary results using 2013 D&B data show that the average distance to the nearest supermarket from residential location was 2.26 miles and there was an average of 8.07 supermarkets within a five-mile buffer around residential location when Euclidian distance was used. When using road network, the average number of stores within a five-mile distance decreased to 5.45. Associations between built food environment exposure variables and odds of adverse birth outcomes will be calculated in subsequent analyses. Differences in access to sources of nutritious food contribute to an individual's built food environment and potentially be associated with health endpoints, including adverse birth outcomes.

Fertility and fecundity

Association Between Exposure to Bisphenols and Phthalates and Female Time to Pregnancy and Subfecundity: Findings from a NYC Pregnancy Cohort Mia Charifson* Linda Kahn Eunsil Seok Shilpi Mehta-Lee Mengling Liu Leonardo Trasande

Bisphenols and phthalates are endocrine-disrupting chemicals commonly found in consumer products and linked to reproductive health and fertility. The goal of this study was to investigate the relation of female bisphenol and phthalate exposure with time to pregnancy (TTP) and subfecundity (TTP >12 months) in the New York University Children's Health and Environment Study (n=400). Chemicals were creatinine-adjusted and imputed below the limit of detection (LOD) as LOD/√2. We used discrete Cox and logistic regression models to estimate associations for each quartile of chemicals measured in first-trimester urine with TTP and subfecundity. To assess the relative importance of each chemical on these outcomes, we employed a novel partial linear single-index mixture model. All models were adjusted for age, body mass index, parity, race/ethnicity, nativity, pre-pregnancy alcohol and folic acid use, and hospital site. Consistent with prior literature, we found little evidence of a link between bisphenols and fecundity, but we unexpectedly observed some positive associations at low doses (Q2 vs. Q1 TTP Fecundability Ratio [FR]: 1.58 [95% confidence interval: 1.16, 2.15]; Subfecundity OR: 0.30 [0.10, 0.77]). Phthalates were consistently associated with longer TTP (lower FOR) and higher odds of subfecundity, although the only group with statistically significant results in all quartiles of exposure was the anti-androgenic phthalates (Q4 vs. Q1 TTP FR: 0.65 [0.47, 0.89]; Subfecundity OR: 4.62 [1.58, 16.9]). The chemical with the highest relative contribution to TTP and subfecundity in the mixtures model was mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP; 75.9% and 41.4%, respectively), an anti-androgenic phthalate. Results were robust to several sensitivity analyses. Overall, we found evidence of negative associations between phthalates and fecundity, warranting further investigation into potential mechanisms and recommendations for public health.

Fertility and fecundity

Association between BMI and Menstrual Cycle Irregularities -Finding the Optimal BMI for Regular Menstruation through Big Data Analysis Shiori Itoi* Makiko Sampei Takayuki Tatsumi Yutaka Osuga Kaori Koga Satoshi Narumi Naho Morisaki

Objective: To evaluate the association between body mass index (BMI) and menstrual cycle irregularities using data retrieved from a smartphone application.

Methods: We analyzed data from 483,520 menstrual cycles from 20,551 women who gave consent and answered in-app questionnaires on background characteristics. Basal body temperature (BBT) readings were also obtained for 4,876 women. Outcomes of interest were standard deviation (SD) of average cycle length (ACL), amenorrhea (if any cycle length ≥90 days), oligomenorrhea (90 days>ACL ≥39 days), and proportion of presumed ovulatory cycle (POC), defined as the proportion of cycles with follicular-luteal BBT difference >0.3 degrees. For all models, cubic spline models were used in consideration of the non-linear association between BMI and outcomes and adjusted for age, parity, marital status, pregnancy desire, exercise level, drinking status, work status, depression level, and education attainment.

Results: ACL, SD, as well as the risk of amenorrhea and oligomenorrhea, showed a distinct J-shaped curve in relation to BMI, with the trough at BMI 20 kg/m^2. The proportion of POC showed a distinct upside-down J-shaped curve in relation to BMI, with a peak at BMI 20 kg/m^2.

Compared with women of BMI 20 kg/m^2, women with BMI 30kg/m^2 had significantly higher SD of ACL [0.49 (95%CI, 0.41-0.56)], higher risk of amenorrhea [OR 1.74 (95%CI, 1.41-2.15))] and oligomenorrhea [OR 1.76 (95%CI, 1.60-1.93)], and lower proportion of POC [OR 0.75 (95%CI, 0.69–0.81)]. Women with BMI 16 kg/m^2 also had significantly higher SD of ACL [0.15 (95%CI,0.02-0.28)], higher risk of amenorrhea [OR 1.68 (95%CI, 1.15-2.44)], and oligomenorrhea [OR 1.46 (95%CI, 1.24-1.71)] but no significant difference was found for POC.

Conclusion: Using a large dataset of in-app logs, we observed that women with BMI 20 kg/m^2 have the most regular menstrual cycles with the least risk of amenorrhea, oligomenorrhea, and the highest proportion of presumed ovulatory cycles.

Fertility and fecundity

Supplement Use Among Couples Seeking Fertility Treatment and Associations with Live Birth Naria Sealy* Sunni L. Mumford Ellen C. Caniglia Julia DiTosto Chanele D. Lomax Erica Boiman Jim Hotaling Bradley Van Voorhis Ginny Ryan Pauline Mendola Enrique F. Schisterman Stefanie N. Hinkle

Background: Dietary supplements are increasingly being marketed towards couples attempting to become pregnant. Studies indicate that micronutrients found in these supplements may be important for pregnancy and fertility, there are limited data on use of dietary supplements within couples seeking infertility treatment and on its association with live birth.

Methods: This was a secondary analysis of data from couples seeking fertility treatment within the Folic Acid and Zinc Supplementation Trial (FAZST) and Impact of Diet, Exercise, and Lifestyle on Fertility Study (IDEAL). Information on supplement use was collected at baseline. Descriptive statistics of supplement use were collected. Poisson models with robust variance were used to estimate risk ratios (RR) and 95% CI for associations between supplement use and live birth, adjusting for confounders.

Results: Among 2370 couples 67% of females used any supplement (66% used a multivitamin) and 45% of males used any supplement (38% used a multivitamin) at baseline. The most used individual supplements among females were folic acid (8%) and fish oil (6%). Fish oil was the most used individual supplement among males (11%), followed by vitamin C (11%). Overall, 35% of couples achieved a live birth. Female use of any supplement use was associated with an increased chance of live birth (adjusted RR: 1.22, 95% CI: 1.04, 1.43). Male use of supplements was not associated with live birth (adjusted RR: 0.98, 95%: 0.87, 1.09). Supplement use within couples was associated with live birth when only the female partner used a supplement (adjusted RR: 1.25, 95% CI: 1.04, 1.50).

Conclusion: Among couples seeking infertility treatment, supplement use was common among both male and female partners, with the majority taking a multivitamin. There is evidence that supplement use in female, but not male, partners is associated with increased likelihood of live birth.

Fertility and fecundity

Target trial emulation of preconception serum vitamin D levels on live birth and pregnancy loss: a couples-based approach Julia DiTosto* Ellen Caniglia Stefanie Hinkle Naria Sealy Chanele Lomax Enrique Schisterman Erica Johnstone Pauline Mendola Jim Hotaling Ginny Ryan Sunni Mumford

Background: Previous studies suggest that higher preconception vitamin D is associated with improved fertility; however, they largely focused on female partners or couples undergoing in-vitro fertilization. We evaluated associations between preconception vitamin D levels in both male and female partners on live birth and pregnancy loss in couples seeking infertility treatment that was primarily ovulation induction/intrauterine insemination.

Methods: Baseline serum 25(OH)D was measured in both partners (N=2370 couples). A target trial framework was used to emulate randomization based on preconception vitamin D status [deficient (<20 ng/mL, ref), insufficient (20-29.9 ng/mL), sufficient (≥30 ng/mL)]. Individual and couple-based models were considered. Log-binomial regression models with multiple imputation for missing data estimated likelihood of live birth adjusting for confounders (Fig). Inverse probability weights account for conception in pregnancy loss models.

Results: At baseline, a majority of female and male partners were vitamin D deficient or insufficient (females 19% and 40%, males 29% and 50%, respectively) while 11% of couples were both deficient. Female vitamin D levels were associated with live birth (sufficient vs. deficient RR 1.3, 95% CI: 1.1, 1.6; insufficient vs. deficient: RR 1.2, 95% CI: 1.0, 1.5). Male vitamin D levels were inconsistently associated with live birth (sufficient vs. deficient RR 1.1, 95% CI: 0.9, 1.3; insufficient vs. deficient: RR 1.2, 95% CI: 1.0, 1.4). Couples who were both sufficient or insufficient vs. both deficient had an increased likelihood of live birth (RR 1.4, 95% CI: 1.1, 1.7). No associations with pregnancy loss were observed.

Discussion: Using a target trial framework, higher preconception vitamin D levels among couples, particularly female partners, were positively associated with live birth and not with pregnancy loss. These results further support an association between preconception vitamin D levels and fertility.

Fetal loss/stillbirth/infant mortality

State and local government expenditures and infant mortality rates in the United States: An updated replication analysis Shivani Sowmyan* Ashley Hirai Jay Kaufman

Background: A recent longitudinal study found that increased state and local government expenditures were associated with reductions in infant mortality rates (IMR). We aim 1) to replicate the original results by Goldstein et. al. and 2) to update the analysis using the latest available data with various improvements, including adjustment for state fixed effects and inflation.

Methods: We utilized publicly posted data assembled by Goldstein et. al. which included a longitudinal, state-level dataset of expenditure data from 2000-2014 and annual 3-year averaged IMR data with a one-year lag to replicate original random effect (RE) model results that included an interaction between time and expenditures and controlled for state poverty rates. We updated the original analysis by adding expenditure data and annual changes in poverty and population through 2017 from the US Census Bureau, updating IMR data through 2019 (2018-2020), and adjusting expenditures for inflation and regional price parities (RPP). State random and fixed effects specification results were compared with the Hausman test.

Results: Replication of the original RE model showed that a standard deviation increase in expenditures was associated with a 0.35 reduction in IMR (95% CI: -0.58 , -0.13). However, this effect was much larger due to misreporting of the smaller time and expenditure interaction (-0.02) as the main effect. The updated RE model with adjustment for inflation and RPP showed an even larger association (-0.63, 95% CI: -0.77 , -0.49) with significant growth over time (-0.02, 95% CI: -0.04 , -0.0). State fixed effects results were similar due to a high intra-cluster correlation (0.75).

Conclusions: With various improvements, most notably adjustment for inflation and state purchasing power, this updated replication analysis generally bolstered the original study findings and showed larger associations between government expenditures and IMR reductions that may be increasing over time.

Gender and sexual identity

Perinatal outcomes and cardiovascular health during pregnancy among birthing people in same-sex and different-sex relationships in Louisiana Dovile Vilda* Maeve Wallace Isabelle Lian Emily Harville

Background: Little is known about perinatal outcomes among birthing people in same-sex relationships compared to people in different-sex relationships, despite differences in preconception risk factors. In addition, while sexual minority women (lesbian, bisexual, and queer) experience higher cardiovascular disease risk, no study so far has investigated the risk of cardiovascular complications during pregnancy in this population.

Methods: We conducted a cross-sectional analysis of vital records data on singleton live births in Louisiana from 2018-2020. We classified births in the female-female relationship as same-sex and female-male relationship as different-sex relationships. Using logistic regression, we estimated associations between having a birth parent in same-sex relationship and cesarean delivery, preterm birth, low birthweight, and low Apgar score, and cardiovascular morbidities (i.e., gestational hypertension, preeclampsia). We adjusted for sociodemographic, preconception, and pregnancy-specific perinatal risk factors. We also examined whether these associations were modified by race/ethnicity.

Results: Compared with birthing people in different-sex relationships, people in same-sex relationships were more likely to have cesarean delivery (adjusted odds ratio (aOR)=1.23; 95% CI=1.01-1.49), preterm birth (aOR=1.43; 95% CI=1.09-1.86), low birthweight infants (aOR=1.39; 95% CI=1.04-1.88), and have newborns with a non-reassuring Apgar score (aOR=1.78; 95% CI=1.05-3.01). No differences were found in cardiovascular complications during pregnancy between the two groups. Effect modification by race/ethnicity was significant for low birthweight, cesarean delivery, and spontaneous delivery ($p<.0.01$).

Conclusion: Birthing people in same-sex relationships experience disparities in several perinatal but not cardiovascular health outcomes. Further research is needed to investigate these differences, particularly at the intersection of sexual identity/orientation and race/ethnicity.

Genetics

Role of genetic ancestry on the relationship between genetic risk score of type 2 diabetes mellitus and birth weight Tesfa Dejenie Habtewold* Richard J. Biedrzycki Fasil Tekola-Ayele

Introduction: Women's genetic risk score for type 2 diabetes mellitus (GRS_{T2D}) has been associated with birth weight; however, the role of genetic ancestry in the relationship is unclear. We investigated whether the association of GRS_{T2D} with birth weight varies based on maternal genetic ancestry composition.

Methods: 1,935 pregnant women self-identified as Hispanic (n=531), White (n=601), African American (n=587), and Asian (n=216) from the NICHD Fetal Growth Studies – Singletons were included. GRS_{T2D} was calculated using 338 variants associated with T2D in the largest trans-ethnic study. The proportions of African, European, Amerindigenous, and East Asian genetic ancestry in the maternal genome were calculated. For each ethnic group, we assessed change in birthweight per unit increase in GRS_{T2D} using linear regression models without and with genetic ancestry proportion: model 1 included sex, gestational age, nativity, insurance, educational status, marital status, age, and parity; model 2 additionally included genetic ancestry, and GRS_{T2D}-genetic ancestry interaction term.

Results: Among Hispanics, GRS_{T2D} was significantly associated with birthweight in the model without genetic ancestry (beta [95% Confidence Interval] = 53 [14, 91] gram (gm)), and strengthened in the model with European ancestry (61 [4, 118] gm), but became weaker and non-significant in the model with Amerindigenous ancestry (49 [-7, 104] gm). Among Whites, GRS_{T2D} was not associated with birthweight in the model without genetic ancestry (26 [-9, 61] gm) but became stronger and significant in the model with European ancestry (52 [2, 102] gm). No associations were significant among African Americans and Asians in models without or with African and East Asian ancestry, respectively.

Conclusion: The performance GRS_{T2D} differed with genetic ancestry even within a self-identified ethnic group, which may be due to gene-environment interplays and limited non-European discovery genomic studies.

Gynecological health

New Long-Acting Reversible Contraceptive Insertions More Than Doubled Among a Commercially Insured, U.S.-Based Outpatient Population from 2010 to 2020 Mekhala Dissanayake* Clara Busse Chase Latour Sara Dejene Andrea Knittel Mollie Wood Alan Kinlaw

Long-acting reversible contraceptives (LARCs) are highly effective, but national trends in new use in outpatient settings are not well characterized.

We used the Merative MarketScan Commercial Claims and Encounters Database to construct a retrospective cohort of women ages 15 to 54 with ≥180 days of continuous enrollment in United States employer-sponsored private insurance from January 1, 2010 to December 31, 2020. We used Current Procedural Terminology (CPT) codes to identify LARC insertions/removals and Healthcare Common Procedure Coding System (HCPCS) codes to classify LARC type. We defined a new LARC insertion as an insertion code without a recent removal code (180 days before insertion) *and* a HCPCS code. We characterized the proportion of insertions by type: implants, non-hormonal intrauterine devices (NHIUD), hormonal IUD (HIUD). We calculated the month-level incidence of new LARC insertions per 10,000 people. Estimates are standardized to the age and state/territory distribution of January 2010.

We identified 1,372,594 new LARC insertions from 2010-2020. The monthly standardized incidence increased from 6.0 insertions per 10,000 people in January 2010 to 14.1 in December 2020. Incidence from March through May 2020 (low of 6.2) was lower than previous months (January: 15.2; February: 13.8), though incidence recovered by July (14.2). The average monthly incidence was lower in 2020 (12.7) compared to 2016-2019 (13.0-14.5). The share of LARCs that were HIUDs was stable across the study period (~68%) whereas implant use increased from 8.5% in 2010 to 21.0% in 2020, and NHIUD use decreased from 19.9% in 2010 to 10.9% in 2020.

New LARC insertion incidence doubled from 2010 to 2020. Incidence was lower early in the COVID-19 pandemic and although it returned to previous levels by July, the monthly average incidence in 2020 was still lower than prior years. Overall, our results demonstrate increasing popularity of LARCs among privately-insured users over this period.

Gynecological health

Vitamin D, calcium, and timing of menopause in a large, longitudinal cohort study Anne Marie Jukic* Dale Sandler Clarice Weinberg Katie O'Brien

Vitamin D status has been inconsistently associated with ovarian reserve and menopause. We used data from the Sister Study cohort to examine the associations of vitamin D supplement use, 25-hydroxyvitamin D (25OHD) level, and calcium supplement use, with the timing of natural menopause. Vitamin D and calcium supplement use were based on a questionnaire at baseline and two follow-up time points, and characterized in multiple ways based on type, dose, and duration of use. Serum samples from a random subset of participants were analyzed for total 25OHD ($25OHD_3$+$25OHD_2$+epi-$25OHD_3$) using liquid chromatography-mass spectrometry. Menopause was assessed at each follow-up as, "Have you had a menstrual period in the past 12 months?" and if not, their age at last menstrual period. We censored women at time of uterectomy or medically induced menopause, death, loss to follow-up or October, 2020. We used multivariable Cox proportional hazard models to estimate HRs and 95% CIs, adjusting for race/ethnicity, education, BMI, alcohol use, smoking status, and physical activity. Among the 13,102 eligible premenopausal participants, 8,897 experienced menopause during follow up. Combined use of a multivitamin and a single vitamin D supplement was associated with slightly earlier menopause (HR(CI): 1.10 (0.98, 1.24). None of the remaining vitamin D or calcium supplement variables were meaningfully associated with timing of natural menopause. A 25OHD level of at least 30 ng/ml was imprecisely associated with earlier menopause (HR(CI): 1.15 (0.85, 1.39), n=906). In total, vitamin D and calcium supplementation were not strongly associated with timing of menopause. Some results indicate that higher levels of vitamin D may be associated with earlier menopause.

Gynecological health

Endometriosis history and prescription medication usage among reproductive-aged women in NHANES 1999-2006 Kristen Upson*, Natalie Barstys Mandy Hall Nicole Talge Kiping Bohnert Christine Hsu Kristen Upson Kristen Upson

Endometriosis is a gynecologic, chronic inflammatory condition characterized by the presence of tissue histologically resembling endometrial glands and stroma outside of the uterus and is associated with a range of comorbidities. The economic burden of endometriosis symptom and comorbidity management has been examined in previous studies using insurance claims data, but few studies have captured the clinical complexity of the condition using prescription medication information in the general population. We examined the history of endometriosis diagnosis and current prescription medication use in a cross-sectional analysis of U.S. women ages 20-54 years using National Health and Nutrition Examination Survey (NHANES) data from years 1999 to 2006 (unweighted n=5,550). History of endometriosis diagnosis and number of current prescription medications were collected by self-report. Prescription number was categorized as ≥2 prescriptions (vs. <2) within 30 days of the NHANES interview, and polypharmacy was defined as the use of ≥5 prescriptions (vs. <5). We conducted log-binomial regression to estimate the prevalence ratios (PRs) and 95% CIs for the relationship between endometriosis history and prescription medication use, adjusting for age, education, insurance status, body mass index, and smoking, and accounting for the complex survey sampling design. Prevalence of endometriosis diagnosis history, current use of ≥2 prescriptions, and polypharmacy were 9%, 32%, and 8% respectively. Those with a history of endometriosis diagnosis (vs. without) had a 50% greater prevalence of taking ≥2 prescription medications (PR 1.5, 95% CI: 1.3-1.7). We observed an even stronger association with polypharmacy use (PR 1.9, 95% CI: 1.3-2.7). These results suggest endometriosis is associated with greater prescription medication use, highlighting the clinical complexity of the condition and the multiple medications that may be needed to manage symptoms and comorbidities.

Gynecological health

Investigating overtreatment: racial/ethnic differences in symptom severity among premenopausal hysterectomy patients in the US South Whitney Robinson* Joacy Mathias Mollie Wood Annie Green Howard Erin Carey Wanda Nicholson Timothy Carey Evan Myers Til Sturmer Kemi Doll

Objective. To evaluate whether symptom severity can explain higher hysterectomy rates among premenopausal non-Hispanic Black versus White patients in the U.S. South

Methods. Using electronic health record data from 1,703 hysterectomy patients (18-44 years old) treated in a large health care system in the US South (2014-2017), we accounted for symptom severity when examining racial/ethnic differences in hysterectomy rates for non-cancerous conditions among premenopausal non-Hispanic Black, non-Hispanic White, and Hispanic patients. We used Poisson Generalized Linear Mixed Modeling to model high symptom severity (>75%ile severity on scores of bleeding, bulk, or pelvic pain) as a function of race/ethnicity. Resulting prevalence ratios [PR] controlled for factors that contraindicate or favor treatment with hysterectomy.

Results. The median age of non-Hispanic White (n=1,050), non-Hispanic Black (n=565), and Hispanic (n=158) patients was 40 years. White and Black patients were mostly insured (insured>95%) while Hispanic patients were often uninsured (insured: 58.9%). Black patients had greater bleeding severity scores compared to Hispanic and White patients (medians=8, 7, and 4 respectively) and greater bulk scores (medians=3, 1, and 0); but pain showed different patterns (medians= 3, 5, and 4). Black and Hispanic patients were more likely to have severity documented on 2+ symptoms (referent: not severe on any symptoms) (adjusted PR [Black vs White]= 3.02 (95% confidence interval [CI]: 2.29, 3.99); adjusted PR [Hispanic vs White]= 2.61 (95% CI: 1.78, 3.83)). While Black and Hispanic patients were more likely to experience severe symptoms, we found no racial/ethnic differences in the number of alternative treatments attempted before hysterectomy.

Conclusion. We did not find evidence of overtreatment of Black patients. However, our findings suggest undertreatment of Black and Hispanic patients with uterine-sparing alternatives earlier in their disease progressions.

Health equity

Disparities in epilepsy over time in Canadian children: A retrospective birth cohort study.
Bénédicte Driollet* Emmalin Buajitti Asma Ahmed Jennifer Hutcheon Laura Rosella Seungmi Yang

Objective. Epilepsy is one of the most common neurologic disorders in children, and few studies have focused on disparities. The objective of this study is to investigate disparities in epilepsy by family socioeconomic position, immigration status, or gender over time in population-based birth cohorts.

Methods. We identified all in-hospital births between 2002 and 2019 in the province of Ontario, Canada, and linked their health records to various administrative data (N=2 342 739). We estimated rates of epilepsy in children <18 years, overall and by gender, maternal eligibility of the Ontario Drug Benefit (ODB) as a proxy of low income, area-based socioeconomic characteristics, and maternal immigration status.

Results. Overall prevalence of epilepsy was 31.6 per 1000 live births (95% Confidence interval 31.3-31.8), with higher rates for boys (33.7, 95%CI 33.3–34.0), children born in low-income families (39.2 95%CI 38.6–39.8), born in highly deprived areas (35.4, 95%CI 34.9–35.9), and children of Canada-born mothers (32.3, 95%CI 32.1-32.6). Gender disparities (boys-girls) remained stable over time (e.g., 5.25, 95%CI 5.24-5.26 in the 2002 birth cohort vs. 5.32, 95%CI 5.32-5.33 in the 2010 cohort). Patterns of socioeconomic disparities were more heterogeneous: the difference increased by ODB (8.69 95%CI 8.69-8.70 in the 2002 cohort vs. 11.90 95%CI 11.89-11.90 in the 2010 cohort), whereas it decreased slightly for area-based measures. In children born to immigrant mothers, although rates decreased steadily over time among those with mothers immigrated from high-income countries, it increased among those born to mothers from low-income countries (27.6, 95%CI 24.3-30.9 in the 2002 cohort vs. 33.9, 95%CI 30.9-37.0 in the 2010 cohort).

Conclusion. In this large representative sample of births in Canada, disparities by gender, socioeconomic position, and maternal immigration status persisted over time, and patterns of changes in the disparities were not homogeneous.

Implementation science

Implementing a Coordinated Referral Process for Home Visiting Programs in NYC Allison Guarino* Allison Guarino Folake Eniola Ericka Moore-Bass

Background: Evidence based home visiting programs are shown to improve maternal and child health outcomes, particularly for families experiencing health inequities due to structural racism and historic neighborhood divestment[1],[2]. Timely referrals increase programs' ability to support families to improve positive parenting behaviors, safe home environments, early childhood intervention[3] and economic self-sufficiency[4]. In 2021, The New York City Department of Health and Mental Hygiene launched the New Family Home Visits Initiative (NFHV) to coordinate referrals to home visiting services for eligible clients- first time parents in neighborhoods most affected by COVID-19, in public housing, or engaged with child services.

Methods: NFHV implemented a Coordinated Intake and Referral (CI&R) system, receiving data for all eligible births from the Office of Vital Statistics. Healthcare navigators then screen and refer to one of five home visiting models. Our descriptive analysis aims to assess whether this system increases uptake of home visiting services for eligible families.

Results: In 2022, the CI&R system identified over 10,300 individuals, 99% reached by a navigator, 54% screened, and 72% and 75% of those screened successfully referred to programs and support services, respectively. Mid-implementation system improvements increased weekly referrals by 17% post deployment. Among clients referred, most identified as Hispanic (47%), new parents (95%), low income (82%), and lived in the Bronx (44%). One-third resided in public housing, and approximately 2% had child services involvement and reported experiencing domestic violence in the preceding year.

Conclusion: The CI&R system shows promise to strengthen home visiting infrastructure in New York City, matching eligible families to programs most aligned with their needs. While the system increases NFHV's reach, challenges with early adoption may slow the speed of program uptake in target communities, an important step in closing service gaps for new families in NYC.

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Infectious disease

Isolating the effects of HIV infection and HIV exposure on epigenetic profiles in infants

Stephanie Shiau* Ziyi Wang Francesca Zumpano Jaya Satagopan Stephen Arpadi Carmen Marsit Emily Barrett

Introduction: Epigenetics offers insight into the mechanisms by which early life HIV infection and HIV exposure *in utero* affects offspring health. However, due to the widespread use of antiretroviral therapy (ART) during pregnancy/infancy, contemporary studies are unable to disentangle the effects of HIV from effects of ART exposure on epigenetic profiles. We used historical specimens collected before ART was in use to examine the role of HIV infection and exposure on DNA methylation (DNAm) profiles in infants at 3 and 12 months of age.

Methods: The Mothers and Infants Cohort Study was a prospective cohort study of pregnant women with and without HIV and their HIV-infected (HIV+), HIV-exposed uninfected (HEU), and HIV-unexposed uninfected (HUU) infants conducted in New York City (NYC) between 1985-1991 when ART was not in use. DNAm on peripheral blood mononuclear cells collected at 3 and 12 months of age was assayed using the MethylationEPIC array (Illumina, San Diego, CA). We tested for differentially methylated (DM) CpG sites (Bonferroni-corrected and ≥5% difference) between HIV groups at 3 and 12 months using the limma package, adjusted for sex and race.

Results: 103 infants (37 HIV+, 33 HEU, and 33 HUU) were included (48% female; 54% Black). Comparing HIV+ to HEU, there were 93 DM CpG sites (58 unique genes) at 3 months and 27187 DM CpG sites (8074 genes) at 12 months. Comparing HIV+ to HUU, there were 1138 DM CpG sites (689 genes) at 3 months and 7902 DM CpG sites (3550 genes) at 12 months. No differences were detected between HEU vs. HUU at 3 or 12 months.

Conclusion: Direct effects of both HIV infection and HIV exposure on the epigenome (in the absence of ART during pregnancy/infancy) were observed at 3 and 12 months of life in infants, with greater divergence observed with age. Further investigations of gene pathways enriched for differential methylation in the ART-naïve epigenome can shed light on the biology of early-life HIV exposure and infection.

Infectious disease

The impact of childhood infection on early child development and school performance: a population-based study Wen-Qiang He* Hannah Moore Jessica Miller David Burgner Olivia Swann Samantha Lain Natasha Nassar

Background: Childhood infection has been associated with adverse child development and neurocognitive outcomes, but studies have had methodological limitations. The aim of this study was to conduct a population-based study to investigate the effect of childhood infection on early child development and school performance.

Methods: A population-based record-linkage study of singleton children born at term (>=37 weeks) in New South Wales, Australia, from 2001 to 2014 ascertained via administrative birth and admitted hospital data linked with early child development (age 4-6 years) and school assessment (age 7-9 years) data collections up to 2019. Association between infection-related hospitalisation (identified through relevant diagnosis codes) from 0-4 years and i) developmental vulnerability and ii) school numeracy and reading was assessed using multivariable Cox regression models with robust sandwich variance estimator to account for clustering, and sensitivity analysis assessing E-values and sibling-pairs discordant for exposure.

Results: Overall, 276,454 infants had a child development outcome and 644,291 a school outcome. Compared with children without an infection-related hospitalization, children hospitalized with an infection were more likely to be developmentally high risk (10.9% vs 8.7%; adjusted HR (aHR) 1.12, 95%CI 1.08-1.15) and have numeracy (3.7% vs 2.7%, aHR 1.22, 95%CI 1.18-1.26) and reading results (4.3% vs 3.1%, HR 1.16, 95%CI 1.12-1.20) below the national minimum standard. The results were likely to be impacted by unmeasured confounding with E-values of 1.48-1.74 and attenuated with minimal to no effect confirmed in the sibling analysis.

Discussion: After taking into account shared familial and environmental factors, childhood infection requiring hospitalization had minimal to no association with developmental vulnerability and poor school performance. However, it is important to prevent childhood infection to avoid acute and long-term complications and adverse health outcomes.

Mental health

Antidepressant treatment patterns among patients with postpartum depression in a US claims database D. Claire Miller* Devika Chawla John Guittar Katie Johansen Taber Andria Del Tredici

Introduction: Postpartum depression (PPD) affects 10-20% of women after childbirth. While antidepressants are recommended to treat PPD, antidepressant treatment patterns are not well characterized. The objective of this study was to characterize the type, duration, and quantity of antidepressant therapies in patients with PPD.

Methods: We conducted a descriptive analysis of a US-based open claims database (Symphony Health). Patients included had an ICD-10 code for delivery (Z37.x) from 2016-2017 and for PPD (F53) within 180 days of delivery. Antidepressant prescription fills in the 365 days after initial PPD diagnosis were used to characterize treatment patterns.

Results: The cohort included 46,346 patients with both a delivery code and a diagnosis of PPD in the 180 days after delivery. Among these patients, 30,331 (65.4%) filled at least one antidepressant prescription in the 365 days after diagnosis. While 49.3% of patients who filled an antidepressant still had an active prescription 180 days after the first fill, 24.3% of patients had one fill in the database and no additional fills. In the 365 days after PPD diagnosis, 30.8% of antidepressant-treated patients received two or more distinct antidepressants, and 10.8% received three or more distinct antidepressants. Sertraline was the most filled first-line antidepressant (53.3%). Later-line therapies were not dominated by any single antidepressant and consisted of 40 different medications.

Conclusions: PPD treatment patterns are heterogeneous. One in 4 patients filled only one antidepressant prescription, suggesting discontinuation. One in 10 patients received three or more treatment lines in the year after diagnosis, suggesting earlier-line treatments were not effective. Sertraline was the most common first-line treatment, but no clear treatment choice was apparent if first-line treatment failed. These data suggest that antidepressant medication discontinuation and switching occur in many patients with PPD.

Mental health

Maternal mental health indicators and gestational weight gain in the 3D prospective cohort study Isabelle Hardy* Catherine Allard Felix Camirand-Lemyre Jean Séguin Catherine Herba Negar Tabatabaei Isabelle Marc Lise Dubois Jean-Patrice Baillargeon William Fraser

Background:

Certain maternal mental health indicators (MMHI) may be associated with gestational weight gain (GWG).

Study Design:

We analyzed data from 2204 pregnant women in the 3D prospective cohort. MMHI were assessed with validated tools in the first trimester (psychiatric history, perceived stress, depressive symptoms, pregnancy-related anxiety, and the quality of marital relations) and at the second study visit (20 weeks) (anxiety, adverse life events, optimism, self-esteem, workplace stress, attachment style and food insecurity). Multiple imputation of missing data was performed. We used 2009 IOM guidelines to categorize average weekly GWG after 20 weeks as insufficient, adequate, or excessive. Associations between each MMHI and GWG categories were assessed using multivariable multinomial logistic regression adjusted for BMI, age, gestational age (GA) at visit 2, GA at delivery, income, education, prematurity, gestational diabetes, preeclampsia and parity. For each model, interactions of body mass index (BMI), parity, ethnicity, income, and newborn sex were assessed and retained for stratification if significant at the level of $p<0.1$. Results are presented as standardized OR (sOR) with [95% CI], and p for interaction=p*i*.

Results:

Among participants with a prepregnancy BMI<18.5, risk factors for excessive GWG were perceived stress (sOR=2.44 [1.24;4.8], p*i* BMI=0.05) and depressive symptoms (sOR=2.58 [1.07;6.20], p*i* BMI=0.06). Among modest-income women (20 000-39 999$), disagreement with the statement “my work is repetitive” was a risk factor for excessive GWG (sOR=1.83 [1.04;3.22], p*i* income=0.06); but among high-income women (>80 000$), it was protective against insufficient GWG (sOR=0.72 [0.56;0.94]) as well as excessive GWG (sOR=0.72 [0.58;0.89]). We did not observe any appreciable associations between the other MMHI and GWG.

Conclusion:

In the 3D cohort, some MMHI were associated with increased odds of excessive GWG among underweight and modest income women.

Methods

The application of simulation to quantifying bias: a framework for reproductive and perinatal epidemiologists Jennifer Dunne* Gizachew Tessema Gavin Pereira

Due to the observational nature of epidemiological studies, they are prone to various types of bias (information, selection, confounding). In particular, reproductive and perinatal epidemiological studies are subject to unique methodological challenges due to unobservable events from pre-conception to birth and the clustering of outcomes across successive pregnancies or multiple births. Therefore, to strengthen the validity of associations drawn from observational studies, it is important for researchers to be able to identify and evaluate potential sources of bias.

Simulations studies involve computational methods to create data by pseudo-random sampling. They are ideal to quantify bias as the process of generating data allows greater control of the biased parameters of interest. Commonly used to test statistical methods, simulation studies are under-used in epidemiology, yet have the potential to quantify the influence of bias on exposure-outcome associations. Current simulation studies in reproductive and perinatal epidemiology lack uniformity in their design, analysis, and reporting. Lack of guidance in the application of simulation to quantify the influence of bias has hampered researchers and peer reviewers.

This paper proposed a framework for the application of simulation studies to quantify the magnitude and direction of biases in reproductive and perinatal epidemiological studies. Using examples, the framework aims to demonstrate the application of simulation to quantify selection, information, and bias resulting from the influence of unmeasured confounding. We illustrated how tools for the design, implementation, and analysis of simulation studies can be applied to quantify bias in epidemiology. Finally, this paper underlines the importance of quantifying bias to remove the uncertainty of exposure-outcome associations in reproductive and perinatal epidemiology.

Methods

Comparison of national estimates of bullying in U.S. adolescents Lindsey Black* Benjamin Zablotsky Amanda Ng Jonaki Bose Jessica Jones Aaron Maitland Stephen Blumberg

Background: Adolescents involved in bullying are at risk for poor mental and physical health. In the US the prevalence of bullying is measured by several different surveys. Adolescent self-report surveys lend themselves to understanding this topic, however due to legal and logistical difficulties related to minors' participation in research, parent-reported measures of bullying are of value. However, it is not known how these data sources compare.

Methods: Bully victimization, bully perpetration, and cyber bully victimization for youth aged 12-17 years were compared using data from the 2021: National Health Interview Survey (NHIS; personal interviews parent-report), National Survey of Children's Health (NSCH; web parent-report), and Adolescent Behaviors and Experiences Survey (ABES; web self-report). For each survey, prevalence and 95% confidence intervals (CI) were estimated overall and by age, sex, and race/ethnicity. Adjusted prevalence ratios (APR) were calculated to determine if associations remained stable.

Results: The prevalence of parent-reported bully victimization (20.7%, 95% CI:19.0-22.5) and perpetration (8.3%, 95% CI:7.1-9.6) from NHIS was lower than NSCH (27.8%, 95% CI: 26.8-29.2; 10.2% 9.4-11.1, respectively). Adolescent self-report estimates of cyber bully victimization from ABES (14.0%, 95% CI:12.5-15.6) were twice as high as parent-report estimates from NHIS (6.2%, 95% CI:5.3-7.2). APR for each bullying measure varied by demographic characteristics, however, all surveys produced the same associations.

Conclusions: The lower prevalence of parent-reported bullying measures in NHIS may be due to social desirability bias associated with interviewer-facilitation that does not affect web-based surveys (NSCH). The lower prevalence of parent-reported bulling measures in NHIS compared to self-report may be due to lack of awareness or unwillingness to report bullying. Regardless, associations between bullying prevalence and sociodemographic characteristics appear similar for three national surveys.

Molecular

Placental and immune cell DNA methylation reference panel for bulk tissue cell composition estimation in epidemiological studies Kyle Campbell* Justin Colacino Joseph Ciarelli Dana Dolinoy Rita Loch-Caruso Vasantha Padmanabhan Kelly Bakulski

DNA methylation perturbations in bulk placental tissue have been linked to adverse perinatal outcomes. To distinguish mechanistic DNA methylation changes from cell composition differences, robust cell type-specific placental DNA methylation profiles are needed. We analyzed 192 new and previously published DNA methylation profiles from 12 cell type-specific fractions, including cytotrophoblasts (n=32), endothelial cells (n=19), Hofbauer cells (n=26), stromal cells (n=29), syncytiotrophoblasts (n=4), six types of adult lymphocytes (n=36), and nucleated red blood cells (n=11), as well as 35 bulk placental tissue samples. Methylation was quantified via the Illumina DNA methylation microarray (450k or EPIC), and common probes were quality filtered (n=407,628 DNA methylation sites). To identify cell type-discriminating DNA methylation sites, we ranked the top 50 hyper- and hypomethylated sites per cell type by F-test, yielding 1,101 sites. To estimate the cell composition of bulk placental tissue, we applied the robust partial correlation deconvolution algorithm using these sites. Consistent with placental biology, bulk placental tissue cell type proportion estimates (mean ± standard deviation) from methylation measures were predominately syncytiotrophoblast (57.8% ± 8.3%), stromal (20.6% ± 5.9%), cytotrophoblast (11.0% ± 4.1%), endothelial (7.5% ± 2.2%), Hofbauer cells (1.5% ± 1.2%), and CD4+ T cells (0.89% ± 0.84%). Other cell types had mean estimates less than 0.5%. This cell type DNA methylation reference panel can robustly estimate cell composition from placental DNA methylation data in epidemiological studies to reveal biological mechanisms and improve casual inference. We will present a software package for community use so that future studies may estimate cell composition in placental tissue for testing with exposure or disease.

Nutrition/obesity

Introduction of complementary foods at 4 months of age and effect on growth in early and middle childhood in the Upstate KIDS cohort Priscilla Clayton* Diane Putnick Ian Trees Akhgar Ghassabian Jordan Tyris Edwina Yeung

The American Academy of Pediatrics and the World Health Organization (WHO) recommend children <2 years old to gradually introduce complementary foods starting at 6 months. Recent evidence shows complementary feeding prior to 6 months may increase obesity risk.

We prospectively explored introduction of complementary foods and anthropometric measures in children. All singletons and one randomly selected multiple from each family were included. Parents reported weight and height acquired from pediatrician visits at 24-36 months (n=2000) and at 7-9 years (n=1348). Age- and sex-standardized weight-, height-, and body mass index (BMI)-for-age z-scores were calculated using the WHO reference. Parents reported whether they introduced solids or liquids (e.g., vegetables, fruits, meats, juice, dairy, etc.) other than breastmilk or formula. Associations between introduction of complementary foods at 4 months and repeatedly assessed anthropometric measures were estimated using linear mixed models adjusting for maternal age, education, race/ethnicity, pre-pregnancy BMI, private insurance, WIC participation, maternal smoking, gestational age, plurality, and breastfeeding.

About 60% infants were introduced complementary foods at 4 months, which was associated with lower maternal college education (24% vs. 30%), WIC participation (17% vs 10%), maternal smoking (10% vs. 2%), and less likely to breastfeed (41% vs. 67%). Compared to infants not introduced to complementary foods at 4 months, BMI-for-age (0.13; 95% CI: -0.004, 0.28) and weight-for-age z-scores (0.15; 0.04, 0.25) were higher in early childhood but these associations were largely attenuated after covariate adjustment (i.e., 0.02; -0.14, 0.19 for BMI; 0.09, -0.03, 0.21 for weight). Results at 7-9 years of age also showed no associations.

After accounting for covariates, complementary feeding did not play a role in child growth. Nevertheless, further investigation of introduction to each type of complementary food is needed.

Nutrition/obesity

Maternal smoking, breastfeeding and growth during infancy: The Norwegian Mother, Father and Child Cohort Study Edmond Shenassa* Edoardo Botteri Hanne Stensheim

Background: Breastfeeding promotes optimal growth during infancy; exposure to cigarette smoke predicts rapid weight gain. Whether breastfeeding by smokers ameliorates or exacerbates suboptimal weight gain, and whether any suboptimal gains can be attributed to ingesting smokers' breastmilk which may be obesogenic remains poorly understood.

Methods: Using data from the Norwegian Mother, Father and Child Cohort Study and Medical Birth Registry of (N=54,522), we examined changes in weight, length, weight-for-length z-score and head circumference between 0-12 months in the context of maternal smoking (0, 1-10, >10 cigarettes/day) and feeding method during the first 6 months (breastfed, formula-fed, mixed-fed). We used generalized linear models, adding an interaction term between smoking and feeding method to evaluate the effect of ingesting smokers' breastmilk.

Results: Among breastfed infants, 1-year gains in weight and length were higher when mothers smoked >10 cigarettes/day than when mothers were non-smokers (176 g, 95%CI: 115, 238; 1.2 mm, 95%CI 0.1, 2.6). Similar gains were observed among mixed-fed (167 g, 95%CI: 110, 223; 2.2 mm, 95%CI: 0.9, 3.5) but not formula-fed infants (119 g, 95%CI: -15, 253; -0.9 mm, 95%CI: -3.7, 1.9). Interaction between heavy smoking and breastfeeding was stronger for length (p=0.04) than for weight gain (p=0.13). No interaction was evident for changes in weight-for-length z-score and head circumference, or between lighter smoking (1-10 cigarettes/day) and breastfeeding.

Discussion: Infants breastfed by heavy smokers grew more rapidly than other infants. However, the excess gains, possibly attributable to ingesting smokers' breastmilk, were not clinically meaningful. Applications of our findings are detailed.

Nutrition/obesity

Should gestational weight gain charts exclude individuals with excess postpartum weight retention? Peter Socha* Kari Johansson Lisa Bodnar Jennifer Hutcheon

Excess postpartum weight retention is a common adverse outcome of high gestational weight gain (GWG), yet individuals with excess postpartum weight retention are not excluded from existing GWG normative charts. We explored the impact of excluding individuals with high postpartum weight retention from GWG charts by comparing GWG distributions including vs excluding individuals with high postpartum weight retention.

We used a cohort of individuals with uncomplicated pregnancies previously used to derive Swedish GWG charts, the Stockholm-Gotland perinatal cohort, which contains population-based records of prenatal visits and delivery admissions, 2008-2014. We defined GWG as the weight change between the first prenatal visit (<14 weeks) and each of 32, 36, and 40 weeks' gestation. Individuals were linked to subsequent pregnancies through 2019, and we calculated interpregnancy weight change as the difference between weight at the start of an index and subsequent pregnancy. We plotted GWG distributions and calculated GWG percentiles, before and after excluding individuals with an interpregnancy weight gain of ≥10kg and ≥5kg, as a proxy for high postpartum weight retention. We stratified results by pre-pregnancy body mass index (normal weight 18.5-24, overweight 25-29, obese ≥30kg/m^2).

Among 55,723 individuals, there were 10,858 GWG measurements at 32 weeks, 17,066 at 36 weeks, and 6,353 at 40 weeks. High interpregnancy weight gain was common, with 17% of the cohort gaining ≥10kg and 34% gaining ≥5kg. Yet, GWG distributions excluding individuals with high interpregnancy weight gain were similar to those that included them, with percentile values largely within 1kg. For example, in normal weight individuals at 40 weeks, the 50th and 97th GWG percentiles were 15kg and 25kg including vs 15kg and 24kg excluding individuals with ≥5kg interpregnancy weight gain.

Excluding individuals with excess postpartum weight retention may not meaningfully impact reference values of GWG charts.

Nutrition/obesity

Do current pregnancy weight gain recommendations balance risks of maternal and child health? Lisa Bodnar* Kari Johannson Jennifer Hutcheon

Institute of Medicine (IOM) pregnancy weight gain guidelines were made without evidence on outcomes linked with high gain like gestational diabetes, preeclampsia, and metabolic syndrome. Thus, their upper limit may be too high and not optimize maternal health. We sought to identify the pregnancy weight gain range that best balances the risks of high and low weight gain by considering multiple health outcomes including maternal perinatal and postpartum health. We used a longitudinal study of nulliparous singleton pregnancies at 8 US sites followed to 5 years postpartum. We converted pregnancy weight gain into gestational age-specific z-scores. We created a composite outcome consisting of ≥1 of the following: gestational diabetes, preeclampsia, unplanned cesarean delivery, excessive postpartum weight retention, postpartum metabolic syndrome, preterm birth, stillbirth, neonatal death, small-for-gestational-age birth, and child obesity. Each outcome was assigned severity points (determined by stakeholders) to reflect its seriousness. We linked weight gain z-scores with the severity-weighted composite outcome using Poisson regression and bootstrapped 95% confidence intervals. Among normal weight participants (n=2344), the mean (SD) total weight gain was 16 (7) kg. The risk of the severity-weighted composite outcome was lowest at a weight gain z-score of -0.7 (13 kg at 40 weeks). Risk increased at z-scores above this value, but confounder-adjusted rate ratios remained within 10% of this nadir at z-scores of 0 (16 kg, the upper limit of the IOM guidelines. In contrast, increases in rate ratios at z-score values below the lowest observed risk were minimal, remaining within 10% until a z-score of -1.4 (9 kg). At a z-score of -0.9 (the lower limit of IOM guidelines, risks were only increased by 2%) These data suggest that pregnancy weight gain lower than the recommendation may not meaningfully increase risk, and high weight gain should be targeted in public health messaging.

Nutrition/obesity

Association of maternal adherence to vegetarian/plant-based diets with pregnancy and perinatal health: findings from the Avon Longitudinal Study of Parents and Children (ALSPAC) in the UK Peiyuan Huang* Gemma Sharp Kate Northstone Carolina Borges

Objectives: To examine the association between maternal adherence to vegetarian (V; as primary exposure)/plant-based diets (PBD; as secondary exposure) with pregnancy and perinatal health.

Methods: There were 233 full-V (228 lacto-ovo-V + 5 vegans) and 357 flexitarians (FLN; 277 pesco- + 80 semi-V) in 11523 British singleton pregnancies. PBD adherence was assessed using 3 indices: the overall (PDI), healthful (hPDI) and unhealthful (uPDI) plant-based diet index, with higher scores representing higher overall, healthy, and unhealthy plant food intakes, respectively. A total of 33 relevant outcomes during the perinatal period were examined. Analyses were adjusted for maternal demographic, lifestyle, and nutrition-related factors.

Results: Women adherent to V/healthful PBD were more socioeconomically advantaged. Compared to non-V, full-V had increased risks of maternal anaemia, perinatal depression, high birth weight, and large for gestational age, and, similar to FLNs, had longer breastfeeding (BF) duration, though underpowered for some rare outcomes. After false discovery rate (FDR) correction for multiple testing, only the associations with maternal anaemia (OR 2.12 [1.31~3.32], P_{FDR}=0.047) and sustained BF (OR 1.84 [1.28~2.66], P_{FDR}=0.047) for full-V remained. The risk of maternal anaemia seemed more evident in FLN (OR 2.56 [1.15~5.69] vs. 0.85 [0.47~1.55]) and full-V (2.98 [1.30~6.81] vs. 1.77 [1.00~3.13]) with no iron supplementation during pregnancy. Higher hPDI was also related to longer BF duration, while higher uPDI was associated with shorter BF duration and reduced birthweight z-score (β -0.01 [-0.02~0.00], P_{FDR}=0.018).

Conclusion: V-women might have a higher risk of anaemia during pregnancy, which could be partially attenuated by taking iron supplements; adherence to unhealthful PBD might be associated with slightly reduced birthweight. We will replicate these findings in other cohorts and explore potential residual confounding in the observed associations.

Nutrition/obesity

Gestational weight gain after bariatric surgery: a population-based matched cohort study in Sweden Huiling Xu* Natalie Holowko Olof Stephansson Elizabeth Arkema Kari Johansson

Gestational weight gain (GWG) after bariatric surgery is not well established. This study investigates the association between having a history of bariatric surgery before pregnancy and GWG, and whether this differs by surgery type.

In this nationwide population-based matched cohort study, 547,829 singleton pregnancies with available total GWG were identified in the Swedish Medical Birth and Pregnancy Registers between 2014 and 2021. Of these, 6394 had a history of bariatric surgery (5489 gastric bypass (GBP) and 905 sleeve gastrectomy (SG)). By using propensity score matching, pregnancies with no history of bariatric surgery were matched to post-bariatric surgery pregnancies on early-pregnancy BMI, pre-pregnancy diabetes/hypertension, maternal age, smoking status, educational level, height, country of birth, birth year (n=6394:6394). Further, within the bariatric surgery group, post-GBP pregnancies were matched to post-SG pregnancies using the same matching factors (n=904:904). GWG was standardized by gestational age into BMI-specific z-scores. Linear regression models were used to compare total GWG z-scores between groups, stratified by early-pregnancy BMI-category.

Regardless of BMI category, post-bariatric surgery pregnancies had lower GWG, compared to matched pregnancies with no history of bariatric surgery. For example, women with a history of bariatric surgery and early-pregnancy overweight women had a GWG z-score of -0.32 (95%CI: -0.36, -0.28; corresponding to 11.9 kg at week 40 (95%CI: 11.7, 12.1), while matched controls had a GWG z-score of -0.01 (95% CI: -0.05, 0.04; 13.6 kg (95% CI: 13.4, 13.9). There was no difference in GWG by surgery type in the matched analysis.

In conclusion, pregnant women with a history of bariatric surgery gained less weight during pregnancy than women with a similar early-pregnancy BMI and no history of bariatric surgery. GWG did not differ by surgical type.

Nutrition/obesity

The Relationship between Prenatal Diet and Gestational Weight Gain: A Study from the Michigan Archive for Research on Child Health Yasamean Zamani-Hank* Md Sakibur Hasan Kelly A Hirko Sarah S Comstock Rita S Strakovsky Jean Kerver

Adequate gestational weight gain (GWG) is critical to promoting optimal pregnancy and birth outcomes, yet only about one-third of women achieve recommended weight gain levels (CDC, 2016). Diverse physiological and sociodemographic factors impact GWG, but the contribution of prenatal diet is particularly important as it presents a modifiable target for intervention. Previously, Hirko et al. (2020) found that consumption of fruits and vegetables (FV) during pregnancy was associated with a lower odds of excessive GWG among women with obesity (OR 0.77, 95% CI 0.60,0.97) in a sample of n=327 pregnant women from a Michigan pregnancy cohort. Here, we present data from a larger sample (n= 1337) from an expanded statewide pregnancy cohort in Michigan. Data on three indicators of prenatal diet (added sugar, dairy, and FV) were collected via survey. GWG was calculated from birth certificate data and categorized as inadequate, adequate (reference category), and excessive based on Institute of Medicine recommendations. Multinomial logistic regression analyses were used to assess associations between each indicator of prenatal diet and GWG in unadjusted and adjusted models controlling for race, infant sex, maternal age, marital status, physical activity, nausea and vomiting during pregnancy, smoking status, pregnancy intention, and depression. We found that FV, dairy, and added sugar were independently associated with higher odds of inadequate (OR 1.2, 95% CI 1.1, 1.3; OR 1.3, 95% CI 1.1, 1.5; OR 1.0, 95% CI 1.0, 1.1) and excessive (OR 1.2, 95% CI 1.2, 1.3; OR 1.4, 95% CI 1.2, 1.6; OR 1.0, 95% CI 1.0, 1.1) weight gain in unadjusted analyses, but these associations became nonsignificant in adjusted models. These results suggest that sociodemographic and other maternal health characteristics may play a larger role in influencing GWG than prenatal diet in this sample.

Nutrition/obesity

Preconception nutritional quality in pregnancy-planning and general-population cohorts: The PrePARED Consortium Lixuan Ji*, Emily Harville Lixuan Ji Janaki Sundaresan Cailey Cranny Ke Pan Danielle Downs Erica Gunderson Gita Mishra Abigail Pauley James Shikany Lauren Wise Lixuan Ji

The preconception period is important for nutrition, to provide physical strength for pregnancy and establish diet for optimal fetal nutrition. Understanding preconception diet ideally includes both planned and unplanned pregnancies. Diet data from 5 cohorts participating in the PrePARED consortium of preconception studies were harmonized (total N=25632). These included four general studies (Australian Longitudinal Study of Women's Health (ALSWH); California Teachers' Study (CTS); Central Pennsylvania Women's Health Study (CePAWHS), a study of rural Pennsylvania women); and the Coronary Artery Risk Development in Young Adults (CARDIA) study, a national study of young Black and Whites, which include data on both planned and unplanned pregnancies; and one study of couples planning pregnancy (Pregnancy Study Online (PRESTO), which recruited from the US and Canada without respect to location). Adherence to the International Federation of Gynecology and Obstetrics (FIGO) (include meat/chicken, fruit and vegetables, fish, dairy, whole grains, and packaged snacks/sugar-sweetened drinks), the Mediterranean diet, and other dietary patterns were calculated in each cohort. Number of recommendations, average score, and cut-offs for quantile-based scales were compared across studies. PRESTO and CTS participants were more likely to have higher education and income than other participants. PRESTO participants were more likely to meet all six of the FIGO recommendations (8.8%; median 4) than participants in the CTS (3.9%, median 4), CARDIA (1.7%, median 4), ALSWH (1%, median 3), or CePAWHS (median 2 of 4 assessed) studies. Median score on the Mediterranean diet was also higher for PRESTO. Adherence to recommendations for optimal pregnancy nutrition is low among reproductive-aged women, although it varies substantially by study population, probably due to education and other socioeconomic variables as well as pregnancy planning status.

Obstetric health

Racial/ethnic Disparity in Severe Maternal Morbidity Following ART Conception Jenna Victory* Sid John Jeff Bone Li Qing Wang Hamideh Bayrampour KS Joseph Sarka Lisonkova

Background. Assisted reproductive technology (ART) that includes egg and sperm manipulation during conception is associated with adverse foetal and infant outcomes. Although racial/ethnic disparities in such outcomes are larger in women following ART, racial/ethnic disparities in severe maternal morbidity (SMM) in women with ART have been understudied.

Objective. To compare SMM rates in women with spontaneous vs ART conception by race/ethnic group.

Methods. We included all singleton live births and stillbirths in the United States, 2016-2017, with data obtained from live birth and foetal death certificates. Rates of SMM (including eclampsia, uterine rupture/intrapartum hysterectomy, blood transfusion, and ICU admission) were contrasted between women with spontaneous vs ART conception, stratified by race/ethnicity i.e., non-Hispanic White (NW), non-Hispanic Black (NB), American Indian/Alaskan Native (AIAN), Asian/Pacific Islander (API), and Hispanic. We used logistic regression to adjust for potential confounders (e.g., age, chronic conditions) and to assess modification of the ART-SMM association by race/ethnicity.

Results. The study included 7,505,189 deliveries (53% NW, 15% NB, 1% AIAN, 7% API and 24% Hispanic). ART was used by 48,584 (0.7%) women and SMM rates were 1.6% and o.7% in ART vs spontaneous conception groups. Odds of SMM was significantly increased in women with ART (adjusted odds ratio [AOR] 2.1; 95% confidence interval [CI] 2.0-2.3). ART-SMM AORs were not different by race/ethnic group, except for uterine rupture/intrapartum hysterectomy where the disparity was larger among Hispanic (AOR 6.1, 95% CI 3.7-10.3) compared with NW women (AOR 3.2; CI 2.5-3.9).

Conclusion. Women who use ART have a 2-fold higher risk of SMM and this increased risk is mostly uniform across all race/ethnicity groups. Hispanic women who conceive following ART have substantially higher risks of severe uterine rupture compared with NW women, and this warrants investigation.

Obstetric health

Comparing fetal ultrasound measures to neonatal anthropometry at the extremes of birthweight Jessica Gleason* Mary Hediger Zhen Chen Jagteshwar Grewal Roger Newman William Grobman Katherine Grantz

Background: Error in birthweight (BW) prediction by estimated fetal weight (EFW) has clinical implications, such as unnecessary cesarean or misclassification of fetal risk in labor. Questions remain regarding optimal timing of ultrasound and which fetal measurements [e.g., head circumference (HC) or abdominal circumference (AC)] contribute to the error between ultrasound estimation of fetal and birth size.

Methods: We compared simple mean differences [95% confidence intervals (CI)] in HC, AC, and EFW between ultrasound and corresponding measures at birth for singletons in the NICHD Fetal Growth Studies. Differences between ultrasound and birth measures within 14 (n=1290) and 7 (n=617) days were compared for SGA (<10^{th} percentile), AGA (10^{th}-90^{th} percentile), and LGA (>90^{th} percentile) newborns.

Results: Average differences between EFW and BW for SGA neonates were: 14 days (-40.2g; CI -82.1, 1.6) and 7 days (13.6g; CI -52.4, 79.7); AGA 14 days (-122.4g; -139.6, -105.1) and 7 days (-27.2g; -50.4, -4.0); and LGA 14 days (-242.8g; -306.5, -179.1) and 7 days (-72.1g; -152.0, 7.9). Differences between fetal and neonatal AC were smaller at 14 vs 7 days and followed the same pattern as EFW where differences were largest for LGA for both intervals. Differences between fetal and neonatal HC were larger at 14 versus 7 days but largest for LGA only at 14 days.

Conclusions: Using a standardized ultrasound protocol, SGA neonates had ultrasound measures closer to actual birth measures compared to AGA or LGA neonates, suggesting slower interval growth. LGA had the largest differences between fetal and neonatal size, and ultrasounds farther from delivery (14 vs 7 days) showed 3-4-fold greater differences in BW, suggesting faster interval growth. Differences in EFW and BW may not be explained by a single fetal measurement; whether it may be improved by incorporation of other knowable factors like fetal growth velocity or body composition should be evaluated in future research.

Obstetric health

Associations between first trimester prediabetes and adverse birth outcomes in a multiethnic population-based retrospective cohort Teresa Janevic* Katharine McCarthy Shelley Liu Victoria Mayer Shelley Liu Frances Howell Luciana Vieira

Little is known about outcomes of pregnancy for pregnant people with prediabetes (HbA1c levels 5.7≤A1c<6.5%), and data is lacking in diverse, multiethnic cohorts. Our objective was to measure associations between prediabetes HbA1c levels in the first trimester with pregnancy outcomes, and to test if associations differed by race-ethnicity or nativity. We used 2015-2017 data from the APPLE Cohort, a population-based cohort of linked HbA1c, birth, and hospital discharge data in New York City. We included pregnant people without prepregnancy diabetes, at least 1 HbA1c measurement in the first trimester, and without elevated A1c (>=6.5%) (n=12,770). We compared prediabetes to normoglycemia (A1c <5.7%). We ascertained gestational diabetes (GDM) and hypertensive disorders of pregnancy (HDP), preterm birth <37 weeks (PTB), cesarean delivery (CD), shoulder dystocia, and macrosomia from the hospital and birth records. We used log binomial regression to estimate relative risks adjusting for pre-pregnancy BMI, prepregnancy hypertension, age, race-ethnicity, nativity, insurance, and education. 15% of pregnant people had prediabetes. Compared to those with normoglycemia, prediabetes was associated with a 2.8 times risk of GDM (95%Confidence Interval(CI)=2.4, 3.2), as well as increased risk of preterm birth (adjusted relative risk (aRR) 1.2 (95% CI: 1.0, 1.5)), CD (aRR: 1.2, 95% CI: 1.1, 1.3) HDP (aRR: 1.2, 95% CI: 1.1, 1.4), and macrosomia (aRR: 1.2 95% CI 1.0, 1.5); the likelihood of shoulder dystocia was reduced (aRR: 0.5, 95% CI: 0.2, 1.0). Effect modification was present by nativity for CD and macrosomia, with associations present only among immigrants (aRR for CD=1.3, 95%CI: 1.1, 1.5; aRR for macrosomia=1.4, 95%CI=1.0, 1.8). All associations were similar by race/ethnicity. HbA1c screening in the first trimester may alert clinicians to patients at increased risk of GDM and other adverse outcomes, particularly among immigrant pregnant people.

Obstetric health

Severe maternal morbidity surveillance: temporal trends and regional variations in Sweden, 1999-2019. Eleni Tsamantioti* Anna Sandström Giulia Muraca K.S. Joseph Katarina Remaeus Neda Razaz

Objective: To quantify temporal trends and regional variations in severe maternal morbidity (SMM) in Sweden with a view to informing clinical practice and population health initiatives.

Methods: We carried out a population-based cohort study using data on all live birth and stillbirth deliveries in Sweden from 01/1999 to 12/2019. SMM types and subtypes were identified based on a standard list (modified for Swedish data), using diagnosis and procedure codes among all deliveries >=22 weeks' gestation (including complications within 42 days after delivery). Contrasts between periods and regions were quantified using rate ratios (RRs) and 95% confidence intervals (CIs). Temporal changes were also assessed using chi-square tests for trend.

Results: Between 1999-2019, there were 59,789 SMM cases among 2,152,787 deliveries, corresponding to 270.2 (95% CI 268.1-272.4) per 1,000 deliveries. SMM rates increased from 1999 to 2006 and then decreased. Severe preeclampsia and HELLP syndrome (100.5 per 10,000 deliveries), severe postpartum hemorrhage (104.1 per 10,000 deliveries), sepsis, and severe mental health disorders were the most common SMM types. Severe hemorrhage rate increased from 94.9 in 1999 to 169.3 per 10,000 deliveries in 2006 and then declined to 111.2 per 10 000 deliveries in 2019 (P for trend <0.0001). Embolism, disseminated intravascular coagulation and shock, acute renal failure, cardiac complications, sepsis, and assisted ventilation rates increased, whereas surgical complications, severe uterine rupture and anesthesia complications declined. Rates of composite SMM in 1999-2019 were higher in Västra Götaland, Värmland, Kronoberg, Uppsala, and Norrbotten, compared with the rest of Sweden, whereas rates were lower in Örebro, Sörmland, Gotland and Jönköping.

Conclusion: The observed spatio-temporal variations in composite SMM and SMM types provide insights and suggest regional priorities for clinical and public health intervention for improving maternal health.

Obstetric health

Trends and Disparities in Postpartum Severe Maternal Morbidity Indicator Categories in California from 1997-2017 Alison El Ayadi* Audrey Lyndon Peiyi Kan Mahasin Mujahid Stephanie Leonard Elliott Main Suzan Carmichael

Background

Most severe maternal morbidity (SMM) research focuses on childbirth, yet risk persists postpartum. Delineating trends and disparities in postpartum SMM by underlying clinical etiologies can support the identification of key clinical and social interventions to improve maternal health and equity.

Methods

We used California birth cohort data from 1997 to 2017 (n= 10,580,096). Postpartum SMM cases were categorized into overall vs non-transfusion SMM, and seven non-transfusion SMM indicator categories (cardiac, renal, respiratory, hemorrhage, sepsis, other obstetric, and other medical SMM). We computed prevalence overall and for each racial and ethnic group. We used logistic and linear regression to estimate associations of race and ethnicity with each SMM outcome and differences in associations across time.

Results

Postpartum SMM overall and non-transfusion occurred in 19.1 and 15.0 per 10,000 births. Sepsis SMM occurred most frequently (4.9 per 10,000 births), followed by cardiac SMM (3.2) and other obstetric SMM (3.1). Compared to non-Hispanic white people, Black people experienced elevated SMM across all categories; US-born Hispanic people experienced elevated overall, renal, and sepsis SMM but reduced hemorrhage SMM; non-US-born Hispanic people experienced reduced SMM across all categories; and Asian and Pacific Islander people experienced reduced cardiac and other obstetric SMM but increased sepsis SMM. Over time, sepsis (905%) and renal (806%) SMM had the largest increase. Disparities increased over time in non-transfusion SMM for US-born and non-US-born Hispanic people. Disparities decreased over time in all categories for Asian and Pacific Islander people and in non-transfusion SMM and sepsis SMM for Black people.

Conclusions

Our research demonstrates the need to explicitly consider SMM and SMM disparities occurring postpartum with broader public health efforts to improve maternal health equity, and these findings can inform quality improvement efforts.

Obstetric health

Maternal mortality in the United States: An alternative perspective on maternal and pregnancy-associated deaths K.S. Joseph* Sarka Lisonkova Amelie Boutin Giulia Muraca Neda Razaz Sid John Yasser Sabr Wee-Shian Chan Azar Mehradabi Justin Brandt Enrique Schisterman Cande Ananth

Background: It is unclear if the rising rates of maternal mortality in the United States reflect changes in surveillance, or a deterioration in maternal health. We examined maternal mortality rates in the US, focusing on the distinction between maternal deaths and pregnancy-associated deaths.

Methods: All deaths in the US, 1999-2020, were included in the study, with rates estimated by underlying and multiple cause-of-death category. Maternal deaths were identified, per current practice, as deaths in pregnancy or in the postpartum period, and alternatively (per definition), as deaths with pregnancy or postpartum causes listed among the multiple causes of death.

Results: Maternal deaths, per current convention, increased by 114% (95% confidence interval (CI) 99 to 130) from 9.55 in 2000-02 (n=1,156) to 20.4 per 100,000 live births in 2018-20 (n=2,280), with increases in all race/ethnicity groups. These increases occurred due to the pregnancy checkbox, which also led to large increases in nonpregnancy-related causes of death, e.g., malignancies as a cause of maternal death increased 54-fold from 0.025 in 2000-02 to 1.34 per 100,000 live births in 2018-20. Under the alternative formulation, maternal mortality rates decreased (-4%, 95% CI -12 to 4) from 10.1 in 2000-02 to 9.64 per 100,000 live births in 2018-20. Deaths due to pre-eclampsia, venous complications, and embolism decreased, while abruption, adherent placenta, renal, cardiomyopathy and chronic hypertension deaths increased. Maternal mortality increased among White women, decreased among Blacks and Hispanics, and remained unchanged among Other race/ethnicity groups. However, maternal mortality rates in 2018-20 were disproportionately higher among Black women.

Interpretation: Identifying maternal deaths by requiring a pregnancy-related cause of death yields a compelling perspective on maternal mortality rates and trends in the US, and provides a clear evidentiary basis for clinical and public health initiatives.

Obstetric health

Definition of optimal symphysis fundal height ranges associated to reduced risk of adverse neonatal outcomes: Data from the Brazilian Maternal and Child Nutrition Consortium Thais Rangel Bousquet Carrilho* Michael E. Reichenheim Helena Mendes Constante Gilberto Kac
Brazilian Maternal and Child Nutrition Consortium

Background/objectives: Monitoring symphysis fundal height (SFH) during prenatal care is recommended to screen individuals at risk of fetal growth restriction in settings where ultrasound access is limited. We aimed to establish optimal SFH ranges to prevent adverse neonatal outcomes based on Brazilian SFH charts.

Methods: Data from 6,088 individuals aged 18-45 years with singleton pregnancies from Brazil were used. Individuals free of hypertensive disorders, diabetes, or diseases affecting fetal growth were selected. SFH (cm) was standardized to gestational age-specific *z* scores according to the Brazilian SFH charts. Outcomes included small-for-gestational-age (SGA, birthweight <10^{th} percentile), large-for-gestational-age (LGA, >90^{th} percentile, according to INTERGROWTH-21^{st}), and preterm birth (<37 weeks). A composite index was defined as the occurrence of any of those outcomes, considering specific weights to account for their relative seriousness. Poisson regression was performed linking SFH *z* scores with the composite outcome, with maternal age and pre-pregnancy body mass index as covariates. SFH ranges associated with the lowest risk of the composite outcomes were identified.

Results: The median SFH at the end of pregnancy was 35 cm (IQR 33-37); 11.5% of the neonates were preterm, 7.7% SGA, and 14.8% LGA. Higher SFH *z* scores were significantly associated with increased preterm birth and LGA probabilities compared with neonates born at term and with appropriate weight, respectively. Lower SFH *z* scores were associated with an increased probability of SGA. SFH between 34.0–36.8 cm at 40 weeks was associated with the lowest risk of these outcomes.

Conclusion: SFH ranges associated with lower risks of preterm birth, SGA, and LGA were identified using an approach that allowed us to consider multiple neonatal outcomes simultaneously. These optimal SFH ranges may help healthcare professionals in the monitoring of SFH to prevent adverse neonatal outcomes.

Obstetric health

Associations between pre-pregnancy obesity and postpartum hospital use among individuals without additional medical comorbidities Teresa Janevic*, Kimberly Glazer Teresa Janevic Natalie Boychuk Natalia Egorova Paul Hebert Jennifer Zeitlin Elizabeth Howell Teresa Janevic

Obesity may be a risk factor for postpartum complications among individuals without other preexisting or gestational conditions. Our objective was to characterize postpartum hospital use (PHU) among people with obesity after excluding medical comorbidities. We studied 2016-2018 linked birth certificate and discharge data on 178,729 births in New York City to individuals without International Classification of Diseases (ICD)-10 codes at delivery for diabetes (gestational, preexisting); hypertensive disorders (preeclampsia, gestational, chronic); pulmonary, cardiac, renal, bleeding, autoimmune, digestive, neuromuscular, or placental disease; anemia; thyrotoxicosis; bariatric surgery; or mental or substance use disorder. We defined PHU as ≥one readmission or emergency department visit within 30 days of delivery discharge. We used ICD-10 codes to specify incident postpartum hypertensive disorder, infection, or hemorrhage during PHU since these are leading mortality causes. We examined associations between pre-pregnancy body mass index (BMI) and PHU using multivariable log binomial regression. PHU incidence in this cohort was 3.7% (n=4001) for those with normal weight (18.5 kg/m^2≤BMI<25), 5.1% (n=2260) for overweight (25≤BMI<30), 6.3% (n=1420) for class I/II (30≤BMI<40), and 9.1% (n=215) for class III obesity (BMI≥40). A monotonic association persisted after adjusting for maternal age, education, insurance, parity, plurality, nativity, race/ethnicity, and late prenatal care. Obesity (any class) was associated with increased risk of PHU with postpartum hypertensive disorder (adjusted risk ratio [95% confidence interval]: 2.2 [1.8-2.7], normal weight referent) and with wound infection after cesarean (1.5 [1.2-1.8]), but not hemorrhage (0.9 [1.7-1.3]). Among patients without other comorbidities, elevated BMI was associated with PHU. Findings can help inform risk stratification to prevent unnecessary hospital use and improve management during the critical fourth trimester.

Obstetric health

The Influence of Preconception Hemoglobin A1c on Gestational Diabetes at First Live Birth Among New York City Adolescents, 2009-2017 Teresa Janevic*, Katharine McCarthy Shelley Liu Luciana Vieira Victoria Mayer Teresa Janevic Teresa Janevic

Nearly one-third of adolescent girls in the U.S. have prediabetes yet less is known about how subclinical glycemic control prior to pregnancy influences the likelihood of pregnancy complications and adverse birth outcomes among adolescents. We examined the influence of preconception hemoglobin A1c level on the likelihood of gestational diabetes at first live birth among adolescents aged 10 to 24 years using a retrospective cohort of linked 2009-2017 NYC birth certificate, hospital discharge, and A1C Registry data. We included those aged 10-24 years with no history of diabetes prior to pregnancy who had at least one preconception A1c test (N=14,284). We examined mean preconception A1c values and values at last preconception test categorized as: no diabetes (A1c<5.7%) or prediabetes (5.7≤A1c<6.5%). Multivariable logistic regression was used to assess the likelihood of GDM at first birth by preconception A1c level, adjusting for pre-pregnancy characteristics. Secondary outcomes included hypertensive disorders of pregnancy, preterm birth, cesarean section and macrosomia. Most (79%) of the sample had ‘no diabetes’ at last preconception test, and 21% had ‘pre-diabetes’. The cumulative incidence of GDM was 5.1%, with higher mean A1c values among those with incident GDM (5.7, 95% CI: 5.7 5.8) than without (5.4, 95% CI: 5.4, 5.4). Adjusting for pre-pregnancy characteristics, those with preconception prediabetes had 2.3 times the likelihood of GDM (95% CI: 1.9, 2.7) than those with no diabetes. Preconception pre-diabetes was also associated with a slight increase in the likelihood of a hypertensive disorder of pregnancy (adjusted odds ratio (aOR): 1.2, 95% CI: 1.0, 1.3), preterm delivery (aOR: 1.2, 95% CI: 1.0, 1.4%) and cesarean section (aOR: 1.1, 95% CI: 1.0, 1.2) and a nonsignificant increase in macrosomia (aOR 1.1: 95% CI: 0.9, 1.4). Results highlight adolescence as a critical window to optimize cardiometabolic health prior to pregnancy and advert excess maternal and fetal risk.

Pharmacoepidemiology

Maternal Acetaminophen Use and Adolescent Behavioral Problems: Discrepancies by Reporter Rashida S. Smith-Webb* Ruby Barnard-Mayers Martha M. Werler Samantha E. Parker

Background: Acetaminophen is commonly used for pain and fever during pregnancy. Research suggests an association between maternal acetaminophen use and poor neurodevelopmental outcomes among offspring. However, studies often rely on maternal report of exposure and outcomes, which is subject to dependent misclassification. We examined the association between maternal acetaminophen use and behavioral problems during adolescence by parent, teacher, and the child.

Methods: We conducted a follow-up study of children born between 1996-2002. Exposure to acetaminophen was assessed via a standardized maternal interview after delivery. Behavioral assessments were conducted during adolescence (ages 11-17) using the Child Behavior Checklist (CBCL), Teacher Report Form (TRF), and Youth Self Report (YSR). Outcomes included internalizing (e.g., anxious) and externalizing (e.g., aggressive behavior) behavioral problems. We used linear regression models to calculate adjusted mean differences (MD) and 95% CI in T-scores. We also calculated weighted MD to account for lost to follow-up.

Results: Among 230 mothers, 66% reported acetaminophen use while pregnant. Acetaminophen use was generally not associated with behavioral problems by any reporter. Adjusted effect sizes varied across reporters. For instance, the MD for anxious/depressed was 1.5 (95% CI: -0.2, 3.2), 0.9 (95% CI: -0.8, 2.6), and -0.5 (95% CI: -2.2, 1.3) for parent, teacher, and self-report, respectively. Weighted results revealed a downward bias of MD based on maternal reported scores whereas those from teacher and youth reports were changed little. For example, the MD for anxious/depressed decreased to 0.9 for parent report but was unchanged for teacher report.

Conclusions: Prenatal acetaminophen use was not associated with behavioral problems during adolescence. Given the discrepancies by reporter and the influence of selection bias evident in maternal reporting, multi-informant assessments are indicated.

Pharmacoepidemiology

Patterns of maternal antifungal use in the National Birth Defects Prevention Study, 1997-2011. Eleni Papadopoulos* Alissa Van Zutphen Martha Werler Meredith Howley Sarah Fisher Paul Romitti

Fungal infections are common among pregnant people. Thus, it is important to study antifungal medications and patterns of use during pregnancy. In this analysis, we described maternal antifungal use among participants in the National Birth Defects Prevention Study (NBDPS). NBDPS was a multi-site, population-based, case-control study of pregnant people from 10/1997 to 12/2011. Participants self-reported information on antifungal use via a telephone interview. For this study, we included 11,427 control participants with pregnancies ending in live births without major birth defects, randomly selected from birth records or hospital discharge lists. We described infant and maternal characteristics, and the route of administration for each reported medication. We examined the prevalence of antifungal medication use during pregnancy and across the study period, overall and by categories of maternal age and race/ethnicity. Antifungal medication use was reported by 283 (2.5%) participants and demographic characteristics were similar between these participants and those who did not report antifungal use during pregnancy. Antifungal use prevalence remained constant through each trimester (trimesters 1 and 2: 1.1%, trimester 3: 1.0%). Prevalence was highest during 1997-2001 (ranging from 1.7-1.9% in each trimester) and decreased in each subsequent period (2002-2006: ranging from 1.0-1.3%; 2007-2011: ranging from 0.3-0.5%). Of 13 reported antifungals, most (69.0%) were indicated for topical use. The most commonly reported antifungals were miconazole (1.0%), clotrimazole (0.2%), fluconazole (0.2%), and terconazole (0.2%). Only marginal variations in antifungal use were observed when stratified by maternal age or maternal race/ethnicity. In our sample, antifungal use was rare, did not vary by trimester, and declined over the study period. Further study is needed to determine if fungal infections or their treatments are declining in pregnant populations.

Pharmacoepidemiology

A Safety Comparison of Continuing Versus Discontinuing Triptans for Acute Migraine Treatment in the First Trimester of Pregnancy Following Pre-pregnancy Triptan Use Jacob Kahrs* Lauren Kucirka Mollie E. Wood

The primary medications prescribed for the acute treatment of migraines outside of pregnancy are triptans. Safety data on triptans in pregnancy is limited but prior studies are relatively reassuring: prenatal triptan use is not associated with many common pregnancy safety outcomes, such as preterm birth or major congenital malformations. Even so, many pregnant migraineurs discontinue triptans out of concern for fetal safety. This study expands on prior literature by examining associations between first trimester triptan use and several pregnancy outcomes.

Using United States commercial insurance claims data from 2004-2015, we identified a cohort of pregnant people who had an International Classification of Diseases, Ninth Revision, Clinical Modification migraine diagnosis code at an inpatient, outpatient or emergency department visit in the 90 days prior to the last menstrual period and filled a prescription for a triptan in the same window. Participants who had a first trimester triptan fill (continuers) were compared to participants who did not have a 1st trimester triptan fill (discontinuers) using generalized linear models. We used inverse probability of treatment weights to account for differences in baseline characteristics including comorbidities, medication use, demographics, healthcare utilization and proxies of disease severity.

Of the 6,081 pregnancies included in this analysis, 1,639 filled a triptan prescription in the first trimester. Triptan continuers had a decreased risk of preterm birth (risk ratio [RR] 0.79, 95% CI 0.66, 0.94) and similar risks of small for gestational age (RR 1.09, 95% CI 0.55, 2.19) and preeclampsia (1.03, 95% CI 0.76, 1.40). We observed increased risks of placental abruption (RR 1.87, 95% CI 0.63, 5.51) and placenta previa (RR 2.03, 95% CI 0.64, 6.47) associated with triptan continuation, albeit with very wide confidence intervals.

These results may be reassuring for pregnant migraineurs who need to continue using triptans.

Pregnancy outcomes

Genetic association study of preterm birth and gestational age duration in a population-based case-control study in Peru Diana Juvinao-Quintero* Sixto E. Sanchez Nelida Pinto Tsegaselassie Workalemahu Liming Liang Michelle A. Williams Bizu Gelaye

Background: Preterm birth (PTB) is an adverse pregnancy outcome affecting ~15 million pregnancies worldwide. Genetic studies have identified several candidate regulatory loci for PTB, but results remain limited to European ancestry populations. Thus, we conducted a genome-wide association study (GWAS) of PTB and gestational age duration (GAD) among Peruvian women. **Methods:** 2,212 women from the Placental Abruption Genetic Epidemiology (PAGE) study participated. PTB cases were women who delivered ≥ 20 weeks' but < 37 weeks' gestation, while controls delivered at term (≥ 37 weeks but < 42 weeks) within 48 hours of the index case. After imputation with TOPMED and quality control, we assessed the additive genetic associations of ~6 million SNPs with PTB and GAD using multiple logistic and linear regression models, respectively, adjusted for maternal age and the first two genetic principal components to account for population stratification. Functional analysis with the FUMA-GWAS tool was conducted among top signals detected with an arbitrary $P < 1.0\times10^{-5}$ in the GWAS. **Results:** Mean GAD was 30±4 weeks in PTB cases (N=933) and 39±1 in the controls (N=1,279). Compared to controls, PTB cases were slightly older and had higher C-sections and vaginal bleeding. No association was identified with PTB or GAD at genome-wide significance. Top suggestive ($P < 1.0\times10^{-5}$) associations with PTB and GAD were seen at rs13151645 (*LINC01182*) and rs72824565 (*CTNNA2*), respectively. The top PTB variants were enriched for biological pathways associated with polyketide, progesterone, steroid hormones, and glycosyl metabolism. For GAD, top variants were enriched for intronic regions and cancer pathways, and these genes were upregulated in the brain and subcutaneous adipose tissue. **Conclusion:** We identified various signals suggestively associated with PTB and GAD in Peruvian women. Top variants were enriched for pathways associated with the metabolism of progesterone and steroid hormones.

Pregnancy outcomes

Violence victimization-related morbidity among pregnant and postpartum women using a population-based, longitudinal dataset Shaina Sta. Cruz* Claire Margerison Alison Gemmill Sidra Goldman-Mellor

Violence against women, including during pregnancy and the postpartum period, is a major public health problem worldwide. Homicides during the perinatal period have recently increased (Wallace 2022), yet, concerningly, these deaths reflect only the most extreme manifestation of violence-related victimization. Far less is known about trends and disparities in pregnancy-associated violence morbidity. Examining emergency department (ED) utilization for violence-related injuries in this patient population can shed light on overall incidence and patterns of risk, despite ED visits comprising a subset of all violent victimization. In this study, we examined trends and disparities in pregnancy-associated violent injury morbidity from 2010-2019 using individually-linked longitudinal, all-payer, population-based statewide data from California. The sample comprised all women with a live-birth hospital delivery in each year from 2010-2018 (~3 million). Annual cohorts of women were followed for 12 months after their delivery hospitalizations to identify subsequent nonfatal ED visits for violent injury (defined using ICD-9/10-CM codes). Analyses included trends in annual incidence rates, including disparities by race/ethnicity and payer. In the 2010 cohort, 12-month incidence of ED visits for pregnancy-associated violent injury was 0.46%; this remained stable for several years and then declined to 0.41% in the 2018 cohort (an overall decrease of 10.9%). In every year, Black women had the highest incidence of ED visits for violent injury compared to White, Hispanic, and Asian/Pacific Islander women. Next steps are to analyze the timing of violence victimization in the perinatal period and investigate sociodemographic trend heterogeneity. While relatively rare, pregnancy-associated violence victimization still affects large numbers of women each year. Better surveillance and prevention efforts are needed.

Pregnancy outcomes

The intergenerational transmission of preeclampsia: examining the unaffected daughters
Aditi Singh* Sage Wyatt Liv Grimstvedt Kvalvik Kari Klungsøyr Rolv Skjærven

Introduction: Previous research has shown that daughters born to mothers with preeclampsia (PE) have an increased risk of developing PE, regardless of their prenatal exposure to PE. To gain further insight into the intergenerational transmission of PE, we examined the risk of PE in the first pregnancies among daughters not prenatally exposed to PE and born to mothers with PE in other pregnancies.

Methods: Using the Medical Birth Registry of Norway (1967-2020), we identified 403 917 mother-daughter units where the daughter was prenatally unexposed to PE. We calculated odds ratio (OR) and 95% confidence intervals (CI) using logistic regression to evaluate the association PE in daughters' first pregnancies and mothers' reproductive history. Daughters born to mothers without PE were the reference group. Models were adjusted for the mothers' and daughters' age at first pregnancy and highest educational status, and daughters' year of birth.

Results: Among daughters unexposed to PE (N=403 917), 0.2% (n=924) were born to mothers with PE pregnancies. Of these daughters, 6.6% (n=61) had PE in their first pregnancy. Daughters born to mothers with PE had an increased risk of developing PE in their first pregnancy (OR 1.88, 95%CI 1.45-2.25). Moreover, daughters had a higher risk of a first PE pregnancy if born to mothers with two pregnancies complicated by PE (OR 5.09, 95%CI 1.98-13.09) than if born to mothers with PE in only one pregnancy (OR 2.07, 95%CI 1.52-2.82). Daughters born to mothers with PE who themselves were born small-for-gestational-age had a higher risk of having a first PE pregnancy (OR 2.4, 95%CI 1.3-4.4) than daughters born appropriate-for-gestational-age (OR 1.85, 95%CI 1.37-2.50); while this was less evident for daughters born large-for-gestational-age (OR 1.38, 95%CI 0.50-3.78).

Conclusion: These findings highlight the heterogeneity in the intergenerational transmission of PE by perinatal factors that need further investigation.

Pregnancy outcomes

Examining the contribution of socioeconomic disadvantage to racial and ethnic disparities in low-risk cesarean birth in California Shalmali Bane* Suzan Carmichael Mahasin Mujahid Elliott Main

In the US, there is substantial variability in the rate of cesarean birth by social factors, such as race/ethnicity and socioeconomic disadvantage. The joint contribution of these factors, especially in a multi-level context, for low-risk cesarean birth has not been examined.

Using a dataset of live birth and fetal death certificates linked with maternal hospitalization data (2007-18), we examined the contribution of multi-level socioeconomic disadvantage (neighborhood deprivation index at the census tract level, maternal education, and insurance) to racial/ethnic disparities in low-risk cesarean (defined as nulliparous, term, singleton, vertex (NTSV)) births. We used Poisson regression models clustered by tract and sequentially adjusted for maternal characteristics, with interaction terms for race/ethnicity and measures of socioeconomic disadvantage.

Among 1,815,933 NTSV births, 26.6% were cesarean. Adjusted RR increased with increasing NDI (e.g., 1.06 95% CI 1.05-1.08 for most deprived vs. least deprived quartile), lower education (e.g., 1.12, 95% CI 1.11-1.13 for high-school education or less vs. college educated), and public insurance (1.11, 95% CI 1.11-1.12 vs. private insurance). When assessing interaction, Black individuals had an elevated RR, relative to White individuals, across all NDI quartiles. Higher education and public insurance status were associated with increased RR for NTSV cesarean for all racial/ethnic groups, relative to White. The most advantaged White individuals had the lowest RR while the least advantaged Black individuals had the greatest RR for cesarean birth.

Our findings suggest that the racial/ethnic disparity in low-risk cesarean is highest among privately insured and more educated individuals, relative to White individuals; Black individuals had a consistently elevated risk of low-risk cesarean regardless of NDI, while the risk for Asian and Hispanic individuals decreased with increasing NDI.

Pregnancy outcomes

Can birth hospital explain racial/ethnic differences in cesarean birth among low-risk births? An analysis of California data, 2007-2018 Shalmali Bane* Suzan Carmichael Mahasin Mujahid Elliott Main Peiyi Kan

In the US, there is substantial variability in low-risk cesarean birth rate by hospitals and race/ethnicity. The contribution of inequitable hospital quality to disparities in low-risk cesarean births is uncertain. Using a dataset of live birth and fetal death certificates linked with maternal hospitalization data (2007-18), we examined the role of birth hospital on racial/ethnic disparities in low-risk cesarean (defined as nulliparous, term, singleton, vertex (NTSV)) births. Poisson regression models clustered by hospital were used to compare racial/ethnic differences in cesarean prevalence, adjusted for maternal and hospital characteristics. We calculated risk-standardized NTSV cesarean prevalence per hospital and used g-computation to assess how the cesarean prevalence by racial/ethnic group would change if all births occurred at the same distribution of hospitals as for White individuals. Among 1,594,277 NTSV births at 212 hospitals, 26.9% were cesarean. Adjusted RRs ranged from 1.01 for US-born Hispanic (95%CI: 0.99-1.05) to 1.28 for Black individuals (95%CI: 1.22-1.33), relative to White individuals. Higher proportions of Black (42.3%), Pacific Islander (40.7%), and AIAN (41.6%) individuals gave birth in hospitals in the lowest tertile of cesarean prevalence, higher proportions of Asian individuals gave birth in the middle tertile (41.0%), and highest proportions of Hispanic individuals (foreign-born: 37.0%, US-born: 39.2%) gave birth in the highest tertile. In the substitution analysis, NTSV cesarean prevalence would be reduced for certain groups but not others, ranging from 87 excess events (0.3% increase) among the Black population to 6,473 avoided events (5.6% decrease) among US-born Hispanic populations. Our findings suggest that rates of cesarean would be reduced in Black, Asian, and Hispanic populations if they gave birth at similar hospitals as white women. Future efforts should consider the role of within-hospital factors.

Pregnancy outcomes

Association between maternal age at conception and select pregnancy outcomes – An analysis of the 2017-2019 National Survey of Family Growth Adaeze Anamege* Kelly Gurka

Background: Various maternal factors are associated with adverse pregnancy outcomes. However, findings from studies on maternal age in the US are inconsistent regarding who is at highest risk of these adverse outcomes. This study aimed to identify the incidence of select pregnancy outcomes by maternal age at conception.

Methods: Data from the 2017-2019 National Survey of Family Growth were analyzed for 6,346 pregnancies among women aged 15-49 years. Women still pregnant with their first child at the time of interview were excluded. Multivariable logistic regression, controlling for education, employment, area of residence, marital status, race, ethnicity, and parity, was used to quantify the association between maternal age and ectopic pregnancy, stillbirth, spontaneous and induced abortion. Analyses were performed in SAS Version 9.4.

Results: A majority of respondents were White (66%) or non-Hispanic (70%). The incidence of induced abortion was highest among the youngest age group (11%), while the incidence of spontaneous abortion (38%) was highest among the oldest age group. The odds of stillbirth increased with increasing maternal age. Women over 40 years of age were three times as likely as women under 20 years of age to have a spontaneous abortion (adjusted odds ratio [AOR]=3.32; 95% Confidence Interval [CI]: 2.02, 5.46). Compared to women under 30 years of age, the risk of ectopic pregnancy was highest among women in their late thirties (AOR=1.72; 95% CI: 0.70, 4.19). Women in their early thirties were nearly half as likely to experience induced abortion as women under 20 years of age (AOR = 0.57; 95% CI: 0.39, 0.83).

Conclusion: Findings from this study confirm the increased risk of an adverse pregnancy outcome among women of extreme maternal ages. Continuous advocacy for increased uptake of prenatal care is needed to ensure early identification of risk factors associated with late conception.

Pregnancy outcomes

Pre-pregnancy and pregnancy disorders, preterm birth, and the risk of cerebral palsy: a population-based study Neda Razaz*

Introduction Cerebral palsy (CP) is the most common cause of childhood physical disability and maternal pre-existing and pregnancy complications are recognized risk factors of CP, but the extent to which their effects are mediated by preterm birth is unknown.

Objective To investigate associations between pre-pregnancy and pregnancy disorders and the risk of CP and to evaluate the extent to which risks are mediated by preterm delivery.

Design, setting, and participants Population-based cohort study in Sweden, including 2,055,378 singleton, non-malformed infants, born between 1999 and 2019. Data on maternal and pregnancy characteristics and diagnoses of CP were obtained by individual record linkages of nationwide Swedish registries.

Exposures Maternal pre-pregnancy and pregnancy disorders.

Main outcome measure Inpatient and outpatient diagnoses were obtained for CP after 27 days of age. Adjusted rate ratios (aRRs) were calculated, along with 95% confidence intervals (CIs).

Results: A total of 515,771 (25%) offspring were exposed to maternal pre-existing chronic disorders, and 3,472 cases of CP were identified, for a cumulative incidence of 1.7 per 1,000 live births. After adjusting for potential confounders, maternal chronic cardiovascular or metabolic disorders, other chronic diseases, mental health disorders, and early pregnancy obesity were associated with 1.89-, 1.24-, 1.26-, and 1.35-times higher risk (aRRs) of CP, respectively. Most notably, offspring exposed to maternal antepartum hemorrhage had a 6-fold elevated risk of CP (aRR 5.78, 95% CI, 5.00-6.68). Mediation analysis revealed that approximately 50% of the effect of these associations was mediated by preterm delivery; however, increased risks were also observed among term infants.

Conclusion: Exposure to pre-existing maternal and pregnancy-related complications, increases the risk of CP in offspring. Although most CP cases occurred in term infants, preterm delivery explained 50% of the overall effect of pre-pregnancy and pregnancy disorders on CP.

Pregnancy outcomes

Lifetime history of low birth weight pregnancies and cognitive function in middle-aged women Diana Soria-Contreras* Jiaxuan Liu Rebecca Lawn Alexandra Purdue-Smithe Francine Grodstein Karestan Koenen Jorge Chavarro Emily Oken

Women with a history of delivering a low birth weight (LBW) infant are at higher risk of cardiovascular disease (CVD). Given the strong association between CVD and cognition, women with a history of LBW may also be at a higher risk of cognitive impairment, but this has not been studied. We evaluated the associations of a lifetime history of LBW with cognitive function among women in the Nurses' Health Study II (NHS II).

In 2014-2019, 15,138 of the 116,429 female nurses enrolled in the NHS II completed the Cogstate Brief Battery, an online cognitive assessment. Analyses were limited to 11,655 nurses with cognitive data who reported ≥1 pregnancy at ≥18 years of age on a reproductive history questionnaire applied in 2009. LBW history was defined as having had a newborn with a birth weight <2500 g in any pregnancy. Outcomes included composite z-scores capturing global cognition, psychomotor speed and attention, and learning and working memory. We used linear regression models adjusted for age at cognitive assessment, race/ethnicity, childhood/adulthood socioeconomic status, education, and pre-pregnancy factors such as chronic hypertension, body mass index, and lifestyle.

Mean (SD) age at cognitive assessment was 61.0 (4.6) y, and 956 (8%) had a history of LBW. In adjusted models, women with a history of LBW had lower mean z-scores in the psychomotor speed and attention (-0.08 [95% CI: -0.14, -0.02]), learning and working memory (-0.05 [-0.10, 0.00]), and global cognition (-0.06 [-0.11, -0.02]) composites compared to those without a history of LBW. We observed a gradient of lower scores with an increasing number of affected pregnancies, i.e., mean difference z-scores in global cognition were -0.05 [-0.10, -0.01] for one and -0.15 [-0.29, -0.01] for two affected pregnancies.

Women with a history of delivering an LBW infant had lower performance on cognitive function tasks in midlife. Additional studies are needed to confirm our findings and understand the mechanisms.

Pregnancy outcomes

Beyond MAVRIC: The effect of transabdominal versus transvaginal cerclage for prevention of early preterm birth in a lower-risk obstetric population Chelsea Messinger* Sonia Hernández-Díaz Albert Hofman Jessica Young Thomas McElrath

The 2020 MAVRIC trial found a strong protective effect of transabdominal cerclage (TAC) relative to transvaginal cerclage (TVC) for the prevention of spontaneous delivery (birth or late miscarriage) before 32 weeks. Trial participants had a prior failed TVC and an average of 2.8 prior spontaneous deliveries <28 weeks. Since MAVRIC, some question whether TAC should be offered to patients with fewer risk factors for recurrent spontaneous preterm delivery. We emulated a target trial to estimate the effect of TAC relative to TVC on preterm delivery <34 weeks within a lower risk population of patients.

We identified a retrospective cohort of adult singleton pregnancies in the United States who received history-indicated cerclage and had 1 prior spontaneous deliveries <34 weeks with or without history of a failed TVC. All eligible patients who received TAC and a random sample of eligible patients who received TVC were included. To estimate risk differences (RD), risk ratios (RR) and 95% confidence intervals (CI), we used inverse probability weighted estimation of cumulative incidence to adjust for confounding and censoring.

195 patients were eligible for inclusion: 91 received TAC and 104 received TVC. Overall, 42% of patients had a history of a failed TVC and an average of 1.5 +/- 0.7 prior spontaneous deliveries <34 weeks. Preterm delivery <34 weeks occurred in 13.2% of pregnancies. The weighted risk of preterm delivery before 34 weeks was 6.0% for TAC (95% CI 2.5%, 10.1%) and 19.1% for TVC (95% CI 7.5%, 30.7%), RD=-13.5% (95% CI -24.8%, -0.1%), RR=0.31 (95% CI 0.12, 0.99). This estimate was robust to several sensitivity analyses.

In a lower risk obstetric patient population than that of the MAVRIC trial, TAC was strongly protective for preterm delivery before 34 weeks compared to TVC. These results must be considered against the risks of TAC, which include mandatory Cesarean delivery at ~37 weeks, for determining whether TAC should be offered to lower-risk women.

Identifying small- and large-for-gestational-age infants using customized neonatal growth charts sid john* KS Joseph

Background There is no consensus on the utility of customizing birth weight-for-gestational age charts by race. We examined the clinical performance and population impact of race-specific small- and large-for-gestational-age (SGA and LGA) cutoffs in relation to serious neonatal morbidity/mortality (SNMM).

Methods The study included all non-anomalous singleton live births at 37-41 weeks' gestation in the United States, 2003-2017, with data obtained from linked live birth and infant death files. Birth weight-specific SNMM, which included 5-minute Apgar score<4, seizures, ventilation and neonatal death, was modeled by gestational week using penalized B-splines. SGA and LGA cutoffs were identified at birth weights where SNMM odds were 10%, 50% and 100% higher than at optimal birth weight.

Findings The study included 31,015,923 White and 6,140,574 Black singletons. At 39 weeks' gestation, SNMM rates were lowest at 3232 g among White females and at 3118 g among Black females. SNMM odds were 10% higher at 2863 g (centiles 19 and 17 of the Intergrowth and WHO charts) and 3685 g (centiles 88 and 85) among White females, and at 2693 g (centiles 9 and 7) and 3544 g (centiles 81 and 76) among Black females. The birth weight cutoff of 2863 g for White SGA females yielded a sensitivity of 12.4% (95% CI 12.2-12.6), a specificity of 89.6% (95% CI 89.6-89.6) and pre and posttest probabilities of 18.6 and 23.8 per 1000, while the cutoff of 2693 g for Black SGA females yielded a sensitivity of 10.9% (95% CI 10.6-11.3), a specificity of 91.1% (95% CI 91.1-91.2) and pre and posttest probabilities of 22.9 and 29.2 per 1000. SGA-associated population attributable fractions were <3% for both races. Findings were similar among males, at other weeks, with other cutoffs, and for outcome components.

Interpretation Identifying SGA and LGA infants using race-customized birth weight-for-gestational age charts does not provide a clinically useful prediction tool or measure of population impact.

Pregnancy outcomes

Infant outcomes for babies born at home in Ireland: a national clinical audit, 2018-2020
Indra San Lazaro Campillo* Indra San Lazaro Jessica Keane Irene O'Farrell Joye McKernan Paul Corcoran Richard Greene Marit L. Bovbjerg

Background. The health and wellbeing of the newborn is a priority when providing maternity care.

Objective. To assess the infant outcomes among women who gave birth at home in Ireland.

Methods. National clinical audit on home birth services (HBS) for three years (2012-2021) in the Republic of Ireland (ROI). Retrospective review of data provided by Self-Employed Community Midwives (SECMs) and Designated Midwifery Officers (DMOs) from clinical maternity notes.

Results. Of the 848 planned home births over the triennial period, 489 infants were born at home, 232 were female (47.8%) and 252 were male (52.0%). The mean birth weight for infants born at home was 3,704 grams. There were no low-birth-weight infants (less than 2,500 grams) born at home. Resuscitation was needed for 6% of infants, including requiring suction, receiving oxygen, use of intermittent positive pressure ventilation or receiving cardiac massage. Eighteen infants who were born at home were transferred to a maternity hospital. The majority of infants were transferred because of respiratory concerns (i.e., tachypnoea, grunting, low oxygen saturation; 61.1%), followed by non-fatal fetal anomalies that required review (22.2%). Eleven of these eighteen infants were admitted to the Special Care Baby Unit (SCBU) or Neonatal Intensive Care Unit (NICU) following transfer, all of which were later discharged alive and well. On the day of the home birth, 97% of women were breastfeeding exclusively, with 95% breastfeeding exclusively on the day of discharge from the care of the SECMs. Women who birthed at home were twice as likely to be breastfeeding exclusively on day of discharge compared to all women who gave birth in the ROI (95% versus 47%). There was one perinatal death among women who gave birth at home in these three years.

Conclusion. Overall, this audit reports positive infant outcomes among a cohort of 489 women who gave birth at home in Ireland for a three-years period.

Pregnancy outcomes

Systematic Review and Meta-analysis of Birthweight and Perfluorononanoic Acid Exposures. J. Michael Wright* Alexandra Larsen Kristen Rappazzo Hongyu Ru Elizabeth Radke Thomas Bateson

Meta-analyses of per- and polyfluoroalkyl substances suggest that some reported birthweight deficits may be due to potential bias from pregnancy hemodynamics (e.g. increased plasma volume) related to biomarker sampling timing differences. We used a systematic review that included potential risk of bias and study sensitivity analysis to identify 34 studies examining changes in mean birthweight in relation to perfluorononanoic acid (PFNA) biomarker measures (e.g., maternal serum/plasma or umbilical cord samples). We fit a random effects model of the overall pooled estimate and stratified estimates based on sample timing and overall study confidence. We detected a -32.9 g (95%CI: -47.0, -18.7) mean birthweight deficit per each ln PFNA increase from 27 included studies. We did not detect evidence of publication bias (p_E=0.30) or between-study heterogeneity in the summary estimate (p_Q=0.05; I^2=36%). The twelve *high* confidence studies yielded a smaller pooled effect estimate (ß= -28.0 g; 95%CI: -49.0, -6.9) than the ten *medium* (ß= -39.0 g; 95%CI: -61.8, -16.3) or four *low* (ß= -36.9 g; 95%CI: -82.9, 9.1) confidence studies. The stratum-specific results based on earlier pregnancy sampling periods in 11 studies showed smaller deficits (ß= -22.0 g; 95%CI: -40.1, -4.0) compared to 10 mid- and late-pregnancy (ß= -44.2 g; 95%CI: -64.8, -23.5) studies and six post-partum studies (ß= -42.9 g; 95%CI: -88.0, 2.2). Overall, we detected mean birthweight deficits for PFNA that were larger and more consistent across studies than previous per- and polyfluoroalkyl substances meta-analyses. Compared to studies with later sampling, birthweight deficits were smaller but remained sizeable for even the earliest sampling periods. Contrary to earlier meta-analyses for perfluorooctanoic acid and perfluorooctane sulfonate, birthweight deficits that were detected across all strata did not appear to be fully explained by potential bias due to pregnancy hemodynamics from sampling timing differences.

Pregnancy outcomes

Variation in risk for neonatal intensive care among TRICARE insured newborns at military and civilian hospitals Celeste Romano* Clinton Hall Anna Bukowinski Thornton Mu Gia Gumbs Ava Marie Conlin Rasheda Vereen JoAnna Leyenaar David Goodman

Objective: To characterize differences in the TRICARE-insured neonatal population and risk for neonatal intensive care unit (NICU) admission between US military and civilian hospitals.

Methods: Singleton births identified in DoD Birth and Infant Health Research program data October 2015–December 2020 were stratified by birth location (military treatment facility [MTF] or civilian hospital); births occurring at civilian hospitals within 40 miles (the catchment area) of an MTF were also ascertained. NICU admission rates (per 100 births) and the frequency of newborn risk factors were calculated by birth location. Modified Poisson regression models estimated associations with risk factors, and marginal R^2 values were calculated to assess model fit.

Results: Of 470,605 births, 36.8% occurred at an MTF, 20.4% at a civilian hospital within an MTF catchment area, and 42.9% at a civilian hospital outside an MTF catchment area. The NICU admission rate was 8.9 and 10.4 among births at MTFs and civilian hospitals, respectively; for births at civilian hospitals within MTF catchment areas, the rate was 12.5. Births at civilian hospitals within MTF catchment areas vs at MTFs were similarly more likely to be preterm (9.1% vs 5.3%) and have low birthweight (5.9% vs 3.9%) and birth defects (5.0% vs 3.1%). Positive associations were observed between risk factors and NICU admission regardless of birth location, but there was greater unexplained variation among births at MTFs (R^2: 0.14) and civilian hospitals outside MTF catchment areas (R^2: 0.19) vs civilian hospitals within MTF catchment areas (R^2: 0.25).

Conclusions: Births at MTFs were at lower risk for NICU admission relative to those at civilian hospitals, particularly civilian hospitals within MTF catchment areas. Furthermore, NICU admission for births at MTFs was not well explained by predictors of newborn need. Baseline population differences should be considered when comparing care received at MTFs vs civilian hospitals.

Pregnancy outcomes

Racial Identification Switching and Health among Birthing Persons in California Jason Bonham* Brenda Bustos Tim Bruckner

Although prior studies indicate that approximately 6% of the population will engage in Racial Identification Switching (RIS), no prior research explores the potential relation between RIS and health outcomes. Using the California birth cohort file from 2005-2015, we examine birthing persons identifying as non-Hispanic White or non-Hispanic Black and with at least two live births over the test period (n= 449,008). We compared perinatal health and sociodemographic characteristics of birthing persons with RIS over time against those without RIS over time. We find that measures of positive maternal and perinatal health correspond with a switch from NH Black to NH white identification, whereas a downward move in maternal and perinatal health and in socioeconomic status varies with a switch from NH white to NH Black identification (all $p<.05$). Future research should, with careful theorizing, disentangle the temporal order of RIS, adverse perinatal health and socioeconomic status.

Pregnancy outcomes

Prenatal Over-the-Counter Acetaminophen Use is Associated with Lower Birthweight in ECHO Cohorts Katelyn Huff* Catherine Bulka Guojing Wu Margaret Adgent Akram Alshawabkeh Brennan Baker Maria Talavera-Barber Traci Bekelman José Cordero Whitney Cowell Zoe Duberstein Amy Elliott Daniel Enquobahrie Akhgar Ghassabian Margaret Karagas Amber Kautz Barry Lester Tengfei Ma Cindy McEvoy Kimberly McKee John Meeker Ruby Nguyen Thomas O'Connor Nigel Paneth Wei Perng Christina Porucznik Sheela Sathyanarayana Hyagriv Simhan Shanna Swan Megan Woodbury Noya Galai Stephen Ehrhardt T. Michael O'Shea Rebecca Fry

Background. Acetaminophen is among the most commonly used over-the-counter (OTC) medications during pregnancy. However, some experimental and epidemiological studies suggest acetaminophen use during pregnancy alters fetal development.

Objective. To evaluate the relationship between prenatal acetaminophen use and the following outcomes: (1) preterm birth, (2) birthweight, (3) small-for-gestational-age (SGA), and (4) large-for-gestational-age (LGA).

Methods. The study population consisted of 8,950 mother-infant pairs from 36 pediatric cohorts participating in the National Institute of Health's Environmental influences on Child Health Outcomes (NIH ECHO) Program. Multiple imputation was performed to address missing covariate data. Regression modelling with inverse probability weighting to account for key confounders was used to examine the relationship between acetaminophen use during pregnancy with each of the four perinatal health outcomes of interest.

Results. Approximately half of the mothers reported using acetaminophen at some point during their pregnancy (n=4,449). After adjustment for relevant covariates, on average, prenatal acetaminophen use was associated with lower birthweight (adjusted β: -41 grams; 95% confidence interval (CI): -59, -22), and lower odds of LGA (adjusted odds ratio (AOR): 0.74; 95% CI: 0.68, 0.81). Further, while not statistically significant, we observed higher odds of SGA (AOR: 1.11, 95% CI: 0.98, 1.25) for those who took prenatal acetaminophen. The adjusted odds ratio for acetaminophen use during pregnancy and preterm birth was near null (AOR: 0.95, 95% CI: 0.88, 1.02).

Conclusions. These results suggest that acetaminophen use during pregnancy is associated with small reductions in fetal growth. Future research is needed to confirm these findings and to test for dose-response effects or windows of susceptibility during pregnancy.

Pregnancy outcomes

Trends in racial/ethnic disparities of postpartum hospital readmissions in California from 1997-2018 Marina Magalhaes*, Curisa Tucker Chen Ma Mahasin Mujahid Alexander Butwick Anna Girsen Ronald Gibbs Suzan Carmichael Marina Magalhaes

Context/Purpose: Substantial racial/ethnic disparities in postpartum readmission (PPR) exist, but little is known about temporal trends in this disparity and factors that contribute to it. Our objective was to explore whether trends in PPR vary by race/ethnicity.

Methods: PPR was defined as hospitalization within 42 days after birth hospitalization discharge, using fetal death and live birth certificates linked to delivery discharge records from 10,711,289 births in California from 1997-2018. We used multivariable logistic regression models stratified by race/ethnicity to estimate the annual change in PPR during the study period and report odds ratios (OR) and 95% confidence intervals (CI) that reflect the total change in odds of PPR from 1997 to 2018. For simplicity, we focus this abstract on comparing results for Black and White individuals. We adjusted models for prenatal (e.g. demographics) and clinical (e.g. comorbidities) factors. We included year-squared in models to allow for non-linearity of trends. To determine whether racial/ethnic disparities changed over time, we calculated risk ratios (RR) in 1997 and 2018 by comparing predicted probabilities from the race-specific models.

Results: The overall prevalence of PPR was 1% (1.7% for Black; 1% for White mothers). In our unadjusted models, the increase in odds of readmission from 2018 to 1997 was 44% for Black mothers (OR: 1.44; CI: 1.35-1.53), compared to 26% for White mothers (OR: 1.26, CI: 1.22-1.31). Adjustment for prenatal and clinical factors somewhat explained these differences. Disparities in PPR over time increased the most for Black mothers (1997: RR 1.7; CI: 1.6-1.8; 2018: RR 1.9; CI :1.8-2.0).

Conclusions: PPR increased during the study period, and it increased the most for Black mothers. Given that PPR varied by race/ethnicity and differences were attenuated by prenatal and clinical factors, it is important to find ways to prevent further increases in PPR especially among groups at highest risk.

Pregnancy outcomes

Maternal opioid use disorder and infant mortality in Wisconsin, 2010-2018 David Mallinson* Hsiang-Hui Daphne Kuo Russell Kirby Lawrence Berger Deborah Ehrenthal

Opioid use disorder (OUD) during pregnancy has increased over the past decade. The extent to which prenatal OUD exposure affects infant mortality (death before 365 days post-birth) is uncertain. We measure the association between maternal OUD during pregnancy and infant mortality with data from a population-based cohort of linked Wisconsin birth records, death records, and Medicaid claims. We also investigate whether that association varies by neonatal opioid withdrawal syndrome (NOWS) diagnosis and by maternal medication-assisted treatment (MAT) for OUD during pregnancy. Our sample consists of Medicaid-paid live deliveries during 2010-2018 (N=235,777 births). There are three measures of OUD exposure: any OUD (no OUD; OUD), OUD-NOWS (no OUD; OUD without NOWS diagnosis; OUD with NOWS diagnosis), and OUD-MAT (no OUD; OUD without MAT; OUD with MAT).

In 5,186 births (2.2%), mothers had OUD during pregnancy. Among these, 2,614 infants (1.1%) had NOWS, and 3,317 births (1.4%) had mothers who received MAT. Approximately 1.3% of OUD-exposed infants died relative to 0.6% of unexposed infants. Stratifying on OUD type, Mortality was greatest in the OUD without NOWS group (1.7%), followed by the OUD with MAT group (1.4%), the OUD without MAT group (1.2%), and the OUD with NOWS group (0.7%). Cox regressions that adjusted for maternal demographics indicated that maternal OUD was positively associated with the incidence of infant mortality (hazard ratio [HR] 2.07; 95% CI 1.60-2.68) relative to no OUD. OUD without NOWS was also associated with infant mortality (HR 2.69; 95% CI 1.98-3.67), as were OUD without MAT (HR 1.66; 95% CI 1.07-2.56) and OUD with MAT (HR 2.34; 95% CI 1.71-3.20). However, OUD with NOWS was not significantly associated with infant mortality. Findings suggest that OUD may increase the risk of infant mortality.

Pregnancy outcomes

Examining the Association between Rurality, Gestational Weight Gain, and Preterm Birth in Appalachia Melissa White* Amy Wahlquist Paula Masters Matthew Loos Megan Quinn

Background: Gaining insufficient weight during pregnancy is associated with increased risk for preterm birth (delivery <37 weeks gestation). Rural populations have lower socioeconomic status, reduced access to care, and higher rates of obesity and pre-pregnancy hypertension relative to non-rural populations, potentially increasing risk for preterm birth.

Purpose: To examine relationships between recommended gestational weight gain (GWG) attainment and rural (vs. non-rural) residence with preterm birth in an Appalachian healthcare system.

Methods: Retrospective electronic health record (EHR) data were extracted for people (N=3023) delivering between January 2018 and December 2020. Bi- and multivariable logistic regression were conducted to estimate the impact of maternal residence on recommended GWG attainment and preterm birth after adjusting for maternal demographic and clinical characteristics using odds ratios (OR).

Results: Nearly 10% of deliveries were considered preterm. Most mothers resided in rural areas (58%), were non-Hispanic white (95%), had non-governmental insurance (53%), never smoked (53%), were partnered (53%), and did not have hypertension (82%) or pre-eclampsia (95%). After adjusting for covariates, primiparity (OR=1.5), multiparity (OR=2.5), hypertension (OR=1.5), and pre-eclampsia (OR=8.9) significantly increased the odds of preterm delivery ($p<0.05$). Rural mothers having excessive GWG had significantly higher odds of preterm delivery than non-rural mothers having excessive GWG (OR=2.1, $p=0.02$).

Discussion: Findings highlight the importance of studying predictors associated with infant mortality at the local or regional level. The interaction between rurality, gaining excessive GWG, and preterm birth emphasizes the need to study these predictors in rural areas. However, missing data and cross-sectional study design were key limitations. Future research directions include follow-up analysis and comparison of results to similar healthcare systems.

Pregnancy outcomes

Prenatal Neisseria gonorrhoeae and preeclampsia subtypes Brandie DePaoli Taylor* Victor Adekanmbi Yuanyi Zhang Abbey Berenson

Background: The role of sexually transmitted infections (STIs) in hypertensive disorders of pregnancy (HDP) is not well understood. A handful of studies suggest that *Chlamydia trachomatis* (CT) and syphilis may increase the risk of HDP. However, the impact of *Neisseria gonorrhoeae* (GC) is largely unknown.

Method of Study: We obtained records from 29,821 singleton births at the University of Texas Medical Branch between 2016-2022. Demographic variables, GC, CT, syphilis, HIV, and hepatitis B testing results and pregnancy outcomes were identified from electronic health records using ICD-10 codes. Primary outcomes of interest included gestational hypertension, severe preeclampsia, superimposed preeclampsia, and preeclampsia with or without a preterm delivery. Secondary outcomes included preterm premature rupture of membranes, chorioamnionitis, and preterm delivery. Logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals. Models were adjusted for maternal age, maternal race/ethnicity, and smoking. E-values were calculated to assess unmeasured confounding.

Results: GC increased the odds of preterm preeclampsia (ORadj. 1.95, 95% CI 1.02-3.73), and preterm birth (OR adj. 1.78, 95% CI 1.22-2.60). GC-chlamydia co-infection was associated with preterm birth (ORadj. 1.77, 95% CI 1.03-3.04). Additional adjustments for infection with other STIs did not alter the results. E-values ranged from 3.0-3.4 suggesting that moderate unmeasured confounding could bias our findings.

Conclusions: GC and GC-CT co-infection appear to increase the odds of preterm preeclampsia and preterm birth. Innate and T-cell immunity plays a role in CT and GC induced reproductive tissue damage, but mechanisms during pregnancy are understudied. To optimize screening and prevention, research is needed to determine the burden of common STIs on HDP, including investigations into biological effects during pregnancy.

Pregnancy outcomes

Progesterone-interferon epsilon interaction reduces the odds of preeclampsia Brandie DePaoli Taylor* Michael Criscitiello Akaninyene Noah Talar Kechinchian Ramkumar Menon Brooke Norwood Fuller Bazer

Background: Novel interferon epsilon (IFNe) is constitutively expressed in the female reproductive tract, but its role in pregnancy is unknown. IFNe expression in the genital tract is regulated by progesterone rather than Toll-like receptors like other type I IFNs. We previously found that elevated vaginal IFNe is associated with preterm preeclampsia and hypothesize that there could be an interaction between maternal progesterone and vaginal IFNe among women who develop preeclampsia.

Method of Study: This pilot study included 15 cases of preterm preeclampsia and 30 normotensive term controls from GAPPS biorepository. Vaginal swabs and paired serum were obtained between 8-20 weeks gestation. ELISA measured serum progesterone (P4), serum IFNe, and vaginal IFNe. Using logistic regression, we examined interaction between log-transformed P4 and IFNe on odds of preeclampsia, adjusting for maternal age, pre-pregnancy body mass index, ethnicity, and gestational age of sample collection. Adjusted linear regression models were used to explore the relationship between P4 and IFNe among cases and controls. Odds ratios (OR) and 95% confidence intervals (CI) are presented.

Results: IFNe was detectable in vaginal swabs but not in maternal serum. There was a significant interaction between IFNe and P4 ($P<0.05$) that reduced the odds of preterm preeclampsia (OR 0.39, 95% CI 0.17, 0.91). Among controls, there was a positive relationship between P4 and IFNe (b 1.81, 95% CI 0.41, 3.20). The trend was in the opposite direction for preterm preeclampsia (b -2.17, 95% CI -8.69, 4.35).

Conclusions: The mechanisms that may explain hormonal regulation of genital tract immune responses are not well understood. Given IFNe research is limited in humans, future studies should determine if dysregulation of P4 and IFNe influences early pregnancy processes such as decidualization, implantation, and placentation.

Social determinants of health

Modification of the association between neighborhood deprivation and adverse perinatal outcomes by Medicaid status? Meredith Dixon* Howard Chang Penelope Howards

Background: Neighborhood deprivation is a multi-dimensional construct representing the social environment through factors such as poverty, education, and employment. Although neighborhood context has been associated with adverse perinatal outcomes, the effects of neighborhood context on perinatal health likely differ by individual resources.

Methods: We created a cohort of singleton deliveries at Emory hospitals from July 2017 through October 2021 using electronic medical records including all live births of at least 20 weeks gestation, with addresses in metro Atlanta (n=18,872). We assigned neighborhood deprivation index (NDI) based on residential census tract and fit binomial identity models to estimate prevalence differences and to evaluate for additive interaction, with NDI as a continuous variable.

Results: Among pregnant people *without* Medicaid (n=11,296), the prevalence of gestational hypertension/preeclampsia was 9.8% higher (95% CI: 8.1% – 11.5%) for people living in high deprivation neighborhoods compared with low deprivation neighborhoods (comparing NDI one standard deviation above the mean to NDI one standard deviation below the mean). Among pregnant people *with* Medicaid (n=7,576), the prevalence difference was 4.7% (95% CI: 2.8% – 6.5%). Thus, the difference in prevalence differences across Medicaid strata was 5.2% (95% CI: 2.7% – 7.7%). The difference in prevalence differences across Medicaid strata was 2.6% (95%CI: 0.8% – 4.5%) for preterm birth. Regardless of Medicaid status, these adverse outcomes were substantially more prevalent in high NDI compared to low NDI neighborhoods. When further stratified on race, Black patients consistently had the highest prevalence of these adverse outcomes, but among people *with* Medicaid, differences between races were substantially reduced.

Conclusion: The association of neighborhood deprivation with certain adverse perinatal outcomes differs by individual socioeconomic status indicators, such as Medicaid status.

Social determinants of health

Associations between postpartum blood pressure and experiences of gendered racial microagressions during obstetric care: a multisite prospective longitudinal cohort study

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Hypertension is a leading cause of postpartum inequities in maternal morbidity and mortality, and racism in healthcare may play a role. We examined if experiences of gendered racial microagressions (GRM) during obstetric care are associated with differences in postpartum blood pressure (BP) in non-White women. We used data (n=369) from the coronaVirus Impact on Birth Equity (VIBE) in the 4th Trimester Study, which prospectively enrolled patients April-October 2022 from four hospitals in Philadelphia and New York City. Participants completed the Gendered Racial Microagressions Scale (adapted by a community panel), and reported postpartum BPs through a text-messaging platform for 90 days. We used mixed-effects linear regression with repeated measures to estimate associations between GRM and postpartum systolic and diastolic BP (SBP, DBP). We adjusted for prepregnancy BMI, race-ethnicity, education, age, parity, and prepregnancy hypertension. We tested effect modification by postpartum period (0-10/11-42/43-90 days), and by hypertensive disorders of pregnancy (HDP) (yes/no). Participants were 10.1% Asian, 37.9% non-Hispanic Black, 41.9% Hispanic, and 10.1% other race-ethnicities; 26.0% had HDP, and 37.6% experienced GRM. Effect modification was not present by postpartum period, but was present by HDP. Among participants with HDP, those who reported ≥1 vs. no GRM had mean SPB over 90 days of 127.0 vs. 124.4 mmHg (adjusted difference (aβ)=4.9, 95%Confidence Interval(CI)=1.8, 7.9)) and mean DPB of 78.4 vs. 77.1 mmHg (aβ= 3.3, 95%CI= 0.2, 6.4). Among participants without HDP, those who reported ≥1 vs. no GRM had mean SPB over 90 days of 117.2 vs. 116.1 mmHg (aβ=1.0, 95%CI= -1.3, 3.4) and mean DPB of 72.4 vs. 71.4 mmHg (aβ =0.9, 95%CI= -1.0, 2.8). GRM during obstetric care is common among non-White women and is associated with higher postpartum SBP and DBP among patients with HDP. Interventions to eliminate GRM in obstetric care may improve postpartum health inequities.

Social determinants of health

Asian-White disparities in obstetric anal sphincter injury: A systematic review and meta-analysis Giulia Muraca*, Meejin Park Susitha Wanigaratne Rohan D’Souza Roxana Geoffrion Giulia Muraca Giulia Muraca

Background and introduction: Obstetric anal sphincter injury (OASI) describes severe injury to the perineum, anal sphincter +/- rectal mucosa following birth and occurs in 4.4% to 6.0% of vaginal births in Canada. Studies from high-income countries have identified an increased risk of OASI in individuals who identify as Asian race vs those who identify as white; we conducted a systematic review and meta-analysis to evaluate this relationship.

Methods: We searched MEDLINE, OVID, Embase, Emcare and Cochrane databases from inception to 2022 for observational studies using keywords and controlled vocabulary terms related to race, ethnicity and OASI. Two reviewers followed PRISMA and MOOSE guidelines. Meta-analysis was performed using RevMan for dichotomous data using the random effects model and the odds ratio (OR) as effect measure with a 95% confidence interval (CI). Subgroup analysis was performed based on Asian subgroups. Risk of bias was assessed using The Joanna Briggs Institute Critical Appraisal tools.

Results: 19 studies conducted in seven countries between 2001-2021 fulfilled eligibility criteria. The average risk of bias score was 6/10. In total, 2,337,883 individuals were included, of which 461,056 identified as Asian and 1,916,827 as white. The rate of OASI was higher among Asian individuals, 6.43% (95% CI 6.36%-6.50%) compared with 4.24% (95% CI 4.21%-4.26%) among white individuals. The meta-analysis showed an increased prevalence of OASI in the Asian group (OR 1.94, 95% CI 1.64–2.28). In studies reporting further details on Asian subgroups (e.g., South Asian, Filipino, Chinese) vs white race/ethnicity the rate of OASI was highest among South Asians (OR 2.23, 95% CI 1.60-3.10).

Conclusion and discussion: Asian individuals, particularly those from South Asia, have higher rates of OASI than white individuals in high-income countries. Few studies have explored underlying causal mechanisms responsible for this relationship. Qualitative and quantitative research to address this knowledge gap is warranted.

Social determinants of health

Changes over time in spatial social polarization and preterm birth in the United States, 1998 to 2019 Brenda Bustos*, Tim Bruckner Abhery Das Joan Casey Alison Gemmill Ralph Catalano Brenda Bustos

Background: Cross-sectional studies find that the Index of Concentration of Extremes (ICE), which measures concentrations of privilege and deprivation in a geographic area, correlates with adverse perinatal outcomes. We, however, know of no work which evaluates this relation longitudinally. This gap in the literature limits assessment of the potentially causal relation between *changes in* regional race-specific deprivation and perinatal health.

Objective: We used a within-county longitudinal approach, among US counties from 1998 to 2019, to determine whether improvements in race-and-income-specific ICE (i.e., away from concentration of poverty among non-Hispanic Black populations) move with a reduced risk of preterm birth.

Method: We obtained incidence of preterm birth using US birth records for 2,851 counties over three distinct epochs: 1998 to 2002, 2006 to 2010, and 2014 to 2018. We anchored these epochs to US Census-derived measures of race-and-income specific ICE . We applied a county “fixed effects” approach which exploits within-county changes in ICE over time and precludes confounding across counties. We, consistent with the literature, examined preterm birth as the outcome.

Results: When using all counties in the sample, we observe no longitudinal relation between ICE and preterm. However, among urban counties (n=431 per epoch, population >1 million), a 1 standard deviation reduction in concentrated poverty among non-Hispanic Black adults corresponds with a reduction in the risk of preterm birth, both overall (coef: 1.19 percent reduction, 95% Confidence Interval [CI]: 0.20, 2.18) and among non-Hispanic Black births (coef: 1.35, 95% CI: -0.13, 2.84).

Discussion: In urban counties only, reductions over time in concentrated poverty (i.e., increases in ICE) in the last 20 years precede reductions in preterm—especially among non-Hispanic Black births.

Social determinants of health

Rurality of Census Tracts and Severe Maternal Morbidity in California (1997-2018) Mahasin Mujahid*, Rachel Berkowitz Peiyi Kan Xing Gao Elleni Hailu Christine Board Audrey Lyndon Mahasin Mujahid Suzan Carmichael Mahasin Mujahid

Introduction: While evidence of increased risk of severe maternal morbidity (SMM) for people living in rural counties exists, no studies have considered rurality at the census-tract level, a more nuanced classification of rurality. We assessed the relationship between census-tract-level rurality and SMM for birthing people in California.

Methods: This California study used vital statistics records linked with birth hospitalization records between 1997 and 2018. SMM was defined by at least one of 21 potentially fatal conditions or lifesaving procedures that people survived. Rural-Urban Commuting Area (RUCA) codes characterized tract rurality dichotomously (rural/urban; RUCA 1) and at four levels (metropolitan/micropolitan/small town/rural; RUCA 2). Covariates included sociocultural, sociodemographic, pregnancy-related, and neighborhood factors. We estimated odds ratios and 95% confidence intervals (CI) using mixed-effects logistic regression models with tract-level clustering.

Results: Out of 10,091,415 births, 1.2% had SMM. Overall, 94.3% of individuals giving birth resided in urban/metropolitan tracts and 5.7% in rural tracts (micropolitan (3.9%), small town (0.9%), rural (0.8%)). In fully adjusted RUCA 1 models, odds of SMM was 10% higher for birthing people in rural vs. urban tracts (95% CI: 1.06, 1.14). In fully adjusted RUCA 2 models, risk of SMM was 17% higher in micropolitan tracts vs. metropolitan tracts (95% CI: 1.12, 1.22); small town and rural estimates contained the null.

Conclusion: The observed relationship between tract rurality and SMM was driven by living in a micropolitan vs. metropolitan tract. Increased risk in micropolitan tracts may result from inequities of access to resources within suburban areas. Our findings using tract-level analysis and a four-level designation highlight nuance gained from more granular assessments and demonstrate the importance of considering rurality at sub-county levels to understand locality-related SMM inequities.

Substance Use

Centers for Disease Control and Prevention's Youth Substance Use Prevention Resource for Action Vanessa Mallory* Douglas Roehler Olga Costa Michelle Culbert Madhumita Govindu Zoe Thanawala Andrew Terranella Jenelle Mellerson Lara DePadilla Michael Calevski Michelle Putnam Elizabeth Hazelwood Hanna Schurman Cherie Rooks-Peck Kristin Holland Starrlett Johnson

Background:

Overdose deaths among youth aged 10-19 increased 109% from 2019 through 2021; simultaneously, cannabis-related ED visits among youth have also increased, and perceptions of risk associated with using cannabis have decreased. Additionally, racial and ethnic minority youth experience unique risk factors (e.g., microaggressions, racial discrimination) that may contribute to increased risk of substance use. The changing substance use landscape, known risks of substance use, and lack of comprehensive resources describing evidence-based prevention efforts underline the need for a resource that identifies youth substance use prevention strategies supported by the best available evidence.

Methods:

To identify these strategies a scoping review of literature was conducted to identify meta-analyses, systematic literature reviews, individual randomized controlled trials and quasi-experimental research studies describing evaluation results of youth substance use prevention policies, programs, and practices. Our review identified relevant prevention strategies and approaches for implementing those strategies were identified.

Results:

The six prevention strategies identified were family/home interventions; promoting protective factors; teaching problem-solving, resiliency, and coping skills; digital health/technology-based; policy; and mass communications. Culturally competent interventions that incorporate a health equity focus were also identified. Interventions like Familias Unidas acknowledge the importance of family in minority communities and their involvement in the intervention process.

Conclusion:

The "Youth Substance Use Prevention Resource for Action" will serve as a comprehensive guide for local- and state-level entities to address youth substance use at all levels of the socio-ecology. By identifying strategies that address inequities in substance use, this resource can be used to address each community's unique needs.

Substance Use

Mortality Risk among Infants with Prenatal Opioid Exposure by Neonatal Opioid Withdrawal Syndrome Diagnosis and Race/Ethnicity Amanda L. Elmore* Jean Paul Tanner Justin Swanson Russell S. Kirby Tanner Wright Anthony Kendle Jason L. Salemi

Introduction

Prenatal opioid exposure (POE) and Neonatal Opioid Withdrawal Syndrome (NOWS) remain prevalent and increase the risk of infant mortality. Infant mortality rates are highest among racial/ethnic minorities. Previous literature has not examined the risk of mortality among infants with POE and/or NOWS past one year of life or by race/ethnicity. We aimed to examine the association between POE and NOWS diagnoses and the risk of mortality for up to five years post-birth, overall and by race/ethnicity.

Methods

We linked birth certificates to birth and delivery administrative records in Florida from 2000-2019. Death certificate data was linked through 2021. We identified POE using a wide range of maternal opioid-related diagnoses at inpatient encounters one year before or at delivery. Infants with a diagnosis indicative of NOWS (779.5 or P96.1) were classified as NOWS+. Mother-infant dyad exposure was categorized as unexposed (POE-/NOWS-), POE+/NOWS-, or NOWS+ (regardless of POE). Differences in survival were examined using Kaplan-Meier curves and Cox proportional hazard models.

Results

Among 3,796,479 maternal-infant dyads, 9,139 (0.24%) had POE and 14,120 (0.37%) were diagnosed with NOWS. Survival probability was lowest among POE+ infants (97.4%). Compared to unexposed infants, the risk of mortality was 3.51 (95% CI: 3.09-3.98) and 1.65 (95% CI: 1.42-1.91) times higher for POE+ and NOWS+ infants, respectively. When stratified by race/ethnicity, the mortality risk for non-Hispanic White infants was similar to the total sample. However, the statistical difference in mortality risk between POE+ and NOWS+ infants was not present for non-Hispanic Black, Hispanic, and non-Hispanic Other infants.

Discussion

Infants with POE and NOWS have a higher risk of mortality through age five. POE infants have the highest risk, suggesting a NOWS diagnosis may be protective. However, this protective effect was not present for all race/ethnicities, which warrants future investigation.

Substance Use

Cannabis Use and Severity of Nausea and Vomiting of Pregnancy: Findings from the National Birth Defects Prevention Study Michelle Klawans* Vahed Maroufy Courtney Byrd-Williams Mark Canfield Kim Waller The National Birth Defects Prevention Study

Introduction: Cannabis use during pregnancy is associated with several adverse birth and childhood outcomes; women should therefore be counseled to discontinue use prior to pregnancy. However, the prevalence of cannabis use during pregnancy continues to increase, and some women report using cannabis to address symptoms of nausea and vomiting of pregnancy (NVP). Our aim was to determine if use of cannabis at pregnancy onset was associated with a decrease in the severity of NVP.

Methods: Using multinomial logistic regression, we analyzed data from 10,887 control participants in the National Birth Defects Prevention Study, a multistate case-control study of birth defects. We defined exposure to cannabis at pregnancy onset as mothers who reported use during the month before and/or the month of conception. We defined NVP as self-reported nausea or vomiting in months 2-6 of pregnancy. Severity of NVP was classified by frequency of episodes per week; mild (1-6 times), moderate (7 to 14 times), and severe (15 or more times). We assessed potential confounders using the 10% change in estimate method and two covariates (cigarette smoking and alcohol consumption) were subsequently included in our final models.

Results: In our sample, 3.9% of mothers used cannabis at pregnancy onset and 71.7% had NVP. Use of cannabis was not associated with mild or moderate NVP. However, women who used cannabis had 1.58 times the odds of reporting severe NVP (95% CI: 1.12, 2.24) compared with no report of use of cannabis.

Conclusion: Our data suggests that use of cannabis at pregnancy onset was associated with increased odds of reporting severe NVP later in pregnancy. This result was in opposition to our hypothesis and may further strengthen recommendations to cease cannabis use prior to pregnancy.

Substance Use

Marijuana use among pregnant and nonpregnant women of reproductive age, 2013–2019
Emily Kobernik* Madison Levecke Romeo Galang Brooke Hoots Douglas Roehler Jean Ko

Background: Marijuana is the most commonly used federally illicit substance among reproductive-age women in the United States. Updated information on marijuana use in this population can inform clinical guidelines and public health interventions.

Objective: To describe national prevalence and factors associated with past-year marijuana use among pregnant and nonpregnant reproductive-age women.

Study Design: This study uses 2013–2019 National Survey on Drug Use and Health data to report weighted prevalence estimates of past-year marijuana use among women 18–44 years stratified by self-reported pregnancy status (at time of survey). Bivariate analyses and general linear regression models with Poisson distribution using appropriate procedures to account for the complex survey design and multi-stage probability sampling identified factors associated with past-year marijuana use by pregnancy status.

Results: Among 878 pregnant and 23,807 nonpregnant women, respectively, past-year marijuana use was reported among 15.2% (95% confidence interval [CI]: 13.9–16.6) and 19.5% (95% CI: 19.2–19.9), of which, 7.7% (95% CI: 5.8–9.6) and 9.0% (95% CI: 8.6–9.4) met DSM-IV criteria for marijuana abuse or dependence. After adjusting for age, race and ethnicity, education, employment, annual household income and health insurance, past-year marijuana use was more likely among pregnant women reporting past-year: tobacco (adjusted prevalence ratio [aPR] 2.41, 95% CI: 1.97–2.95), alcohol (aPR 3.92, 95% CI: 2.87–5.36) or other illicit drug use (aPR 2.63, 95% CI: 2.24–3.10) and similarly, more likely among nonpregnant women reporting past-year: tobacco (aPR 2.18, 95% CI: 2.11–2.26), alcohol (aPR 4.17, 95% CI: 3.78–4.59) or other illicit drug use (aPR 2.43, 95% CI: 2.36–2.51) compared to those reporting no substance use.

Conclusions: These results may be useful for clinicians and public health initiatives addressing marijuana use alone or with other substances among reproductive-age women.

Substance Use

Changes in Polysubstance Use of Marijuana and Nicotine Products During Pregnancy: Distribution and Associations with Breastfeeding Practices Xiaozhong Wen*, Fatima Mohammed Deryn Ramsoomair Xiaozhong Wen Xiaozhong Wen

Background: Pregnancy can motivate women to quit substance use. We examined the distribution of changes in polysubstance use of marijuana and nicotine products during pregnancy and their associations with breastfeeding practices.

Methods: We conducted a secondary data analysis of 21,410 mothers enrolled in Phase 8 of the Pregnancy Risk Assessment Monitoring System in 2016-2020. Mothers reported the use of marijuana (MJ), combustible cigarettes (CC), and electronic cigarettes (EC) during the 3 months before pregnancy and the last 3 months of pregnancy. They also reported breastfeeding practices, including breastfeeding initiation, status, and duration. We used multivariable log-binomial regression to estimate risk ratio (RR) and 95% confidence interval (CI) for the associations of changes (discontinuing vs. continuing) in CC, MJ, and EC use during pregnancy with breastfeeding initiation and status at 2 months, adjusting for confounders.

Results: The complete discontinuation rate during pregnancy was 25.2% among MJ/CC users, 49.4% among MJ/EC users, and 25.9% among MJ/CC/EC users. Among MJ/CC users, those who continued both (38.9% vs 74.1%; confounder-adjusted RR, 0.84 [95% CI;0.79-0.89]), discontinued MJ only (36.8% vs 74.1%; 0.81 [95% CI, 0.73-0.89]), or discontinued both during pregnancy (55.9% vs 74.1%; 0.93 [95% CI, 0.88-0.99]) had lower breastfeeding rates at 2 months compared to non-users. Among MJ/CC/EC users, those who continued all 3 substances (29.4% vs 74.1%; 0.77 [95% CI, 0.66-0.91]) or discontinued EC use only during pregnancy (34.0% vs 74.1%; 0.83 [95% CI, 0.71-0.97]) had a lower breastfeeding rate at 2 months compared to non-users. Similar results were observed for breastfeeding initiation but to a less extent.

Conclusions: Among U.S. women, discontinuing MJ/CC/EC use was common during pregnancy. Polysubstance use of MJ/CC/EC use was associated with compromised breastfeeding practices, which could be mitigated by quitting CC use during pregnancy.

Substance Use

Prevalence of smoking before, during, and after pregnancy, United States, 2016-2020

Madison Levecke* Megan O'Connor Lauren Kipling Emilia Sigrid Pasalic Cheryl Robbins Jean Ko

Background: Smoking before, during, and after pregnancy increases the risk for many pregnancy complications and adverse maternal and infant outcomes. Public health guidance and effective interventions exist for smoking cessation during pregnancy yet smoking remains one of the most common preventable causes of infant morbidity and mortality.

Objective: To estimate the prevalence of smoking before, during, and after pregnancy in 2016-2020 and assess smoking behaviors around the time of pregnancy.

Study Design: This study uses Pregnancy Risk Assessment Monitoring System (PRAMS) survey data to report weighted prevalence estimates of self-reported smoking status before, during, and after pregnancy among women with a live birth in 2016–2020 in 23 PRAMS jurisdictions. A trend analysis was conducted to compare the prevalence of smoking before, during, and after pregnancy over the study years. Patterns of smoking cessation during pregnancy and smoking relapse in the postpartum period among women who reported any smoking was also examined.

Results: Overall in 2016–2020, 15.7% of women smoked before, during, or after pregnancy. In those 5 years, smoking 3 months pre-pregnancy decreased from 17.5% to 13.1%; smoking in the final 3 months of pregnancy decreased from 7.8% to 6.0%; and smoking 2-6 months postpartum decreased from 11.3% to 8.1% (linear tests for trend $P<0.001$). Among women who reported any smoking in the study period before, during, or after pregnancy, 55% quit smoking from pre-pregnancy to pregnancy; among the women who quit smoking during pregnancy, 34% resumed smoking postpartum.

Conclusions: Smoking prevalence estimates decreased before, during, and after pregnancy in 2016–2020. However continued comprehensive tobacco cessation efforts for pregnant and postpartum women are critical, including integration of clinical guidelines for tobacco use screening and treatment into maternity care protocols.

Violence or abuse victimization

Population-level patterns of obstetrical and gynecological health care utilization in the 12-months following an emergency department encounter for sexual assault in a universal health care system Katherine Muldoon* Katherine Muldoon Hailey Mitchell Robert Talarico Kari Sampsel Mark Walker Shi-Wu Wen

Background: Little is known about obstetrical and gynecological (OBGYN) health care use among survivors of sexual assault. The objective of this study was to document OBGYN health care utilization patterns in the 12-mo following an emergency department (ED) encounter for sexual assault.

Methods: This retrospective matched cohort study uses health administrative data from 2013-2018 to identify survivors of sex assault who presented for care at 197 EDs in Ontario, Canada. Cases were identified through the National Ambulatory Care Reporting System, Discharge Abstract Database, and Registered Persons Database. Follow-up encounters were identified through the Ontario Health Insurance Plan, a single-payer universal health insurance plan, and OBGYN specialists were identified through specialty designation codes. Data are presented in proportions and median (med) and interquartile ranges (IQR) for continuous measures. Sexual assault cases were compared to controls matched by age and ED admission date within 7 days.

Results: Between 2013-2018, there were 15 365 ED encounters for sex assault among female individuals. In the 12-mo post-ED admission, OBGYNs provided care to 2330 (15.2%) survivors of sexual assault within med 137 (IQR:50-242) days, and 8882 (19.4%) matched-controls within 84 (IQR:22-202) days. Comparing cases to controls, the most common codes applied by OBGYNs were disorders of menstruation (17.8% vs 18.4%), normal uncomplicated pregnancy (17.4% vs 27.6%), family planning/contraception/abortion (17.0% vs 14.9%), and cervical erosion or dysplasia (13.9% vs 8.8%).

Conclusion: This study found over 15% of survivors saw an OBGYN in the 12-months following an ED admission for sexual assault, consulting for both pregnancy and non-pregnancy related conditions. The most common consultations were for menstruation, healthy pregnancy, advice on family planning, and cervical erosion or dysplasia.

Women’s health

A prospective study of hypertensive disorders in pregnancy and subjective cognitive decline
Alexandra Purdue-Smithe* Janet W. Rich-Edwards Deborah L. Blacker Kathryn M. Rexrode

Subjective cognitive decline (SCD), defined as self-reported deterioration in cognitive function, is increasingly recognized as an early risk state for dementia. Emerging research suggests that hypertensive disorders in pregnancy (HDP) may be associated with greater risk of dementia in women during late life, but whether HDP are associated with SCD during midlife is unknown. We prospectively examined associations of self-reported HDP with SCD among 49,038 parous participants of the Nurses’ Health Study II with data on lifetime pregnancy history and SCD, and no history of pre-pregnancy cardiovascular disease, type II diabetes, or chronic hypertension. SCD was assessed in 2017 (at median age 63 years) via participants’ responses to 7 questions, which were summed to a total SCD score (0-7) and then categorized as good (0; 57%), moderate (1-2; 31%), and poor (≥3; 12%). Multinomial regression models were used to estimate OR (95% CI) for moderate and poor compared to good SCD score. After adjusting for age, income, and pre-pregnancy BMI and other health and behavioral factors, HDP in a first pregnancy (9%) was associated with greater odds of a poor SCD score (OR=1.15; 95% CI=1.05-1.26), but not a moderate SCD score (OR=1.03; 95% CI=0.96-1.11), compared to those with normotensive first pregnancies. Preeclampsia was slightly more strongly associated with a poor SCD score (adjusted OR=1.16; 95% CI=1.04-1.30) than gestational hypertension (adjusted OR=1.12; 95% CI=0.96-1.32). In stratified analyses, HDP in a first pregnancy was more strongly associated with a poor SCD score in older than in younger women (SCD assessment at >63 years OR=1.23; 95% CI=1.05-1.43 vs. ≤63 years OR=1.10; 95% CI=0.98-1.24). Our results suggest that HDP is a risk factor for SCD in midlife, which may reflect early neuropathological changes related to dementia. Women with a history of HDP may benefit from enhanced monitoring for cognitive change during midlife and dementia risk factor management.

Women’s health

Gestational Diabetes and Subsequent Metabolic Dysfunction: An NHANES Analysis (2011-2018) Sandie Ha*, Andrew Williams Kelly Schultz Sandie Ha Sandie Ha

Background. Gestational diabetes (GDM) complicates approximately 10% of pregnancies, with the highest rates among Asian women. Data suggest GDM is associated with an increased risk for future chronic health conditions, yet data specific to Asian women are sparse. We explored the association between prior GDM and metabolic dysfunction with data that allows for estimates specific to Asian women.

Methods: Data were drawn from National Health and Nutrition Examination Survey for 7,227 women with a prior pregnancy. GDM(yes/no) was defined using the question “During pregnancy, were you ever told by a doctor or other health professional that you had diabetes, sugar diabetes or gestational diabetes?” Metabolic dysfunction(yes/no) was based on 4 biomarkers: systolic blood pressure(≥130mmHg), waist circumference(≥88cm), HDL cholesterol(<50mg/dL), and HbA1c(≥6.5%). Logistic regression estimated odds ratios(OR) and 95% confidence intervals(CI) for the association between prior GDM and metabolic outcomes, overall and by race. Models were adjusted for sampling weights, demographic and behavioral factors.

Results. Overall, women with prior GDM had 44% greater odds of increased waist circumference(OR:1.44; 95%CI:1.06,1.97), yet prior GDM was not associated with blood pressure, HbA1c, or HDL cholesterol. In race-specific analyses, prior GDM was associated with increased risk of elevated HbA1c among Asian(OR:3.18; 95% CI: 1.08, 9.36), Mexican American(OR:2.62; 95%CI:1.18,5.80) and Black(OR:2.54; 95%CI:1.33,4.86) women, yet not among White(OR:1.04; 95%CI:0.45,2.41) or Other race/ethnicity(OR:2.21; 95%CI:0.73,6.70) women. Prior GDM was associated with elevated SBP among Mexican American women, and low HDL among Black women.

Discussion. Results suggest that prior GDM is a stronger predictor of elevated HbA1c among Asian women than other women. More research is needed to understand racial/ethnic differences in the association between prior GDM and metabolic dysfunction.

Women’s health

Higher maternal plasma testosterone levels are associated with more persistent nausea in pregnancy Brad Ryva* Susan Schantz Rita Strakovsky

Background: Nausea in pregnancy is common but has unclear etiology, especially if it persists later into pregnancy. To examine possible hormonal mechanisms, we evaluated overall and fetal sex-specific associations of maternal sex-steroid hormones with nausea duration.

Methods: Central Illinois pregnant women reported nausea since conception or last study visit (yes/no) at median 13, 17, 23, 28, 34 weeks gestation and at delivery. In women who experienced nausea (n=223), we categorized nausea experience as either nausea ending by or persisting past 17 weeks gestation (typical nausea or persistent nausea, respectively). We quantified progesterone, estradiol, and testosterone levels in fasting plasma samples collected at median 17 weeks gestation. Using covariate-adjusted binary logistic regression models, we evaluated associations of hormones with the odds of experiencing persistent than typical nausea and explored differences by fetal sex with an interaction term.

Results: Most women were ≥30 years old (59%), non-Hispanic White (79%), and college educated (82%). Of women who experienced nausea, 36% reported persistent nausea. Progesterone and estradiol were not associated with nausea duration overall or by fetal sex. However, each 10% increase in testosterone was associated with 5% (Odds Ratio (OR): 1.05; 95% Confidence Interval (CI): 0.99, 1.11) higher odds of experiencing persistent than typical nausea. These associations were stronger in women carrying males, where each 10% increase in testosterone was associated with 8% (OR: 1.08; 95% CI: 1.00, 1.17) higher odds of experiencing persistent than typical nausea, and no association was observed in women carrying females (OR: 1.04; 95% CI: 0.96, 1.10).

Conclusion: Higher testosterone was associated with elevated odds of persistent nausea, especially in women carrying males. Future studies should validate these results in other populations and consider implications of our findings for maternal and fetal health.

Women’s health

Pregnancy history at age 40 as a marker of cardiovascular risk Liv Grimstvedt Kvalvik* Rolv Skjærven Gerhard Sulo Aditi Singh Quaker E Harmon Allen J Wilcox

Background: Individual pregnancy complications (such as preeclampsia, small birth weight and preterm delivery) have been linked to increased maternal risk of cardiovascular disease. We assessed how well a woman’s total pregnancy history at age 40 predicts her risk of dying from atherosclerotic cardiovascular disease (ASCVD).

Methods: In this population-based, prospective study we used data from The Medical Birth Registry of Norway, the National Cause of Death Registry, the National Education Database and the Population Registry, Statistics Norway in the period 1967-2020. We identified 854 442 women born after 1944 or registered with a pregnancy in 1967 or later, and surviving to age 40. Our main outcome was the hazard ratio of ASCVD mortality up to age 69 for 40-year-old women, as predicted by exposure categories of combined parity (0, 1, 2 3, or 4 recorded pregnancies) and number of complicated pregnancies (preterm delivery <35 gestational weeks, preeclampsia, placental abruption, perinatal death (stillbirth or death within first 7 days) and term or near-term birth weight <2700grams). Women with three pregnancies and no complications had lowest ASCVD risk and served as the reference group. Estimates were adjusted for women’s birth year.

Results: Among women reaching age 40, risk of ASCVD before age 69 increased with greater number of complicated pregnancies in a strong dose-response fashion, reaching 24-fold risk (95% confidence interval 11-54) for women with four complicated pregnancies. Based on pregnancy history alone, 19% of women at age 40 (including nulliparous women) had ASCVD mortality risk in the range of 2.5 to 5-fold.

Conclusions: Pregnancy history at age 40 is highly predictive of ASCVD mortality over the next 30 years. Pregnancy history at age 40 could be useful as a routine clinical screen to identify at-risk women young enough to benefit from intervention, and perhaps even before clinical markers of CVD risk have fully emerged.

Women’s health

Body mass index and uterine fibroid development: a prospective study Quaker Harmon* Stacy Patchel Sheri Denslow Ganesa Wegienka Donna Baird

Fibroids are hormonally dependent benign tumors of the uterus with significant morbidity. Increased adiposity, as measured by body mass index (BMI), alters hormone concentrations, and has inconsistent associations with fibroid prevalence. We assessed the association between repeated measures of BMI and fibroid incidence and growth in the Study of Environment, Lifestyle & Fibroids (SELF). SELF followed 1,610 women self-identified as “African American” or “Black”, ages 23-35 from the Detroit, Michigan area with ultrasound every 20 months for 4 visits (5 years). Weight and height were measured at enrollment and weight was measured at every follow-up visit. Baseline BMIs ≥30 kg/m^2 were common (59%). Participants with incident fibroids (n=294) were identified among those who were fibroid free at the enrollment ultrasound (n=1230). Fibroid incidence was modeled using Cox models. Fibroid growth, scaled to 18-months, was estimated for individual fibroids as the difference in log-volume between visits and was modeled using linear mixed models accounting for within-woman and within-fibroid correlations. All models used time-varying BMI, and adjusted for time-varying demographic, reproductive, and contraceptive factors. Compared to BMI<25 kg/m^2 those with BMI 30-<35 kg/m^2 had increased fibroid incidence (adjusted hazard ratio (aHR) 1.37, (95% CI 0.96, 1.94)) while those with BMI≥40 kg/m^2 had reduced incidence (aHR 0.61, (95% CI 0.41, 0.90)). A non-linear association was corroborated using continuous BMI with a restricted cubic spline (p-value=0.0007, indicating nonlinearity) (Figure 1). Fibroid growth had inconsistent and mostly small magnitude associations with BMI. BMI is only a crude measure for studying the health effects of adiposity. More detailed measures of hormonal, metabolic, and DNA-damaging sequelae of adiposity are needed to better understand the non-linear association we observe.

Women’s health

Obstetrics risk factors among infants who received therapeutic hypothermia (TH) in Ireland: a five-year cohort, 2016-2020 Indra San Lazaro Campillo* Julie McGinley Paul Corcoran Aenne Helps Sarah Meaney Peter McKenna Peter Filan Richard Greene John Murphy

Background. The risk of long-term morbidity or mortality for infants requiring therapeutic hypothermia (TH) as treatment for neonatal encephalopathy is significant. A rate reduction may be achieved by identifying relevant antenatal and intrapartum risk factors.

Objective. To assess the obstetrics factors that are associated with infants who received TH in the Republic of Ireland (ROI) for 5 years (2016-2020).

Methods. Retrospective reviews of inpatient medical records have been used as a gold standard approach when assessing multiple outcomes and rates of adverse events.

Results. There were 301,940 infants born in the ROI between 2016 and 2020, with 357 having received therapeutic hypothermia (TH). The risk of TH among multiparous women was 0.80 (95% CI=0.63-0.99) per 1,000 births, compared to the risk of 1.78 (95% CI=1.55-2.04) per 1,000 births for nulliparous women. The risk of TH was 2.78 (95% CI=1.94-4.0, p-value<0.001) times higher among nulliparous women. After adjusting for maternal age, the risk ratio associated with nulliparity was almost identical to the crude risk ratio at 2.36 (95% CI=1.90-2.93). This association was not seen after adjusting for parity. Infants with a birthweight in the 50-89th centile range had the lowest risk of TH, at 0.9 per 1,000 births. The risk was 30% (RR=1.30, 95% CI=1.02-1.67) and 54% (RR=1.54, 95%CI =1.08-2.2) higher among infants in the 10-49th and >90th birthweight centile ranges, respectively, but the risk was doubled for infants with a birthweight under the 10th centile (RR=2.81, 95%CI = 1.79-4.41). The risk of an infant receiving TH was 18.4 (95%CI =13.3-24.9) per 1,000 women if the delivery was affected by shoulder dystocia compared to 1.1 (95% CI=1.0-1.2) per 1,000 women if there was no reported shoulder dystocia.

Conclusion. Nulliparity, estimated fetal weight <10th centile and shoulder dystocia are risk factors for TH which require particular attention in their clinical management.

Women’s health

Prevalence and factors associated with excessive weight during pregnancy in South Carolina:2015-2021 Sarah Simpson* Sarah Simpson Angela Malek Chun-Che Wen Brian Neelon Dulaney Wilson Julios Mateus John Pearce Kalyan Chundru Jeffery E. Korte Hermes Florez Kelly J. Hunt

Background: The objective of the study was to assess the prevalence and associated factors of excessive weight gain during pregnancy among a population-based cohort in South Carolina.

Methods: This study included 301,553 live full term singleton births from 173,722 Non-Hispanic White (NHW), 91,036 Non-Hispanic Black (NHB), 22,387 Hispanic and 14,408 women of other race/ethnic groups from 2015 to 2021. Pre-pregnancy BMI based on CDC classification was collected via birth certificate. Gestational weight gain (GWG) adequacy was defined as inadequate, adequate and excessive based on IOM 2009 recommendations for weight gain during pregnancy based on pre-pregnancy BMI. GWG adequacy was dichotomized as excessive vs. inadequate and adequate.

Results: 24.9% gained inadequate weight, 25.5% gained adequate weight and 49.7% gained excessive weight during pregnancy. The prevalence of excessive weight gain among underweight, normal, overweight, and obese women was 29.5%, 39.5%, 60.1% and 55.6 %, respectively. Trends in excessive weight gain remained stable over time across race-ethnic groups. Being overweight (RR=1.57, 95% CI: 1.55-1.58) or obese (RR=1.47, 95% CI: 1.46-1.49) prior to pregnancy was associated with excessive weight gain compared to normal weight, while less likely among underweight (RR=0.75, 95% CI: 0.72-0.77). High school education, some college and college education or higher was associated with excessive weight gain. Smoking and parity were also associated with excessive weight gain. NHBs, Hispanics, and other racial/ethnic minorities were less likely to gain excessive weight than NHWs. Age, Medicaid, WIC and residence were not associated with excessive weight gain.

Conclusions: The prevalence of excessive weight gain during pregnancy remains high. Pre-pregnancy overweight and obesity was associated with excessive weight gain. Additionally, race/ethnicity, education, parity, and smoking are significant predictors of excessive weight gain during pregnancy.

Factors associated with excessive weight gain during pregnancy in South Carolina.

Characteristic	**Odd Ratios (95% CIs)**
Time	0.99 (0.99-1.00)
Age (10-year unit increase)	0.99 (0.98-0.99)
Race/Ethnicity	
Non-Hispanic White	1.00
Non-Hispanic Black	0.85 (0.84-0.86)
Hispanic	0.79 (0.78-0.81)
Other	0.81 (0.79-0.83)
BMI Classification	
Normal	1.00
Underweight	0.75 (0.72-0.77)

Overweight	1.57 (1.55-1.58)
Obese	1.47 (1.46-1.49)
Education	
Less than high school	1.00
High school graduate	1.09 (1.07-1.10)
Some College	1.15 (1.13-1.16)
>= College Graduate	1.15 (1.14-1.17)
Medicaid Status (yes vs. no)	0.98 (0.97-0.99)
Women, Infants and Children (WIC) (yes vs. no)	1.02 (1.01-1.03)
Residence (rural vs. urban)	0.99 (0.98-1.00)
Previous Live Birth/Still Born (no vs. yes)	1.15 (1.14-1.16)
Smoking (yes vs. no)	1.10 (1.08-1.11)

Women’s health

Multiple Job Holding, Job Change, and Relationships with Gestational Diabetes and Pregnancy-Related Hypertension — United States, October 1997–December 2011 Amel Omari* Miriam Siegel Carissa Rocheleau Kaori Fujishiro Kristen Van Buren Dallas Shi A.J. Agopian Suzanne Gilboa Paul Romitti National Birth Defects Prevention Study

Background: Gestational diabetes and pregnancy-related hypertension are serious maternal health conditions which could be influenced by social determinants of health, including occupation. Many health surveys ask only about participants’ main job, limiting the study of detailed working patterns in relation to maternal morbidities. We used National Birth Defects Prevention Study (NBDPS) data to investigate associations between multiple job holding and job change shortly before and throughout pregnancy and gestational diabetes and pregnancy-related hypertension.

Methods: We analyzed three maternal self-reported working patterns (multiple job holders, job changers, single job holders) during the three months before and throughout pregnancy of 8,140 NBDPS participants who delivered a live-born child without a birth defect. “Multiple job holders” worked >1 job simultaneously during at least part of this time, “job changers” worked >1 job with no overlap in timing, and “single job holders” (referent) worked 1 job. We used multivariable logistic regression to estimate associations between working pattern and self-reported gestational diabetes and pregnancy-related hypertension, adjusting for maternal age and education. We explored effect modification by household income, peak weekly working hours, and maternal race/ethnicity.

Results: Multiple job holders had higher odds of gestational diabetes (adjusted odds ratio [aOR]: 1.5; 95% CI: 1.1–2.1) and pregnancy-related hypertension (aOR: 1.5; 95% CI: 1.0–2.2) compared with single job holders. Multiple job holders with a household income of <$30,000 per year, 32–44 peak weekly working hours, and Hispanic and/or non-White race/ethnicity had higher odds of gestational diabetes compared with single job holders in respective categories. We observed no associations between job change and outcomes.

Conclusions: Detailed occupational information is important for exploring relationships between occupation and maternal health. Non-standard work arrangements and instability related to working multiple jobs could drive observed associations with maternal morbidities. Further research is warranted to replicate findings.

Women's health

Long-term Impact of In Utero Exposure to Air Pollutants on Risk of Obesity and Chronic Hypertension in Adult Women: Findings from a Multigenerational Cohort Michelle Pearl* Kimberly Berger Joan Casey Alan Hubbard Kara Rudolph Andrew Rosenberg Dorothy Maffei Marty Kharrazi

Background: Fetal exposure to air pollutants may have lasting health effects. We investigated the long-term impact of women's *in utero* air pollution exposure on their health during reproductive years.

Methods: The study included 112,726 white and 48,115 Black women who delivered a live birth in California from 2007-2011 (Generation 2 [G2]) and were linked to their own California birth record from 1982 onward (Generation 1 [G1]). Annual census tract particulate matter (PM2.5) and nitrogen dioxide (NO2) estimates were linked to G1 and G2 births, representing women's *in utero* and adult exposure, respectively. Pre-pregnancy obesity (BMI≥30; POB) and chronic hypertension (CH) were obtained from G2 live birth and delivery hospital discharge records. We used targeted maximum likelihood estimation (TMLE) to estimate adjusted risk difference (RD) for total effects of *in utero (IU)* exposure quartiles (vs. lowest quartile) on POB and CH, and longitudinal TMLE to estimate controlled direct effects holding adult exposure quartile constant.

Results: Prevalence of POB and CH was 24.3% and 1.5% among Black women, and 19.4% and 1.0% among white women. POB risk among Black women increased with Q4 of *IU* PM2.5 (RD=3.1, 95% confidence interval [0.8, 5.4]) and NO_2 (1.8 [0.1, 3.5]); and with Q2 of *IU* PM2.5 among white women (1.5 [0.9, 2.1]), but decreased with *IU* NO_2 among white women (Q2: -0.9 [-1.5, -0.3]; Q3:-2.2 [-2.9, -1.6]). CH risk increased with Q2 of *IU* PM2.5 among both Black (0.2 [0.1, 0.4]) and white (0.4 [0.0, 0.9]) women. but decreased with Q2 of *IU* NO_2 (-0.54 [-0.96, -0.12]) among Black women. Direct effect RDs for *IU* NO_2 and CH varied greatly depending on adult exposure, while others generally corroborated total effect RDs. Most RDs did not follow a dose-response.

Conclusion: There is some evidence that *in utero* exposure to PM2.5 increases risk for pre-pregnancy obesity and chronic hypertension regardless of adult PM2.5 exposure, while relations with NO_2 may be more complex.

Big Data/Machine Learning/AI

A simulation study of bias in the mediated association between maternal obesity and caesarean section delivery Jennifer Dunne* Gizachew Tessema Amanuel Gebremedhin Gavin Pereira

Mediation analysis is conducted under the assumption of no unmeasured confounding. However, bias from unmeasured confounding has the potential to distort mediated exposure-outcome associations. The aim of this simulation study was to determine the total effect of maternal obesity on caesarean section delivery when mediated by the pregnancy complication of pre-eclampsia. We also estimated the magnitude and direction of bias resulting from unmeasured confounding on this mediated association. We simulated data from an observed pregnancy cohort in Western Australia and a range of values for the prevalence of maternal obesity, pre-eclampsia, caesarean section delivery and an unmeasured confounder U. Additionally, we simulated the odds ratio for the selection effects (maternal obesity → pre-eclampsia, pre-eclampsia → caesarean section delivery, U → pre-eclampsia, U → caesarean section delivery) based on realistic assumptions. Overall, we found that conditioning on the mediator of pre-eclampsia had a negligible impact on the association between maternal obesity and caesarean section delivery. When we compared the total effect, including the influence of the mediator and unmeasured confounder, to the direct effect drawn from the observed cohort we found a negligible downward bias of 1%. By extrapolation, we conclude that results of studies that intended to estimate the total effect of maternal obesity on caesarean section delivery are not biased by over-adjustment for pre-eclampsia.

Birth defects

Periconceptional intakes of micronutrients involved in folate metabolism may further reduce risk of neural tube defects in offspring: A United States population-based case-control study of women meeting the folic acid recommendations Julie Petersen* Rashida Smith-Webb Gary Shaw Suzan Carmichael Tania Desrosiers Eirini Nestoridi Anne Marie Darling Samantha Parker Maria Politis Mahsa Yazdy Martha Werler

Background. Neural tube defects (NTDs) occur in offspring of some women who consume folic acid for prevention. Other micronutrients involved in methylation or folate metabolism may further protect against NTDs. We investigated whether intakes of B6, B12, choline, betaine, methionine, thiamine, riboflavin, and zinc, alone or in combination, were associated with NTD risk in offspring of women meeting the folic acid recommendations.

Methods. Data were from the National Birth Defects Prevention Study (US population-based, case-control), restricted to 1999-2011 deliveries with daily maternal periconceptional folic acid supplementation or estimated dietary folate equivalents ≥400 µg. Cases were NTD-affected livebirths, stillbirths, or terminations (n=1227). Controls were livebirths without a major birth defect (n=7095). Each micronutrient was categorized as higher or lower intake based on food frequency questionnaire data and self-reported supplement use. We estimated NTD associations for higher versus lower intake of each micronutrient with ORs and 95% CIs, adjusted for age, race/ethnicity, education, and study center. In secondary analysis, we stratified by offspring sex.

Results. NTD associations were weak to modest for each micronutrient in isolation but were considerably stronger with concurrent higher intakes of multiple micronutrients. For instance, NTD odds were halved with higher intakes of ≥4 versus ≤1 of the micronutrients (OR 0.53, 95% CI 0.33, 0.86). The strongest association was observed with concurrent higher intakes of B6, B12, choline, betaine, and methionine (OR 0.26, 95% CI 0.09, 0.77) compared with higher intake of ≤1 micronutrient. Associations comparing higher intakes of ≥4 versus ≤1 of the micronutrients were slightly stronger among females.

Conclusion. Our findings support that NTD prevention, in the context of folic acid fortification, can be augmented through intakes of methyl donors and other micronutrients involved in folate metabolism.

Birth defects

A Deterministic Selection Bias Analysis of the Etiologic Association Between Periconceptional Folic Acid Supplementation and Spina Bifida in Offspring Due to Differential Participation in the National Birth Defects Prevention Study Julie Petersen* Andrew Olshan Jacob Kahrs Mollie Wood Nedghie Adrien Samantha Parker Gary Shaw Amy Herring Meredith Howley Paul Romitti Maria Politis

Background: A previous National Birth Defects Prevention Study (NBDPS) investigation reported an OR of 1.0 (95% CI 0.7, 1.2) for the association between spina bifida and periconceptional folic acid supplementation. This observation was unexpected given the wealth of research, including randomized trials, finding that folic acid supplementation can reduce spina bifida risk by 40–60%.

Methods: We conducted a deterministic multidimensional bias analysis in the NBDPS to investigate if there are plausible scenarios of differential participation that could explain the observed null association. We assumed the true OR was at least 0.7 given prior studies and based estimates for the prevalence of folic acid supplementation in the underlying source population from US-based reports of periconceptional folic acid use (20–40%). We also searched the literature and employed causal diagrams to consider if there are theoretical factors that could drive the differences in participation by case-control and exposure status and result in structural selection bias via collider stratification.

Results: If folic acid supplementation was overrepresented, relative to the US source population, in both the participating cases and controls, but more so among the cases, selection bias would be substantial enough to shift the OR from 0.7 (hypothesized truth) to 1.0 (observed). This scenario seemed plausible given that the literature supported common factors related to participation and folic acid use. Specifically, both participation and folic acid use tend to be higher among individuals who identify as Non-Hispanic White, planned the pregnancy, and/or have higher educational attainment.

Comment: Our investigation supported that differential participation is a plausible explanation for why a null finding between folic acid and spina bifida was observed in the NBDPS. However, other potential explanations, such as recall bias, are possible and warrant further investigation.

Birth defects

Recurrence of congenital heart defects in siblings Wen-Qiang He* Samantha Lain Antonia Shand David Winlaw Gary Sholler Gillian Blue Natasha Nassar

Background: The recurrence risk of congenital heart disease (CHD) increases with a known family history of this condition, but few studies have investigated the risk of CHD recurrence among siblings. This study aims to examine the recurrence risk of CHD in siblings within a population-based cohort and combine results in a systematic review and meta-analysis.

Method: All liveborn infants from 2001 July 1st to 2019 December 31st in New South Wales, Australia with a recorded diagnosis of CHD (ICD10-AM codes: Q20-Q26.9) up to one year of age were identified using linked birth and hospital admission records. Sibling pairs were identified using the unique project number of each mother. The recurrence risk ratio (RR) was calculated using log-binomial models with CHD in the older sibling as exposure and CHD in the younger sibling as outcome, adjusting for year of birth, maternal age, and maternal diabetes. A systematic review was then conducted using MEDLINE and Web of Science databases with relevant data extracted and pooled with findings from this study using random-effects model.

Result: A total of 734,237 sibling pairs (including 15,090 twins) corresponding to 1,246,046 births were included. Among sibling pairs, the prevalence of CHD in the younger sibling was 219.9 per 10,000 for those with CHD in the older sibling compared to 83.6 per 10,000 where the older sibling did not have CHD (adjusted RR 2.63, 95%CI 2.19-3.13). Recurrence RR of severe CHD was 4.19 (95%CI, 2.37-7.41). For twins, the recurrence RR of any CHD was 32.85 (95%CI 21.49, 50.21). Four studies including this study were included in the meta-analysis. The recurrence RR in siblings of any CHD was 2.92 (95%CI, 1.84-4.65) and severe CHD was 3.95 (95%CI, 0.99-15.66) with I^2= 0%.

Conclusion: The overall risk of having a sibling with CHD increased almost 3-fold, and 4-fold for severe CHD, when the older sibling was affected. Findings provide important information for pregnancy counseling and aids risk prediction.

Birth defects

Maternal Exposure to Ambient Air Pollution During Pregnancy and Prevalence of Congenital Limb Defects: a Focus on Racial Disparities Olufunmilayo Arogbokun Knutson* Thomas Luben Jeanette Stingone Lawrence Engel Chantel Martin Andrew Olshan

Background: Birth defects account for 20% of all infant deaths; yet, the causes of birth defects remain widely unknown. Among suspected causes are environmental exposures, such as air pollution. Racial disparities in air pollution exposure and congenital limb defect prevalence have been observed. However, racial differences in the association between air pollution exposure during pregnancy and limb defect prevalence have not been investigated. Methods: To investigate the relationship between air pollution and congenital limb defects, we carried out a cohort study using North Carolina birth certificate data (from 2003-2015) that were linked to the state's birth defect registry. Particulate matter ≤2.5 microns ($PM_{2.5}$) and ozone exposure during weeks 3-9 of pregnancy were assigned to each pregnancy using exposure estimates from the Environmental Protection Agency's Downscaler Model. A 7-week average of maternal $PM_{2.5}$ and ozone exposure at the geocoded address at birth were assigned. We created single- and co-pollutant log-binomial models for the full study population and also for racially-stratified analyses that examined non-Hispanic Black and non-Hispanic White pregnancies. Results: We observed positive associations between both pollutants and limb defects. In adjusted, co-pollutant, categorical $PM_{2.5}$ models, we observed a positive, increasing monotonic trend. The largest prevalence ratio (PR) was seen in the highest exposure concentration of $PM_{2.5}$ (>12 µg/m^3) during pregnancy (aPR (95% CI): 1.16 (0.94, 1.44)). No clear differences were observed in racially-stratified models of $PM_{2.5}$ and limb defects, though racial differences were seen for ozone. Conclusion: Ambient $PM_{2.5}$ and ozone exposure early in pregnancy may be associated with increased prevalence of congenital limb defects. Also, exposure to ozone during pregnancy may be impacting non-Hispanic Black and non-Hispanic White pregnancies differently. More epidemiologic studies are necessary to confirm findings.

Birth defects

Does Selection Bias Explain Reduced Odds of Hypospadias with Exposure to Tobacco Smoke During Pregnancy? Jacob Kahrs* Mollie E. Wood Nedghie Adrien Julie M. Petersen Elizabeth C. Ailes Amy Herring Meredith Howley Samantha E. Parker Maria D. Politis Paul A. Romitti Gary M. Shaw Andrew F. Olshan The National Birth Defects Prevention Study

A meta-analysis of 15 case control studies of maternal smoking and offspring hypospadias found a pooled odds ratio (OR) of 0.9 (95% confidence interval [CI] 0.85, 0.95). We evaluated whether selection bias due to differential participation may explain this finding using previously published results from the National Birth Defects Prevention Study (NBDPS), a large population-based case control study in the United States (US).

We conducted deterministic bias analyses with a range of bias parameters reflecting selection fractions representing differential participation that varied by both case/control status and smoking. We then used the resulting fractions to simulate source populations from which cases and controls were drawn and estimated selection bias adjusted ORs for the association between smoking and hypospadias. Simulated source population estimates of smoking prevalence were drawn from the Pregnancy Risk Assessment Monitoring System.

The original published NBDPS OR for active smoking in pregnancy was 0.8 (95% CI 0.7, 1.0). Selection bias adjusted ORs remained below 1.0 if the selection fraction of smoking-exposed cases was lower than exposed controls and/or the selection fraction of smoking-unexposed cases was greater than the unexposed controls. Selection bias adjusted ORs moved toward or across the null in scenarios where smoking-exposed case mothers were less likely to participate than unexposed case mothers. When simulated participation was similar to observed participation for NBDPS (65% of hypospadias cases, 64% of controls) and smoking prevalence was similar to the US birthing population (e.g., 21%) but was higher in cases than controls (e.g., 25% vs 20%), the selection bias adjusted OR could be as high as 1.33.

Realistic differences in participation for smoking-exposed versus unexposed cases and controls may explain previously observed reduced odds of hypospadias associated with maternal smoking.

Birth defects

Sibling Birth Defects Recurrence in Florida, 1998 to 2019 Jean Paul Tanner* Jason Salemi

Background: Birth defects are the leading cause of infant death and can adversely affect the quality of a child's, and his or her family's life. With the average American family consisting of more than one child, it is important to quantify the sibling birth defect recurrence risk to create evidence for preventive care and health services for families. The purpose of this study is to investigate the recurrence risk of birth defects in siblings in Florida from 1998 to 2019.

Methods: The Florida Birth Defects Registry was used to identify infants born between 1998-2019 with select birth defects. Sibling pairs were identified from maternally-linked infant records. Chi-squared tests were used to compare socio-demographic and perinatal characteristics of infants, by the presence of a birth defect. Adjusted multivariable logistic regression models were used to investigate the recurrence odds ratio (ROR) of birth defects in siblings by similar and dissimilar anatomical groupings.

Results: We observed a 200% (99% CI: 1.9-2.1) increased odds of birth defect recurrence in sibling pairs, with the highest recurrence risk present if the older sibling had an orofacial (ROR: 17.6, 99% CI: 13.0-23.8) or a central nervous system defect (ROR:7.1, 99% CI: 2.9-17.2). Younger siblings had a statistically significantly increased odds of an anatomically dissimilar birth defect from the older sibling when their older siblings had a central nervous system (ROR:1.7, 99% CI: 1.3-2.4), gastrointestinal (ROR:1.5, 99% CI: 1.1-2.0), or orofacial (ROR:1.4, 99% CI: 1.0-1.8) defect.

Conclusions: Infants whose older siblings have a birth defect are at increased likelihood of being born with a birth defect. Although the magnitude of this increased likelihood varied by the type of birth defect in the older sibling and whether the younger sibling were to have an anatomically similar or dissimilar birth defect, our study findings support a direct association of birth defect recurrence.

Birth defects

Using data linkage of novel biobank data with administrative health data to inform genomic analysis for precision medicine treatment of congenital heart disease Samantha Lain* Gillian Blue Bridget O'Malley David Winlaw Gary Sholler Sally Dunwoodie Natasha Nassar

Aim: We aimed to assess utility of data linkage of clinical biobank and administrative health data to identify and validate patient outcomes following surgical treatment for congenital heart disease (CHD), to inform a future study of genetic variants.
Methods: Children born from 2002-2014 undergoing surgery for CHD in New South Wales, Australia were identified from the Kids Heart Biobank, and their records linked with hospital admission and deaths data collections. Children were grouped by CHD lesion (septal defects, complex CHD, malformation of outflow tract) and age at first cardiac surgery (neonatal, infant, childhood). Children in each lesion/age-at-surgery group were classified into 'favourable' and 'non-favourable' cardiovascular outcome groups based on variables in linked dataset including: death or morbidity (e.g cardiac arrest, stroke), time in intensive care (ICU), length of stay (LOS), time on mechanical ventilation. An independent, blinded medical record audit was conducted to validate outcomes of 200 randomly chosen children from two outcome groups.
Results: There were 1872 children in the biobank dataset that linked to hospital or death data. Outcomes for children in each lesion/age-group were identified and then ranked. Those in lowest quartile in each group (n=476) were defined as having a 'non'favourable' cardiovascular outcome and those in highest quartile (n=487) a 'favourable' outcome. The medical record audit found concordant outcome groups for 183/192 (95%) of records. The main reasons for discrepancy were additional information available via data linkage, or clinical judgement of ICU stay/LOS.

Conclusion: Data linkage of a clinical biobank with health data is a feasible and reliable method to identify patient outcomes. This approach will enhance genomic analysis to investigate the relationship between genetic variation and clinical outcome and identify genetic hallmarks of patients at-risk of non-favourable cardiovascular outcomes.

Child health and development

Preterm birth and educational and economic outcomes during adulthood Asma Ahmed* Eleanor Pullenayegum Sarah D. McDonald Jason Pole Shahirose Premji Marc Beltempo Fabiana Bacchini Prakeshkumar S. Shah Petros Pechlivanoglou

Background: Preterm birth (PTB) at <37 weeks gestation affects approximately 10% of births worldwide; however, data on the socioeconomic outcomes of these children is limited and inconclusive. We aimed to examine the effect of PTB on individuals' income, employment, and educational attainment during adulthood.

Methods: Using linked administrative data from Statistics Canada, we created a population-based cohort of children born in Canada between 1983 and 1996. We tracked these individuals until the end of 2018 (age 21-34 years) to ascertain the following outcomes ≥18 years: annual employment income, employment rate, and education enrollment and attainment. We estimated mean differences and RR using generalized estimating equations and multinomial regressions, accounting for differences in baseline characteristics using exact matching and adjusting for age and period effects.

Results: Out of ~3.8 million births, approximately 7% of infants were born preterm. Infants born preterm, on average, earned -2,331 CAD (95% CI: -2,656, -2,007) lower per year than those born at term and were 4% (RR 0.96, 95% CI 0.96 to 0.97)) less likely to be employed. In a subsample of 1991-1996 births (~2 million births), those born preterm were less likely to have enrolled in postsecondary education (RR 0.85 (0.84, 0.87) for college and 0.76 (0.75, 0.77) for university enrollment at age 18-22 years) and to graduate (RR 0.82 (0.80, 0.83) for <bachelor's degree; 0.74 (0.72, 0.75) for a bachelor's degree, and 0.74 (0.70, 0.78) for postgraduate education). The risks of these outcomes were inversely proportional to gestational age (GA). Estimates for those born <28 weeks were -10,356 CAD (-12,177, -8,535) per year for mean income differences and RR 0.14, 95% CI 0.10 to 0.21, for graduation with > bachelor's degree.

Conclusion: Individuals born preterm had lower educational and economic achievements in their second and third decades after birth than those born at term, and the risks were higher with decreasing GA at birth.

Hearing loss and its association with autism spectrum disorder Nicole Talge* Sarah Keim Samrawit Yisahak Brooke Ingersoll

Auditory processing difficulties are commonly observed with autism spectrum disorder (ASD), including hyposensitivity to sound. Contributions of hearing loss to this phenomenon are unclear because the association between hearing loss and ASD is not well-characterized. This knowledge gap has implications for diagnostic assessment and intervention strategies for ASD and co-occurring conditions.

We analyzed cross-sectional, caregiver-reported data from the National Survey of Children's Health (2016-2020). Our sample included children with data on the presence or absence of hearing loss and ASD (ages 2-18; n=150,327). We used logistic regression to evaluate the association between hearing loss and: 1) ASD diagnostic status (no, yes), 2) ASD symptom severity (none, mild, moderate/severe), and 3) the co-occurrence of ASD with intellectual disability (ID) which includes 30% of children with ASD (neither, ASD only, ID only, both). Analyses were weighted for the study sampling scheme; the no diagnosis group for each outcome served as the referent.

Approximately 1% (SE=0.1) and 3% (SE=0.1) of children had diagnoses of hearing loss and ASD, respectively. Hearing loss was associated with ASD (OR=2.7, 95%CI 1.8, 3.9), with 4% (SE=1.3) of children with ASD having hearing loss compared to 1% (SE=0.1) of children without ASD. These associations were stronger in the context of moderate/severe ASD symptoms (OR=3.5, 95%CI 2.1, 5.7) relative to mild symptoms (OR=1.8, 95%CI 1.1, 3.1) and among children with co-occurring ID (OR=5.0, 95%CI 2.8, 9.0) or ID only (OR=8.6, 95%CI 6.0, 12.4) relative to ASD only (OR=2.4, 95%CI 1.5, 3.8). Findings persisted after adjusting for socio-demographics, insurance status, and preterm birth.

Hearing loss is associated with ASD, particularly- though not exclusively- among children with more severe symptoms and co-occurring ID. Future research is needed to investigate impacts on the timing of ASD and hearing loss diagnoses along with receipt of interventions.

Child health and development

Relationships between Maternal, Offspring, and Pregnancy Factors and Extracellular Vesicle and Particle miRNAs in Prenatal Maternal Plasma and Postpartum Human Milk: A Pilot Study Caitlin Howe* Meghan Muse David Armstrong Diane Gilbert-Diamond Jiang Gui Anne Hoen Thomas Palys Brock Christensen Margaret Karagas

Introduction: MicroRNAs (miRNAs) carried by extracellular vesicles and particles (EVPs) in maternal circulation during pregnancy and in breast milk postpartum are hypothesized to facilitate maternal-offspring communication and contribute to developmental programming. However, the factors that influence them remain largely unknown.

Methods: EVP miRNAs were extracted from maternal plasma samples collected at approximately 24-28 weeks gestation and paired breast milk samples collected at approximately 6 weeks postpartum from 54 participants in the New Hampshire Birth Cohort Study. 798 miRNAs were profiled using the Nanostring nCounter platform. Associations between maternal, offspring, and pregnancy factors and maternal EVP miRNA levels were investigated using covariate-adjusted robust linear regression models.

Results: 142 miRNAs were detectable in ≥60% of plasma samples, and 200 miRNAs were detectable in ≥60% of milk samples; 92 miRNAs were common between the two sample types. Shared detectable miRNAs in plasma and breast milk were poorly correlated with each other ($|r| < 0.25$). Total milk EVP miRNA counts were significantly ($P = 0.018$) lower among mothers with a BMI >25 kg/m^2 compared with mothers with a BMI between 18 and 25 kg/m^2 prior to pregnancy. Infant age at breast milk collection was inversely associated ($FDR < 0.05$) with two miRNAs (miR-146a-5p and miR-130b-3p) in breast milk EVPs. Maternal pre-pregnancy BMI and gestational age at sample collection were not significantly associated with plasma EVP miRNA levels. Other factors investigated, including maternal parity, education, gestational weight gain, delivery mode, infant sex, and gestational age at delivery, were not significantly associated with maternal EVP miRNAs in either sample type.

Conclusions: MiRNA levels in breast milk EVPs may be influenced by pre-pregnancy weight status and infant age. Additional research is needed to investigate possible implications for offspring health.

Child health and development

Gestational trajectories of glycemic biomarkers and placental epigenetic aging: findings from a multi-ethnic pregnancy cohort study Tesfa Dejenie Habtewold* Cuilin Zhang Richard J. Biedrzycki Katherine L. Grantz Una Grewal Fasil Tekola-Ayele

Background: Maternal prenatal glycemia status is critical for maternal and fetal health, yet its impact on placental aging is unclear. This study investigated whether longitudinal trajectories of glycemic biomarkers during pregnancy are associated with placental epigenetic aging in race/ethnicity-pooled and -stratified pregnant women.

Methods: Glycemic hemoglobin (hbA1c), glucose, and insulin were measured in maternal plasma from blood collected at four consecutive gestation times in the NICHD Fetal Growth Studies – Singletons (n=301; 77 White, 72 Black, 102 Hispanic and 50 Asian). Placental epigenetic age was estimated using Mayne's clock, control placental clock (CPC), robust placental clock (RPC), and refined RPC (rRPC). Placental epigenetic age acceleration (PAA) was estimated by regressing epigenetic age upon gestational age. The trajectory of each glycemic biomarker was determined by group-based trajectory modeling and its association with PAA was tested using covariate-adjusted linear regression.

Results: Four hbA1c (low, medium, moderate, and high), two glucose (low and high), and two insulin (low and high) trajectories were identified. Glycemic trajectories were not associated with PAA in the full sample. Among black women, compared to low trajectory, medium and moderate hbA1c trajectories were associated with increased PAA (Mayne's clock: $\beta_{moderate}$=1.60, p=0.01; CPC clock: β_{medium}=0.79, p=0.03; CPC clock: $\beta_{moderate}$=0.73, p=0.03), whereas high hbA1c trajectory was associated with decreased PAA (rRPC clock: β_{high}=-1.41, p=0.02). Among white women, medium hbA1c trajectory was associated with increased PAA (Mayne's clock: β_{medium}=1.35, p=0.04). Among Hispanic women, high glucose trajectory was associated with increased PAA (RPC clock: β_{high}=0.36, p=0.03).

Conclusion: Persistently elevated glycemic levels during pregnancy may be linked to accelerated or decelerated placental aging, which vary by race/ethnicity.

Aortic Dissection in the Young: A Population-Based Investigation of Texas Patients, 1999-2019 Sara Stephens* Bita Salamat Sophia Martin Pirouz Shamszad Shaine Morris

Introduction: Aortic dissection (AD) in children and young adults is exceptionally rare. Studies identifying incidence beyond single tertiary centers are limited. We aimed to identify the population-based incidence of AD, its associated mortality, and characteristics associated with AD in Texas.

Methods: Using the Texas Inpatient Public Use Data File, we retrospectively evaluated 1999-2019 hospitalizations for patients <20 years old admitted for AD. Population census data was used to calculate overall and age-specific incidence rate of AD per person-year. Subjects were grouped by diagnosis: traumatic injury, congenital heart disease (CHD)-associated intervention, connective tissue disorder, hypertension, or unspecified. Mixed-effects logistic regression controlling for age as a fixed variable and hospital as a random effect was performed for inpatient mortality.

Results: One-hundred eighty-two patients were included (70.0% male). The population-based incidence of AD was 1.2 cases per 1 million person-years, with a bimodal distribution showing peak incidence in infancy and late teens. Mortality was 10%. Most frequent concurrent diagnoses were trauma (31.3%), CHD-associated intervention (29.1%), hypertension (10.4%), and connective tissue disorder (5.5%). One-quarter (23.1%) had no associated explanatory diagnoses. Era was the only significant factor associated with mortality, with patients hospitalized 2015-2019 having 92% lower odds of dying compared to those admitted 1999-2004 (OR 0.08, 95% CI 0.01-0.72, p=0.025).

Discussion: Findings confirmed AD’s rarity in young people. Patients most frequently had AD with traumatic injury, followed by surgery, which may suggest a high proportion of iatrogenic cases in children. A diagnosis associated with connective tissue disorder was a minority. Mortality improved over time, which is posited to be due to improved early recognition of pediatric AD.

Infant Phenol Exposure and Growth: The Infant Feeding and Early Development Study

Danielle Stevens* Mandy Goldberg Margaret Adgent Helen Chin Donna Baird Virginia Stallings Walter Rogan David Umbach Kelly Ferguson

Background: Phenols are ubiquitous environmental chemicals that may perturb human development. Infancy is a period of increased susceptibility to environmental exposures, and infant growth patterns characterized by heightened BMI (level) or rapid BMI development (trajectory) contribute to obesity.

Aim: Investigate associations between phenols and growth in infancy.

Methods: We analyzed data from 199 US infants in a racially diverse prospective cohort of healthy, term singletons conducted 2010-2014. Exposure to bisphenol A, benzophenone-3, dicholorophenols (DCP), parabens, and triclosan was assessed in urine collected at 6-8 and 12 weeks, creatinine-corrected, and averaged across repeated measures. BMI was collected at a mean of 10 study visits between birth and 36 weeks. Adjusted linear mixed effects spline models estimated differences (β [95% confidence intervals (CI)]) in BMI z-score for a one-interquartile range (IQR) increase in individual phenols. Growth mixture models determined trajectories of normalized BMI z-score, and adjusted multinomial logistic regression models estimated the relative risk ratio (RRR [95% CI]) for associations between individual phenols and trajectories.

Results: A one-IQR increase in 2,5-DCP was positively associated with BMI z-score across infancy (12 weeks: 0.21 [0.01, 0.41], 24 weeks: 0.23 [0.04, 0.42], 36 weeks: 0.20 [-0.02, 0.42]). Similar associations were observed for parabens. Growth mixture models identified four BMI z-score trajectories: decreasing BMI (n=52), expected growth (n=74), increasing BMI (n=48), rapid growth (n=25). Relative to normal growth, a one-IQR increase in Benzophenone-3, 2,4-DCP, and 2,5-DCP was positively associated with relative risk of rapid growth (2.39 [1.22, 4.69], 1.79 [1.00, 3.20], and 2.35 [1.25, 4.42], respectively).

Conclusions: In a diverse cohort of US infants, phenols were positively associated with BMI z-score (level) and rapid BMI z-score development (trajectory), suggesting obesogenic effects.

Child health and development

Prenatal Organophosphate Pesticide Exposure and Fetal Biometry Eleanor Medley* Leonardo Trasande Mrudula Naidu Yuyan Wang Akhgar Ghassabian Linda Kahn Sara Long Yelena Afanasyeva Kurunthachalam Kannan Shilpi Mehta-Lee Whitney Cowell

Organophosphate (OP) pesticide exposure during pregnancy may be associated with reduced fetal growth, though studies are limited and results have been mixed. We aimed to investigate associations between prenatal OP pesticide exposure and fetal biometry and determine if associations vary by fetal sex. In the New York University Children's Health and Environment Study cohort, prenatal urinary concentrations of 6 dialkyl phosphate (DAP) metabolites of OP pesticides were measured at 3 time points. Fetal biometrics were obtained from ultrasounds in the second (n=793) and third (n=543) trimesters. Estimated fetal weight and biometry z-scores were calculated using Intergrowth-21st standards. Covariates included age, education, race/ethnicity, parity, pre-pregnancy BMI, and tobacco exposure. Associations between pregnancy-averaged, creatinine-adjusted, log-transformed ΣDAP and fetal biometry z-scores were determined through linear models for each ultrasound timepoint and stratified by child sex. In the second trimester, one log-unit increase in ΣDAP was associated with lower estimated fetal weight (-0.15 SD; 95% CI: -0.29, -0.01), head circumference (-0.11 SD; CI: -0.23, -0.004), biparietal diameter (-0.15 SD; CI: -0.27, -0.02), and abdominal circumference (-0.13 SD; CI: -0.26, 0.01) measures in females. In the third trimester, one log-unit increase in urinary ΣDAP was associated with lower head circumference (-0.14 SD; CI: -0.28, 0.001), biparietal diameter (-0.12 SD; CI: -0.26, 0.02), and femur length (-0.12 SD; CI: -0.27, 0.04) measures in males. Most of these associations remained consistent when the sample was restricted to participants without gestational diabetes, pre-eclampsia, or pregnancy-induced hypertension. Our results suggest that prenatal OP pesticide exposure is negatively associated with fetal growth and affects fetal biometry trajectories in a sex-specific manner, with females affected earlier in gestation and males affected later in gestation.

Child health and development

Associations between maternal adiposity and early childhood growth trajectory and obesity

Michael Bloom* Hua Min Grace Lawrence Alma Fuller Kathi Huddleston

Childhood obesity is a critical public health issue with a multifactorial etiology. Our aim was to investigate associations of maternal adiposity with early childhood growth trajectory. We enrolled 4580 pregnant women from northern Virginia into a prospective birth cohort between 2012-2019. Participants completed a study questionnaire and we abstracted their obstetrical data from the medical record. We queried child's weight every 6 months through 36 months of age. We included 1466 male and 1420 female singleton term deliveries in this analysis; 38.9% non-Hispanic white, 32.3% Hispanic, 9.9% Asian, 2.6% non-Hispanic Black, and 17.3% other or missing race/ethnicity. The mean (standard deviation) self-reported pre-pregnancy BMI was 25.5 (5.0) kg/m^2 and mothers gained a mean of 14.1 (6.1) kg during pregnancy. Child growth velocity Z-score, defined as the difference between sex- and age-standardized body mass Z-scores using the World Health Organization (WHO) growth standard, was associated with greater prepregnancy BMI (β=0.005, 95% confidence interval (CI): 0.001, 0.009) in a mixed effects regression model, adjusted for pregnancy weight gain, age, education, race/ethnicity, birth weight, and child sex. The covariate-adjusted association with pre-pregnancy BMI was stronger when limited to the 0-6 month growth interval (β=0.012, 95%CI: 0.002, 0.022), which was also associated with pregnancy weight gain (β=0.004, 95% CI: 0.000, 0.008). Defined as body mass ≥ 85 %ile for sex and age, child overweight/obesity at 36 months was associated with greater pre-pregnancy BMI (β=0.002, 95%CI: 0.001, 0.00) in a covariate-adjusted logistic regression model, and the association was partially mediated by birth weight (23.8%) and 0-6 month child growth velocity Z-score (12.8%). Our results suggest that maternal adiposity may be more strongly associated with early childhood growth trajectory and adiposity than pregnancy weight gain but requires confirmation in other study populations.

Metal co-exposures in relation to serum lipid levels during childhood in the Rhea mother-child cohort in Greece Gyeyoon Yim* Katerina Margetaki Megan Romano Shohreh Farzan Maria Kippler Marina Vafeiadi Leda Chatzi Caitlin Howe

Background

Growing evidence suggests that cardiovascular disease, the leading cause of mortality worldwide, develops over the lifetime, often beginning in childhood. Exposure to metals may contribute to dysregulation of lipid levels during childhood. However, previous epidemiologic studies have mainly focused on evaluating the impacts of single metal exposures on lipid levels in adults.

Objectives

To investigate the joint and individual associations of metal mixture exposures with lipid levels during childhood.

Methods

The current cross-sectional study included 297 mother-child pairs from the Rhea Cohort Study in Heraklion, Greece. Seven metals (cadmium, cobalt, mercury, manganese, molybdenum, lead, and selenium) were measured in child blood at 4 years of age. Serum lipid measures included total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL). To determine the joint and individual impacts of child metal exposures (log-transformed) on lipid levels, Bayesian kernel machine regression (BKMR) was employed as a multi-pollutant approach. Models were adjusted for maternal education and child sex, secondhand smoke exposure, and fish consumption.

Results

BKMR identified a positive association between the metal mixture and both TC and LDL. Of the seven metals, selenium (median 90.6 [IQR=83.6, 96.7] µg/L) was assigned the highest posterior inclusion probability for both TC (0.89) and LDL (0.85). A difference in LDL of 4.76 mg/dL (95% CI=-0.12, 9,64) was observed when blood selenium was set to its 75^{th} versus 25^{th} percentile, holding all other metals at their median values.

Conclusion

Higher blood selenium concentrations during childhood may increase LDL. Given that selenium is an essential element which may have benefits in small quantities, additional studies in populations that span a wider range of selenium intake are needed to elucidate the full dose-response relationship between this element and child lipid levels.

Child health and development

How to capture dynamic features of infant growth: A comparison of methods for modeling growth across the first two years Elizabeth Widen* Rachel Rickman Shalean Collins Josh Miller Maricianah Onono Pauline Wekesa Saralyn Foster Sera Young Charlotte Lane

Infants and young children experience dynamic changes in growth in the first two years of life. Several growth modeling methods exist, including latent class growth mixture modeling (LCMM), SuperImposition by Translation And Rotation (SITAR), and longitudinal random effects models. Each has unique benefits and limitations. Longitudinal models quantify simple, interpretable differences in growth. SITAR provides insight into average growth dynamics, in size, velocity, and timing. LCMM identifies subgroups within a population which experience similar growth. The use of more than one approach in the same population may provide additional insight beyond any single method. Using these approaches, we compare findings about the dynamics and determinants of linear growth and skinfold changes during the first two year of life in a mixed HIV-status birth cohort (n=247) in Kisumu, Kenya. All infants experienced poor linear growth. Across the three methods, HIV-exposed, -uninfected (HEU) infants grew less optimally than HIV-unexposed, -uninfected (HUU). In longitudinal models, HEU infants showed shorter linear growth (b=-0.35 cm, 95% CI:-0.63,-0.06) than HUU infants. Using SITAR, we find that difference in linear growth were due to smaller size (-1.15, 95% CI: -1.90, -0.41), not growth velocity. Using LCMM, 3 growth trajectory subgroups were identified; HEU infants were more likely to belong to groups that experience a linear decline in LAZ across time or a steep decline at 7 months. HEU was not associated with sum-of-skinfolds pattern trajectories, or size or velocity with SITAR. Using multiple analytic methods allowed the identification of differences in linear size between HEU and HUU infants, but found no differences in postnatal growth velocities. This suggests that differences are accumulated prenatally. Investigators interested in growth modeling should consider using multiple methods concurrently to examine growth patterns, their determinants, and health outcomes.

Special educational provision for children with neurodevelopmental conditions: a national cohort using linked health and education records for England Ania Zylbersztejn* Vincent Nguyen Ruth Gilbert Katie Harron

Introduction: One in three children in England have Special Educational Needs (SEN) recorded during school. We examined variation in recorded SEN for pupils with neurodevelopmental conditions associated with higher need for SEN intervention.

Methods: We developed a national cohort of children entering primary school (aged 5-6) in academic years 2009/10-2014/15 in England using linked health and education records from the ECHILD database. Children were followed-up for 6 years until the end of primary school.

We identified pupils with neurodevelopmental conditions (autism, learning disability, hyperactivity disorders, developmental delay, cerebral palsy, epilepsy, sensory impairments, perinatal conditions, other associated conditions) using hospital records at ages 0-4 years old. Recorded SEN (school-level *SEN support* or more intense provision via *Education, Health and Care plan, EHCP*) was indicated using education records at ages 5-10.

For each condition, we estimated the proportion of children with recorded SEN support/EHCP at the start (Year 1), the end (Year 6) and ever during primary school.

Results: The cohort included 3,675,796 children. 17% had SEN support recorded in year 1, 17% in year 6 and 30% had ever recorded SEN support. Corresponding rates for EHCPs were 1.7%, 3.6% and 3.7%.

116,309 (3.2%) of children had a neurodevelopmental condition, of whom, 41% had ever recorded SEN support and 29% had ever recorded EHCP (ranging from 16% of children with perinatal conditions, to 70% of children with cerebral palsy and approx. 85% of children with autism and learning disability). The proportion of children with a neurodevelopmental condition and recorded SEN support declined from 28% in year 1 to 21% in year 6, while the proportion with EHCPs increased from 21% to 27%, respectively.

Conclusions: Children with neurodevelopmental conditions have varying level of recorded SEN. Further work will examine contribution of geographic, health and socioeconomic factors to variation in SEN provision.

Child health and development

Duration of general anesthesia exposure in early childhood and subsequent child development and school performance: a novel record linkage study using operating room data Francisco Schneuer* Samantha Lain Natasha Nassar

Aims: We investigated the effect of general anesthesia (GA) duration in early childhood on school entry development and school performance outcomes

Methods: We included children term-born in New South Wales, Australia without major congenital anomalies or neurodevelopmental disability with either a school-entry developmental assessment or Grade-3 (aged 8-9 years) school test results in 2008-2019. We compared children exposed to general anesthesia aged <4 years in the state's largest tertiary pediatric hospital to a propensity score-matched group without any hospitalization, and with biological siblings. We used operating room data to ascertain GA duration linked to birth, hospital admission, developmental assessment and school performance information. Outcomes included developmental vulnerability in five domains and scoring below the national minimum standard in five school performance domains.

Results: We included 9,961 children (exposed n=3,334; unexposed n=6,627) with developmental assessment and 21,104 (exposed n=7,071; unexposed n=14,033) with school performance information. The median cumulative GA exposures for both cohorts were 57 (43-77) and 55 (42-75) minutes, respectively. Children exposed for <90 minutes and ≥90 minutes had 18% and 42% increased odds of being developmentally vulnerable in physical health and wellbeing, respectively (adjusted odds ratio (aOR) 1.18; 95%CI 1.00-1.40; aOR 1.42; 95%CI 1.10-1.85) with no association with other domains. Exposure to ≥90 minutes of GA was associated with between 38% and 80% increased odds of poor scores in numeracy (aOR, 1.80; 95% CI 1.32-2.46), reading (aOR 1.38; 95%CI 1.01-1.89), writing (aOR 1.78; 95%CI 1.23-2.56) and spelling (aOR 1.50; 95%CI 1.11-2.03). These results were not consistent when comparing biological siblings.

Conclusion: Although children exposed to GA for more than 90 minutes had increased risk of poor development and poor numeracy scores, no effects were found in biological siblings. Findings suggests effects be all or partially attributable to unmeasured confounding. The uncertainty of the effects of long exposure warrants caution from parents and clinicians when deciding to undergo procedures in the child that may be avoided or delayed.

Child health and development

Optimum core temperature and initiation of active cooling among infants who received therapeutic hypothermia (TH) treatment in Ireland Indra San Lazaro Campillo* Indra San Lazaro Campillo Julie McGinley Paul Corcoran Aenne Helps Sarah Meaney Peter McKenna Peter Filan Richard Greene John Murphy

Background. In line with practice guidelines, TH should be initiated within six hours of birth and should be continued for 72 hours. The optimum core temperature of 33°C to 34°C is targeted over this 72-hour period.

Objective. To assess the average age when target temperature was reached among infants who received therapeutic hypothermia (TH) in the Republic of Ireland, 2019-2020.

Methods. Retrospective reviews of inpatient medical records have been used as a gold standard approach when assessing multiple outcomes and rates of adverse events. In Ireland, TH is provided in four tertiary maternity hospitals. All babies born in the remaining 15 units requiring TH are transferred to one of these four centres.

Results. Of the 148 infants who received TH during the two-year period 2019-2020, 66% of the infants were born in a tertiary hospital (n=98 of 148). During the same period, according to HIPE data, 53% of all the mothers who gave birth in hospital did so in a tertiary hospital (n=60,286 of 113,198). Thus, TH was provided to 1.63 infants per 1,000 mothers who gave birth in a tertiary hospital (inborn, 95% CI=1.3-1.9) and 0.95 infants per 1,000 mothers who gave birth in a non-tertiary hospital (outborn, 95% CI=0.82-1.15), a 72% difference (Risk ratio=1.72, 95% CI=1.22-2.42, p-value <0.001). More than 85% of the 49 infants transferred for neonatal TH treatment required respiratory support (n=42), and two-thirds required sedation (n=33) in-route to the tertiary unit. Targeted temperature was reached at 4:12 hours (median: 3:47 hours) (SD=2:48) of average of age for inborn compared to 10:21 hours (median: 10:30 hours) (SD=7:18) for outborn infants. This difference was statistically significant, p-value <0.001.

Conclusion. The vast majority of all infants, both inborn and outborn, achieved optimum core temperature within six hours of birth. However, inborn infants achieved core temperature earlier than outborn babies.

Child health and development

Similarities between perinatal mother and child miRNA expression profiles Helen Foley* Joshua Millstein Sandrah Eckel Theresa Bastain Carmen Marsit Carrie Breton

Background. Circulating miRNA may play a key role in maternal-fetal communication during pregnancy and contribute to downstream effects from pregnancy complications. However, little is known about the relationship between maternal and child miRNA expression profiles. In this study, we compare late pregnancy maternal miRNA expression and cord blood miRNA expression to identify groups of co-expressed miRNA and assess them for association with pregnancy complications.

Methods. Eighty-nine mother-child pairs from the MADRES study were profiled for 800 miRNA on the Nanostring platform. 468 miRNA were recorded above sample-specific background in at least 5% of samples. miRNA expression profiles were clustered using Weighted Gene Network Correlation Analysis (WCGNA) and tested for association with six factors: BMI, gestational diabetes mellitus (GDM), gravidity, fetal sex, hypertension, and gestational age at birth.

Results. Overall, miRNA expression profiles showed some similarity between maternal and child samples (Rand Index =0.70). Three clusters of miRNA expression were associated with GDM in cord blood plasma, but not in matching maternal plasma, and the other five factors were not associated with any clusters in either sample type. miRNA in clusters associated with GDM have been associated with insulin regulation, transcription factors, and signaling pathways that may be related to downstream effects of GDM in children.

Conclusion. While miRNA expression was largely similar between late-pregnancy maternal samples and child cord blood samples, miRNA clusters associated with GDM were only identified in cord blood, suggesting that GDM effects in neonates and children may carry over after birth. Future research may investigate later consequences of GDM exposure in young children.

Child health and development

Prenatal Phthalate Exposure and Anogenital Distance in Male and Female Infants at 12 months Akhgar Ghassabian*, Nicole Salvi Yuyan Wang Mengling Liu Linda Kahn Leonardo Trasande Akhgar Ghassabian Akhgar Ghassabian

Introduction

Anogenital distance (AGD) is a proxy measure for *in utero* androgen exposure. Higher exposure to phthalates—commonly used plasticizers that are known endocrine disruptors—during the fetal period of sexual development has been associated with shorter AGD in males. The impact of prenatal phthalate exposure on female AGD is understudied.

Methods

Data were from the NYU Children's Health and Environment Study, a NYC birth cohort (2016-2019). Phthalate metabolites were quantified in maternal urine samples collected at <18 weeks of gestation. We measured anus to clitoris (AGD_{AC}) and anus to fourchette (AGD_{AF}) distances in female infants, and anus to scrotum (AGD_{AS}) distance, anus to penis (AGD_{AP}) distance, and penis width in male infants around 12 months. We examined associations of 12 phthalate metabolites, phthalic acid, and 2 phthalate groupings, ∑di(2-ethylhexyl)phthalate (DEHP) metabolites and ∑anti-androgenic phthalates, with infant AGD, adjusted for infant age, weight-for-length Z scores, and urinary dilution.

Results

416 infants had both phthalate exposure and AGD data (214 males and 202 females). In males, higher mono(carboxy-isononyl) phthalate (mCINP) was associated with shorter AGD_{AP} (parameter estimate, b=-0.329, 95%CI: -0.585, -0.072) and higher monobutyl phthalate (mBP) with shorter penile width (b=-0.002, 95% CI: -0.004, -0.0001). In female infants, higher mBP and mono-isobutyl phthalate (mIBP) were associated with longer AGD_{AC} (b=0.024, 95%CI: 0.0003, 0.048 and b=0.023, 95%CI: 0.001, 0.045, respectively). We observed a negative association between ∑anti-androgenic phthalates and penile width in male infants and a positive association between ∑anti-androgenic phthalates and AGD_{AC} in female infants.

Conclusion

Negative associations of phthalate exposure with AGD_{AP} and penile width in male infants and positive associations with AGD_{AC} in female infants suggest that the effect of prenatal phthalate exposure on fetal reproductive development varies by sex.

COVID-19 Pandemic

COVID-19 and Maternal Substance Use during Late Pregnancy Min Chung* Haeni Lee Xiaozhong Wen

The coronavirus disease 2019 (COVID-19) pandemic has potential impacts on substance use. We examined if e-cigarette (EC), combustible cigarette (CC), and Marijuana (MJ) use among U.S. pregnant women was affected in the early stage of the pandemic using data from Phase 8 of the U.S. Pregnancy Risk Assessment Monitoring System. We included mothers who gave birth between June 2016 and December 2020 and had data on EC use in late pregnancy (N=119,772), CC in late pregnancy (N=119,997), and/or MJ during pregnancy (N=44,433). Logistic regression was used to fit the pre-COVID trend of EC, CC, and MJ use based on periodic prevalence between from June to September (Jun-Sep) of 2016 and from October to December (Oct-Dec) of 2019. Expected prevalence during the pandemic (from June to December of 2020) was estimated from regression models and was compared with the observed prevalence (and 95% confidence intervals).

There was an increase in EC use among pregnant women from Jun-Sep 2016 (1.01%) to Oct-Dec 2019 (1.93%). The observed (Obs) prevalence of EC use was similar to the expected (Exp) prevalence in Jun-Sep (Obs 1.48% vs. Exp 1.50%) but significantly diverged in Oct-Dec (Obs 1.93% vs. Exp 1.56%, 95% CI: 1.23-1.97) in 2020. There was a decrease in CC use from Jun-Sep 2016 (7.37%) to Oct-Dec 2019 (6.65%). Observed and expected prevalence of CC use significantly diverged in both Jun-Sep (Obs 6.29% vs. Exp 5.47%, 95% CI: 4.67-6.40) and Oct-Dec (Obs 6.65% vs. Exp 4.60%, 95% CI: 3.61-5.84) in 2020. MJ use remained stable between Jun-Sep 2016 (4.07%) and Oct-Dec 2019 (4.69%). The observed and expected prevalence of MJ use was similar in Jun-Sep (Obs 4.81% vs. Exp 4.61%) and Oct-Dec (Obs 4.69% vs. Exp 4.60%) of 2020.

We concluded that U.S. pregnant women had a higher prevalence of EC and CC use, and a similar prevalence of MJ use during the COVID-19 pandemic, compared to the expected prevalence based on the historical trend.

COVID-19 Pandemic

COVID-19 Prevalence and Trends Among Pregnant and Postpartum Individuals in Maine by Rurality and Pregnancy Conditions Charlie Grantham* Christina Ackerman-Banks, MD Heather Lipkind, MD, MS Kristin Palmsten, ScD Katherine Ahrens, MPH, PhD

Objective: To estimate COVID-19 diagnosis prevalence and trends among pregnant and postpartum individuals in Maine by rurality and common pregnancy conditions.

Methods: We used the Maine Health Data Organization's All Payer Claims Data to identify deliveries during 2020-2021. We identified COVID-19 during pregnancy (Apr 2020 to Dec 2021 deliveries) and during the first 6 months postpartum (Jan 2020 to Jun 2021 deliveries) using the ICD-10 diagnosis code U071 on medical claims. We used Joinpoint regression software to model trends. We stratified the analysis by rurality of residence (based on ZIP code) and by common pregnancy conditions: gestational diabetes (GDM), hypertensive disorders of pregnancy (HDP), and prenatal depression.

Results: We included 13540 deliveries in our pregnancy and 10891 deliveries in our postpartum analysis. COVID-19 diagnosis prevalence among pregnant individuals increased from 0.5% in Apr 2020 to 10.4% in Dec 2021 (Oct 2020 was the start of slope [0.43 per month], $p<.01$). COVID-19 diagnosis prevalence postpartum increased from 0.2% in Jan 2020 to 3.2% in Jun 2021 deliveries (slope=0.16 per month, $p<.01$). Trends in prevalence of COVID-19 diagnosis among pregnant individuals living in urban areas were distinct from those living in rural areas ($p=.02$), with a steeper slope during the first months of the pandemic in urban areas; trends postpartum were similar ($p=0.51$). Trends in persons with prenatal depression showed a steeper increase in COVID-19 diagnosis prevalence in pregnancy after Dec 2020 ($p<.01$) and postpartum overall ($p<.01$) compared to those without prenatal depression. Persons without vs. with GDM had a steeper increase in COVID-19 diagnosis postpartum ($p<.01$).

Conclusion: COVID-19 diagnosis among pregnant and postpartum individuals in Maine showed distinct patterns by rurality of residence and select pregnancy conditions. This information can be used for assessing the impact of the COVID-19 pandemic on maternal and infant health.

COVID-19 Pandemic

Systematic review of COVID-19 vaccine decision-making, uptake, and hesitancy among adolescents aged 12 to 17 years old Brianna Agnew* Honorine Uwimana Marie-Claude Couture Timothy Callaghan Onyebuchi Arah Annette Regan

Vaccination remains the best strategy to prevent COVID-19-associated morbidity and mortality. COVID-19 vaccine prevalence among adolescents (61.5%) has recently stalled and remains lower than adults aged ≥25 years (82%). While prior research has focused on the parental/caregiver perspective of adolescent vaccine uptake, we need an up-to-date understanding of the adolescent perspective. We conducted a systematic review of the factors associated with COVID-19 vaccine decision-making, uptake, and hesitancy among adolescents aged 12-17 using four databases: CINAHL, EMBASE, PubMed, and SCOPUS. Inclusion criteria were: i) studies reporting on factors associated with COVID-19 vaccine uptake, hesitancy, or intention to vaccinate, ii) among adolescents aged 12 – 17 years, iii) published in English or Spanish. Two team members independently screened 4,137 research papers and agreed to full text review 299 studies for potential inclusion.

After assessing 166 full-text articles (to date), 11 studies conducted in seven countries have met eligibility criteria. A preliminary narrative analysis of four cross-sectional studies found low vaccine uptake among teens (South Korea: 50%; U.S.: 52% – 58%; Israel; 64%). The majority of adolescents reported participating with their family in vaccine decision-making (65.7%); 17.8% made their own decision, and 16.4% stated their parent/caregiver decided alone. Compared to parents/caregivers, teens reported higher levels of trust in family and friends (40%), school (20%), and social media (20%) for vaccine information and more commonly reported fear of needles (21%) and unvaccinated friends (17.1%) as reasons for vaccine hesitancy. Adolescents provide critical insights into their own COVID-19 vaccine uptake, hesitancy, and decision-making, that may diverge from their parents/caregivers. Better understanding adolescent factors associated with COVID-19 vaccination is necessary to create effective interventions to improve vaccination rates.

COVID-19 Pandemic

Association of the COVID-19 Pandemic and SARS-CoV-2 Infection During Pregnancy with Maternal and Infant Outcomes, South Carolina, 2018-2021 Jihong Liu* Maria Sevoyan Yiwen Shih Peiyin Hung Xiaoming Li

Background: This study aims to examine the associations of SARS-CoV-2 infection and the COVID-19 pandemic with maternal and infant outcomes.

Methods: Data came from the South Carolina (SC) COVID-19 Cohort, novel linkages of statewide COVID testing and vital records data for all women giving a singleton birth during pre-pandemic (01/2018-02/2020) (n=101,517 births) and peri-pandemic (03/2020-12/2021) (n=81,372 births) periods. SARS-CoV-2 infection was categorized as no COVID-19 testing, COVID-19 positive, or COVID-19 negative during pregnancy and intrapartum. Based on self-reported symptoms, COVID-19 severity was classified into three groups: asymptomatic, mild, and moderate/severe symptoms. Multivariable logistic regressions were used to examine the differences in maternal and infant outcomes by pandemic period and SARS-CoV-2 infection status.

Results: During the pandemic, 8.3% of birthing people in SC were infected by SARS-CoV-2. Among COVID-positive cases, 56.4% were asymptomatic, 30.6% had mild symptoms, and 13% had moderate/severe symptoms. Compared with pre-pandemic, significant increases were observed in low birthweight (<2500 grams, adjusted OR (aOR): 1.04, 1.01-1.08), preterm birth (<37 weeks, aOR: 1.03, 1.00-1.07), NICU admission (aOR: 1.10, 95% CI: 1.06-1.13), gestational diabetes (aOR: 1.16, 95% CI: 1.11-1.20), and gestational hypertension (aOR: 1.08, 95% CI: 1.05-1.12) during the pandemic. Compared with pre-pandemic, birthing people with COVID infection also had increased odds of preterm birth (aOR: 1.14, 1.05-1.24), NICU admission (aOR: 1.23, 1.13-1.34), and gestational hypertension (aOR: 1.21, 1.12-1.32). Compared to asymptomatic people, people with moderate/severe symptoms had increased odds of preterm birth (aOR: 1.42, 1.13-1.78).

Conclusions: Adverse maternal and infant health outcomes were increased during the COVID pandemic and were higher among people with SARS-CoV-2 infection, especially those with moderate/severe symptoms.

Disability status

Pregnancy intendedness and preconception health risks by severity of maternal disability, 2019-2020 Abigail Newby-Kew* Anne Valentine Monika Mitra Ilhom Akobirshoev Jonathan M. Snowden Willi Horner-Johnson

Background: Women with disabilities are more likely to have unintended pregnancies and experience preconception health risks, which may each contribute to adverse perinatal outcomes. It is not yet known how these risks vary by severity of disability. Closing that gap will help identify where interventions are most needed.
Methods: We analyzed 2019-2020 PRAMS data from 23 sites that included the Washington Group Short Set of Questions on Disability (n=36,569). We examined associations of disability severity (none [reference group], mild, or moderate/severe) with pregnancy intendedness and preconception health risks, using multivariable Poisson regression with robust standard errors to calculate adjusted prevalence ratios (aPRs) and 95% confidence intervals (CIs) while controlling for sociodemographic characteristics. Preconception health risks included smoking, heavy drinking, high blood pressure, diabetes, no multivitamin use, and experiencing abuse, depression, or obesity.
Results: Of respondents, 33.6% had mild disability (some difficulty) and 6.3% had moderate/severe disability (a lot of difficulty). Women with either mild (aPR 0.85; 95%CI 0.82,0.87) or moderate/severe (aPR 0.79; 95%CI 0.72,0.88) disability were less likely to describe their pregnancy as intended, compared to women with no disability. The likelihood of experiencing three or more preconception health risks increased by severity of disability: mild (aPR=1.86; 95% CI: 1.53,2.25); moderate/severe (aPR=2.41; 95% CI: 1.97,2.95).
Conclusions: Pregnancies among women with disabilities are less likely to be intended, which may limit opportunities to prepare for healthy pregnancy. Disabled women, especially those with more severe disability, are vulnerable to preconception health risks that could potentially be mitigated before conception. Our findings highlight the need for improvements in family planning and preconception health care for disabled women.

Disability status

Neonatal outcomes in births to Black and Hispanic women with physical disabilities Willi Horner-johnson* Bharti Garg Aaron Caughey Ilhom Akobirshoev Monika Mitra

Background: Neonates of women with physical disabilities have increased risk of poor outcomes. Risks may be compounded for neonates of disabled women in minoritized racial and ethnic groups, but little is known about outcomes at this intersection.

Methods: We used linked hospital discharge and vital records data from California, 2000-2012. We identified women with physical disabilities using ICD-9 codes for major injuries, congenital anomalies, musculoskeletal disorders, or nervous system disorders. We excluded multiple gestations and gestational ages <23 weeks or >42 weeks. We compared neonates of women in 5 groups (Black and Hispanic with and without physical disabilities, White with physical disabilities) to those of non-Hispanic White women without disabilities. We used multivariable logistic regression to assess associations with small for gestational age (SGA), low and very low birthweight, still birth, infant death, Apgar score <7 at 5 minutes, congenital anomalies, and NICU admission, while controlling for sociodemographic and clinical confounders.

Results: Neonates of Black disabled women had the highest odds of SGA (Odds Ratio (OR)=3.04, 95% confidence interval (CI): 2.54, 3.64), low birthweight (OR=3.84, 95% CI: 3.18, 4.64), and NICU admission (OR=2.00, 95% CI: 1.68, 2.38); CIs did not overlap with those for non-disabled Black women or disabled White women. Neonates of disabled Hispanic women had larger odds than non-disabled Hispanic women or disabled White women for SGA, low birthweight, very low birthweight, and congenital anomalies.

Conclusions: Neonates of Black and Hispanic women with physical disabilities are more likely to have adverse outcomes than neonates of non-disabled women in the same racial and ethnic group or non-Hispanic White women with disabilities. Further research is needed to better understand how racism and ableism intersect to increase risk, and to identify effective strategies for reducing disparities and improving outcomes.

Environment/climate change

Parental preconception exposure to per- and polyfluoroalkyl substances in relation to birthweight Leah Martin*, Yu Zhang Vicente Mustieles Leah Martin Yang Sun Alexandra Hillcoat Zainab Bibi Nicole Torres Ayanna Coburn-Sanderson Irene Souter John C. Petrozza Yi-Xin Wang Carmen Messerlian Leah Martin

Background

Although prenatal per- and polyfluoroalkyl substances (PFAS) exposure has been associated with lower birthweight, the influence of preconception PFAS exposure in either parent is absent.

Methods

This study included 312 mothers and 145 fathers with a singleton live birth from a prospective preconception cohort of subfertile couples seeking fertility treatment at a clinic in Massachusetts, USA. Six PFAS compounds were quantified in baseline serum samples. Birthweight was obtained from delivery records and low birthweight (LBW) was defined as < 2500 grams. We utilized linear regression, logistic regression, and quantile-based g computation to examine the associations between maternal or paternal serum PFAS concentrations (log-2 transformed single compound concentration or quartiles of the total mixture) and birthweight and LBW, adjusting for confounders.

Results

The mean (SD) age was 34.5 (3.8) years for mothers and 36.6 (5.1) years for fathers. Most of the participants were white, non-smokers, and nulliparous. Maternal preconception serum concentrations of perfluorooctane sulfonate (PFOS) (-161.4 g, 95% CI: -268.3, -54.6), perfluorohexane sulfonate (PFHxS) (-94.3 g, 95% CI: -180.4, -8.1), and the total PFAS mixture (-96.9 g, 95% CI: -195.8, 2.0) were inversely associated with birthweight. Maternal preconception serum PFOS concentration was associated with an increased risk of LBW (OR: 1.87, 95% CI: 1.09, 3.21). In contrast, paternal preconception serum concentrations of PFOS (144.5 g, 95% CI: -10.0, 299.0) and PFHxS (111.5 g, 95% CI: -16.9, 240.0) were positively associated with birthweight.

Conclusion

In this prospective cohort of subfertile couples, maternal preconception exposure to PFOS, PFHxS, and the total PFAS mixture was associated with lower birthweight, while opposite associations were found with birthweight for paternal preconception PFOS and PFHxS exposure. Future studies with larger sample sizes are needed to validate these findings.

Environment/climate change

Racial disparities in the association between phthalate mixtures and measures of male fetal genital development Meghana Varde* Michael S. Bloom Abby G. Wenzel John W. Brock John R. Kucklick Rebecca J. Wineland Roger B. Newman

Phthalates are endocrine disrupting chemicals found in personal care products, medications, and plastic food and beverage packaging. Phthalates have anti-androgenic properties and may affect fetal genital development. Studies have also shown a racial disparity in phthalates exposure among women in the U.S. We conducted a prospective birth cohort study of phthalate mixtures and measures of fetal genital development in a racially-diverse population to investigate potentially disparate effects. Mid-gestation (18-22 weeks) urine was collected from 198 women who identified as Black and 197 women who identified as white in Charleston, SC between 2011-2014. We measured eight phthalate monoester metabolites in urine using liquid chromatography coupled to tandem-mass spectrometry. We used Bayesian kernel machine regression to estimate the associations between the mixture of phthalate metabolites and anogenital distance measures and penile dimensions at birth, among 229 singleton male infants. We adjusted for urinary specific gravity, maternal age, body mass index, education level, cigarette smoking, and birth weight z-score. Infants of women who identified as Black at the 75%ile of the phthalate mixture had lesser anopenile distance (-1.23 mm; 95% credible interval (CI): -2.71, 0.25), penile length (-0.66 mm; 95%CI: -2.19, 0.87), penile width (-0.28 mm; 95%CI: -0.91, 0.36), and penile volume (-29.13 mm^3; 95%CI: -105.29, 47.03) than infants at the 50%ile, with little difference found in the associations among infants of women who identified as white. Monobutyl phthalate, monobenzyl phthalate, monomethyl phthalate, mono(2-ethylhexyl) phthalate, and mono(2-ethyl-5-oxohexyl) phthalate were important drivers of the associations. The results suggest different associations between gestational exposure to a phthalates mixture and fetal genital development among women in a racially-diverse population.

Environment/climate change

Iron status does not Mediate the Association of an Industry-Relevant Metal Mixture with IQ in Italian Adolescents Samantha Schildroth* Linda Valeri Baoyi Shi Alexa Friedman Roberta F. White Katarzyna Kordas Donatella Placidi Robert O. Wright Donald Smith Roberto G. Lucchini Megan Horton Birgit Claus Henn

Background: Metals have been associated with adverse neurodevelopmental outcomes in children.

Epidemiological evidence suggests that these associations may be mediated by essential nutrients like iron (Fe). However, few studies have investigated Fe status as a possible mediator of a metal *mixture* with neurodevelopment.

Methods: We used cross-sectional data from 383 adolescents (10-14 years) in the Public Health Impact of Metals Exposure Study. Manganese (Mn), chromium (Cr), and copper (Cu) were quantified in hair; lead (Pb) was quantified in whole blood using ICP-MS. Ferritin, a marker of Fe status, was quantified in serum using immunoassays. The Wechsler Intelligence Scale for Children (WISC) was administered to assess intelligence quotient (IQ). We used Bayesian Kernel Machine Regression Causal Mediation Analysis (BKMR-CMA) to estimate natural direct effects (NDEs) and natural indirect effects (NIEs), adjusting for *a priori* selected confounders. Betas (β) and 95% credible intervals (CIs) were estimated.

Results: Median concentrations for Mn, Cr, Cu, Pb and ferritin were 0.08 µg/g, 0.05 µg/g, 9.4 µg/g, 1.3 µg/dL and 27.0 ng/mL, respectively. Although individual metals (e.g., Cu, Pb) were associated with IQ, there was limited evidence that the overall mixture was materially associated with IQ. The NDE, reflecting the direct association not mediated through Fe status for an increase in the overall mixture from its 25^{th} to 75^{th} percentiles, was null for verbal IQ (β=-0.30, 95% CI= -2.28, 1.52), performance IQ (β=0.06, 95% CI=-1.31, 1.54), and full-scale IQ (β=-0.05, 95% CI=-1.56, 1.40). There was no evidence of mediation by Fe status, where the NIEs for each IQ scale were null.

Conclusion: In this Fe-replete population, there was no evidence that the metal mixture was jointly associated with IQ through either direct or indirect pathways. Fe-deficient populations may be more susceptible to metals neurotoxicity, and should therefore be examined in future studies.

Environment/climate change

Preconception Serum Per- and Polyfluoroalkyl Substances (PFAS) and Risk of Spontaneous Abortion in a Prospective Cohort of North Americans: Preliminary Findings Samantha Schildroth* Amelia K. Wesselink Michael D. McClean Ganesa Wegienka Elizabeth E. Hatch Lauren A. Wise

Background: Per- and polyfluoroalkyl substances (PFAS) are a class of endocrine-disrupting chemicals that are ubiquitous in the environment. Prior studies have linked PFAS exposure with increased risk of spontaneous abortion (SAB, pregnancy loss <20 weeks gestation), but few studies have measured PFAS before pregnancy or have captured early SAB (<8 weeks).

Methods: We used data from Pregnancy Study Online (n=163), a prospective cohort study of North American females aged 21-45 years (2015-2021), to assess associations between PFAS concentrations and self-reported SAB (pregnancy loss <20 weeks' gestation). We quantified five PFAS in preconception serum samples using isotope dilution tandem mass spectrometry. We used Cox proportional hazards regression to estimate hazard ratios (HRs) and 95% CIs, adjusting for *a priori* selected confounders. We further stratified results by parity status (parous vs. nulliparous), as pregnancy is an important route of PFAS elimination.

Results: Median concentrations (ng/mL) for PFOS, PFOA, PFNA, PFHxS, and PFDA were 2.8, 1.3, 0.4, 0.8, and 0.2, respectively. Spearman correlations between PFAS ranged from 0.38 (PFHxS vs. PFDA) to 0.84 (PFOS vs. PFNA). Nearly 19% (N=30) of participants reported SAB during follow-up, with 50% of losses occurring <8 weeks' gestation. In adjusted models, the HR for an interquartile increase in PFNA concentrations was 1.6 (95% CI=0.6-4.4). Associations for other PFAS were generally null. Among parous participants, there was a consistent trend of increased risk of SAB with increasing concentrations for all PFAS, and associations were strongest for PFOS (HR=3.0, 95% CI=0.5-19.6) and PFNA (HR=2.4, 95% CI=0.4-15.2).

Conclusions: Preliminary findings indicate that preconception PFAS concentrations are associated with increased rate of SAB, particularly among parous participants, though results were imprecise. Further work includes expanding the sample size and examining the influence of PFAS mixtures on SAB.

Environment/climate change

Short term air pollution exposure during pregnancy and acute changes in markers of immune function measured in maternal blood plasma Catherine Yount* Sally Thurston Kristin Scheible Yihui Ge Zhenchun Yang Philip Hopke Yan Lin Richard Miller Susan Murphy Jessica Brunner Daniel Kaplan Xing Qiu Yiping Pang Emily Barrett Thomas O'Connor Junfeng Zhang

Background
Air pollution exposure during pregnancy has been associated with fetal growth restriction, for which maternal immune activation is a hypothesized mechanism. We hypothesized that acute exposure to air pollutants during pregnancy would be associated with greater immune activation, and that this effect may not be equal across trimesters.
Methods
In each trimester, pregnant participants in the UPSIDE cohort study (Rochester, New York) provided plasma, which was assayed for immune markers (C-reactive protein, TNFα, fractalkine, CSF, IFNg, IL1β, IL2, IL4, IL5, IL6, IL7, IL8, IL10, IL12-p70, IL21, and IL23). We matched participants' residential addresses to 1 km2 grids using spatial temporal models to modeled daily PM2.5 and NO2 exposure during pregnancy. Using generalized additive models, we estimated the difference in immune markers associated with interquartile range increases in mean PM2.5 and NO2 concentrations 1 to 7 days prior to the blood draw, adjusting for smoking, employment, age, race, education, Women, Infants, & Children Program use, pre-pregnancy BMI, ambient temperature and relative humidity, and gestational age. We then included interaction terms of NO2 with indicator variables for trimester to determine whether immune marker/pollutant associations differed across trimesters.
Results
IQR increases in NO2, but not PM2.5, concentrations in the previous 1-7 days were significantly associated with higher fractalkine, IL10, IL17a, IL1β, IL2, IL21, IL23, IL4, and IL7. For example, an IQR increase in NO2 concentration on the day of the blood draw was associated with a 11.3% increase (95% CI = 4.1, 19.0) in IL 10. When allowing for trimester specific slopes, we observed a 6.3% increase (-2.1%, 15.4%) in IL10 in trimester 1, a 12.3% increase (3.8%, 21.5%) in trimester 2 and a 16.8% increase (7.0%, 27.4%) increase in trimester 3. We observed similar effects across trimesters for the other immune markers.
Conclusions
An increase in NO2 concentration in the prior week was associated with increased concentrations of multiple immune markers, with larger effects observed in trimesters 2 and 3. Exposure to traffic pollutants may have acute impacts on general immune activation, particularly in mid to late pregnancy.

Environment/climate change

Tampon use as a source of toxic metal exposure: Results from NHANES 2001-2004 Mandy Hall*, Kristen Upson Mandy S. Hall Jenni Shearston Kathrin Schilling Beizhan Yan Nancy K. Reame Nicole Talge Claire Schertzing Marianthi-Anna Kioumourtzoglou Mandy Hall

Tampons, used by 50-86% of US menstruators, absorb and retain menstrual fluid in the vagina. They are composed of cotton, rayon, or their mixture, derived from cotton plants and wood pulp that can accumulate metals present in soil and water. It is plausible that metals in tampons can be absorbed by the permeable vaginal mucosa, and directly enter systemic circulation. The one prior study to investigate this association observed increased whole blood total mercury levels with tampon use, but no associations with cadmium or lead. We investigated these associations in a cross-sectional study using data from the National Health and Nutrition Examination Survey (NHANES), years 2001-2004. In a subset of menstruators ages 20-49 years whose first day of last menstrual period (LMP) was in the past 30 days (unweighted n=1,220), data were available on tampon use in the past month and lead, cadmium, and total mercury concentrations measured in whole blood. We conducted multivariable linear regression to estimate the percent difference in blood metal concentrations and 95% CIs with tampon use, adjusting for age, education, smoking, parity, and the other metals. In the study sample, 62% of menstruators (unweighted n=681) reported using tampons in the past month. Those who used tampons (vs. non-users) had 11% higher total mercury levels in whole blood (95% CI: 1%, 23%). When restricting the sample to those with first day of LMP in the past 7 days (unweighted n=342), the association was stronger (28%; 95% CI: 1%, 63%). No association was observed with cadmium (1%, 95% CI: -10%, 13%). We observed an inverse association between tampon use and lead levels (-9%, 95% CI: -16%, 0%) that persisted in analyses among those with first day of LMP in the past 7 days. Our results, along with the prior study, suggest that tampon use is associated with increased mercury exposure. This is concerning given the known adverse effects of mercury exposure and the frequency of tampon use in the US.

Environment/climate change

Housing characteristics, in-home environmental exposures, and lung function in a safety net population of children with asthma Matthew Bozigar* Catherine Connolly Kim Vermeer Luis Carvalho Robyn Cohen Julianne Dugas Jon Levy Patricia Fabian

Objective: The health effects of in-home environmental exposures (IHEEs) including asthma triggers are challenging to examine in large populations. We investigated the influence of housing and IHEEs on lung function among children with asthma visiting a safety net hospital.

Methods: We merged clinical lung function data from electronic health records (EHRs) for 1,070 children from Boston Medical Center to publicly available geospatial data on housing and census tract characteristics and previously predicted probabilities of IHEEs – indoor cockroach and rodent presence. We fit two Bayesian hierarchical models of percent predicted forced expiratory volume in one second (FEV_1%) with and without IHEEs as latent variables to identify confounders.

Results: The study population had a mean age of 10.2 years, was 58% male, and 75% identified as Black. In fully adjusted models, we found 6.4% lower FEV_1% (95% confidence interval, CI: -9.3%, -3.5%) from a one-unit increase in the log odds of the probability of cockroach presence, and no significant association with rodents (point estimate: -0.1, 95% CI: -3.5%, 3.4%). Living in public housing, housing built before 1950 and after 1980, were associated with 5.1% (95% CI: 1.6%, 8.6%), 5.8% (3.7%, 7.9%), and 2.7% (95% CI 0.0%, 0.6%) higher FEV_1%, respectively. Living in a Black residentially segregated census tract was associated with 3.9% lower FEV_1% (95% CI: -6.4%, -1.4%).

Discussion: In this safety net population of children with asthma, cockroach allergen presence predicted from EHRs and geospatial housing and neighborhood characteristics such as housing age and racial residential segregation were associated with differential lung function. Our unique approach provided evidence that IHEEs confounded the relationship between housing, neighborhood characteristics, and lung function. Observational environmental epidemiological studies can articulate the health effects of underlying and modifiable indoor environmental exposures.

Environment/climate change

Drinking Water Arsenic and Blood Hemoglobin among Women in Rural Northern Bangladesh: Comparing Associations in Pregnancy and Postpartum Tyler J. S. Smith* Jessie P. Buckley Ana Navas-Acien Alexander van Geen Rebecca C. Fry Hasmot Ali Rezwanul Haque Saijuddin Shaikh Towfida Jahan Siddiqua Kerry Schulze Keith P. West Jr. Alain B. Labrique Christopher D. Heaney

BACKGROUND: Arsenic exposure has been negatively associated with hemoglobin (Hb) in adults, but evidence in pregnancy is mixed. Hb determinants may differ during pregnancy given profound changes in hemodynamics (*e.g.*, plasma volume expansion). We compared associations between drinking water arsenic and blood Hb in pregnancy and postpartum among women in rural northern Bangladesh, where prevalence of iron deficiency is low.

METHODS: We enrolled pregnant women (n=784) in the early second trimester (median [IQR] gestational week: 14 [13-15]) in Gaibandha District, Bangladesh, 2018-2019. We measured drinking water arsenic (w-As) and iron (w-Fe) by ICPMS and Hb by real-time assay. In women with singleton live births (n=722) and complete data, we used linear regression to estimate mean differences in Hb per IQR-unit difference in w-As at enrollment (Visit 1; n=719), ~28 days post-enrollment (Visit 2; n=698), <1 month postpartum (Visit 3; n=527), and 3 months postpartum (Visit 4; n=551), adjusting for w-Fe, age, gestational week (Visits 1 and 2), parity, education, living standards index, mid-upper arm circumference, and husband's smoking.

RESULTS: Median (IQR) w-As was 5.27 (0.48, 25.0) µg/L. Median (IQR) Hb was 11.8 (11.2, 12.4), 11.3 (10.7, 11.9), 11.7 (10.7, 12.8), and 12.3 (11.7, 12.9) at Visits 1-4, respectively. Unadjusted and adjusted mean differences (95% confidence intervals [CI]) in Hb (g/dL) per IQR-unit difference in w-As were 0.23 (0.11, 0.36) and 0.25 (0.07, 0.43) at Visit 1, 0.22 (0.10, 0.33) and 0.21 (0.04, 0.38) at Visit 2, 0.41 (0.19, 0.64) and 0.10 (-0.23, 0.43) at Visit 3, and 0.18 (0.03, 0.32) and 0.05 (-0.16, 0.25) at Visit 4. The difference between unadjusted and adjusted postpartum estimates was due mostly to w-Fe adjustment.

CONCLUSION: After adjustment, w-As was positively associated with Hb in pregnancy but not postpartum. Pregnancy-specific mechanisms (*e.g.*, reduced plasma volume expansion and hemodilution) should be evaluated.

Environment/climate change

Cross-sectional associations of urinary phthalate and serum PFAS biomarkers with serum total 25 hydroxyvitamin D levels in childhood: The HOME Study Taylor M. Etzel*, Katherine Marquess Taylor Etzel Bruce Lanphear Andrew Hoofnagle Kim Cecil Aimin Chen Yingying Xu Kimberly Yolton Heidi Kalkwarf Joseph Braun Jordan Kuiper Jessie Buckley Taylor M. Etzel

Background: Exposure to endocrine disrupting chemicals, such as phthalates and per-/poly-fluoroalkyl substance (PFAS), may disrupt vitamin D metabolism and adversely affect health. These relations have been assessed in adults but not children. We investigated associations of urinary phthalate and serum PFAS biomarker concentrations with serum total 25 hydroxyvitamin D [25(OH)D] levels at ages 8 and 12 years in the HOME Study.

Methods: We performed a cross-sectional analysis of data on 233 children of women enrolled during pregnancy in a prospective cohort study in Cincinnati, OH (2003-2006). We measured 9 phthalate metabolites in spot urine samples and 4 PFAS and total 25(OH)D in serum samples collected at ages 8 (n=186) and 12 (n=186). We categorized children as vitamin D deficient if total 25(OH)D was <20ng/mL (age 8: 15.6%, age 12: 32.3%). Using generalized estimating equations to account for repeated measures within-child, we estimated differences in 25(OH)D (linear regression) and odds of vitamin D deficiency (logistic regression) per interquartile range (IQR) increase in concurrent log2 biomarker concentrations. We also used quantile-based g-computation to estimate associations of a simultaneous IQR increase for all phthalate and PFAS biomarkers with vitamin D outcomes. We adjusted for covariates such as race, sociodemographics, BMI z-score, diet, and season.

Results: Urinary phthalate metabolite and serum PFAS concentrations were weakly associated with higher total 25(OH)D and lower odds of vitamin D deficiency though most confidence intervals crossed the null. In mixtures analyses, an IQR increase in all phthalate and PFAS biomarkers was associated with 6.3 ng/mL (95% CI: 2.9, 9.8) higher total 25(OH)D and 0.3 (95% CI: 0.2, 0.8) times the odds of vitamin D deficiency.

Conclusions: Combined phthalate and PFAS exposure was associated with higher total 25(OH)D levels and lower odds of vitamin D deficiency in HOME Study children.

Fertility and fecundity

Differences in Assisted Reproductive Technology Use among Cisgender Women with Same-Sex versus Different-Sex Partners: Findings from a Prospective Cohort across the U.S.

Kodiak Soled* Tabor Hoatson Brent Monseur Bethany Everett Aimee Huang Colleen Reynolds Payal Chakraborty Sarah McKetta Sebastien Haneuse Brittany Charlton

Background: Women with same-sex partners form biological families in myriad ways, including through sexual intercourse, and, for those without access to sperm, social networks and medically assisted reproductive technology (ART). Emerging evidence suggests this population increasingly wants to form biological families, yet little is known about their ART use.

Methods: The Growing Up Today Study is a longitudinal cohort based in the U.S. (n=27,805). Participants were 9–16 years of age at baseline (1996 initial enrollment) and biennial follow-up is ongoing. We identified cisgender women with same-sex and different-sex partners and assessed ART use using logistic models, accounting for participant clustering using generalized estimating equations. We also assessed pregnancy status, conception attempts, and ART methods.

Results: A sizable portion of participants were pregnant or trying to conceive in 2019 (15% of those with same-sex partners vs 26% of those with different-sex partners). Nearly 80% of pregnant participants with same-sex partners (n = 29) used ART from 2005 – 2019 compared to 17% of those with different-sex partners (n = 588; $p<0.0001$). Among participants who used ART, those with same-sex partners used different ART methods compared to those with different-sex partners ($p<0.0001$); differences were largest for intrauterine insemination (55% among those with same-sex partners vs 21% among those with different-sex partners), gamete/zygote intrafallopian transfer (7% vs 0%), intracytoplasmic sperm injection (7% vs 11%), and ovulation medication alone (0% vs 30%).

Conclusions: A bourgeoning number of cisgender women with same-sex partners are forming biological families and using ART more often than their peers with different-sex partners to achieve this. Differences in ART methods reflect different clinical needs (e.g., ovulation medications alone indicate infertility). Providers need to be prepared to competently care for this growing population.

Fertility and fecundity

Life course economic hardship and fecundability Molly Hoffman* Collette Ncube Sharonda Lovett Ruth Geller Chad Coleman Amelia Wesselink Lauren Wise

Background: The influence of life course economic hardship on fertility is not well studied.

Methods: We examined the association between life course economic hardship and fecundability (per-cycle probability of conception) among 6,014 participants enrolled in Pregnancy Study Online, a North American preconception cohort study. We estimated fecundability from follow-up questionnaires completed every 8 weeks. Beginning in 2019, we invited past and current participants to complete a supplemental questionnaire about adversity across the life course. Economic hardship was defined by self-report of “not having enough money to pay for food, rent, or mortgage,” “having to borrow money to pay for medical expenses,” or “receiving public assistance or welfare” in the following life stages: childhood (age ≤11), adolescence (ages 12-17), and adulthood (age ≥18). Current wealth was defined by self-reported length of time participants could maintain their standard of living and stay in their home had they suddenly lost all sources of household income. We used proportional probabilities regression models adjusted for age and socio-demographic factors to estimate fecundability ratios (FRs) and 95% confidence intervals (CI).

Results: Economic hardship (ever vs. never) was associated with reduced fecundability (FR=0.90; 95% CI 0.84-0.95). Fecundability was further reduced among those who experienced economic hardship in all life stages (FR=0.83; 95% CI 0.75-0.92) and adulthood only (FR=0.87; 95% CI 0.80-0.95). Compared with those who could maintain their standard of living for >1 year had they lost all sources of income, those able to maintain their standard of living for <2 months had slightly lower fecundability (FR=0.92; 95% CI 0.84-1.01).

Conclusions: Life course cumulative exposure to economic hardship, economic hardship in adulthood, and less current wealth were associated with delayed conception.

Fertility and fecundity

Fine particulate matter during susceptible windows of spermatogenesis and impact on semen quality Lindsey M. Russo* J Richard Pilsner Timothy P Canty Neil J Perkins Pauline Mendola Enrique F Schisterman Sunni L Mumford Carrie J Nobles

Background: Studies have suggested a detrimental association between fine particulate matter ($PM_{2.5}$) and semen quality in countries with high levels of air pollution. However, a data gap exists in exploring the relation between $PM_{2.5}$ and semen quality parameters in countries with low to moderate $PM_{2.5}$ levels, such as the U.S.

Methods: We examined the relation between $PM_{2.5}$ and semen quality in the Folic Acid and Zinc Supplementation Trial (FAZST) (2013-2017) in male partners of couples seeking infertility treatment in the Salt Lake City, Utah region (n=2,015). We evaluated four windows of susceptibility to ambient $PM_{2.5}$ during spermatogenesis (Mitosis, Meiosis I-II, Spermiogenesis, Spermiation). Semen quality parameters were assessed at enrollment and at 2-, 4-, and 6-month intervals. $PM_{2.5}$ was abstracted from EPA Downscaler models for the Salt Lake City region and averaged across each susceptible window. Generalized estimating equations and 95% confidence intervals considered four repeated semen sample measures for each participant, and adjusted for season, ambient temperature, and participant characteristics. Season was assessed as a potential effect modifier.

Results: Overall, a 1 µg/m3 increase in $PM_{2.5}$ across the 74-day spermatogenesis window [$PM_{2.5}$ median (IQR): 7.2 (6.0, 9.0) µg/m3] was associated with lower sperm concentration in the warm season (% change: -2.00 (-3.95, -0.01). $PM_{2.5}$ was associated with lower percent motility and percent progressive motility in the warm season, particularly during spermiation [% progressive motility, aMD: -0.35 (-0.60, -0.10)] and spermiogenesis [aMD: -0.60 (-0.89, -0.32)], the periods where sperm acquire motility due to epididymal transit. No clear associations were observed between $PM_{2.5}$ and morphology, or with motility in the cold season.

Conclusion: Findings from this study help fill in the research gap showing low to moderate concentrations of $PM_{2.5}$ exposure in the U.S. may impact the spermatogenesis developmental process.

Fertility and fecundity

Dietary supplement use in relation to markers of ovarian reserve and response to controlled ovarian hyperstimulation among oocyte donors Audrey Gaskins*, Robert Hood Heather Hipp Jacqueline Lee Zsolt Nagy Daniel Shapiro Audrey Gaskins Audrey Gaskins

Studies among infertile women undergoing autologous in vitro fertilization suggest that certain dietary supplements may have beneficial effects on ovarian reserve and oocyte quality; however, the evidence is sparse. No studies have been conducted among young, healthy women. Our objective was to examine the association of dietary supplement use with markers of ovarian reserve and response among nonidentified oocyte donors.

We included 598 oocyte donors who underwent 957 ovarian stimulation cycles at a private fertility clinic in Georgia (2008-2021). Donors provided information on demographic, reproductive, and lifestyle characteristics, including current supplement use prior to their first retrieval. Antral follicle count (AFC) was measured with transvaginal ultrasonography on cycle day 3. Following controlled ovarian hyperstimulation and oocyte retrieval, the mature oocytes were vitrified. Generalized estimating equations with a Poisson distribution and robust standard errors were used to examine the associations of dietary supplements to AFC and number of mature oocytes retrieved adjusted for age, body mass index, race/ethnicity, parity, exercise, education, and year.

The oocyte donors had a mean age of 25.8 years and 72% identified as White. The median AFC and number of mature oocytes retrieved was 35 and 23, respectively. Use of dietary supplements was low: only 16% reported multivitamin use, 4% reported B vitamin use, and <2% reported vitamin C, fish oil, calcium, or vitamin D use. Most of the dietary supplements were not associated with AFC or mature oocyte count. Women who used fish oil supplements had significantly higher AFC (% difference: 20.6; 95% CI 3.2, 41.0) and number of mature oocytes retrieved (% difference: 55.3; 95% CI: 27.9, 88.6) compared to women who reported no fish oil supplement use.

Our results suggest that fish oil supplementation may positively influence ovarian function, even among young, healthy women.

Fetal loss/stillbirth/infant mortality

Investigating the Patterns and Determinants of Pregnancy Loss: The Unique Opportunity of a Preconception Cohort in Pakistan Michelle Dimitris* Sajid Soofi Arjumand Rizvi Yaqub Wasan Imran Ahmed Zulfiqar Bhutta

Introduction: Pregnancy loss is the outcome of approximately 30% of conceptions. Early pregnancy losses are often systematically missing from datasets, which may bias studies of prenatal exposures and postnatal outcomes. We examined the patterns and determinants of pregnancy loss in a population-based cohort in rural Pakistan. **Methods:** The Matiari Empowerment and Preconception Supplementation Study (MaPPS), of which our study is an extension, was a cluster randomized-controlled trial that investigated the effect of preconception multiple micronutrient supplementation on nutrition and birth outcomes. The MaPPS trial quarterly monitored women aged 15-24, regardless of pregnancy intent, for ongoing pregnancy. We examined risk of pregnancy loss by gestational age, and stratified risk curves by pre-pregnancy characteristics. **Results:** Among 17048 consenting households in which 25447 eligible women lived, we analyzed 4401 pregnancies of which 377 ended in pregnancy loss (243 miscarriages/abortions and 134 stillbirths). Mean (standard deviation) gestational age at pregnancy detection was 8.9 (3.7) weeks among those that ended in miscarriage/abortion, 14.7 (7.0) weeks among stillbirths, and 14.5 (6.9) weeks among livebirths. Accordingly, we calculated risk of loss by allowing pregnancies to contribute follow-up time from: a) 0 weeks gestational age and b) the gestational age at pregnancy detection. Risk of pregnancy loss tended to decline from 8 to 20 weeks gestational age, though absolute risks differed by method of calculation; risks ranged from 0.3-1.2% at 8 weeks and 0.2-0.3% at 20 weeks. Preliminary results indicated that this pattern differed by pre-pregnancy self-reported health status. **Conclusion:** In this population-based cohort, the risk of pregnancy loss was highest at the lowest gestational ages, and steadily decreased to mid-pregnancy. Our completed study may provide insight on the correlates of pregnancy loss, and whether it is amenable to intervention.

Gender and sexual identity

Covariate Adjustment in LGBTQ+ Health Disparities Research: Aligning Methods with Assumptions Colleen Reynolds* Jarvis Chen Brittany Charlton

In 2016, the NIH designated LGBTQ+ individuals (i.e., lesbian, gay, bisexual, transgender, queer, and all sexual and gender minorities) as a health disparities population. The growing interest in studying the health of LGBTQ+ populations merits revisiting the methodological approaches researchers employ. We elucidate how researchers can identify appropriate adjustment sets for both descriptive and causal questions using directed acyclic graphs (DAGs). To illustrate these points, we simulated a simplified example using pregnancy loss as the outcome, wherein we generate 1,000 datasets with a sample size of 10,000 individuals.

We first argue that in descriptive research, adjustment should be minimal as there are implicit value judgments in adjusting for nuisance variables. Using the example of sexual orientation-related disparities in pregnancy loss, we demonstrate how such adjustment can obscure the magnitude of disparities. Second, we motivate why covariates that are commonly used in LGBTQ+ health disparities research (e.g., health insurance status) are mediators, not confounders, and how adjusting for these variables in causal research can induce bias by blocking part of the indirect effect of exposure on the outcome.

Next, we illustrate the complexity of mediation analyses with social exposures due to mediator-outcome confounding induced by exposure (e.g., adult socioeconomic status), and compare potential approaches, such as inverse probability weighting (IPW) and randomized intervention analogues. Finally, we demonstrate how incorporating heterosexism (i.e., stigma and discrimination) as an unobserved node in our DAG can guide decision-making on appropriate adjustment sets. For example, by eliminating the effects of sexual orientation (i.e., through method of conception) on pregnancy loss using IPW, sexual orientation can be used as a proxy for the discriminatory effects of heterosexism.

Global health

Prediction models for antenatal care attendance in Ethiopia Clara Pons-Duran* Bryan Wilder Frederick G.B. Goddard Bezawit Mesfin Hunegnaw Sebastien Haneuse Delayehu Bekele Grace J. Chan

Background. In low-resource settings, coverage of at least four antenatal care (ANC) visits remains low. As a first step towards enhancing ANC attendance, this study aims to develop a series of predictive models to identify women who are at high risk of failing to attend ANC in a rural setting in Ethiopia.

Methods. This is a cohort study conducted in the Birhan field site, Amhara region. Using data of a surveillance system and a pregnancy cohort, we developed and internally validated a series of logistic regressions with regularization (LASSO), and ensembles of decision trees. Discrimination was estimated using the area under the receiving operator characteristic curve (AUC). Three prediction time points were considered: conception, and gestational weeks 13 and 24. All models were internally validated using 5-fold cross validation to avoid overfitting.

Results. The study sample size was 2195. Mean age of participants was 26.8 years (Standard Deviation [SD] 6.1) and mean gestational age at enrolment was 25.5 weeks (SD 8.8). A total of 582 women (26.5%) did not attend any ANC visits during cohort follow-up. We observed AUC in the range of 0.61-0.70, with higher model performance for ensembles of decision trees (AUC 0.62-0.70), and for models predicting ANC attendance with available data at weeks 13 and 24 (AUC 0.66-0.70).

Conclusion. This study presents a series of prediction models for ANC attendance with modest performance. The developed models may be useful to identify women at high risk of missing their ANC visits to target interventions to improve attendance rates. This study opens the possibility to develop and validate easy-to-use tools to predict health-related behaviors in settings with scarce resources.

Gynecological health

History of endometriosis diagnosis and current quality of life in U.S. women: Results from NHANES 2001-2006 Mandy S. Hall* Natalie Barstys Jennifer Watling Neal Lucy Thompson Sawsan As-Sanie Nicole Talge Arianna Foster Kristen Upson

Endometriosis, a chronic gynecologic condition, can confer substantial pain symptoms, including pelvic pain and dysmenorrhea. As such, endometriosis has been associated with poorer mental health, productivity, and health-related quality of life (HRQOL). Prior studies have mostly been conducted among endometriosis patients in the clinical setting. To investigate the impact of endometriosis on HRQOL in a nationally representative sample of the U.S. population, we conducted a cross-sectional analysis using data from the National Health and Nutrition Examination Survey years 2001-2006. In women ages 20-54 years (unweighted n = 4,232), data were available on four HRQOL “Healthy Days Measures” ascertaining current general health (excellent, very good, good, fair or poor) and number of days in the past month when physical health or mental health was “not good” or when physical or mental health kept one from doing usual activities, such as self-care and work. History of endometriosis diagnosis was obtained by self-report. We conducted log-binomial regression to estimate the prevalence ratios (PR) and 95% CIs between endometriosis and HRQOL measures, adjusting for age, education, smoking, and body mass index. The prevalence of endometriosis diagnosis was 9% (unweighted n=296). Those with a history of endometriosis diagnosis had a 20% increased prevalence of fair/poor health status (PR 1.2, 95% CI: 1.0-1.6), ≥14 physically unhealthy days (PR 1.2, 95% CI: 0.9-1.8), and ≥14 mentally unhealthy days (PR 1.2, 95% CI: 0.8-1.7) in the past month. History of endometriosis diagnosis was associated with a 70% increased prevalence of ≥14 inactive days in the past month due to poor physical or mental health; those diagnosed with endometriosis ≥10 years ago (vs. no endometriosis) had twice the prevalence of ≥14 inactive days (PR 2.0, 95% CI: 1.2, 3.5). These results highlight the substantial impact of endometriosis on current HRQOL in U.S. women, warranting further investigation.

Health equity

Respectful Maternity Care Collaborative: Top 10 Research Priorities to Eliminate Black Maternal Health Disparities Afua Nyame-Mireku* LaTasha Snell Gatling Zainab Jah Susan Perez Yasmine Griffiths Carmen Green

Background: Black birthing people are often excluded from lead or partnering roles in research despite often being included as subjects. This causes a missed opportunity for Black birthing people to develop research topics that are important to them. The National Birth Equity Collaborative (NBEC) has established the Respectful Maternity Care Collaborative (RMCC), a formalized partnership of stakeholders where Black birthing people initiate, design, and lead research initiatives. The RMCC developed a research agenda for Black maternal health based on the knowledge and experiences of Black birthing people and stakeholders.

Methods: From February 2022 to April 2022, NBEC distributed *The Future of Black Birthing Research*, a survey on eradication strategies for Black maternal health disparities, to NBEC staff, birth equity stakeholders, and the general public via social media and email. The qualitative survey results were thematically analyzed to identify research priorities. In October 2022, NBEC hosted the RMCC Virtual Convening, a convening of Black birthing people and stakeholders, to prioritize the survey themes and develop a research agenda that addresses the Black maternal health crisis.

Results: Ten research priorities were identified (1 = Highest priority, 10 = Lowest Priority): 1) Systemic Change, 2) Full Spectrum Perinatal Care Integration, 3) Culturally Safe Care, 4) Personal Decision-Making, 5) Birth worker and Healthcare Professional Pipeline 6) Investing and Funding, 7) Listening and Supporting Black Birthing People and their Villages, 8) Availability and Access to Respectful and Quality Perinatal Care, 9) Accessible and Respectful Education and Resources, and 10) Professional Development.

Conclusions: The RMCC is a model for building knowledge and opportunities for Black birthing people to be equitable partners in research. This research agenda should be elevated and used to develop research that eliminates maternal disparities.

Health equity

Experiences of discrimination in a North American preconception cohort study Sharonda M. Lovett* Lauren A. Wise Renée Boynton-Jarrett Jasmine Abrams Amelia K. Wesselink Chad M. Coleman Ruth J. Geller Andrea S. Kuriyama Molly N. Hoffman U. Vivian Ukah Erika L. Sabbath Collette N. Ncube

Background: Experiences of discrimination perpetuate social and economic adversities, which may have detrimental effects on reproductive outcomes. We characterized patterns of self-reported discrimination in a preconception cohort.

Methods: Beginning in 2019, we invited former and current participants of Pregnancy Study Online to complete a supplemental questionnaire with items adapted from Williams' Major Experiences of Discrimination and Everyday Discrimination scales, and Krieger's instrument on coping with discrimination. Participants self-identified as female, were aged 21-45, residents of the U.S. or Canada, and trying to conceive without fertility treatment. We conducted a descriptive analysis among 7,443 respondents to describe patterns in experiences of discrimination, including attributions and coping strategies.

Results: Overall, 49% of participants reported ≥1 experience of lifetime discrimination and 83% reported ≥1 experience/year of everyday discrimination. Most Black participants reported 'race or ethnicity' as one of the main attributions for their experiences of discrimination (79%), while 'sex or gender' was the most common attribution reported by all other race and ethnicity groups (range: 67-68%). The most frequently reported type of lifetime discrimination was 'job (hiring, promotion, firing)' (35%), followed by 'school' (23%) and 'getting medical care' (15%). Reports of everyday discrimination (≥1 times/year) included being 'treated with less courtesy or respect' (64%), others 'acting as if you are not smart' (64%), being 'threatened or harassed' (55%), 'receiving poorer service than others' (36%), and others 'acting as if they are afraid of you' (16%). Among those reporting any discrimination, 58% reported 'talking to others' and 71% reported 'accepting experiences as a fact of life.'

Conclusions: These data show a high prevalence of experiences of discrimination among pregnancy planners, with attributions that varied by race and ethnicity.

Health equity

Socio-structural correlates of non-barrier contraceptive access among sex workers in Vancouver, Canada: Findings from a longitudinal cohort study (2010-2021) Emma Stirling-Cameron* Andrea Krüsi Jennie Pearson Charlie Zhou Esteban Valencia Shira Goldenberg

Background: Women sex workers (SWs) face substantial health inequities, including a high burden of unintended pregnancy. Migrant women are overrepresented in precarious employment, including sex work, and face additional barriers to healthcare due to intersecting socio-structural factors including immigration status, stigma, and criminalization. Given limited epidemiological evidence regarding socio-structural barriers to non-barrier contraceptive access—including the role of migration—we examined socio-structural factors associated with contraceptive access among a prospective cohort of women SWs in metropolitan Vancouver, Canada, from 2010-2021.

Methods: Baseline and semi-annual questionnaire data were drawn from an open, community-based cohort of women SWs (January 2010 – September 2021). Complete case bivariate and multivariable logistic regression using generalized estimating equations (GEE) modeled socio-structural correlates of experiencing difficulties accessing contraceptives in the past 6 months, including the role of migration timing. Non-barrier contraceptive use included pills, IUDs, injectables, end emergency contraception.

Results: Analyses included 7340 observations among 958 SWs. Over the course of follow-up, 22.4% of participants (n = 214) reported difficulties in accessing non-barrier contraceptives.Multivariable GEE analysis indicated recent (<5 years; AOR: 1.84, 95% CI: 1.09, 3.08) and long-term migrants to Canada (>5 years; AOR: 1.14, 95% CI: 0.78, 1.68) faced higher odds of experiencing difficulties accessing non-barrier contraceptives. Self-reported regular healthcare access (AOR: 0.66, 95% CI: 0.45, 0.95) and age (AOR: 0.95, 95% CI: 0.94, 0.96) were associated with lower odds of experiencing barriers to contraceptives.

Conclusion: To address enhanced barriers to contraceptive access among migrant women in sex work, there is a critical need to scale-up of newcomer-specific, culturally-safe, and confidential sexual and reproductive health services, alongside structural interventions to decriminalize and destigmatize sex work.

Infectious disease

Epidemiologic Characteristics of Clostridioides difficile in Pediatric Patients in Tennessee

Jasmine Watkins* Glodi Mutamba Mike Norris Daniel Muleta Christopher Wilson

Tennessee conducts population based *Clostridioides difficle* (CDI) surveillance as part of CDC's Emerging Infections Program (EIP). Pediatric cases are a small percentage of all CDI cases causing data to be scarce. Surveillance data from 2016-2020 were studied for cases ≤19 years of age. An incident case is a laboratory confirmed *C. difficile* test for a person residing in Davidson County that is ≥1 year old. Healthcare facility onset (HCFO) cases were defined as a case where incident stool was collected ≥3 days after admission to a hospital or in a long-term care facility resident; all other cases are community onset (CO). CO cases are classified as community-associated (CA) or healthcare facility associated (CO-HCFA). CO-HCFA cases had an overnight stay in a healthcare facility ≤12 weeks prior to the date of incident stool collection (DISC). 202 of 3723 (5.4%) cases were pediatric cases. 99 cases were male (49.1%); 103 cases were female (50.9%). 30 cases were (46.2%) ≤5 years old; 35 (53.8%) cases were 6 to 19. Nucleic acid amplification test (NAAT) was the most common testing method (191/202 [94.5%]). 62 (30.7%) cases had an underlying condition; infectious bowel diseases were the most common (18/202 [9%]). 100 (49.5%) cases received antimicrobial therapy ≥12 weeks to DISC. 3 (1.5%) cases were reported deceased; all were HCFO cases. The average time between DISC and death was 102 days. Cases were more likely to be classified as CO than HCFO (185/202 [91.6%] versus 17/202 [8.4%], $P<0.0001$). Cases were more likely to be classified as CO-CA than CO-HCFA (171/202 [84.7%] versus 31/202 [15.3%], $P<0.0001$). 65/202 (14.9%) cases were prescribed antibiotics; metronidazole was prescribed more than vancomycin (35/65 [53.9%] versus 30/65 [46.1%], $P=0.3805$). The trend of CDI cases among pediatric population need to be monitored. Improved infection prevention and community education are needed to reduce community onset infection rates

Mental health

Maternal Postpartum Depressive Symptoms and Infant Growth Indices Xuanxuan Zhu* Jihong Liu Prema S Bhattacharjee Bo Cai Sara Wilcox

Background. Previous studies are inconclusive about associations between maternal postpartum depression and infant growth. Most studies have examined major postpartum depression and ignored subclinical postpartum depressive symptoms. Further, many studies have focused on mothers with normal pre-pregnancy body mass index, even though women with overweight/obesity are more likely to have elevated postpartum depressive symptoms. This study aims to evaluate the longitudinal effect of maternal depressive symptoms among overweight/obese mothers on infant growth in the first year of life.
Methods. Data came from a randomized controlled trial designed to promote healthy weight gain during pregnancy and postpartum weight loss among women who were overweight/obese before pregnancy. The Edinburgh Postpartum Depression Scale (EPDS) assessed depressive symptoms at 6 months after delivery. Infants' weight, length, head circumference, arm circumference, triceps skinfold, and subscapular skinfold were measured at 6- and 12-postpartum months. Their z-scores were obtained to show the growth indices. Linear mixed models were used to assess the aforementioned association.
Results. Of 170 mother-infant dyads, the mean age of mothers was 29.9 years (± 5.0) with 43.5% being Black. The mean EPDS score was 4.1 (± 4.2). After adjusting for covariates, EPDS scores were negatively associated with infants' mean of length-for-age z-scores at 12-months of age (β = -0.05, 95% Confidence Interval: -0.09, -0.01, p-value = 0.01). Maternal depressive symptoms were not associated with other infant growth indices at either 6- or 12- months postpartum.
Conclusion. Having more postpartum depressive symptoms was negatively associated with infant's length during the first year of life. It is necessary to raise awareness among women and their families to pay more attention to maternal mental health since better mental health is not only good for mothers but also translates to better growth outcomes for infants.

Mental health

Past 30-day suicide attempts among women ages 18–55 years with past 30-day nonmedical prescription opioid use Emily Kobernik* Carla DeSisto Laura Welder Madison Levecke Mishka Terplan Jean Ko

Background: The opioid overdose crisis continues to be a public health concern and rates of suicides with opioid-involvement have increased over time.

Objective: To describe the prevalence of and factors associated with past 30-day suicide attempt and past 30-day suicide attempt only when high or in withdrawal from alcohol or drugs among women with past 30-day nonmedical prescription opioid use.

Methods: Estimates are reported among women 18–55 years with self-reported past 30-day nonmedical prescription opioid use from 338 locations in 35 states using January 2018–December 2020 National Addictions Vigilance Intervention and Prevention Program data. Bivariate analysis and multinomial logistic regression models identified factors associated with past 30-day suicide attempt and past 30-day suicide attempt only when high or in withdrawal from alcohol or drugs.

Results: Among 10,095 women with past 30-day nonmedical prescription opioid use, 2.7% reported a suicide attempt, and 1.5% reported a suicide attempt only when high or in withdrawal from alcohol or drugs. Non-Hispanic Black women reported the highest rate of suicide attempt (4.5%), and American Indian/Alaska Native women reported the highest rate of suicide attempt only when high or in withdrawal from alcohol or drugs (2.7%). The strongest measures of association for suicide attempt and suicide attempt only while high or in withdrawal from alcohol or drugs, respectively, were an extreme alcohol problem as defined in the dataset (adjusted odds ratio [aOR] 2.84, 95% confidence interval [CI]: 1.80–4.47), and no stable living arrangement (aOR 2.66, 95% CI: 1.78–3.98).

Conclusions: These results provide insight on suicide attempts among reproductive-age women misusing opioids and may help address population-specific risk and protective factors and tailoring culturally relevant, upstream public health interventions for groups disproportionately affected by opioid misuse and non-fatal suicide attempts.

Methods

A novel quantification technique for intervillous fetal vasculature of the placenta Andrea Kozai* Lauren Skvarca W. Tony Parks Abbi Lane Bethany Barone Gibbs Janet Catov

Introduction: The placenta is responsible for nutrient transfer throughout pregnancy and is implicated in adverse pregnancy outcomes (APOs) due to structural adaptations that impact perfusion and fetal angiogenesis. Maternal vascular malperfusion (MVM) lesions are often found in placentas from APOs, but these lesions are only described dichotomously as “present” or “absent”. Continuous metrics of placental structure are needed to characterize placental health and function.

Methods: Tissue sections (N=64) of formalin-fixed, paraffin-embedded human placenta from live births were obtained from a biobank repository and stained with CD34 antibody to highlight vascular endothelial cells and hematoxylin to highlight villous tissue. The Aperio ImageScope Positive Pixel Count algorithm quantified pixels positive for CD34 antigen (numerator) and total pixels (denominator); the ratio represented the proportion of villous space occupied by vascular endothelium. Two ratio calculations were employed: all villous tissue (Whole Slide protocol), and four 600μm^2 areas of intermediate and terminal villi (Quadrant protocol). Both protocols were evaluated for effect sizes associated with smoking status (ever vs never, self-report) and subtypes of MVM lesions (pathology report abstraction, n=30).

Results: Ratios (mean$\pm$SD) were significantly higher using the Quadrant protocol compared to the Whole Slide protocol (0.31$\pm$0.06 vs 0.27$\pm$0.05, $p<0.01$) but the protocols were strongly correlated ($r=0.84$). Any subtype of MVM lesion was noted in 15 of 30 pathology reports. Effect sizes for associations were similar between protocols. Medium effect sizes were found for smoking, accelerated villous maturation, and small placental size (Cohen’s *d* ranges 0.48-0.58).

Conclusion: This method provides continuous quantification of fetal vasculature in the placenta. Future research can examine this measure with relation to markers of pregnancy health and placental function.

Methods

Recruitment and Retention of Longitudinal Prenatal and Postpartum Survey Cohorts

Montana Hunter* Elysia Larson

Background: Recruitment and retention of birthing cohorts may require specific strategies given the distinct physical and mental burdens experienced by this population.

Methods: We evaluated the participant- and program-level factors that impact attrition and retention of aprospective longitudinal cohort consisting of patients receiving prenatal care at a large academic hospital in Boston, MA from April 2020 to present and who gave birth after February 2020. Prenatal participants were offered an initial prenatal survey and follow-up surveys every 5 weeks until delivery, as well as one postpartum survey sent 5-7 weeks after delivery. Risk ratios (RR) and confidence intervals (CI) were computed.

Results: Of prenatal (n=2,025) and postpartum (n=2,217) participants approached, 797 (39.4%) and 696 (31.4%) enrolled in the study, respectively. Prenatal participants that only received a phone call reminder as compared to those that only got an email reminder were 2.82 time as likely to complete the survey (95% CI: 2.17-3.65) while postpartum participants with only a phone reminder were 0.86 times as likely to complete the survey compared to those that only got an email (95% CI: 0.80-0.93). Both cohorts responded well to lottery-style incentives, with over 50% of recruited participants responding to survey(s), No incentive resulted in ~30% survey completion for both cohorts while receiving guaranteed gift cards had mixed effects with 25.0% prenatal and 51.8% postpartum survey completion. Postpartum participants were more likely to complete surveys late evening and early morning than prenatal cohorts. Non-white participants were 0.64 times as likely to complete a prenatal survey (95% CI: 0.43-0.97) and 0.77 times as likely to complete a postpartum survey (95% CI: 55-1.08) as white participants.

Conclusions: Reminder methods and specific incentive structures may increase survey response and retention during the perinatal period

Nutrition/obesity

Prenatal dietary patterns and infant weight trajectories from the 3rd trimester to 2 years of age Nan Ji* Luis Maldonado Mark Johnson Sandrah Eckel William Gauderman Thomas Chavez Dema Faham Brendan Grubbs Deborah Lerner Rima Habre Shohreh Farzan Theresa Bastain Carrie Breton

Background/Aims: Although maternal diet during pregnancy has been associated with fetal and newborn development, few diet studies have evaluated in utero growth measures and postnatal weight trajectories along a continuum. This study aims to (1) assess associations between prenatal dietary patterns and weight trajectories from the 3rd trimester through 2 years of age; and (2) determine whether these associations vary by gestational complications (diabetic and/or hypertensive disorders).

Methods: Fetal weights during the 3rd trimester were abstracted from maternal ultrasound records for the women participating in the Maternal and Developmental Risks from Environmental and Social Stressors (MADRES)—a pregnancy cohort of predominantly low-income Hispanic/Latina women in Los Angeles. Infant weight measures were abstracted from medical records. Two maternal dietary patterns previously identified in MADRES participants were examined in relation to weight trajectories using piecewise linear spline models (N=398). The first dietary pattern included a higher intake of vegetables, oils, and fruits (VOF). The second dietary pattern included a higher intake of solid fats, refined grains, and cheese (SRC).

Results: In the whole population and those without gestational complications, both VOF and SRC were associated with decreased growth from the 3rd trimester to age 3 months. For women with gestational complications, comparing to the lowest quartiles, the growth rate from the 3rd trimester to age 3 months was significantly decreased in children of mothers in the 4th quartile of VOF pattern scores, but significantly increased in children of mothers in the 3rd quartile of SRC pattern, with relative changes in growth of 0.66% [95%CI 0.48%, 0.92%] and 1.50% [95%CI 1.07%, 2.10%], respectively.

Conclusion: Both dietary patterns during pregnancy could impact infant weight gain trajectories, with a stronger impact on early infancy. These associations vary by gestational complications.

Nutrition/obesity

Experience and transmission of past, current, and child food insecurity Marisa Tsai* Elissa Epel Janet Tomiyama Cindy Leung Mahasin Mujahid Hilary Hoynes Barbara Laraia

Food insecurity (FI) is associated with poorer physical and mental health outcomes across the life course. However, there is limited research showing how FI changes, both across an individual's life course and intergenerationally, and what factors affects its transmission. This study examines the dynamics of FI transmission and assesses potential familial and socioeconomic moderators.

The National Heart, Lung, and Blood Institute (NHLBI) Growth and Health Study is a longitudinal cohort study of mothers (n=624, ages 36-43 years) and their children (n=645; n=331 were over 10 years old, ages 10-17 years). Data were collected between 1987-2019. Three validated measures for FI were used: the Past Food Insecurity Scale was used to assess FI of the mothers during their childhood; the 18-item USDA household food security module measured current household FI of the mothers in adulthood; and the Child Food Security Assessment assessed current child-reported FI for children over 10 years old. In pre-registered analyses, associations between past maternal FI and current maternal FI, current maternal FI and current child FI, and past maternal FI and current child FI were examined using hierarchical multivariate logistic regression, controlling for sociodemographic factors (e.g., income, education, race, marital status). Moderation by SES (e.g., education, income) and marital status was also assessed.

Among mothers, FI was reported by 32.42% for past maternal FI and 22.46% for current maternal FI. Among children, 53.17% reported current child FI. Past maternal FI was associated with current maternal FI (OR: 5.57, 95% CI: 3.25,9.54). Current maternal FI was associated with current child FI (OR: 2.07, 95% CI: 1.10,3.89). However, past maternal FI did not predict current child FI, and there was no evidence of moderation by sociodemographic factors.

Results suggest that FI may be perpetuated through the life course and intergenerationally.

Nutrition/obesity

Di(2-ethylhexyl) terephthalate partially mediates associations of maternal diet quality with mid-pregnancy glucose homeostasis DIana Pacyga* Diana Pacyga Joseph Braun Susan Schantz Rita Strakovsky

Background: Healthy diets support pregnancy and fetal health, but diet is also a major source of chemicals, including the plasticizer di(2-ethylhexyl) terephthalate (DEHTP), to which pregnant women are increasingly exposed. We previously observed higher DEHTP was associated with worse maternal glucose homeostasis. Currently, we evaluated associations of maternal diet quality with glucose homeostasis and mediation of this relationship by DEHTP.

Methods: At 13 weeks gestation, 295 Illinois women with relatively high socioeconomic status completed a food frequency questionnaire (reflecting the prior 3 months) to calculate the Alternative Healthy Eating Index 2010 (AHEI-2010). We quantified two DEHTP metabolites from pools of five first-morning urines collected monthly at 13-34 weeks gestation. We measured 16 metabolic biomarkers in fasting plasma samples collected at 17 weeks gestation, which we reduced to five uncorrelated principal components (PCs): glucose homeostasis, cholesterol, lipids, insulin, and inflammation. Adjusted linear regression models evaluated associations of AHEI-2010 with metabolic PCs and molar-summed DEHTP metabolites. We tested if DEHTP partially mediated associations of AHEI-2010 with metabolic PCs using the causal mediation framework.

Results: Overall, each 10-point increase in AHEI-2010 (indicating better diet quality) was associated with 0.2 (95% confidence interval (CI): 0.1, 0.3) lower (more favorable) glucose homeostasis PC scores, but not with the other PCs. Each 10-point increase in AHEI-2010 was also associated with 17.2% (95%CI: 5.4, 27.6) lower urinary DEHTP levels. In mediation analyses, lower DEHTP levels explained 11.7% of the association between better AHEI-2010 and lower glucose homeostasis PC scores.

Conclusion: Our results suggest associations of better maternal diet quality with favorable mid-pregnancy glucose homeostasis can be partially attributed to lower DEHTP exposure, which should be corroborated in other populations.

Nutrition/obesity

Associations of maternal first-trimester diet quality with gestational weight gain Kelsi Morris* Diana Pacyga Sue Schantz Rita Strakovsky

Background: Pregnancy is characterized by higher energy needs, leading to gestational weight gain (GWG) that supports fetal development. However, prior studies evaluating the role of specific dietary patterns in GWG have been mixed/null. Hence, we evaluated associations of maternal diet quality with GWG and considered differences by pre-pregnancy body mass index (ppBMI).

Methods: At median 13 weeks gestation, 456 Illinois women with relatively high socioeconomic status completed a semi-quantitative food frequency questionnaire (reflecting the past 3 months) to calculate the Alternative Healthy Eating Index 2010 (AHEI-2010). We calculated gestational age- and ppBMI-specific GWG z-scores (GWGz, based on an international reference chart) using weight before pregnancy and at median 38 weeks gestation. We calculated ppBMI (kg/m^2) from self-reported pre-pregnancy weight and height, and categorized women as having under-/normal weight (BMI<25), overweight (BMI=25-29.9), or obesity (BMI≥30). Using adjusted linear regression models, we evaluated associations of AHEI-2010 with GWGz and included an interaction term to explore differences by ppBMI.

Results: Women had mean AHEI-2010 scores of 52 points (out of 100; min, max: 26, 79), mean weight gain of 14.8 kg (min, max: -10.9, 38.1) at median 38 weeks gestation, and 23% and 24% had overweight and obesity, respectively. Overall, AHEI-2010 was not associated with GWGz. However, in overweight women, every 10 point increase in AHEI-2010 (reflecting better diet quality) was associated with 0.2 (95% confidence interval (CI): 0.0, 0.4) higher GWGz ($P_{interaction} = 0.16$). AHEI-2010 was not associated with GWGz in women with under-/normal weight (β: 0.0; 95%CI: -0.2, 0.1) or obesity (β: 0.0; 95%CI: -0.2, 0.2).

Conclusions: Only in women with overweight, better maternal diet quality was related to higher pregnancy weight gain. Additional studies should replicate these findings and consider potential implications for maternal and child health.

Nutrition/obesity

Pregnancy weight gain and longer-term cardiometabolic disease Kari Johansson* Lisa M Bodnar Olof Stephansson Jennifer A Hutcheon

Excess pregnancy weight gain could increase a pregnant individual's risk of later cardiometabolic diseases. Yet, current Institute of Medicine (IOM) guidelines for weight gain during pregnancy were established in the absence of evidence on how weight gain is linked with postpartum cardiometabolic health. We aimed to establish the association between pregnancy weight gain and risk of cardiometabolic disease at 4-12 years postpartum.

Our study population included 82,570 deliveries to nulliparous individuals in the population-based Swedish Stockholm-Gotland perinatal cohort, 2008-2015. Pregnancy weight gain was standardized into gestational age-specific z-scores, and categorized as <-2.0, -2.0 to -1.1, -1.0 to -0.6, -0.5 to +0.49 (reference), +0.5 to +0.9, +1 to 1.9, ≥+2.0. New-onset postpartum cardiometabolic disease (type 2 diabetes, hypertension, and cardiovascular disease) occurring up to 2019 was identified from ICD-codes and ATC-codes from national health care registers. The association between pregnancy weight gain and cardiometabolic disease was estimated using BMI-stratified pooled multivariable adjusted log binomial regression to account for differential follow-up times.

Over 4-12 years of follow-up, the rate of cardiometabolic disease was 5% in normal weight, 8% in overweight, 12% in obese class I, and 15% in obese class II and III individuals. In normal weight individuals, risk of cardiometabolic disease became increased as of a z-score of +1 (RR=1.2 [95%CI: 1.1, 1.4] for z-scores +1 to 1.9 and 1.7 [1.4 to 2.1] for z-scores ≥2). Trends were similar in overweight and obese individuals (overweight: RR=1.3 [1.1 to 1.5] and 1.7 [1.2 to 2.4]; obese class I: RR= 1.2 [0.9, 1.6] and 1.8 [1.0, 3.1]), but became imprecise for class II and III obese idivduals.

High pregnancy weight gain is linked with increased risks of longer-term maternal cardiometabolic disease. Pregnancy weight gain recommendations should take risks of this adverse health outcome into account.

Nutrition/obesity

Dietary Food Group Interactions during Pregnancy and Birthweight: Findings from the Maternal And Developmental Risks from Environmental and Social Stressors (MADRES) Study Luis Enrique Maldonado* Claudia Toledo-Corral Genevieve Dunton Tingyu Yang Carrie Breton Shohreh Farzan Theresa Bastain

BACKGROUND

Dietary food group interactions in pregnancy and their role on birthweight have been difficult to capture using traditional statistical methods due to high food collinearity.

METHODS

Participants (n=497) in MADRES – an ongoing, prospective pregnancy cohort of predominantly low-income Hispanic/Latina individuals – completed up to 2 staff-administered 24-hr diet recalls in the 3rd trimester of pregnancy. Birthweight was abstracted from electronic medical records (99.6%); z-scores were estimated using the INTERGROWTH-21st reference. We used 25 MyPyramid food group equivalents in multivariable Bayesian Kernel Machine Regression (BKMR) models on birthweight and assessed dose-response plots of each individual diet factor while fixing a second factor at the 25th, 50th, and 75th percentiles and keeping other foods at their medians. For food pairs that showed evidence of interaction by BKMR, we verified them by testing continuous-by-categorical (tertiles) interaction terms using multivariable ordinary least squares (OLS). We considered $p<0.10$ as potentially meaningful interactions.

RESULTS

Bivariate plots from BKMR models suggested 2-way interactions between citrus fruit and whole grains, processed meats, and between whole- and refined grains. OLS findings showed interactions only between citrus fruit and whole grains ($p=0.095$) and processed meats ($p=0.082$) and between whole- and refined grains ($p=0.084$). Greater whole grain ($\beta=0.19$, 95% CI: 0.01, 0.37) and processed meat ($\beta=0.19$, 95% CI: 0.02, 0.37) intakes were associated with higher birthweight only in the highest citrus fruit tertile, while greater refined grain intake was associated with lower birthweight ($\beta=-0.56$, 95% CI: -0.91, -0.21) only in the lowest whole grain tertile.

CONCLUSION

In pregnancy, citrus fruit and whole grain intake may modify the relationship between other foods and birthweight. BKMR may be valuable for identifying important diet interactions previously missed by traditional methods.

Obstetric health

Identifying and Tracking Intrapartum Transfer Between Birth Facilities: A New Approach with Medicaid Claims Data David Mallinson*, Madelyne Greene Xue Gong David Mallinson HeeJin Kim David Mallinson

People who give birth in low-resource areas are at greater risk for adverse obstetric outcomes. When high-level care is needed, mothers are often emergently transferred from lower-level facilities to higher-level facilities. Little is known about intrapartum maternal transfer between facilities or its impact on obstetric outcomes. We aimed to develop a measure of intrapartum transfer from Medicaid claims, compare it to the birth record indicator of transfer, and describe population patterns in transfer.

Using linked birth records and Medicaid Claims data from Wisconsin residents who gave birth between 2011-2019 (N=235,378), we developed an indicator of intrapartum transfer by identifying the birth hospitalization and then locating claims at a separate hospital on overlapping dates. We described this sample and compared it to individuals with transfer indicated on the birth record. Additionally, logistic regressions estimated the odds of transfer based on NCHS 2013 residence county category and Level of Maternity Care of the originating hospital (I through IV, where IV is highest).

We identified 2,409 transfers in Medicaid claims and 2,466 transfers from birth records. However, only 767 cases had overlapping transfer indication from both sources. Using the claims indicator, people living in rural counties had higher rates of transfer (adjusted odds ratio [OR] 2.06, 95% confidence interval [CI] 1.65-2.57) and most often delivered at a Level III facility. Those who presented to a hospital at any level above I had lower rates of eventual transfer (Level II adjusted OR 0.40, CI 0.43-0.46).

Preliminary evidence from this analysis suggests that our claims-based measure of transfer may be more accurate than the birth record transfer indicator. Further research will evaluate intrapartum transfer in a clinically actionable way and investigate the relationship between intrapartum transfer and severe maternal morbidities. This study is a first step in understanding this understudied phenomenon.

Obstetric health

Disparities in Gestational Diabetes Mellitus by Race/Ethnicity, Nativity, and Pregnancy Pre- and During the COVID19 Pandemic in the United States, 2018 to 2021 Min Kyung Kim* Tamarra James-Todd Lucy Chie MyDzung Chu

Background: Asian American and Pacific Islanders (AAPI) have the highest proportion of foreign-born (FB) residents and also the highest risk of gestational diabetes mellitus (GDM), which may be due to acculturative stress and discrimination. We sought to understand the associations between AAPI race, FB status, and GDM prevalence pre- and during COVID19 to explore whether heightened anti-Asian racism and xenophobia during COVID19 impacted GDM prevalence.

Method: We used the 2018-2021 US National Center for Health Statistics natality administrative dataset (N=14,848,870). FB was proxy for exposure to acculturation-related risk factors and race/ethnicity was evaluated as a social construct for racial discrimination. We calculated prevalence odds ratios (OR) for GDM using multivariable logistic regressions to assess the associations between race/ethnicity, nativity, and GDM by delivery year.

Results: Both AAPI non-Hispanic (NH) and FB women had higher odds of GDM compared to White-NH (OR: 2.21, 95% CI: 2.17, 2.24) and US-born (1.36, 95% CI: 1.36, 1.37) women, respectively, with increased odds for women in both groups ($p_{\text{AAPI-NH + FB interaction}} <0.001$). By delivery year, prevalence of GDM increased significantly from 2018 to 2021 (2018: 6.7%; 2019: 6.9%; 2020: 7.8%; 2021: 8.3%) ($p_{\text{trend}} <0.001$). The association of AAPI-NH race and GDM did not change pre- (2.22, 95% CI: 2.19 2.25) vs. during COVID19 (2.22, 95% CI: 2.18, 2.26). However, the association of FB status and GDM slightly decreased pre- (1.38, 95% CI: 1.36, 1.39) vs. during COVID19 (1.36, 95% CI: 1.34, 1.38) ($p_{\text{interaction}} = 0.07$).

Discussion: AAPI-NH and FB women continued to have the highest risk of GDM compared to their racial/ethnic and US-born counterparts, with slight differences in GDM risk observed during COVID19 for FB women, which could be due to sociopolitical changes. Our findings underscore the need to better understand socio-structural drivers of reproductive health inequities in these populations.

Obstetric health

Risk of early and late-onset preeclampsia burden by race in California Ruofan Yao*, Bo Park
Ruofan Yao Julianne Byun Ruofan Yao

Background: Early onset preeclampsia is thought to be associated with abnormal placenta development in the first to the early second trimester. In contrast, late-onset preeclampsia is hypothesized to be related to maternal immune activation late in pregnancy. There are likely genetic variations that predispose individuals of various ethnic backgrounds to develop these conditions. Therefore, we set out to evaluate the risk of early and late-onset preeclampsia based on their stated racial/ethnic background.

Methods: The primary outcome of interest was early and late-onset preeclampsia, which was defined as having been diagnosed with preeclampsia ICD-9 codes and gestational week. Those who had early onset preeclampsia were compared to those who delivered before 34 weeks. Those who had late onset were compared to those who delivered after 34 weeks. Multivariate logistic regression models were used to estimate the risk of early and late-onset preeclampsia.

Results: Of the 3,098,578 pregnancies analyzed, Asians showed decreased odds (adjusted OR [95% CI]) 0.84 [0.79 – 0.88] and 0.8 [0.78 – 0.82] of developing both early and late-onset preeclampsia, respectively compared to White. Interestingly, when we further breakdown the Asian race into 11 Asian Americans and Pacific Islanders (AAPI) subgroups, we observed that Pacific Islanders showed an increased risk of early and late-onset preeclampsia compared to Whites. Other Asian American subgroups retained the reduced risk of early and late-onset preeclampsia compared to Whites.

Conclusion: There are variations in early and late preeclampsia risk during pregnancy across AAPIs, highlighting the need to disaggregate AAPI data when studying pregnancy complications and risk factors.

Obstetric health

Racial/Ethnic and Geographic Disparities in Vaginal Birth after Cesarean Delivery in the US between 2011-2021 Rana Chehab* Assiamira Ferrara Mara Greenberg Amanda Ngo Yeyi Zhu

Background

Vaginal birth after cesarean (VBAC) is associated with lower maternal morbidity and complications in future pregnancies than repeat cesarean delivery; however, data on recent VBAC rates in US are lacking. We examined VBAC rates between 2011-2021 and by race/ethnicity and region of birth.

Methods

We conducted a serial, cross-sectional analysis using National Center for Health Statistics data among 5,841,858 individuals who delivered live births in 2011-2021, were 15-44 years old at delivery, and had previous cesareans. We calculated VBAC annual percent change (APC) using Joinpoint regression and rate ratio (RR) by race/ethnicity and birth region. P-values<0.05 were considered statistically significant.

Results

VBAC rate increased overall from 10.1% in 2011 to 14.5% in 2021 (APC: 3.9%) and across all race/ethnicity groups (APC range: 2.8% among Blacks and 4.7% among Hispanics) and birth regions (APC range: 2.3% in Northeast and 6.1% in West), all *P*-values<0.05. In 2021, VBAC rate was 15.4% among American Indian or Alaska Natives, 15.6% among Asian or Pacific Islanders (A/PI), 14.3% among Blacks, 13.7% among Hispanics, and 14.8% among Whites. Further, VBAC rate varied by region in 2021: 17.3% in the Midwest, 16.2% in the West, 15.8% in the Northeast, and 11.7% in the South. VBAC rate among A/PI, Blacks, and Hispanics compared to Whites was higher in the Midwest (RR: 1.28, 1.26, 1.15, respectively) but lower in the West (RR: 0.88, 0.93, 0.83, respectively), all *P*-values<0.05. VBAC rate was lower among A/PI and Hispanics in the Northeast (RR: 0.87 and 0.85, respectively) but higher among A/PI in the South (RR: 1.15) compared to Whites, all *P*-values<0.05. No other significant differences in VBAC rate were noted.

Conclusions

Despite the increase in VBAC rate, it falls short of the recommendations, with noted racial/ethnic and geographic disparities. Targeted interventions are warranted to further support VBAC and provide equitable care for all pregnant individuals.

Obstetric health

Trends and Disparities in Severe Maternal Morbidity Indicator Categories During Childbirth Hospitalization in California from 1997-2017 Alison El Ayadi* Audrey Lyndon Peiyi Kan Mahasin Mujahid Stephanie Leonard Elliott Main Suzan Carmichael

Background

In the United States, severe maternal morbidity (SMM) is increasing and characterized by substantial racial and ethnic disparities. Understanding trends and disparities across time by underlying clinical etiologies may reveal specific, actionable pathways to equitable care.

Methods

We used California birth cohort data from 1997 to 2017 (n= 10,580,096). SMM cases were categorized into overall vs non-transfusion SMM, and seven non-transfusion SMM indicator categories (cardiac, renal, respiratory, hemorrhage, sepsis, other obstetric, and other medical SMM). We computed prevalence overall and for each racial and ethnic group (Black, White, Hispanic/Latino, Asian/Pacific Islander, Other. We used logistic and linear regression to estimate associations of race and ethnicity with each SMM outcome and differences in associations across time.

Results

SMM and non-transfusion SMM occurred in 116 and 54 per 10,000 births. Hemorrhage SMM occurred most frequently (27 per 10,000 births) followed by other obstetric (11), respiratory (7), and sepsis, cardiac, and renal SMM (5), and other medical SMM (3). Across SMM categories, racial and ethnic disparities were evident for most groups compared to non-Hispanic white people, with the most pronounced relative disparities for Black people. Over time, sepsis SMM had the largest relative increase (713%) and sepsis and hemorrhage SMM had the largest absolute increase (17 per 10,000 births). Disparities increased over time for respiratory SMM among Black, US-born Hispanic, and non-US-born Hispanic people and for sepsis SMM among Asian or Pacific Islander people. Disparities decreased over time for sepsis SMM among Black people yet remained large.

Conclusions

Our research further supports the critical need to address SMM and disparities in SMM as a significant public health priority in the United States and suggests that analyses of SMM using intermediate grouping by affected organ system may reveal helpful nuance for intervention while mitigating sample size limitations.

Obstetric health

SARS-CoV-2 Infections and Severe Maternal Morbidity in the United States: A National Retrospective Electronic Health Records Cohort Study Jihong Liu* Peiyin Hung Tianchu Lyu Chen liang Adiba Promiti Yiwen Shih Jiajia Zhang Xiaoming Li

Background: To examine the associations of SARS-CoV-2 infection, its severity and timing, with risks of severe maternal morbidity (SMM).

Methods: We used electronic health records (EHR) from the National COVID Cohort Collaborative (N3C), a clinical data repository from >75 healthcare systems across 50 states, restricting to women who gave a live birth between March 1, 2020 and May 31, 2021 (209,289 childbirths). COVID severity was determined using the WHO Clinical Progression Score (CPS): mild (CPS: 1-3) and moderate/severe (CPS: 4-10). SMM during pregnancy through 42 days postpartum was defined as diagnoses or procedures suggestive of any of the 20 CDC-recommended SMM indicators (excluding blood transfusion) using EHR phenotyping protocol. Log-binomial models were used to estimate adjusted relative risks (aRR) of SMM.

Results. The cohort was 30.6 years old (±5.9), racially diverse (17.1% Black, 19.6% Hispanic, 5.4% Asian, and 8.1% other races), of which 9% were infected by SARS-CoV-2. Of COVID cases, 65.3% were mild, 34.7% were moderate/severe COVID; 71.3% were first infected during pregnancy, and 28.7% infected at delivery or <42 days after delivery. SMM rate was 148.5 cases per 10,000 births with a higher prevalence among Black births (260.0 cases) than White births (120.5 cases). Compared to those without COVID, SARS-CoV-2 infection was associated with increased risks of SMM (aRR: 1.91, 95% CI: 1.73-2.10). SMM risks were higher among those with mild symptoms (aRR: 2.05, 1.84-2.28), those with moderate/severe symptoms (aRR: 1.65, 1.41-1.94), those infected during pregnancy (aRR: 1.26, 1.10-1.43), and those infected at delivery or early postpartum (aRR: 3.61, 3.20-4.08).

Conclusions. SARS-CoV-2 infection, its severity, and especially the diagnosis at delivery or early postpartum were associated with increased risks of SMM. These findings suggest an urgent need to prevent and intervene SARS-CoV-2 infections among birthing people to prevent SMM in the US.

Obstetric health

Race and Socioeconomic Status in Preeclampsia Severity and Fetal Growth Marni Jacobs*, Priscilla Ngu Jinyoung Bae Megan Corn Carolina Diaz Luevano Kelsey Pinson Richard Wolf Louise Laurent Marni Jacobs Marni Jacobs

Preeclampsia (PE) is a hypertensive disorder that is a major contributor to preterm births and pregnancy related deaths. Black women have a higher rate of PE, however, the association between race and severity of PE remains unclear. This study aims to analyze how race (Non-Hispanic White, Hispanic, Non-Hispanic Black, Asian, other/mixed race) and socioeconomic status (SES) affect the severity of hypertensive disorders of pregnancy and related outcomes.

This is a retrospective case-control study of patients who delivered at a single medical center from January 1- December 31, 2019. Patients with ICD-10 codes associated with hypertensive diseases during pregnancy (O10-16) were identified via electronic medical record review, and severity of hypertensive disorders was adjudicated by a board-certified maternal-fetal medicine specialist. Hypertensive disorder severity and small for gestational age (birth weight < 10th percentile for gestational age, SGA) were compared across patient's self-identified race/ethnicity, primary language, and health insurance status using Chi-square, Fisher's Exact and Kruskal-Wallis tests.

Among 151 women with hypertensive disorders during pregnancy, 90 presented severe PE, while 61 presented mild PE or mild or severe gestational hypertension (GHTN). Race and ethnicity across severe PE included: 36% Non-Hispanic White, 39% Hispanic, 13% Black, 10% Asian. No significant differences were found for neither the severity of PE nor SGA status across race, ethnicity, language, and insurance type. Neither Social Vulnerability Index (SVI) quartiles, nor Healthy Places Index (HPI) quartiles showed an association with hypertension severity.

Despite documented higher rates of PE amongst Black women, our study indicates no associations between race, ethnicity, or SES and the severity of GHTN and SGA status. Future studies should focus on identifying the factors that contribute to the increased rates of PE amongst Black women to alleviate the disparity.

Obstetric health

Midwifery care among pregnant people with and without chronic conditions Elizabeth Simmons* Karen Sheffield-Abdullah Anna Austin Alyssa Mansfield Kavita Singh Mollie Wood

The prevalence of chronic conditions in pregnant individuals is increasing. An alternative to care with obstetrician-gynecologists (OB-GYN), midwifery-care uses fewer interventions with similar outcomes. Midwives typically oversee low-risk pregnancies, but they can comanage care of higher risk patients. The aim of this study was to describe use of midwives in a cohort of pregnant individuals with and without chronic conditions in the U.S.

A cohort of pregnant individuals was identified using the Merative Marketscan Commercial Claims and Encounters Database 2004-2015. Individuals 18-55 years old were included if they had a live or stillbirth, continuous insurance and prescription drug coverage (6 months prior to last menstrual period to 30 days after delivery). Individuals were classified as having pre-gestational diabetes and/or chronic hypertension and as initiating prenatal care with a midwife, OB-GYN, or other provider. Descriptive statistics were calculated and compared between patients with pre-gestational diabetes, chronic hypertension, both or neither.

Of 1,556,804 pregnancies in 1,547,461 individuals, 1% had pre-gestational diabetes (n=16,656), 2% had chronic hypertension (n=34,049) and 0.2% had both (n=3,138). On average, individuals with neither condition were younger, delivered at a later gestational week, and used the healthcare system less than those with either or both conditions. Overall, 1.4% of individuals initiated prenatal care with a midwife (n=20,155). Midwifery care at prenatal initiation was lower among those with pre-gestational diabetes (0.8%), chronic hypertension (0.8%) and both conditions (0.5%).

Midwifery care was low in this cohort, especially among those with chronic conditions, which might indicate a lack of access to midwives in this population. Midwives could be an underused resource in managing the increasing number of pregnancies to individuals with chronic conditions. Further research is needed on why midwives are underutilized.

Occupational

Medical Students' Perspectives on Pregnant or Parenting Colleagues Samuel Wilcox* Abigail Christmas Victoria Bright Jean Kerver Ph.D.

Background:

Despite barriers, many medical students are pregnant or parenting with limited institutional support. We assessed medical students' perspectives about underlying bias and resource gaps.

Methods:

A survey link was distributed to all students in a single medical school (n= 806). Survey content included 55 questions regarding demographics, family planning, resources, and opinions about bias against pregnant medical students with likert scale response options (1-7). Descriptive analyses and one-way analysis of variance were used.

Results:

The survey response rate was 13.2% (n=106). Respondents were in their 1st (n=29), 2nd (n=29), 3rd (n=36), and 4th (n=15) year of medical school. The survey was not targeted to women, yet the majority of respondents (76%) identified as female. Few respondents (3.8%) had been pregnant during medical school, 4.8% were currently attempting to get pregnant, and most (61.7%) planned to have children. The majority (71.3%) indicated that their plans for having children would influence their choice of medical specialty. Further, 66% reported choosing to delay pregnancy with 78% of those citing career and education as the reason.

For the statements, "pregnant medical students are more likely to experience bias than their fellow male classmates who are parents" and "pregnant medical students face bias", females had significantly higher scores than males, indicating strong agreement, whereas males had higher scores for the statement "pregnant medical students feel supported" ($p<0.05$ for all). Means for the statements with the strongest overall agreement were: Pregnant medical students are resilient (6.6), face additional challenges (6.5), and parental leave should be available in medical school (6.4).

Conclusion:

To promote equity and inclusion in medical education and specialty choice, efforts are needed to support students who are pregnant or parenting by decreasing existing biases and offering parental leave.

Omics

Effects of Maternal Adverse Childhood Experiences on Intergenerational DNA methylation Signatures Sahra Mohazzab-Hosseinian* Joseph Wlemels Carrie Breton Nicholas Mancuso Erika Garcia Crystal Marconett Tracy Bastain Helen Foley Deborah Lerner Nathana Lurvey Karina Corona Caitlin Howe

Abstract

Introduction

Adverse Childhood Experiences (ACEs) refers to the collection of traumatic events that occurs before a child turns 18 years old. The effects of early life adversity, maltreatment, and/or ACEs have been studied extensively within humans and animal models in relation to DNA methylation. Most human studies rely on retrospective reports of ACEs examined as either domains experienced (neglect, household dysfunction, abuse) or the cumulative number of ACEs. Few studies have explored the two factors within the same modelling framework. Such factors are important to consider in tandem, especially in the context of causal associations where dose and domain of ACEs may contribute to variability in the outcome.

Objectives

This study first examined the effect of the number of ACEs experienced on DNA methylation while accounting for interaction by domain of ACE in a multigenerational population from the Maternal and Developmental Risks from Environmental and Social Stressors (MADRES) pregnancy cohort. Then, the intergenerational transmission of ACE-associated DNA methylation was explored using paired, whole blood prenatal (N = 240, n = 120) and cord blood infant (N = 63) DNA methylation profiles on the Infinium MethylationEPIC kit. Effects of DNA methylation on higher order expression was explored using paired maternal and infant RNA-sequencing samples.

Methods

As the exposure we used a four-level categorical indicator variable for ACEs: none (ACE =0), low (ACE 1-3), moderate (ACE 4-6), and high (ACE > 6). Then, the direct causal effect of ACEs on maternal DNA methylation was estimated. To determine if these effects showed evidence for intergenerational transmission, the Barron and Kenney model for mediation analysis was used. Normalized RNA-sequencing was used with differentially methylated regions in a correlative analysis in maternal and infant samples.

Results

In our maternal samples, ACE scores displayed some shared but mostly distinct effects across categorical ACE predictors. *PTPRN2* displayed a direct causal effect on maternal DNA methylation in the low ACE group. This effect was persistent across the domain of abuse, and in the maternal RNA-sequencing expression analysis. Additionally, *COMT/TXNRD2* displayed an intergenerational effect that persisted in the Barron and Kenney model for mediation.

Conclusion

Effects of ACEs are variable on maternal and infant DNA methylation profiles. There is some

evidence for an intergenerational effect of trauma, supported by overlapping effects in the *COMT/TXNRD2* gene.

Pharmacoepidemiology

Internal validation of gestational age estimation algorithms using ICD-10 Z3A codes in women undergoing fertility treatment Yu-Han Chiu* Roger Logan Sonia Hernández-Díaz

Healthcare utilization databases present an important source for studying the safety of medications during pregnancy. Algorithms to assign gestational age based on the International Classification of Disease (ICD)-9 codes indicative of gestational age at the end of pregnancy have been shown to be accurate for live births; they are less accurate for non-live birth. The introduction of ICD-10 Z3A codes denoting weeks of gestation at prenatal visits provides an opportunity to improve upon earlier algorithms. Yet, the accuracy of Z3A codes to inform the timing of gestation at each visit requires evaluation. Using a convenient sample of pregnancies conceived by assisted reproductive technologies (ART) or intrauterine insemination (IUI) in the MarketScan database, we compared the estimated gestational age at the end of pregnancy using (1) a previously validated algorithm based on the end-of-pregnancy codes (method A) and (2) an algorithm based on both Z3A and end-of-pregnancy codes (method B), against the estimates based on time since ART/IUI procedure (as a reference standard). We identified 11,191 pregnancies conceived by ART or IUI who had a record of positive pregnancy tests within 4 weeks from the procedure date. Overall, method B estimates were closer to the reference standard than method A for both live birth and non-live birth. For full-term live births, agreement of estimated gestational age within 7 days was 65.4% by method A and 94.5% by method B. For preterm live births, agreement within 7 days was 63.8% by method A and 90.8% by method B. For stillbirth, agreements within 7 days of the reference were 17.2% for method A and 89.3% for method B. The corresponding estimates were 26.6% and 38.7% for spontaneous/unspecified abortion; and 10.3% and 75.6% for elective termination. Algorithms that incorporate Z3A codes improve the accuracy of gestational age estimation in healthcare databases, especially for preterm live births and stillbirths.

Pharmacoepidemiology

Concomitant Use of Antidepressants and Benzodiazepines during pregnancy: A Retrospective Study of 1,404,013 Pregnant Women in Taiwan Lin-Chieh Meng*, Hui-Min Chuang Lin-Chieh Meng Fei-Yuan Hsiao Lin-Chieh Meng

Introduction

Maternal use of psychotropic agents, such as antidepressants or benzodiazepines (BZDs) have been widely studied due to concerns of their neonatal adverse outcomes. Co-administration of these drugs during pregnancy may further aggravate such risks. The study aimed to evaluate the temporal trends and identify predisposing factors associated with the concomitant use of antidepressants and BZDs among pregnant women.

Method

A nationwide cohort study was conducted using Taiwan’s national health insurance claims and birth certificate databases from 2012 to 2018. We captured all prescriptions (including starting date and days of supply) of antidepressants and BZDs at each trimester of all identified pregnant women. Logistic regression models were adopted to investigate predisposing factors associated with the concomitant use of antidepressants and BZDs.

Result

Of 1,404,013 pregnancies, 12,108 (0.9%) received prescriptions of antidepressants, of whom 8,161 (67%) also received prescriptions of BZDs at any trimester. Women with psychiatric conditions such as depression (adjusted odds ratio [aOR], 2.43 [95% CI 2.23-2.64]), anxiety (1.96 [1.80-2.14]), bipolar disorder (2.23 [1.83-2.73]), and insomnia (1.82 [1.66-2.00] were more likely to receive concomitant prescriptions of BZDs and antidepressants. Alcohol users (2.21[1.34-3.64]) were also more likely to receive concomitant prescriptions of these two drugs.

Conclusion

Among pregnant women who use antidepressants, concomitant use of BZDs was prevalent. Such concomitant use was seen at each trimester during pregnancy, although it was most prevalent at the first trimester. Underlying mental conditions and were associated higher likelihood of concomitant use of antidepressants and BZDs.

Policy

Effects of changes in GA limits in abortion law on pregnancies; national study in Japan

Yuko Yanagawsa* Naho Morisaki

Appropriateness of abortions is constantly debated in many countries and regions, and related laws have changed over time based on various ethical, religious, medical, and political backgrounds. However, research on the impact of such legal changes on pregnant women and health care providers has been scarce.

We studied the impact of the change in upper limits for legal abortion from 24 to 22 weeks GA that occurred on January 1, 1991 in Japan. Using national vital statistics data on all abortions, stillbirths and livebirths of 1989-1994, we observed changes in abortions rates (cases per pregnant women) and proportion of pregnancies ending as abortions for each week of gestation, as well as in birthweight of fetuses aborted at 20-21 weeks GA, by interrupted time-series analyses.

After the change, abortion rates at 19 weeks (incidence risk ratio (IRR) 1.13 (95%CI 1.01-1.26), 20 weeks (IRR 1.28 (95%CI 1.15-1.43)) and 21 weeks (1.33 (95%CI 1.18-1.50)) gestation increased but not at 18 weeks or less. Proportion of pregnancies ending as abortions decreased for women who were in their 19th week (IRR 1.13 (95%CI 1.01-1.26), 20th week (1.33 (95%CI 1.19-1.48)), and 21st week (1.38 (95%CI 1.23-1.55)) of pregnancy, but not for those in 18th week or less. Proportion of pregnancies ending as stillbirth among those in or past 22th week GA did not change (p=0.46). Mean birth weight of fetuses aborted at 20-21 weeks gestation increased significantly by 15.8 (95%CI 4.1-27.4) grams.

Lowering of the legal limit of GA for abortions in Japan led to a subtle increase in abortions at 18-21 weeks not sufficient to cancel out the reduction in proportion of pregnancies ending as abortions for those already in or past their 18th week in pregnancy. Lack of increase in stillbirths past the limit and increase in birthweight among abortions under the limit, suggest abortions conducted beyond new limit were registered as abortions conducted earlier in pregnancy rather than listed as stillbirths.

Pregnancy outcomes

The Association between in utero Cannabis Exposure and Neonatal Outcomes in a Large Integrated Healthcare Delivery System Lyndsay Avalos* Sara Adams Stacey Alexeeff Nina Oberman Monique Does Deborah Ansley Amy Conway Nancy Goler Alisa Padon Lynn Silver Kelly Young-Wolff

Despite the increasing prevalence of prenatal cannabis use, research evaluating the association between *in utero* cannabis exposure and adverse neonatal outcomes has been largely inconclusive. This study evaluated associations between *in utero* cannabis exposure and adverse neonatal outcomes. We conducted a population-based retrospective birth cohort study of children born (January 1, 2011-July 31, 2020) to pregnant Kaiser Permanente Northern California members universally screened for cannabis use via self-report and/or urine toxicology. Data were ascertained from electronic health records. A directed acyclic graph (DAG) informed the study design and analytic model. Multivariable logistic regression was conducted. *In utero* cannabis exposure was defined as any use (yes versus no; primary) and frequency of use (among those with self-report data; secondary). Of the 364,915 infants, 6.2% (n=22,626) were exposed to cannabis *in utero*. *In utero* cannabis exposure was associated with greater odds of low birthweight (aOR:1.19, 95%CI: 1.12, 1.27), SGA birth (aOR:1.23, 95%CI: 1.17, 1.29), preterm birth (aOR:1.06, 95%CI: 1.01, 1.13), and NICU admission (aOR:1.06, 95%CI: 1.01, 1.11), with a trend noted for early preterm birth (aOR:1.11, 95%CI: 1.00, 1.24) and respiratory support (aOR:1.07, 95%CI: 0.97, 1.18), after adjustment for exposure to other *in utero* substances and additional potential confounders. A dose-response relationship emerged for associations with low birth weight and SGA birth. Sensitivity analyses excluding individuals with other substance use during pregnancy produced similar results. *In utero* cannabis exposure was associated with an increased likelihood of adverse neonatal outcomes. Care for individuals considering pregnancy and pregnant individuals should include education about the adverse neonatal health effects associated with prenatal cannabis use, and cannabis policy on labeling, marketing and public education should address neonatal risks.

Pregnancy outcomes

Trends in adverse maternal and perinatal health outcomes associated with mode of delivery following a previous cesarean section: a population-based cohort study Azar Mehrabadi* Maggie M. Brown Christy C. Woolcott Emily Gray Heather Ezurike John Fahey Heather Scott Anthony B Armson Victoria Allen

Objective

To describe time trends in adverse maternal and perinatal health outcomes associated with a planned vaginal birth versus a planned repeat cesarean section after a previous cesarean delivery. To explore risk factors associated with adverse outcomes over time.

Methods

This population-based cohort study included all singleton pregnancies ≥37 weeks gestation with one previous cesarean and without contraindications for a trial of labour in Nova Scotia, Canada, from April 1, 2003 to March 31, 2021. The main outcome measures were severe maternal morbidity and severe perinatal and neonatal morbidity and death. Adjusted risk ratios (aRRs) and 95% confidence intervals (CIs) were calculated using Poisson regression analyses, accounting for confounders using inverse probability weighting.

Results

Among 12 681 pregnancies (4% aged ≥40 years), 5138 (40.5%) had a planned vaginal birth. Among those with a planned vaginal birth versus a planned repeat cesarean, severe maternal morbidity increased over time from 5.9 vs 5.0 per 1000 deliveries in 2003-08 (aRR 1.13, 95% CI 0.45, 2.81) to 25.5 vs 5.6 per 1000 deliveries in 2015-21 (aRR 4.4, 95% CI 2.2, 8.6). The increase was driven by a marked rise in uterine rupture among planned vaginal births from 3.2 to 13.5 per 1000 deliveries from 2003-08 to 2015-21. There was no notable change in the risk of overall severe perinatal and neonatal morbidity and mortality by planned mode of delivery over time.

Conclusions

There was a temporal rise in severe maternal morbidity among those undergoing a planned vaginal birth versus a repeat cesarean section, that was driven by a rise in uterine rupture. It is unclear what accounts for the increase in uterine rupture among those planning a vaginal birth following a previous cesarean delivery.

Pregnancy outcomes

Associations between gestational exposure to air pollution and birthweight in a North Carolina birth cohort Alison K. Krajewski* Thomas J. Luben Joshua L. Warren Kristen M. Rappazzo

Previous studies reported birthweight (BW) is associated with exposure to criteria air pollutants. Due to the variability in the magnitude of reported associations, we used quantile regression to evaluate the magnitude of the association between gestational exposure to fine particulate matter ($PM_{2.5}$), nitrogen dioxide (NO_2), or ozone (O_3) and BW among term births in a North Carolina birth cohort from 2003-2015 (n:1,252,811). Modeled daily $PM_{2.5}$, NO_2, and O_3 concentrations were aggregated to census tract, linked to residential address at delivery, and averaged across each trimester of pregnancy. Quantile regression estimated the change (and 95% CI) in mean BW across deciles of BW per 1-unit increase in $PM_{2.5}$, NO_2, or O_3, adjusted for gestational parent marital status, race/ethnicity, age at delivery, and Medicaid status. The daily mean (SD) concentrations were 10.9 (2.2) $\mu g/m^3$ for $PM_{2.5}$, 15.8 (6.6) ppb for NO_2, and 41.6 (3.5) ppb for O_3. During the first and third trimesters, we observed higher BW with higher $PM_{2.5}$ concentrations across all deciles, but lower BW with higher $PM_{2.5}$ concentrations during the second trimester across all but the highest decile. Generally, we observed higher BW with higher NO_2 concentrations and lower BW with higher O_3 concentrations across trimesters and deciles of BW. Overall, the largest magnitude quantile regression coefficients for lower BW associated with higher air pollutant concentrations were for second trimester $PM_{2.5}$ exposure and first and second trimester O_3 exposure, whereas the largest magnitude coefficients for higher BW were for higher NO_2 concentrations during each of the three trimesters. While the overall magnitude of associations with BW were relatively small across pollutants and trimesters, evaluating these associations may help to identify critical windows of exposure that have the greatest risk to changes in BW.

Pregnancy outcomes

Contextualizing relationship quality between mother and father of the baby during pregnancy: A latent class analysis Rosemary Adaji* Carmen Giurgescu Dawn Misra

Background: Understanding of contextual variables is pertinent to interpreting findings linking socio-environmental correlates of health outcomes, including birth outcomes. For example, in the psychosocial domain of pregnancy, constructs such as relationship quality are multidimensional. However, analytical approaches in many studies mainly focus on one or two proxy indicators independently (e.g., social support). Such an approach is inadequate, especially when correlation among these indicators is likely high. This study aims to identify a construct of mother of the baby with the father of the baby (FOB) relationship quality during pregnancy using multiple self-reported relationship indicators among Black women.

Methods: This is a secondary data analysis from a subsample of 404 Black pregnant women who participated in the Biosocial Impacts on Black Births study, a prospective cohort study. Participants completed questionnaires at 19-29 weeks' gestation including six measures of woman's relationship with the FOB: 1) contact with FOB, 2) FOB involvement, 3) overall relationship, 4) change in relationship prior to pregnancy to during pregnancy, 5) social support from FOB, and 6) conflict with FOB. Latent class analysis was used to identify and classify the relationship construct.

Results: We identified three classes of mother-FOB relationship quality: good, conflictual, and no relationship. Good relationship comprised 50% of responses, while conflictual, and no relationship comprised 29% and 21%, respectively. Class names were assigned based on theoretical knowledge of how mother-father relationships have been defined in previous literature.

Conclusion: Characterizing complex constructs using methods like latent class analysis could help identify subgroups of women or individuals who are at increased risk of adverse health outcomes or who could benefit from specific public heath interventions based on their shared characteristics.

Pregnancy outcomes

ApoE ε2 carrier status is associated with increased HDL in pregnancy and decreased fetal growth Marni Jacobs*, Cassandra Wauer Carolina Diaz-Luevano Amy Kung Abbas Hakim Morgan Meads Anelizze Castro-Martinez Mana M Parast Louise C Laurent Marni Jacobs Marni Jacobs

Maternal lipids have been linked with higher risk for poor birth outcomes. However, genetic influences on lipid levels during pregnancy and linked fetal outcomes are unknown. Apolipoprotein E (ApoE), has three major alleles (ε2, ε3, ε4), and the ε4 allele has been associated with pregnancy loss and decreased fertility. The aim of the present study was to determine the relationship between ApoE genotype, circulating lipid levels during pregnancy, and fetal growth restriction and associated placental findings. In this case-control study, serum samples of pregnant women who delivered a small-for-gestational age (SGA) infant (birthweight < 10th percentile, n = 50) were matched by gestational age (GA) at the time of sample collection in a 1:2 ratio with healthy appropriate-for-gestational age (AGA) pregnancies (n=100). To control for the effect of hypertension on SGA, patients with hypertensive disorders were excluded. No differences in mean maternal age (31.4 vs. 32.1 years) or GA at delivery (37.7 vs. 36.9 weeks) were noted. ApoE allele distributions and lipid levels were compared between cases and controls and among placental pathological findings using chi-square and ANCOVA. No significant differences in ApoE allele distribution or carrier status, or low-density lipoproteins (LDL) levels, were noted between groups. However, SGA cases had significantly higher maternal levels of high-density lipoprotein (HDL) than controls (73.3 vs 65.2 mg/dL, p = 0.002).

Pregnancy outcomes

Maternal mitochondrial DNA copy number is associated with longer gestational length in a Michigan pregnancy cohort Maria Cinzori (Kloboves)* Megan Nicol Zheng Zhou Jaclyn Goodrich Nicole Talge Joseph Gardiner Jean Kerver Rita Strakovsky

Background: Gestational length predicts both short- and long-term child health outcomes. Carrying a pregnancy to term is energetically demanding, requiring extensive metabolic adaptations. Mitochondria regulate metabolic processes, and mitochondrial DNA copy number (mtDNAcn) may be a marker of mitochondrial function. However, the relationship between mtDNAcn and gestational length has not been studied.

Methods: Pregnant Michigan women (n=394) from the Archives for Research on Child Health (ARCH) cohort provided sociodemographic information and blood spots at median 11 weeks gestation. We extracted DNA from blood spots and measured NADH-ubiquinone oxidoreductase chain 1 (*ND1)* expression, a mitochondrial gene and mtDNAcn marker, using real-time quantitative PCR. Gestational length (wks) was obtained from birth certificates. Multivariable linear regression models accounting for important sociodemographic, lifestyle, and health factors evaluated the association of ln-transformed mtDNAcn and gestational length (cubed, due to left-skewness). Quantile regression was used to determine if associations differed across the gestational length distribution.

Results: Many (42%) mothers were non-White and 68% had an annual family income of <$25,000. Median gestational length was 39 wks (25^{th}, 75^{th} percentiles: 38, 40), and 8% of births were preterm (<37 wks gestation). Using linear regression, mtDNAcn was only modestly positively associated with gestational length. Using quantile regression, associations were exclusive to lower quantiles of gestational length. Only at the 5^{th}, 15^{th}, and 25^{th} percentiles, each 10% increase in mtDNAcn was associated with 0.25 (95%CI: 0.18, 0.32), 0.11 (95%CI: 0.02, 0.20), and 0.08 (95%CI: 0.01, 0.15) wk longer gestation, respectively.

Conclusions: It is possible that mitochondrial adaptations may be especially important in women who deliver earlier. Future experimental studies are needed to understand the roles of mitochondria in gestational length.

Pregnancy outcomes

Examining the role of work domains on preterm birth among Black mothers Florence Kizza*
Dawn Misra

Background

Preterm birth contributes to the majority of neonatal mortality and morbidity and long-term neurological disabilities. How work factors impact risk of preterm birth is a relatively neglected area of study, especially among Black women who are the group at highest risk for preterm birth. The aim of the present study was to examine the effect of various domains of work on the risk of preterm birth among Black women.

Methods

We performed a secondary analysis based on data from a hybrid retrospective and prospective cohort study of African American women residing in Baltimore (2001-2004). A total of 872 women were enrolled in the parent study and 856 of these women had data on preterm birth. Preterm birth was defined as less than 37 weeks of gestation completed. Multivariable logistic regression analyses were used to determine the role of work factors on the risk of preterm birth and to adjust for the effect of potential covariates (depression, social support, hassles during pregnancy, marital status, maternal age and education). Results are presented as odds ratios (OR) and 95% Confidence Intervals (95% CI).

Results

155 (18.1%) participants had preterm birth. In adjusted models, women whose jobs required working very fast had an increased risk of preterm birth (OR=1.62; 95% CI: 1.01,2.60). Having a job that required a lot of physical effort was also associated with increased risk of preterm birth but not statistically significant (OR: 1.43; 95% CI: 0.78, 2.63). Similarly, women whose jobs required moving or lifting heavy loads had high odds of preterm birth but this association was not statistically significant (OR: 1.24; 95% CI: 0.78, 1.20).

Conclusion

Pregnant women whose work involves strenuous or physically demanding activities are at increased risk of preterm birth. These findings highlight the need to develop social and economic policies that are focused on accommodation reforms that will improve the livelihood of pregnant women in the workforce.

Pregnancy outcomes

Daily physical activity and nocturnal glucose in pregnant people with gestational glucose intolerance Bethany Rand* Jill Maples Scott Crouter Christina Peterson Nikki Zite Kimberly Fortner Samantha Ehrlich

PURPOSE: This study examined the relationships of daily minutes (min) of moderate to vigorous intensity physical activity (MVPA), light intensity activity (LPA), and total activity (MVPA + LPA) with nocturnal (12AM- 6AM) glucose levels in individuals with gestational glucose intolerance (GGI). **METHODS:** Data come from the Project Wellness pilot randomized controlled trial (i.e., baseline). Participants concurrently wore a Dexcom G6 continuous glucose monitor and an ActiGraph CentrePoint Insight Watch activity monitor for 7 days. The TwoRegressions algorithm estimated min by min metabolic equivalents of task (METs) for periods in which the devices were worn, and mins per day at ≥ 3.0 METs and <3 METs, indicative of MVPA and LPA, respectively, were summed. PROC MIXED in SAS, with an autoregressive covariance structure, estimated the associations of 10 min blocks of MVPA, LPA, and total activity with nocturnal: mean glucose, percent time in range (TIR; 60-99 mg/dL), and glucose area under curve (AUC). AUC was calculated in R, using 12AM glucose as the starting point and the trapezoid method. **RESULTS:** Nine participants with mean gestational age 31 weeks [standard deviation (SD) 1.8] contributed a total of 66 days of data. On average, they amassed 56 mins of daily MVPA (SD 32) and 321 mins of LPA (SD 98). Mean nocturnal glucose was 88 mg/dL (SD 13) and TIR 86% (SD 28). For each 10 min increase in MVPA, there was a 1.5 mg/dL increase in mean nocturnal glucose (P= .004), a 3.3% decrease in TIR (P=.03), and a 26,575 mg/dL increase in AUC (P=.02). Estimates for LPA and total activity did not attain statistical significance. Mean nocturnal glucose and AUC also increased with each passing day (both P<.02). **CONCLUSION:** Findings suggest that MVPA may negatively affect nocturnal glucose levels in pregnant people with GGI. Future studies with concurrent dietary intake data are needed to investigate the potential role of compensatory behaviors in this population.

Pregnancy outcomes

Lifetime history of gestational diabetes and cognitive function in middle-aged women Diana Soria-Contreras* Jiaxuan Liu Rebecca Lawn Alexandra Purdue-Smithe Francine Grodstein Karestan Koenen Emily Oken Jorge Chavarro

Women who experience gestational diabetes mellitus (GDM) during their lifetime are at higher risk of hypertension, type 2 diabetes, and other conditions that increase their risk of cognitive impairment and dementia. Despite this, the relationship between GDM and cognitive function has not been established. We evaluated the associations of a lifetime history of GDM with cognitive function among women in the Nurses' Health Study II (NHS II).

The NHS II enrolled 116,429 female nurses in 1989. In 2014-2019, 15,138 participants completed the Cogstate Brief Battery, an online cognitive assessment. We restricted this analysis to 11,711 nurses with cognitive data who reported ≥1 pregnancy at ≥18 years of age in a reproductive history questionnaire applied in 2009. GDM history was defined as having had at least one pregnancy affected by this condition. Outcomes included composite z-scores for global cognition, psychomotor speed and attention, and learning and working memory. We used linear regression models adjusted for age at cognitive assessment, race and ethnicity, childhood and adulthood socioeconomic status, education, and pre-pregnancy factors such as chronic hypertension, body mass index, and lifestyle.

Mean (SD) age at cognitive assessment was 61.0 (4.6) years and 354 (3%) participants had a history of GDM. In adjusted models, women with a history of GDM, vs. those with no history, had mean difference z-scores of -0.06 (95% CI: -0.16, 0.03) in the psychomotor speed and attention composite, -0.003 (95% CI: -0.08, 0.07) in the learning and working memory composite, and -0.03 (95% CI: -0.10, 0.04), in the global cognition composite. In a secondary analysis, we observed similar null associations among women who developed type 2 diabetes after GDM.

We did not find associations between a lifetime history of GDM during the reproductive years and cognitive function at midlife. Additional studies, ideally with a larger sample of exposed women and longer follow-up, are needed.

Pregnancy outcomes

A prospective study of subjective preconception sleep health and hypertensive disorders of pregnancy Chad M. Coleman* Amelia K. Wesselink Traci N. Bethea Tanran R. Wang Andrea S. Kuriyama Elizabeth E. Hatch Lauren A. Wise

Background: Hypertensive disorders of pregnancy (HDP)—defined as gestational hypertension, preeclampsia, and eclampsia—are leading causes of pregnancy-related morbidity and mortality in the United States. While studies report associations between sleep-disordered breathing and HDP, few studies have evaluated subjective (self-assessed) sleep health and HDP.

Methods: We examined prospectively the association between subjective sleep health and HDP risk among 5,730 participants enrolled in Pregnancy Study Online, a North American preconception cohort study. On the baseline questionnaire, participants reported their sleep duration (hours/night) in the past month and their frequency of trouble sleeping at night in the past two weeks (all the time, most of the time, slightly more than half the time, slightly less than half the time, some of the time, and at no time). We identified HDP diagnoses via questionnaires and birth registries. We used log-binomial regression models to estimate risk ratios (RRs) and 95% CIs for the association between both sleep measures and HDP risk, adjusting for socio-demographic, behavioral, and reproductive factors.

Results: About 14% of participants with a pregnancy that progressed beyond 20 weeks of gestation and no pre-pregnancy hypertension had a HDP diagnosis. 21% of participants slept <7 hours/night in the past month and 18% experienced trouble sleeping ≥half the time. Compared with 7-<9 hours/night (recommended sleep), RRs for sleep durations of <6, 6-<7, and ≥9 hours/night were 1.18 (95% CI 0.88-1.58), 1.05 (95% CI 0.87-1.26), and 0.99 (95% CI 0.75-1.31), respectively. Compared with participants who had no trouble sleeping, RRs for participants who had trouble sleeping <half the time and ≥half the time were 0.98 (95% CI 0.84-1.15) and 1.06 (95% CI 0.87-1.29), respectively.

Conclusions: Short preconception sleep duration may be associated with increased HDP risk. We will evaluate sleep during pregnancy in future analyses.

Pregnancy outcomes

Occurrence of Spontaneous Preterm Birth Within 5 days of Preterm Labor Testing Status by Gestational Week Categories Nehaa Khadka* Michael J. Fassett Nana Mensah Vicki Y. Chiu Chantal C. Avila Fagen Xie Jiaxiao Shi Meiyu Yeh Michael Ruma Philipp Mueller Darios Getahun

Background: Early detection of preterm labor (PTL) is important to identify patients at-risk of preterm births. We describe the clinical utilization of two testing tools commonly used to identify risk of preterm birth (transvaginal ultrasound [TVUS] and fetal fibronectin [fFN] testing) at PTL evaluation visits and present the proportion of spontaneous preterm births (sPTB) following a PTL evaluation visit in a large integrated healthcare delivery system**.**

Methods: This retrospective cohort study from Kaiser Permanente Southern California used electronic health records data (2009-2020) to identify 427,698 singleton pregnancies. sPTB was defined using Natural Language Processing to extract triage data for PTL evaluation. PTL evaluation was performed using TVUS measuring cervical length and/or fFN testing. Gestational age was determined using a clinical estimate combining the last menstrual period and first-trimester ultrasound. Chi-square test was used to estimate p-values.

Results: During the first PTL evaluation(n=101,095), the overall sPTB rates increased by gestational weeks: $24^{0/7}$-$25^{6/7}$ weeks (2.4%), $28^{0/7}$-$29^{6/7}$ weeks (2.4%), $30^{0/7}$-$31^{6/7}$ weeks (3.3%), and $32^{0/7}$-$34^{6/7}$ weeks (8.9%) except at $26^{0/7}$-$27^{6/7}$ weeks (1.9%). Pregnancies that did not receive fFN or TVUS testing at the first PTL evaluation visit at $32^{0/7}$-$34^{6/7}$ weeks had a higher proportion of sPTB (11.0%) than those who received both TVUS and fFN (1.8%) or fFN only (1.8%) or TVUS only (4.6%), P<.001. Among all PTL evaluation visits (n=151,701), the highest proportion of sPTB was observed at $32^{0/7}$-$34^{6/7}$ weeks of gestation, where sPTB was greatest for those who did not receive fFN or TVUS (11.1%) followed by those who received TVUS only (5.4%), fFN only(2.7%), and both fFN and TVUS (2.2%), P<.001.

Conclusions: This study highlights the importance of testing at PTL triage evaluation visits. Identifying at-risk women prone to deliver preterm may allow for timely intervention to improve maternal and fetal outcomes.

Pregnancy outcomes

Changes in obstetric intervention and perinatal outcomes during the COVID-19 pandemicKS Joseph*, Sophie Simon Sid John Sarka Lisonkova Neda Razaz Guilia Muraca Amélie Boutin Mohamed Bedaiwy Justin Brandt Cande Ananth KS Joseph KS Joseph

Background: Covid-19 pandemic had profound infection-related effects along with disruption of health services. We quantified the overall pandemic-related changes in obstetric intervention and perinatal outcomes.

Methods: We studied all deliveries in the United States from 2015 to 2021 using data from National Center for Health Statistics. We quantified obstetric intervention rates by month, including clinician-initiated preterm (preterm labour induction/caesarean) and post-term birth rates. We examined perinatal outcomes (stillbirth, preterm birth and macrosomia) among singletons and in high-risk groups (pre-existing diabetes/hypertension, hypertensive disorders and twins). Interrupted time series analyses were used to estimate changes in pre-pandemic (Jan-2015 to Feb-2020) and post-pandemic (Mar-2020 to Dec-2021) periods and at pandemic onset.

Results: The study included 26.6 million births. During the pre-pandemic period, clinician-initiated preterm birth rates increased by 0.02 per 100 live births per month (95% confidence interval 0.01-0.02) from a baseline of 4.1 per 100 live births. Pandemic onset reduced the frequency of such births by 0.2% (95% CI 0.1-0.3), followed by an increase of 0.01% per month (95% CI 0.01-0.02). Stillbirth rates declined by 0.005 per 1000 total births per month (95% CI 0.002-0.008) during the pre-pandemic period from a baseline of 5.8 per 1000 total births. Pandemic onset increased stillbirth rates by 0.43 per 1000 total births (95% CI 0.2-0.7), followed by a decrease of 0.06 per month (95% CI 0.03-0.10). Stillbirth rates in April 2020 were higher than rates in any month in the previous 5 years (estimated excess of 120-200 stillbirths). Similar pandemic-related decreases in preterm and post-term birth rates and increases in macrosomia rates were observed.

Interpretation: Pandemic-related disruption of fetal surveillance and obstetric services resulted in transient declines in obstetric intervention and increases in stillbirth rates.

Pregnancy outcomes

Rate of gestational weight gain after gestational diabetes diagnosis and its association with cesarean delivery and infant size for gestational age Emily Liu* Assiamira Ferrara Monique Hedderson

Pregnant people diagnosed with gestational diabetes mellitus (GDM) are recommended to change their diet and physical activity to achieve glycemic control, which may also impact rate of gestational weight gain (GWG). While two of the most common complications of GDM – excess fetal growth and cesarean delivery – are influenced by GWG, the association between rate of GWG after GDM diagnosis and perinatal complications is unclear.

In a cohort of 14,122 singleton full-term births among GDM pregnancies at Kaiser Permanente Northern California between 2011 and 2018 with universal GDM screening we examined the relationship between rate of GWG after GDM diagnosis and cesarean delivery and infant size for gestational age. Rate of GWG per week between GDM diagnosis and delivery was categorized into excessive, adequate, or inadequate according to the Institute of Medicine guidelines. We explored effect modification by pre-pregnancy BMI categories of normal (< 25.0), overweight (25.0-29.9), and obese (≥ 30.0).

After diagnosis, the median rate of GWG was 0.23 kg/week; 54% had inadequate and 29% had excessive rate of GWG. One-third (32%) had cesarean delivery and 14% were large- (LGA) and 9.6% were small-for-gestational-age (SGA). Excessive GWG rate after GDM diagnosis increased risk of cesarean delivery (RR: 1.16, 95% CI: 1.08-1.26) and LGA (RR: 1.25, 95% CI: 1.13-1.41) and decreased risk of SGA (RR: 0.77, 95% CI: 0.64-0.92) compared to adequate GWG rate. Inadequate GWG rate after GDM diagnosis was associated with decreased LGA risk (RR: 0.57, 95% CI: 0.51-0.64), increased SGA risk (RR: 1.44, 95% CI: 1.25-1.66) and no cesarean delivery risk. In analyses stratified by pre-pregnancy BMI, risk of LGA and SGA for excessive and inadequate GWG rate weakened in higher pre-pregnancy BMI categories but remained statistically significant. Results suggest that helping pregnant people with GDM achieve the recommended rate of GWG after their diagnosis may improve perinatal outcomes.

Pregnancy outcomes

Increasing Preterm Delivery trends in South Carolina Kalyan Chundru* Kalyan Chundru Jeffrey Korte Chun-Che Wen Brian Neelon Dulaney Wilson Julio Mateus John Pearce Sarah Simpson Hermes Florez Kelly Hunt Angela Malek

Abstract

Introduction: With preterm delivery (PTD) trends rising in the U.S. and the multitude of complications for neonates, we aimed to assess the early impact of the COVID-19 pandemic and change in trends in PTD in South Carolina (SC).

Methods: Our study used 2015-2021 SC vital records data for singletons (n=338,784) born to non-Hispanic White (NHW), non-Hispanic Black (NHB) and Hispanic women. PTD was defined on the birth certificate as delivery <37 weeks gestation. Generalized estimating equation modified Poisson regression was used to assess the pandemic's impact on PTD. A fixed changepoint at the first quarter (Q1) of 2020 was fitted to test the change in slope of PTD trends.

Results: In SC, the overall PTD rate rose (9.09% to 10.26%) from 2015 to 2021, with the largest differences observed for NHB women compared to NHW and Hispanic women. The relative risk (RR) for PTD with a one quarter increase in time was 1.0055 (95% CI: 1.004-1.006). PTD increased steadily throughout the study period, with no time-race interaction before (p=0.35) or after (p=0.30) the changepoint. Adjusting for demographic factors (race-ethnicity, maternal age, education, Medicaid eligibility, urban vs. rural residence and use of Women, Infants and Children [WIC] services) attenuated PTD trends in this population (Figure 1). The RR for the prevalence of PTD with a one quarter increase in time was 1.003 (95% CI: 1.002-1.004). The prevalence of PTD for an average NHB woman was highest in the first quarter of 2021 (RR=0.115, 95% CI: 0.112-0.118] and in the last quarter of 2021 (RR=0.125, 95%: CI 0.122-0.128) compared to an average NHW or Hispanic woman in SC (Table1).

Conclusion: Although we did not observe a significant change in PTD trends before vs. after the pandemic's early phase, the steady rise in PTD and racial-ethnic group differences is concerning. Women delaying childbearing and clinical risk factors may be contributing to current PTD trends in this population.

Table 1: Prevalence of PTD for an average woman in SC.

	1st Quarter of 2015			4th Quarter of 2021		
Ethnicity-Race	Estimate	95%CI	p value	Estimate	95% CI	p value
non-Hispanic Black	0.115	(0.112, 0.118)	<.0001	0.125	(0.122, 0.128)	<.0001
non-Hispanic White	0.078	(0.076, 0.080)	<.0001	0.085	(0.083, 0.087)	<.0001
Hispanic	0.061	(0.058, 0.064)	<.0001	0.066	(0.063, 0.070)	<.0001

Demographic Factors	Relative Risk (RR) of PTD	95% CI	p value
One Year Increase in Women's Age	1.030	(1.028, 1.032)	<.0001
non-Hispanic Black	1.471	(1.435, 1.508)	<.0001

Hispanic	0.782	(0.761, 0.818)	<.0001
Education: High school	0.865	(0.836, 0.895)	<.0001
Education: Some College Education (No Degree)	0.789	(0.761, 0.818)	<.0001
Education: College Graduate	0.618	(0.594, 0.644)	<.0001
Medicaid Access	1.231	(1.199, 1.265)	<.0001
WIC Services	0.908	(0.886, 0.931)	<.0001
Rural	1.006	(0.982, 1.030)	0.6044

Pregnancy outcomes

Differences in Maternal Health Outcomes among U.S.-born and Foreign-born Black Birthing People Mariah Jiles* Kim Harley Ndola Prata

Despite the multitude of research conducted on the health of Black birthing people in the United States in recent years, little information is provided on the nationality or country of origin for these individuals. Black American populations in research are largely represented as monoliths, which obscure the potential impacts that country of origin and nationality can have on health outcomes. As public health begins to grapple with the impacts that toxic stress and racism can have on birth outcomes, it will be helpful to examine how these experiences differ within Black American populations.

This study examines differences in maternal morbidity rates among the U.S.-born and Foreign-born Black people who gave birth in a U.S. hospital in 2021. I utilize natality data which totals over 3 million births total from 2021. My selected population includes individuals who self-identify as Black, are primiparous, having singleton births and have noted natality and morbidity data provided. I first examine the amount of people in each population who experienced a maternal morbidity, then analyze which type of 5 maternal morbidities were reported (maternal transfusion, perineal laceration, ruptured uterus, unplanned hysterectomy and/or admission to the intensive care unit). This study adds to current knowledge about extensive racial disparities of maternal health outcomes in the United States, and allows us to begin to examine how nationality can impact the experiences of Black birthing people.

Pregnancy outcomes

Understanding the role of childhood nurture, abuse, and stability on incident gestational diabetes in the Coronary Artery Risk Development in Young Adults study (CARDIA) Kaitlyn Stanhope* Erica Gunderson Shakira Suglia Sheree Boulet Denise Jamieson Catarina Kiefe Kiarri Kershaw

Objective: To estimate the association between positive (nurture, stability) and negative (abuse) aspects of maternal childhood family environment with gestational diabetes (GDM) and effect modification by pre-pregnancy body mass index (BMI) or maternal race.

Methods: We used CARDIA data over 30 years (1985-2016) on individuals with >20 week pregnancies after baseline (1985-86), no pre-pregnancy diabetes and complete data on the Childhood Family Environment Questionnaire (retrospectively assessed once at year 15, 2000-01). We used the overall score and three subscales: abuse, nurture, and stability as continuous, separate exposures. We fit log binomial models with generalized estimating equations to account for multiple pregnancies per individual and calculated crude and adjusted risk ratios and 95% confidence intervals. Age at delivery, parity, race (black or white), and parental education (as a proxy for childhood SES) were potential confounders and pre-pregnancy BMI and race potential effect modifiers.

Results: We included 748 individuals (39% Black, age at baseline 18-32 years) with 1891 pregnancies, 142 of which (7.5%) were complicated by GDM; For all four exposures, a worse childhood family environment was associated with increased risk of GDM. The estimated association was strongest for abuse, with a 1 point increase on the abuse subscale (e.g., from “rarely or never” to “some or little of the time”) associated with a 40% increased risk of GDM (aRR: 1.4, 95% CI: 1.1, 1.7). There was multiplicative interaction by BMI with a stronger association among individuals who were overweight/obese at the preceding CARDIA exam than among those who were normal/underweight. There was no evidence of interaction by race.

Conclusions: Higher levels of childhood trauma were associated with increased risk of GDM, with possible effect modification by BMI.

Pregnancy outcomes

Variation in Breastfeeding Initiation and Duration by Mode of Childbirth: A prospective, population-based study Edmond Shenassa*, Lindsay Mallick Edmond Shenassa Edmond Shenassa

Less than half of infants in high-income countries breastfeed until 6 months of age, despite well-known benefits including prevention against infections for infants. One potential barrier to long-term breastfeeding is birth by cesarean section (C-Section), which can invoke long-term difficulties. After we conducted a structured review of literature published between January 2000 and June 30, 2022, we found that the literature to date has not fully elucidated this relationship using critical methods, like conditioning on breastfeeding or conducting a time to event analysis, disaggregated mode of birth by type of C-section. We analyzed data from 14,414 mother-infant dyads enrolled in the United Kingdom-based prospective Millennium Cohort Study, beginning in 2001. Using multivariable logistic regression, we examined the association between mode of birth (vaginal, emergency C-section, and elective C-section) and likelihood of breastfeeding initiation. We then applied adjusted Accelerated Failure Time survival models to examine the associations between mode of birth and duration of any and exclusive breastfeeding. Relative to vaginal births, women with planned (but not emergency) C-section were less likely to initiate breastfeeding (odds ratio: 0.84, 95% Confidence Interval (CI): 0.71-0.99), but that those with either planned and unplanned C-section discontinued both any and exclusive breastfeeding sooner. However, for planned C-section, there were larger differences for time to cessation of any breastfeeding (Time Ratio (TR): 0.75, 95%CI: 0.64-0.89), than unplanned C-section (TR: 0.85, 95%CI: 0.74, 0.97) compared with vaginal births. Practical implications of these finding for supporting breastfeeding among those having had a C-section are discussed.

Pregnancy outcomes

Do Religiosity and Spirituality Modify the Association Between Adverse Childhood Experiences and Preterm Delivery? A Latent Class Moderation Analysis Yasamean Zamani-Hank* Ahnalee Brincks Nicole Talge Jaime Slaughter-Acey Claire Margerison

Religiosity (R) and spirituality (S) have been identified as potential protective factors that may buffer against life stressors to promote positive pregnancy outcomes. No studies to date have evaluated the relationship between adverse childhood experiences (ACEs), R, S, and preterm delivery (PTD). Using a latent class moderation analysis, we evaluated whether R and S modified the relationship between membership in two identified latent classes of women (high ACE prevalence class vs. low ACE prevalence class) and preterm delivery among a sample of n=3,884 women from the National Longitudinal Study of Adolescent to Adult Health (1994-2018) who had a pregnancy that ended in a live birth. Data on six ACEs (sexual, physical, and emotional abuse; neglect, family member suicide attempt or death, foster care placement), PTD, R, S, and race were collected via self-report. A composite childhood SES construct included parental occupation and education, family income, and public assistance receipt. A Wald test was conducted to assess whether R and S modified the relationship between the two latent classes and PTD in the overall sample and in stratified analyses by race and SES. We found that neither R or S modified the association between latent class membership and odds of PTD for the majority of race and SES subgroups (p>.05, respectively). However, in the overall sample, we found that among women with high levels of religiosity, the odds of PTD were higher in the high ACE vs. low ACE class (OR 3.4, 95% 1.2-9.7). Similarly, among women with high levels of spirituality, the odds of PTD were higher in the high ACE vs. low ACE class (OR 3.4, 95% CI 1.4-8.4). These results indicate that R and S may be protective against PTD for women with a lower prevalence of ACEs but not for women with higher prevalence of ACEs. These findings suggest that R and S may not operate equally for all women in all contexts of adversity, highlighting the need to consider adversity thresholds.

Pregnancy outcomes

Lifetime exposure to abuse modifies associations between PFAS & gestational hypertension Tamarra James-Todd*, Kathryn Tomsho Emma V. Preston Jennifer J. Stuart Janet Rich-Edwards Marie-France Hivert Emily Oken Jorge E. Chavarro Sheryl Rifas-Shiman Briana Stephenson Ami Zota Tamarra James-Todd Tamarra James-Todd

Background: Psychosocial stressors can modify the associations between environmental toxicant exposures and adverse pregnancy outcomes. We sought to examine whether early life exposure to physical and/or sexual abuse modified the association between PFAS and HDP.

Methods: Project Viva participants recruited during pregnancy from obstetric practices in eastern Massachusetts from 1999-2002, who provided an early pregnancy blood sample comprised the analytic population. Maternal plasma concentrations of 8 PFAS were measured in samples collected at a median 9.7 weeks of gestation. HDP data were abstracted from medical records and classified as normotensive (ref.), gestational hypertension, and preeclampsia. Participants with chronic hypertension were excluded. History of physical or sexual abuse (yes/no) was self-reported via a Personal Safety Questionnaire in early pregnancy. Associations of early pregnancy concentrations of individual PFAS with HDP were estimated via multinomial logistic regression with interaction terms for log-2 transformed PFAS and abuse, controlling for race/ethnicity and age.

Results: Among 1,247 participants, 39% had experienced abuse. We observed higher odds of gestational hypertension per doubling of PFOA, PFOS, and PFNA concentrations with significant effect modification by abuse (interaction p-values: PFOA=0.01, PFOS=0.03, PFNA=0.03). The ORs (95% CIs) for gestational hypertension associated with a doubling of PFOA, PFOS, and PFNA among those with a history of abuse were 2.36 (1.35, 4.12), 1.98 (1.20, 3.26), and 2.07 (1.18, 3.63). The corresponding estimates among women with no history of abuse were 0.98 (0.66, 1.45), 1.08 (0.76, 1.54), and 0.98 (0.68, 1.40). PFAS concentrations were not associated with odds of preeclampsia and we did not find evidence of effect modification by abuse.

Conclusion: History of abuse appears to modify associations between PFAS and gestational hypertension. Future work should seek to replicate these findings.

Social determinants of health

Heterogeneity in self-reported hospital experiences in the 2020 North Dakota Pregnancy Risk Assessment Monitoring System COVID-19 Supplement Julia Wilson-Peltier*, Andrew Williams Julia Wilson-Peltier Lexie Schmidt Grace Njau Matthew Schmidt Anastasia Stepanov Julia Wilson-Peltier

Background. There is limited research on hospital experiences of mothers who gave birth during the COVID-19 pandemic. This analysis describes COVID-19 hospital experiences of mothers in North Dakota(ND).

Methods. Data for 1588 women(weighted) was drawn from the 2020 ND Pregnancy Risk Assessment Monitoring System(PRAMS). Participants reported 'yes' or 'no' regarding hospital experiences during delivery(received information on protecting baby from COVID-19, masking when caring for baby, masking when others were present, if they were separated from baby, and if baby was tested for COVID-19), social support(family member/friend present, husband/partner present) and breastfeeding(received information on protecting baby during breastfeeding, masking while breastfeeding, pumping to avoid infecting baby, and trouble consulting a lactation specialist). Data were summarized using weighted percentages by race, age, income, education, and marital status.

Results. The sample was primarily White(80.3%), married(75.3%), and no college degree (57.9%), and 30.2% had income ≤$47,999. Compared to American Indian(AI) mothers, White mothers had lower rates of receiving information on protecting baby(57.4% vs 43.1%.), masking when caring for baby(13.6% vs 7.6%), masking when others were in the room(54% vs 38.6%), and baby being tested for COVID-19(27.3% vs 3.7%). For social support, 100% of White mothers reported having their husband/partner present compared to 75% of AI mothers. For breastfeeding experiences, White mothers reported lower rates of masking while breastfeeding and trouble consulting a lactation specialist than AI mothers. Hospital experiences, social support, and breastfeeding also differed by marital status, education, income, and age.

Discussion. Results suggest differences in hospital experiences for mothers by demographic factors during the COVID-19 pandemic. These data may inform culturally safe healthcare practices to provide equitable experiences for all patients.

Social determinants of health

County-level indicators of residential racial segregation and neonatal anthropometry in the NICHD Fetal Growth Studies Jessica Gleason* Pauline Mendola Zhen Chen Kathryn Wagner Calvin Lambert Marion Ouidir William Grobman Roger Newman Katherine Grantz

Background: Racial and ethnic differences in fetal growth and birth size have not been explained by individual SES factors. We explored whether differences may be partially explained by residential racial segregation.

Methods: We linked participant zip codes from a pregnancy cohort (2009-2013) to county-level data from the American Community Survey to calculate 2 indices of segregation: racial isolation and racial evenness (Thiel's H, corresponding to the proportion of multiple race/ethnic groups in a county). Using hierarchical modeling to account for county-level clustering and a causal mediation analysis adjusted for individual sociodemographics, we calculated the extent to which racial differences in birthweight (BW) and length (BL) could be explained by residential segregation. We also tested for effect modification using hierarchical models by each race/ethnic group.

Results: Compared to Non-Hispanic white (NHW, n=431), county-level racial evenness in neonates of Asian mothers (n=334) mediated 21.0% (95% CI 2.3, 39.7%) of the difference in BW and 49.6% (-8.7, 98) in BL; 28.5% (7.3, 64.4) of the difference in BW for neonates of Hispanic women (n=454); and no proportion of the difference in BW or BL for neonates of non-Hispanic Black (NHB, n=395) women. No mediation was observed for racial isolation. When testing for effect modification, there was no association between racial evenness and birthweight for Asian, Hispanic, or NHB women, but neonates of NHW women were 27.8g (6.5, 49.1g) larger for every 0.1 unit (10%) decrease in evenness and 39.8g (2.4, 76.6g) larger for every 0.1 unit increase in isolation.

Conclusions: Indicators of residential racial segregation partially explained differences in BW and BL for Asian and Hispanic women compared to NHW. As county composition skewed toward NHW, neonates of NHW women had larger birthweight, which may indicate a differential impact of structural factors associated with residential segregation across race/ethnic groups.

Social determinants of health

Relationships between subjective socioeconomic status and birth outcomes Julia Porth* Bobby Cheon

Background: Socioeconomic inequalities in preterm birth (PTB) and low birth weight (LBW) persist in the United States. Internalized, psychological processes due to low perceived socioeconomic status (SES) relative to others ("subjective SES") may be one pathway linking SES to disparities in PTB and LBW. This analysis investigated relationships between subjective SES and women's experiences delivering a child who was born preterm or had a low birth weight. **Methods:** Data came from the National Longitudinal Study of Adolescent to Adult Health. Subjective SES was assessed at Wave 4 (collected in 2008-09 when participants were aged 24-33) via the MacArthur Scale of Subjective Social Status (range 1-10). Relationships between subjective SES, PTB, and LBW in deliveries occurring between Wave 4 and Wave 5 (2016-18, participants aged 33-41) were assessed using logistic regressions accounting for complex survey design and clustering of births by mother. **Results:** The PTB sample included 1,293 births from 838 mothers and the LBW sample included 1,257 births from 818 mothers. Participants had an average subjective SES score of 5.24 (standard deviation: 1.78) in both samples. Higher subjective SES was associated with slightly higher odds of PTB (odds ratio [OR] for a one-unit increase in subjective SES: 1.11, 95% confidence interval [CI]: 0.95, 1.29), though the 95% CI contained the null. Associations between subjective SES and LBW were weaker (OR: 1.04, 95% CI: 0.82, 1.32). Accounting for perceived stress at Wave 4 did not change the results. **Conclusions:** Findings suggest higher subjective SES may be associated with increased odds of PTB, though results should be confirmed in other samples. Future research should further probe these relationships to examine if other measures of perceived SES inequality are associated with PTB and LBW.

Social determinants of health

Family relationships and depressive symptoms during pregnancy among Black women Lisa A. DeRoo* Sharon K. Davis Cleopatra H. Caldwell Dawn Misra

A close relationship with the father of the baby (FOB) has been linked with women's reduced risk of depressive symptoms during pregnancy, but little is known about other family relationships and maternal depression. We analyzed data from the Life-course Influences on Fetal Environments Study (2009-2011), a cohort of 1,410 new Black mothers in Metropolitan, Detroit. During postpartum interviews, women were asked about the closeness of their relationships with the FOB, their parents and the FOB's mother. The 20-item Center for Epidemiologic Studies Depression Scale (CES-D) was used to measure depressive symptoms. Poisson regression was used to estimate risk ratios (RR) and 95% confidence intervals (CI) for clinical depression (CES-D score 16+) adjusting for potential confounders. Relationship closeness for each parent, taking into account FOB relationship, was examined as follows: both FOB and parent close, FOB close and parent neutral/cold, FOB neutral/cold and parent close, and both FOB and parent neutral/cold (referent). 41.5% of women were clinically depressed. Close relationships with their mother (RR=0.82; 95% CI 0.67, 0.99), the FOB's mother (RR=0.82; 95% CI 0.64, 1.06), and their father (RR=0.88; 95% CI 0.70, 1.10), suggested a decreased risk of depression even when FOB relationship was neutral/cold. Risk estimates were most protective when both the FOB and parent relationships were close: RR=0.55 (95% CI 0.46, 0.66) for their mother; RR=0.52 (95% CI 0.43, 0.63) for the FOB's mother; and RR=0.60 (95% CI 0.49, 0.74) for their father. Along with the FOB relationship, close relationships with parents and the FOB's mother were protective against the risk of depression during pregnancy. A supportive family context may positively influence maternal mental health and thus improve birth outcomes among Black women.

Social determinants of health

Characterizing gestational parents in a census tract by residence in or out of a historical redlining HOLC polygon Kristen Rappazzo*, Monica Jimenez Adrien Wilkie Christine Gray Alison Krajewski Kristen Rappazzo Lynne Messer Thomas Luben Kristen Rappazzo

Background/Aim:

Around the mid-1930s, the Home Owners' Loan Corporation (HOLC) ranked urban neighborhoods as least to most desirable in terms of perceived mortgage stability, documenting fine-scale spatial variability in a structural racist practice (i.e., redlining). We evaluated how extending the fine-scale spatial variability represented by HOLC polygons to larger geopolitical boundaries (i.e., census tracts [CT]) may contribute to selection bias in epidemiologic studies of redlining by assessing demographics across five historically redlined cities in North Carolina (NC). We compared individuals who resided in an HOLC polygon to individuals who resided in the corresponding census tract but not in an HOLC polygon.

Methods:

Geocoded NC birth records (2003-2015) were assigned HOLC grade A (Best), B (Still desirable), C (Declining), or D (Hazardous) using a "point-in-polygon" approach. HOLC grade was assigned to CT based on the grade of the HOLC polygon(s) covering the majority of the land area. We used Chi-square test of proportions to compare race/ethnicity, age, and Medicaid eligibility of gestational parents, and gestational age, birth weight, and presence of a birth defect among infants in an HOLC polygon to those in the same census tract but residing outside a polygon

Results:

Our analysis included 83,130 residential addresses in 142 CT; 32968 (47.2%) in an HOLC polygon, and 43887 (52.8%) in an HOLC CT but not in an HOLC polygon. There was a higher proportion of non-Hispanic (NH) white gestational parents living in HOLC polygons than in HOLC CT; the opposite was observed for NH Black, Hispanic, and Asian gestational parents. The proportion of infants born preterm (<37 weeks) or low birth weight (<2500 g) was higher in HOLC polygons compared to HOLC CT.

Conclusions:

This comparison of demographics suggests there are differences between individuals who reside in an HOLC polygon and those who do not but live in the same census tract.

Lifetime Racial Discrimination in Healthcare Settings and Preconception, Prenatal, and Postpartum Care Utilization using the Pregnancy Risk Assessment Monitoring System

Bonnie Bloxom* Maria Ness Suzanne Zane

Introduction

Racism in healthcare settings negatively impacts healthcare utilization among Hispanic, non-Hispanic (NH) American Indian/Alaska Native, NH Black/African American, NH Asian, NH Pacific Islander/Native Hawaiian, and NH Multiracial individuals. Associations between racial discrimination and healthcare utilization have not been explored in Oregon's birthing population.

Methods

We used 2016-2020 Oregon Pregnancy Risk Assessment Monitoring System data, which sampled people with a recent live birth. Lifetime experience of racial discrimination in healthcare settings (LDHCS) was created from a state-added yes/no question that asked "Have you ever experienced discrimination while getting any type of health or medical care …because of…My race or skin color?"

We used three multivariable logistic regression models to estimate adjusted odds ratios (AOR) and 95% confidence intervals (CI) for the association between LDHCS and preconception checkup, adequate prenatal care (PNC) Kotelchuck index, and postpartum visit (PPV). Analysis sample (unweighted n=6891) excluded non-Hispanic White respondents. Models controlled for demographic variables, prenatal depressive symptoms, chronic diabetes or hypertension, and having a personal doctor. The PNC and PPV model included a yes/no risk variable (yes if one or more of gestational diabetes, gestational hypertension, eclampsia, or previous preterm birth were present), and parity.

Results

The weighted prevalence of LDHCS was 8.1%. LDHCS was positively associated with a preconception checkup (AOR: 1.13; CI 1.03-1.24), negatively associated with having adequate PNC (AOR: .78; 95% CI .73-.84), and negatively associated with attending a PPV (AOR: .76; 95% CI .69, .84).

Conclusion

LDHCS was associated with higher odds of a preconception checkup and lower odds of having adequate PNC and a PPV. Lower utilization of PNC and PPV represents a missed opportunity to detect problem(s) and to prevent adverse maternal and infant health outcomes.

Substance Use

Comparison of Demographic and Clinical Characteristics of Birthing People and their Infants with and without Neonatal Abstinence Syndrome in Massachusetts, 2020-2021

Alyssa M. Pochkar* Mahsa M. Yazdy Hanna M. Shephard Eirini Nestoridi

The Massachusetts (MA) Department of Public Health conducts active, state-wide, population-based surveillance to identify infants with neonatal abstinence syndrome (NAS) per the Council of State and Territorial Epidemiologists (CSTE) NAS (Tier 1) Standardized Case Definition. Surveillance data were used to assess characteristics of birthing people and infants in MA. It is important to identify risk factors and disparities among this population, and link birthing people and their infants to treatment and services. Potential cases were identified by NAS-related ICD-10-CM diagnostic codes and documentation of NAS on birth certificates. Cases underwent medical record abstraction and clinical review and classification, with additional information derived from birth certificates to ascertain self-reported demographic information. We compared distributions of demographic and clinical characteristics for birthing people and infants with and without NAS born during April 1, 2020 – March 31, 2021, in MA. Among 67,542 live births, 829 (1.2%) infants were classified as having NAS. Non-Hispanic (NH) White pregnant people were overrepresented (80.9%) in the NAS population when compared to the population without NAS (57.6%). Most (86.0%) dyads classified as having NAS were publicly insured versus 35.7% of those without NAS. More than a third (38.1%) of persons delivering an infant with NAS received inadequate prenatal care, compared with only 10.3% of birthing persons of infants without NAS. A greater proportion of infants with NAS were born moderate to late preterm (18.1%) compared to those without NAS (7.5%). Understanding differences in demographic and clinical characteristics of birthing person-infant dyads with NAS in MA may help inform clinicians and other providers about the needs for care, treatment, and referral to appropriate services for pregnant persons with a history of substance use and their infants.

Substance Use

Experiences of Discrimination and Treatment Outcomes Among Pregnant and Postpartum People with Opioid Use Disorder Nichole Nidey* Angel Ehrenschwender Joyce Xu Emily DeFranco Christine Wilder Aaron Murnan Mishka Terplan

OBJECTIVE
Experiences of discrimination among pregnant and postpartum people with opioid use disorder (OUD) are common and likely affect utilization of medication for OUD (MOUD), which is associated with reduced risk of overdose and death. The objective of our study was to examine experiences of discrimination among pregnant and postpartum people with OUD by healthcare setting (prenatal care and substance use disorder (SUD) treatment) and estimate its effect on the risk of not using MOUD treatment as prescribed, MOUD discontinuation, return to substance use, and overdose.

STUDY DESIGN
Patient-stakeholders co-designed survey questions to measure self-reported outcomes related to MOUD treatment utilization, return to use, and overdose. A modified Healthcare Discrimination Scale (HDS) was used to measure discrimination during pregnancy. The effect of discrimination experienced by healthcare setting on postpartum MOUD utilization, return to use, and overdose was estimated using log-binomial models to calculate the relative risk (RR) of each outcome.

RESULTS
Among the 100 participants enrolled in the study, 57 reported experiencing discrimination, 56 within prenatal care and 33 within SUD treatment settings. Discrimination within prenatal care (RR 2.6, 95% CI 1.06, 6.40) and SUD treatment (RR 3.26, CI 1.59, 6.70) were associated with increased risk of not using MOUD as prescribed. Discrimination within SUD treatment settings was associated with greater than two-fold increased risk of MOUD discontinuation (RR 2.56, CI 1.19, 5.54) and return to use (RR 2.36, CI 1.18, 4.73)**.**

CONCLUSION
Experiences of discrimination were common, especially within prenatal care settings, and discrimination was associated with poor MOUD treatment outcomes and risk of return to use. Institutional policies, provider-focused trainings, and accountability practices are needed to address discrimination within healthcare settings to improve outcomes for pregnant and postpartum people with OUD.

Substance Use

Birth Interventions Among Women with Opioid Use Disorder Stephanie Mallahan* Linnea Linde-Krieger Lela Rankin Stacey Tecot Alicia Allen

Background: Rates of opioid overdose in the year following delivery are higher among cesarean compared to vaginal delivery (12.9 vs. 9.9 per 10,000 live births). Exogenous administration of the hormone oxytocin (i.e., Pitocin) is also higher among women who deliver via cesarean compared to vaginal births. To identify risk factors for postpartum opioid relapse and overdose, this study tested differences in birth interventions in a sample of women with and without opioid use disorder (OUD).

Methods: At week 1 postpartum, participants (n=29 OUD, n=10 control) completed a semi-structured birth interview. Participants reported mode of delivery (i.e., vaginal, cesarean) and if they had received Pitocin to augment labor. Descriptive statistics (counts, percentages) and a Fisher's exact test to determine differences between groups, were completed in Stata.

Results: Participants were on average 30 years old (standard deviation 5.25 years), and 84% (n=33) were white. All those with OUD were involved in treatment of some kind, with 76% (n=22) taking medication for OUD. Cesarean deliveries accounted for 41.4% (n=12) in the OUD group compared to 50% (n=5) in the control group (p=0.72). Reported use of Pitocin during labor did not differ by group (57.7% OUD, 85.7% control, p=0.22). A significant relationship was found between use of Pitocin and mode of delivery (p= 0.014) in the OUD group.

Discussion: We did not find significant differences in mode of delivery or use of Pitocin by group. However, examining mode of delivery and Pitocin use together revealed a significant relationship for those with OUD, suggesting that OUD group participants were more likely to deliver by cesarean if they received Pitocin. While Pitocin is short acting, it has an unknown role in postpartum opioid relapse. Due to the high risk of postpartum relapse, further research should consider the clinical implications of Pitocin and cesarean delivery (e.g., pain management) for mothers with OUD.

Substance Use

Prenatal exposure to delta 9-tetrahydrocannabinol, neonatal adiposity, and postnatal growth trajectories: The Healthy Start study Brianna Moore* Katherine Sauder Emily Hebert Adrienne Hoyt Erica Wymore Allison Shapiro Gregory Kinney Dana Dabelea

Background: Cannabis use during pregnancy is associated with lower birth weight. Less is known about how cannabis exposure may influence postnatal growth, and whether breastfeeding modifies this association.

Methods: We followed 128 mother-child pairs from Colorado through age 3 years. Prenatal exposure to cannabis was determined by measuring seven common cannabinoids (including delta 9-tetrahydrocannabinol [Δ9-THC] and cannabidiol [CBD]) and their metabolites in maternal urine collected mid-gestation. Generalized linear models estimated the associations between prenatal exposure to Δ9-THC-metabolites (alone or in combination with any other cannabinoid) with neonatal body composition. A mixed-effects model estimated the association between prenatal exposure to Δ9-THCand BMI z-score trajectories. Interaction by breastfeeding was assessed by including a product term in a mixed-effects model.

Results: In our study, 12% (n=15) children had prenatal exposure to any cannabinoid. Of these, 9% (n=12) had prenatal exposure to Δ9-THC alone. Offspring exposed to Δ9-THC alone were smaller at birth (mean difference in birth weight: -216g, 95% CI: -458, 27, p=0.08; mean difference in adiposity: -2.1%; 95% CI: -4.2, -0.04, p=0.04) and grew more rapidly in early childhood (0.50 increase in BMI z-score per square root year; 95% CI: 0.19, 0.82; p<0.01). Breastfeeding modified this association, such that BMI z-scores at 3 years were higher among Δ9-THC-exposed, formula-fed offspring (1.00; 95% CI: -0.05, 2.04; p=0.06) but no difference observed among those who were exclusively breastfed for at least 5 months.

Conclusions: Prenatal exposure to Δ9-THC may alter early-life growth. Breastfeeding may stabilize growth among Δ9-THC-exposed offspring, but the impact of lactational exposure to Δ9-THC is a concern and requires further investigation. Parents and parents-to-be should be informed of the risks of cannabis use during pregnancy and while breastfeeding.

Substance Use

Association between maternal e-cigarette use during pregnancy and low gestational weight gain Xiaozhong Wen* Marjorie Thomas Lufeiya Liu Aye Moe Peter Duong Malkijah Griffiths Ambra Munlyn

Objective: To evaluate the risk of low gestational weight gain (GWG) in women who use electronic cigarettes (e-cigarettes), combustible cigarettes, or both e-cigarettes and combustible cigarettes (dual use) during pregnancy.
Methods: We conducted a secondary analysis of the data from 176,882 singleton pregnancies in the 2016–2020 US Pregnancy Risk Assessment Monitoring System (PRAMS). Postpartum women self-reported their use of e-cigarettes and/or cigarettes during the last 3 months of pregnancy. Low GWG was defined as a total GWG less than 12.7 kg, less than 11.3 kg, less than 6.8 kg, and less than 5 kg (<28, <25, <15, and < 11 lb) for women with underweight, normal weight, overweight, and obesity, respectively. We used multivariable logistic regression to estimate the odds ratios (ORs) of low GWG, adjusting for confounders.
Results: In this national sample, 921 (weighted percentage, 0.5%) women were e-cigarette users, and 1,308 (0.7%) were dual users during late pregnancy. Compared with non-users during late pregnancy (40,090, 22.1%), cigarette users (4,499, 28.0%) and dual users (427, 26.0%) had a higher risk of low GWG, but e-cigarette users had a similar risk (237, 22.1%). Adjustment for sociodemographic and pregnancy confounders moderately attenuated these associations: confounder-adjusted ORs 1.26 (95% confidence interval [CI] 1.18–1.35) for cigarette users, 1.18 (95% CI 0.96–1.44) for dual users, and 0.99 (95% CI 0.78–1.27) for e-cigarette users.
Conclusions: Unlike combustible cigarette use, e-cigarette use during late pregnancy does not appear to be a risk factor for low GWG.

Violence or abuse victimization

Racial Disparities in Adverse Childhood Experiences and the Association with Interpersonal Violence During Pregnancy in North Dakota (ND PRAMS 2017-2020) Lexie Schmidt*, Andrew Williams Lexie Schmidt Julia Wilson-Peltier Grace Njau Matthew Schmidt Anastasia Stepanov RaeAnn Anderson Lexie Schmidt

Background. In North Dakota (ND), American Indian (AI) women have a greater prevalence of adverse childhood experiences (ACEs) than White women and experience a higher prevalence of interpersonal violence. Those exposed to ACEs are more likely to experience interpersonal violence, however evidence regarding racial disparities in this association among pregnant women is limited.

Research Questions. Are ACEs associated with interpersonal violence during pregnancy? Do these associations vary between AI and White women?

Methods. Data for 2,582(weighted n=33,312) AI and White women were collected from the 2017-2020 ND Pregnancy Risk Assessment Monitoring System survey. Participants self-reported(yes/no) to 10 ACEs(high ACES ≥2). “Any interpersonal violence” variable was created if participants reported “yes” to experiencing violence from a husband/partner, ex-husband/partner, family member, or someone else during pregnancy. Logistic regression estimated odds ratios and 95% confidence intervals for associations between high ACEs, individual ACEs, and exposure to violence during pregnancy, adjusted for maternal demographic and health factors.

Results. AI women with high ACEs were 3.13 times(95%CI:1.86,5.27) and White women with high ACEs were 7.31 times(95%CI:2.23,23.93) more likely to experience violence, compared to those with low ACEs. Increased risk of experiencing violence during pregnancy was observed for all ACEs among all women, yet ORs were higher among White than AI women.

Discussion. For AI and White women, high ACEs, verbal abuse, physical abuse, an incarcerated household member, a mother who experienced violence, and feeling unloved during childhood were associated with increased risk of experiencing violence during pregnancy. The ACEs with the highest OR for AI women was having a mother who experienced violence, and for White women was physical abuse. Lower ORs among AI women likely reflect higher prevalence of ACEs among AI women compared to White women.

Violence or abuse victimization

Mediating pathways of neighborhood violence on adverse pregnancy outcomes in California
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Neighborhood violence may contribute to adverse pregnancy and perinatal health outcomes. The contribution of mediating pathways, such as coping behaviors and medical conditions, is not well understood which limits understanding of the mechanisms underlying health disparities in historically minoritized populations exposed to neighborhood violence.

We examined mediating pathways from acute changes in neighborhood violence to adverse perinatal outcomes, restricting analyses to within-neighborhood comparisons to control for time-constant neighborhood factors by design.

We combined California neighborhood violence data with hospital records of singleton live births from 2007-2011. We estimated the excess risk of infant mortality, neonatal mortality, preterm birth, gestational diabetes mellitus (GDM), and preeclampsia among birthing individuals exposed to acute increases in neighborhood violence. We estimated risk differences with targeted maximum likelihood estimation, adjusting for individual- (age, race, parity, education, insurance, conception year and season) and time-varying neighborhood- (temperature, precipitation, unemployment) level potential confounders. Substance use and maternal infection during pregnancy were analyzed as mediators.

Acute increases in community violence were associated with elevated risk of GDM (2.2/1000 RD 95% CI (1.4/1000, 3.1/1000)), preeclampsia (2.4/1000 RD 95% CI (1.6/1000, 3.1/1000)), and preterm birth (0.9/1000 RD 95% CI (0.0/1000, 1.7/1000)). Both maternal infection and substance use mediated effects on all outcomes. Across all outcomes, maternal infection had a larger mediating role than substance use. For example, 21% and 16% of the effect of acute violence on preterm birth was mediated by maternal infection and substance use, respectively. Future analyses will consider additional mediators and estimate mediation effects by racial/ethnic group.

Women’s health

History of multifetal gestation and long-term maternal mortality Susanna Mitro* Rajeshwari Sundaram Yan Qiao Jessica Gleason Edwina Yeung Stefanie Hinkle Pauline Mendola James Mills Sonia Grandi Sunni Mumford Enrique Schisterman Cuilin Zhang Katherine Grantz

Background: Preeclampsia and preterm birth are linked to maternal cardiovascular (CV) risk. Multifetal gestation (twins, etc.) increases the risk of these pregnancy complications, but etiologies may differ from that of singletons. We examined whether multifetal versus singleton gestation was associated with long-term maternal mortality in a diverse U.S. cohort.

Methods: We ascertained vital status as of 2016 via linkage to the National Death Index and Social Security Death Master File of 44,174 mothers from the Collaborative Perinatal Project (CPP; 1959-66). Cox proportional hazards models with maternal age as the time scale assessed associations between history of spontaneous multifetal gestation (in last CPP observed pregnancy or prior pregnancy(ies)) and all-cause and CV mortality, adjusted for demographics, smoking, and preexisting conditions. We calculated hazard ratios (HR) for all-cause mortality over the study period and until age 70 (premature mortality).

Results: Of eligible women, 1,672 (3.8%) had a history of multifetal gestation. Women with versus without a history of multifetal gestation were older, more likely to have a preexisting condition, and more likely to smoke. By 2016, 51% of women with and 38% of women without a history of multifetal gestation had died (unadjusted all-cause HR=1.14 (95% confidence interval (CI): 1.07, 1.23)), but after adjustment for smoking and preexisting conditions, history of multifetal gestation was not associated with all-cause (adjusted HR=1.00 (95%CI: 0.93, 1.08)) or CV mortality (adjusted HR=0.99 (95%CI: 0.87, 1.11)) over the study period. However, history versus no history of multifetal gestation was associated with 11% lower risk of premature all-cause mortality (adjusted HR=0.89 (95%CI: 0.82, 0.96)).

Conclusions: In a cohort with over 50 years of follow-up, history of multifetal gestation was not associated with all-cause mortality. Still, multifetal gestation may be associated with lower risk of premature mortality.

Women’s health

Predictors of Per- and Polyfluoroalkyl Substances (PFAS) Concentrations in Maternal Plasma in the New Hampshire Birth Cohort Study Yuting Wang* Jiang Gui Caitlin Howe Jennifer Emond Lisa Gallagher Margaret Karagas Megan Romano

Per- and polyfluoroalkyl substances (PFAS) are related to various health outcomes and food is a common source of PFAS exposure. Dietary predictors of PFAS have not been adequately explored among pregnant individuals. We examined dietary predictors of plasma PFAS concentrations among 649 pregnant individuals enrolled during 2009-2018 in the New Hampshire Birth Cohort Study. PFAS concentrations, including perfluorohexane sulfonate (PFHxS), perfluorooctane sulfonate (PFOS), perfluorooctanoate (PFOA), perfluorononanoate (PFNA), and perfluorodecanoate (PFDA), were measured in maternal plasma collected at ~24 to 28 gestational weeks. Information on sociodemographic, lifestyle, and reproductive factors were collected from prenatal questionnaires and diet from food frequency questionnaires at ~24 to 28 gestational weeks. We used adaptive elastic net (AENET) to predict plasma PFAS concentrations on a training set (n=521) and tested model performance on a test set (n=128). We used multivariable linear regression to assess associations of dietary predictors selected by AENET models and plasma PFAS concentrations, adjusting for enrollment age, parity, previous breastfeeding duration, gestational week of blood sample collection, and enrollment year. Higher egg, fish/seafood, red processed meat, and popcorn intake during pregnancy predicted higher PFAS concentrations in AENET models, while higher fruit and whole grain intake predicted lower PFAS concentrations. Each 1 serving/day increase in egg intake was associated with a 9.6% (95% CI: 0.8,19.2), 9.4% (2.0,17.2), and 24.9% (13.3,37.6) increase in plasma PFOS, PFOA, and PFDA concentrations respectively. Each 1 serving/day increase in fruit intake was associated with a -4.5% (95% CI: -8.0, -0.9) decrease in PFOS concentrations. Our study suggested intake of certain dietary associated with plasma PFAS concentrations among pregnant individuals, which can inform interventions to reduce PFAS burden for both mothers and offspring.

Women’s health

CLINICAL CHARACTERISTICS OF ANOVULATORY MENSTRUAL CYCLES Joseph Stanford* Shahpar Najmabadi

Women of reproductive age have an incidence of anovulation in the range of 3-10% of cycles, depending on the woman’s age, and the biomarker used to identify ovulation. Presumably, women with subfertility may have higher incidence of anovulatory cycles. We aimed to 1) describe the proportion of anovulatory cycles in fertile and subfertile women; 2) examine the lengths of ovulatory and anovulatory cycles by woman’s age and fertility status. We conducted a secondary data analysis, combining data from four cohorts of women, followed for 1-3 years. Women recorded vaginal bleeding and mucus discharge daily. We used the peak day of cervical mucus within a cycle as the indicator of ovulation in the cycle. We used generalized linear mixed models stratified by cycle ovulatory status, age, and fertility status to describe cycle length. The combined data included 4477 cycles from 771 women: 581 presumably fertile women with 3324 cycles, 190 subfertile women with 1153 cycles. Overall, 5.0% of cycles (n=224) were anovulatory: 3.5% of cycles of fertile women (n=115), and 9.5% (n=109) cycles of subfertile women). Among nonconception cycles (4235), overall cycle length was 30.73 days, 95% confidence interval (CI) 30.32, 31.15. When controlled for gravidity (none vs ≥1) and fertility status (fertile vs subfertile), among ovulatory cycles, younger women (<30) had significantly longer cycles compared to older women (30.93 days, 95% CI 30.35, 31.510) vs (29.28 days, 95% CI 28.52, 30.04). There was a significant difference in anovulatory cycle length by fertility status: anovulatory cycles of subfertile women were significantly shorter than fertile women (30.90 days, 95% CI 28.71, 33.09) vs (36.53 days, 95% CI 32.09, 40.96). Overall, both short (<24 days) and long (>35 days) cycles were more frequent among anovulatory cycles than among ovulatory cycles (7.1% vs 1.1%, and 19.2% vs 10.3%, respectively).

Women’s health

Association between serum 25-hydroxyvitamin D and antimüllerian hormone Anita Subramanian* Quaker E. Harmon Lia A. Bernardi Mercedes R. Carnethon Donna D. Baird Erica E. Marsh Anne Marie Z. Jukic

Background: Vitamin D has been associated with fertility and reproductive outcomes. Antimülleiran hormone (AMH) is considered a marker of ovarian reserve. The objective of this study was to examine the association between 25-hydroxyvitamin D [25(OH)D] concentration and ovarian reserve as measured by AMH.

Methods: Cross-sectional analysis of African American participants living in the Detroit, Michigan area, ages 23-35 years, using enrollment data from prospective cohort study designed to assess fibroid development. Participants (N=1591) included those without polycystic ovarian syndrome, pregnancy, and non-missing AMH or 25(OH)D measures at baseline. Linear regression was used to examine the associations between categorical 25(OH)D (ng/ml: <12, 12-<20, 20-<30, ≥30) and continuous natural log transformed AMH. Logistic regression was used to estimate the odds ratio for high or low AMH.

Results: Participants had a mean age of 29 years (standard deviation: 3.0 years). The 25(OH)D levels were low in this population with 29% of participants having levels less than 12 ng/ml, 41% with levels from 12-<20 ng/ml, 22% with levels from 20-<30 ng/ml, and 8% with levels ≥30 ng/ml. In models adjusted for age, BMI, hormonal contraceptive use, smoking and exercise, compared to 25(OH)D levels <12 ng/ml, AMH was 11% higher (95% CI: -0.07, 0.28) for 25(OH)D levels ≥30 ng/ml. Those with 25(OH)D ≥30 ng/ml, had higher odds of high AMH (>7.8 ng/ml, based on the 90th percentile) (OR [95% CI]: 1.47 [0.77, 2.81]). Exclusion of participants with irregular cycles and very high AMH, which might indicate undiagnosed PCOS, did not alter the association.

Conclusion: Higher 25(OH)D was imprecisely associated with higher AMH. To further explore this association, studies should examine populations with higher 25(OH)D levels and AMH measured at multiple time points to determine if long-term changes in 25(OH)D impact AMH levels.

Women’s health

Differences in birth hospitalization experiences during the COVID-19 pandemic by maternal race and ethnicity, Pregnancy Risk Assessment Monitoring System, 2020 Jessica Meeker*, Regina Simeone Mehreen Meghani Jessica Meeker Lauren Zapata Romeo Galang Beatriz Salvesen von Essen Ada Dieke Sascha Ellington Jessica Meeker

The COVID-19 pandemic changed obstetric care. Many hospitals implemented mitigation measures to prevent COVID-19 transmission. It is unclear whether approaches implemented during the COVID-19 pandemic were equitably experienced by women of different race and ethnicities.

Our analysis of the 2020 Pregnancy Risk Assessment Monitoring System (PRAMS) included 12,879 women who had a live, in-hospital birth, from April–December 2020, and responded to questions about experiences with COVID-19 during the birth hospitalization. These experiences were having their baby tested for COVID-19, being separated from their baby due to COVID-19, and not being allowed a support person during their labor and delivery, among others. Weighted percentages of birth hospitalization experiences were calculated. Adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) estimated associations between maternal race and ethnicity and birth hospitalization experiences.

Overall, 12.3% of women reported their baby being tested for COVID-19, 3.6% reported being separated from their baby, and 1.8% reported not being allowed a support person. These experiences differed by maternal race and ethnicity. Compared to non-Hispanic white women, American Indian/Alaska Native (aPR=2.7, CI: 1.2-6.3), Hispanic (aPR=2.2, CI: 1.5-3.1), non-Hispanic Black (aPR=2.4, CI: 1.7-3.5), and non-Hispanic Asian (aPR=2.9, CI: 1.7-4.9) women were more likely to report being separated from their baby due to COVID-19. American Indian/Alaska Native (aPR=5.3, CI: 1.8-15.4) and non-Hispanic Black (aPR=2.3, CI: 1.3-4.1), compared to non-Hispanic White, women were more likely to report not being allowed a support person.

Women reported a range of birth hospitalization experiences, with variation by race and ethnicity. COVID-19 mitigation measures may have been unequally experienced by racial and ethnic minorities. The impact of some hospitalization experiences on maternal and infant well-being is unclear.

Women’s health

Maternal glucose level and future risk of developing cardiovascular diseases: a systematic review Na Zeng* Wendy Wen Daniel J Corsi Wenshan Li Taddele Kibret Shi Wu Wen

Introduction Hyperglycemia during pregnancy has been considered one of the risk factors for cardiovascular diseases (CVD) for women. Although the evidence regarding the association between gestational diabetes mellitus (GDM) and subsequent cardiovascular disease has been synthesised, there is a lack of systematic review covering the evidence of the association between the specified glucose level and future risk of CVD. This systematic review and meta-analysis therefore aim to summarise existing evidence on the association between maternal glucose level and the risk of future CVD in pregnant women with or without a diagnosis of GDM.

Methods and analysis This systematic review protocol was developed following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) guidelines. The protocol of this review was registered in PROSPERO (registration number: CRD42022363037). Comprehensive literature searches were performed in the following electronic database: MEDLINE, EMBASE and CINAHL to identify relevant papers from inception to December 31, 2022. All observational studies (case control studies, cohort studies, cross-sectional studies) will be included. Two reviewers performed the abstract and full-text screening based on the eligibility criteria through Covidence. The Newcastle-Ottawa Scale (NOS) was used to assess the methodological quality of included studies. The study results were reported in the sequence of main outcomes, secondary outcomes, for overall and each type of glucose level separately.

Results Four studies were identified in this review, including two retrospective cohort studies and two retrospective case-control studies. A total of 347,727 women were included in this review. All these studies were rated as good or high quality, which were assessed with a score of 7 and above. Among these four studies, three of them were in Israel and one was in Canada. Two studies assessed specified glucose level measured by glucose challenge test (GCT), whereas the other two studies focused on glucose level without specification of glucose test. For those glucose level measured by GCT, one study showed that women with GCT >11.1 mmol/L and GCT (10-11.1mmol/l) are more likely to develop cardiovascular morbidities, with HR of 2.00 (95% CI 1.40-2.87) and 2.13 (95% CI 1.54-2.93) respectively, compared to those with GCT 7.2 have an increased risk of cardiovascular morbidity requiring hospitalization, with HR of 1.25 (95% CI 0.90–1.73), compared to those with glucose 7.2 mmol/L and less; whereas the other study found out women with glucose level > 5.5mmol/L have higher risk of atherosclerotic morbidity (HR 1.29, 95% CI 1.1-1.5) compared to those with glucose level between 4.4 and 5.5mmol/L. One of those studies also treated the glucose level measured by GCT as a continuous variable, which showed that for each nmol/L glucose increase, the risk of the CVD will be increased, with HR 1.13 (95% CI 1.04–1.22).

Conclusion Women with hyperglycemia are more likely to have increased CVD and relevant comorbidities. However, there is a lack of research pertaining to the association of glucose level measured by fasting glucose or other types of post-loaded glucose tests. Further research is warranted regarding the relationship between specified glucose measurements during pregnancy and CVD.

Women’s health

Transfers to hospital of women registered to give birth at home: a national clinical audit, 2018-2020 Indra San Lazaro Campillo* Indra San Lazaro Campillo Jessica Keane Irene O’Farrell Sarah Meaney Joye McKernan Paul Corcoran Richard Greene Marit L. Bonvbjerg

Background. There is little evidence on the frequency of transfers among women who planned a homebirth, or on the indications for transfer.

Objective. To the describe the flow of hospital transfers among women who registered for a home birth in Ireland.

Methods. National clinical audit on home birth services (HBS) for three years in the Republic of Ireland (ROI). Retrospective review of data provided by Self-Employed Community Midwives (SECMs) and Designated Midwifery Officers (DMOs) from clinical maternity notes.

Results. 848 women registered for a home birth from 2012 to 2021 in the ROI. 33.4% were referred to a maternity hospital due to complications in the antepartum period. Post maturity (14%), prolonged pre-labour rupture of membranes (11%) and small for gestational age (9%) were the most common reasons. 22% of women transferred antenatally returned to the care of the SECMs following review. Of the 627 women who began labouring at home, 22% were transferred with nulliparous women bring more likely (33% v. 8%). Of the 136 women who required intrapartum transfer, 131 gave birth in hospital, three women gave birth at home but were transferred in before the 3rd stage was complete, and two women gave birth in transit. Over 90% of intrapartum transfers were during the 1st stage of labour. Failure to progress in labour (27%) and maternal request for medical analgesia (27%) were the main reasons. The mean time it took to transfer was 32.1 minutes. Almost 50% of women who had an intrapartum transfer, were transferred in less than 30 minutes. Another 50% took between 30 and 60 minutes. Only 5% took over 60 minutes. Thirty-eight women who gave birth at home were transferred in the postpartum period. Postpartum haemorrhage (32%) and extensive perineal tear (26%) were the most common reasons.

Conclusion. As demonstrated, transfer of care to the maternity hospital for women registered for home birth is a key factor to consider when providing HBS.

Women’s health

How is the newborn’s weight and length at birth affected by maternal diabetes? Thomas Skogvold* Nils-Halvdan Morken Linn Marie Sørbye Rolv Skjærven Kari Klungsøyr

Introduction: Gestational diabetes is a pregnancy complication while type 1 and type 2 diabetes are chronic conditions. Diabetes during pregnancy is known to increase average birthweight of the fetus. Less is known about whether the different subtypes differentially affect fetal size.

Aim: To explore how maternal diabetes subtype differentially affects fetal weight and length at birth.

Method: We identified 483 346 nulliparous women who gave birth to a viable singleton child between 1999-2020 using the Medical Birth Registry of Norway. We studied newborn size in diabetic mothers stratified by infant sex and diabetes subtype (pregestational -type 1 and type 2, or gestational diabetes), with non-diabetic mothers as the reference group. Generalized additive models in R were used to describe size by length of gestation. Mean values and 95% confidence intervals (CI) were evaluated by analysis of variance.

Results: Among nulliparous women giving birth in Norway (1999-2020), 3% were registered with diabetes during their first pregnancy. Of these women 0,7% had pregestational and 2,1% gestational diabetes. Generalized additive models showed that newborn length and weight differed by diabetes subtype (pregestational or gestational). Mean birthweight at week 38 for offspring of non-diabetic mothers (3217g, 95%CI 3213-3220g) was lower than for pre-gestational and gestational diabetes (3641g, 95%CI 3612-3671g and 3381, 95%CI 3363-3400g, respectively). The effects were more apparent for weight than length at birth. The largest relative difference in size was found among those born between gestational week 28 and 38 (day 196 and 266).

Conclusion: In the Norwegian population, maternal pregestational diabetes was associated with higher average birthweight and average body length. Gestational diabetes did not affect weight and length at birth to the same degree.

Women’s health

Dairy Intake and Uterine Fibroid Development: A Prospective Study Ky’Era Actkins* Ganesa Wegienka Donna Baird Lauren Wise Quaker Harmon

Uterine fibroids (UF), benign tumors of the uterus, are associated with severe gynecologic morbidity and are the primary indication for hysterectomy in the United States. Dairy intake has been associated with decreased UF risk in some studies. We examined the association between dairy intake and UF development in the Study of Environment, Lifestyle and Fibroids (SELF), a prospective cohort of 1,693 Black/African American women aged 23-35 years at baseline (2010-2012). We assessed UF incidence, growth, and loss with ultrasound every 20 months over 5 years. Dairy intake was collected via questionnaire at every visit as cups of cow’s milk (<0.5, 0.5-0.9, 1-1.4, and ≥1.5 cups/day). Total dairy intake (≤1 or >1 serving/day) was also calculated using a food frequency questionnaire at baseline. We used Cox proportional hazards models to evaluate UF incidence among those without UF at baseline. Growth was calculated as the change in log-volume for UFs matched across visits, and it was analyzed on a by fibroid basis. UF loss was defined as a reduction in UF number between visits and was modeled with Poisson regression. Models were adjusted for age, body mass index, sociodemographic variables, and fibroid characteristics. The majority (62%) of participants consumed <0.5 cups of cow’s milk daily. There were no associations observed between UF incidence and milk consumption or total dairy. However, UF growth decreased by 6.8% (95% confidence interval (CI) -14.6%, 1.8%) for those drinking ≥0.5 cups of milk. This association was slightly stronger for total dairy, with higher intake (>1 serving/day) leading to a 9.6% (95% CI -18.3%, -0.1%) decrease in UF growth and an increase in UF loss (RR=1.1, 95% CI 0.9, 1.5). Our data suggest a protective association between dairy intake and UF growth and loss, but not incidence. These outcomes have not been examined previously and should be explored in populations with higher dairy intake.

Women’s health

No increased risk of cardiovascular death after preeclampsia in over 40% of women: a population based cohort study Sage Wyatt* Liv Grimsvedt-Kvalvik Kari Klungsøyr Truls Østbye Aditi Singh Rolv Skjærven

Introduction: Preeclampsia (PE) most commonly appears only in the first pregnancy among women. Previous literature estimated cardiovascular disease mortality risk to be doubled after PE. But this estimate is biased by including high risk groups, such as one-child mothers and recurrent PE.

Aim: To estimate the risk of cardiovascular death in women with PE by parity, preterm delivery and stillbirth

Methods: Using data from the Medical Birth Registry of Norway, the Norwegian Cause of Death Registry, and the Norwegian Population Registry, we identified 891,076 mothers with first pregnancies registered between 1967–2013. Our primary outcome was mothers’ cardiovascular death between age 40 – 69, defined as death caused by ischemic heart disease, cerebrovascular disease, or peripheral arterial disease. The reference group was women with no preeclamptic pregnancies. Our exposure was PE in the first pregnancy among women who had no PE in later pregnancies by considering interactions with preterm and stillbirth. The association between the exposure and outcome was estimated by Cox proportional hazard model, adjusted for education, mother’s age at first birth, year of birth and marital status.

Results: 5.2% of mothers (891,076) had term PE in their first pregnancy and 1.0% of mothers had preterm PE in their first pregnancy. 44% of mothers (30,665) with PE only had PE in the first pregnancy and no PE in later pregnancies. Among mothers with two pregnancies, mothers with a first term preeclamptic pregnancy and no PE in their second pregnancy did not exhibit an elevated risk of cardiovascular death (HR 1.0, 95%CI 0.8–1.3). The same trend was observed in mothers with 3 children after excluding mothers with stillbirths (HR 1.1, 95%CI 0.8 – 1.6).

Conclusion: Multiparous women with term PE only in the first pregnancy and no preeclamptic pregnancies later have no increased risk of death from cardiovascular causes.