



Annual Meeting Abstract Book

2019

Minneapolis, Minnesota

SPER 2019 Abstract Book

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Student Prize Paper Award

Dominique Heinke, PhD

Massachusetts Department of Public Health

Risk of stillbirth among fetuses with non-syndromic major birth defects: a population-based cohort study

Heinz Berendes International Travel Award

Can Liu, PhD

Karolinska Institutet

Perinatal health of refugee and asylum-seeking women in Sweden 2014-17: a register-based cohort study

Rising Star Award

Wei Perng, PhD

Colorado School of Public Health

Mentoring Award

Emily Oken, MD MPH

Harvard Medical School

President's Award

Cande Ananth, PhD MPH

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ABSTRACTS

MATERNAL OCCUPATIONAL OIL MIST EXPOSURE AND BIRTH DEFECTS — UNITED STATES, 1997–2011

Miriam Siegel, Carissa M. Rocheleau, Candice Y. Johnson, Martha A. Waters, Christina C. Lawson, Tiffany Riehle-Colarusso, Jennita Reefhuis (Division of Surveillance, Hazard Evaluations, and Field Studies, National Institute for Occupational Safety and Health)

Background: Over one million U.S. workers in approximately 40 industries are exposed to metalworking fluids. When metalworking fluids are aerosolized, workers can be exposed to the resultant oil mists through skin contact or inhalation. A previous CDC birth defect cluster investigation at a steel strip manufacturing company found oil mists were one common exposure among fathers of infants born with heart defects. A potential explanation was take-home exposure — workers wore oil mist-contaminated clothes home from work, exposing pregnant partners. However, little research exists on reproductive effects of direct maternal occupational oil mist exposure. We aimed to investigate associations between occupational oil mist exposure during pregnancy and a spectrum of birth defects. **Methods:** We analyzed population-based case-control data from the multisite National Birth Defects Prevention Study. We evaluated occupational exposure among 22,011 mothers of infants with birth defects and 8,140 mothers of infants without birth defects. To estimate associations between oil mist exposure during pregnancy and individual birth defects, we used logistic regression to calculate odds ratios (OR) and 95% confidence intervals (CI), controlling for study site and smoking status. **Results:** Manufacturing jobs, particularly apparel manufacturing, comprised the largest groups of exposed mothers. Mothers of infants with septal heart defects (OR: 1.8; CI: 1.1–3.3), especially perimembraneous ventricular septal defects (OR: 2.5; CI: 1.2–5.2), were more likely to be exposed to oil mists than control mothers. Associations for both defects were stronger for mothers with higher exposure (OR: 2.3; CI: 1.1–4.9, OR: 2.8; CI: 1.1–7.6, respectively) than lower exposure. **Conclusions:** Results support an association between maternal occupational oil mist exposure and septal heart defects. Further research could evaluate reproductive effects of occupational oil mist exposure.

ORGANOPHOSPHATE PESTICIDE EXPOSURE IN PREGNANCY AND FETAL GROWTH Kelly Ferguson, Michiel van den Dries, Romy Gaillard, Anjoeka Pronk, Suzanne Spaan, Henning Tiemeier, Vincent Jaddoe (NIEHS)

Perturbations in fetal growth may have adverse consequences for childhood and later life health. Organophosphate pesticide (OP) exposure has been associated with reduced birth weight at delivery but results are not consistent. We investigated this question by utilizing ultrasound measures of size in utero in combination with measures from delivery. Within the Generation R Study, a population-based prospective cohort conducted between 2002-2006 in Rotterdam, The Netherlands, we measured dialkyl phosphates (DAPs), OP metabolites, in urine samples from early, mid, and late pregnancy and created subject-specific averages to estimate OP exposure (n=784). Ultrasound measures of head circumference, femur length, and estimated fetal weight from mid and late pregnancy and delivery measures were converted to standard deviation scores (SDS). Associations with DAP averages were examined in linear mixed effects models that included an interaction term between gestational age at measurement and DAP average to investigate whether the relationship changed over time. Windows of vulnerability to exposure were assessed by modeling urinary DAPs from each visit in relation to growth measurements. All analyses were adjusted for relevant confounders. At 20 weeks gestation, a 10-fold increase in average DAPs was associated with a -0.53 SDS decrease in fetal length (95% confidence interval [CI]=-0.83, -0.23) and a -0.32 SDS decrease in estimated fetal weight (95% CI=-0.59, -0.04). Effect estimates were greatest in magnitude for DAP concentrations measured early in pregnancy. Associations between DAPs and length and weight at 40 weeks were null. In conclusion, maternal urinary DAPs were associated with decreased fetal weight and length measured during mid-pregnancy, but not at delivery.

PERFLUOROALKYL SUBSTANCES AND THYROID HORMONES IN EARLY PREGNANCY; FINDINGS IN THE DANISH NATIONAL BIRTH COHORT (DNBC) Zeyan Liew, Kosuke Inoue, Beate Ritz, Cecilia Ramlau-Hansen, Birgit Bjerre Høyer, Bodil Hammer Bech, Tine Brink Henriksen, Eva Cecilie Bonefeld-Jørgensen, Stine Linding Andersen, Jørn Olsen (Yale School of Public Health)

BACKGROUND: Thyroid hormones (THs) during pregnancy are essential for fetal brain development. Perfluoroalkyl substances (PFASs), synthetic chemicals widely applied in a variety of industrial and consumer products, have been demonstrated to interfere with thyroid function in adults. We evaluated the associations between six types of PFASs and thyroid function in early pregnancy using samples collected in the Danish National Birth Cohort (DNBC) during 1996-2002. **METHODS:** A cross-sectional analysis was conducted using 1,366 maternal blood samples collected in the DNBC during week 5 to 19 of gestation (median 8.3 week). We estimated changes of serum thyrotropin (TSH) and free thyroxine (fT4) levels according to each of the six PFASs plasma concentrations (ng/mL) analyzed per inter-quartile range (IQR) increase or by exposure quartiles, adjusting for gestational week of blood sampling and other potential confounders. We also estimated the gestational-week-specific relationship between PFASs and TSH or fT4. Binary outcomes for hyper- or hypo-thyroid profiles were also evaluated. **RESULTS:** Overall, there was no apparent association between each of the PFASs and the TSH or fT4 levels or the risk for subclinical hyper or hypo-thyroid status. However, the gestational-week-specific analyses suggested possible dynamic differences in TSH comparing the highest quartile for several PFASs to the lower quartiles; the TSH values were higher for PFOS, PFOA, PFHxS and PFHpS from gestational week 5 to 10 but the trend reversed after gestational week 10. **CONCLUSIONS:** We did not find strong associations between PFASs and TSH or fT4 values among women enrolled in the DNBC most of whom were healthy and without thyroid disorders. We observed possible gestational-week-specific relationships for high PFASs exposures and TSH in early gestation, but replication is needed for these results that were less precise and unexpected a priori.

THE “NEW” SECONDHAND SMOKE: E-CIGARETTE USE IN US HOUSEHOLDS WITH CHILDREN Jenny Carwile, Abby Fleisch, Katherine Ahrens (Maine Medical Center)

Background E-cigarette aerosols are widely perceived as safe to non-users. However, these aerosols contain potentially harmful compounds including nicotine and volatile organic compounds that nonusers can be exposed to through inhalation, ingestion, or dermal contact. The prevalence of households with children exposed to secondhand aerosols from e-cigarettes in the US is unknown. **Methods** We used pooled data from 2016-2017 US Behavioral Risk Factor Surveillance System to calculate the prevalence of self-reported current e-cigarette use among adults with at least one child (≤ 18 years) in the household, overall and by state in the US. We used average marginal predictions from logistic regression to calculate the prevalence difference for adult e-cigarette use by child asthma status, overall and by adult combustible cigarette use. We used survey procedures to account for the complex survey design and weighted estimates to represent the adult population in the US. **Results** During 2016—2017, (4.9% [95% CI: 4.7, 5.1]) of US adults with a child in the home reported current use of e-cigarettes. In the continental US, prevalence ranged from 2.3% (95% CI: 1.5, 3.4) in the District of Columbia to 7.7% (95% CI: 6.5, 9.0) in Oklahoma. E-cigarette use was more prevalent among adults living with a child with asthma (5.6%) versus adults living with a child without asthma (4.8%) (prevalence difference=0.8% [95% CI: -0.05, 1.7]). The prevalence of e-cigarette use did not vary by child asthma status after stratification by adult combustible cigarette use (current, former, never). **Conclusion** Nearly 5% of US adults living in a household with children are e-cigarette users; these children are potentially exposed to secondhand aerosols, an amalgam of compounds with yet unknown health consequences. Future studies should explore the characteristics and exposure levels of children living with adults who use e-cigarettes.

PRE- AND POSTNATAL PM_{2.5} EXPOSURE AND CHILDHOOD LIPID LEVELS IN THE PROGRESS COHORT Laura McGuinn, Allan Just, Itai Kloog, Marcela Tamayo-Ortiz, Citlalli Osorio-Yáñez, Andrea Baccarelli, Martha M Téllez-Rojo, Robert Wright (Icahn School of Medicine at Mount Sinai)

Background: Studies have identified associations between air pollution and lipid levels in adults, suggesting a mechanism by which air pollution contributes to cardiovascular disease (CVD). However, little is known about the association between early life air pollution exposure and lipid levels in children. Given that elevated lipid levels may track from childhood to adulthood, research in children may provide insight into the early origins of CVD. Methods: We used data from 466 mother-child pairs from a prospective birth cohort in Mexico City. Daily PM_{2.5} predictions were estimated using a 1km satellite-based exposure model and averaged over trimesters, entire pregnancy, and the first year of life. We assessed associations with several lipid measures at 48 months of age, including HDL, LDL, total cholesterol and triglycerides. Linear regression models were used to estimate change in lipid levels with each $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} for each of the different pre- and postnatal time periods. Quantile regression was additionally used to assess if the PM_{2.5} effect varied for individuals with low vs high lipid concentrations. Models were adjusted for socioeconomic status, pre-pregnancy body mass index, and age and sex of the child. Results: We observed associations between PM_{2.5} and LDL levels for exposures during the third trimester ($\beta=0.99$, 95%CI: 0.52, 1.46). There was additionally an increasing trend in the effect estimate across higher quantiles of LDL concentrations during the third trimester ($\beta=0.40$, 95%CI: -0.29, 1.22 for the 10th percentile of LDL concentrations and $\beta=2.16$, 95%CI: 1.45, 2.73 for the 90th percentile). Conclusions: PM_{2.5} exposure in late pregnancy may be a critical window for elevated LDL cholesterol in children. Effects were strongest among children with the highest LDL levels which may represent a sensitive subpopulation. Future analyses will use distributed lag regression to further define time specific effects.

PRENATAL EXPOSURE TO SYNTHETIC OXYTOCIN AND RISK OF SUBSEQUENT ATTENTION DEFICIT HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER IN DANISH AND FINNISH CHILDREN Lonny Stokholm, Mette Juhl, Nicole M Talge, Mika Gissler, Carsten Obel, Katrine Strandberg-Larsen (The University of Copenhagen, Denmark)

DESIGN OF STUDY: A cross-national population-based register study **PURPOSE:** Studies have indicated an increased risk of Attention Deficit Hyperactivity Disorder (ADHD) and a small, sex-specific effect on Autism Spectrum Disorder (ASD) among children prenatally exposed to obstetric oxytocin. Since oxytocin is used in approximately half of all deliveries among nulliparous women, these potentially deleterious effects are of concern. The present study aims to examine whether prenatal oxytocin exposure for labor induction and augmentation is associated with ADHD and ASD in offspring born in Denmark and Finland. **METHODS:** In this population-based study, we use data from the national registers in Denmark and Finland. Singletons born in Denmark 2000-2010 (n=577,380) or Finland 1991-2010 (n=945,543) who survived infancy were included in the study population and followed until December 31st 2015. ADHD and ASD were defined using diagnostic codes. In the definition of ADHD, we also included information on prescribed and redeemed ADHD-medication. The cox-regression model with Hazards Ratios (HRs) and 95% confidence intervals modeled with age as underlying time scale was used to estimate the associations. **RESULTS:** Obstetric oxytocin was used in 31% and 46% of the deliveries in Denmark and Finland, respectively. In unadjusted analyses, prenatal oxytocin exposure was associated with slightly increased risk of both ADHD and ASD. However, adjustment almost entirely attenuated the associations: ADHD: (HR=1.03, 95% CI, 1.01-1.05) and ASD: (HR=1.05, 95% CI, 1.02-1.08). The results were similar in Denmark and Finland, and for boys and girls. **CONCLUSION:** Obstetric oxytocin for labor induction and augmentation has no effect on risk of either ADHD or ASD. Our results help to allay any concerns of prenatal use of oxytocin causing ADHD and ASD.

PRENATAL STRESSFUL LIFE EVENTS AND SEX-TYPICAL PLAY BEHAVIOR IN EARLY CHILDHOOD

Jeremy Lessing, Nicole Bush, Alexis Zavez, Sally W. Thurston, Sheela Sathyanarayana, Ruby Nguyen, Sarah Evans, Shanna Swan, Emily Barrett (Rutgers Robert Wood Johnson Medical School)

Introduction: Animal models suggest prenatal stress may impact the prenatal endocrine environment to feminize males and masculinize females. In humans, limited work suggests that prenatal stress is associated with masculinized development and play behavior in girls, with no associations observed in boys. We used data from a multi-center pregnancy cohort (TIDES) to examine the relationship between stressful life events (SLEs) during pregnancy and sex-typical play behavior at age 4. **Methods:** Women completed a 3rd trimester questionnaire on SLEs (n=541; 259M/282F). When children turned 4, mothers completed the Preschool Activities Inventory (PSAI), which assesses sex-typical play behavior; higher composite scores indicate more masculine play. We fit covariate-adjusted linear regression models that included interactions of sex with both PSAI and parental attitude to examine the sex-specific associations between SLEs (dichotomized as 0 vs 1+) and PSAI scores. **Results:** As expected, composite scores were significantly higher in boys than girls ($\beta = 15.17$, $p < 0.001$). Compared to children of mothers with no SLEs, composite scores among children of stressed mothers were non-significantly lower in both males ($\beta = -1.58$, 95% CI: -4.28, 1.11) and females ($\beta = -1.78$, 95% CI: -4.34, 0.77). Maternal education ($\beta = 2.73$, 95% CI: -0.52, 5.98) and parental attitudes about sex-atypical development (boys: $\beta = 1.05$, 95% CI: 0.30, 1.79; girls: $\beta = -1.38$, 95% CI: -2.22, -0.55) were the strongest predictors of composite scores. In both sexes, prenatal stress was non-significantly associated with lower masculine and higher feminine sub-scale scores. **Conclusions:** Contrary to previous work, prenatal SLEs were not associated with sex-typical play behavior. Importantly, maternal education and parental attitudes about sex-typical development were strong predictors of maternal-reported sex typical play, indicative of a need for future work using objective measures of play.

EARLY CHILDHOOD GROWTH TRAJECTORY AND LATER COGNITIVE ABILITY: EVIDENCE FROM A LARGE PROSPECTIVE BIRTH COHORT

Asma Ahmed, Michael Kramer, Jonathan Bernard, Maria Esther Perez Trejo, Richard Martin, Emily Oken, Seungmi Yang (McGill University)

Background: Most previous studies on associations between child growth and cognitive ability have been based on size at one time point or on growth between two time points and a single measure of cognition. **Methods:** In a sample of 12,368 healthy Belarusian children born at term, we examined associations of individual-specific growth trajectories over the first 6.5-years of life with cognitive scores at 6.5 and 16 years and with change in cognition between those ages. We estimated growth trajectories using the Super Imposition by Translation and Rotation (SITAR) model for the overall pattern over the first 6.5 years and the Jenss-Bayley (JB) model to differentiate growth in infancy from post-infancy. Cognitive ability was measured using the Wechsler Abbreviated Scales of Intelligence at 6.5 years and the self-administered computerized NeuroTrax test at 16 years. **Results:** When we examined the growth over the whole period of 6.5 years, overall length/height between birth and 6.5 years was positively associated with the cognitive scores at age 6.5 and 16 years [+2.5 IQ points, 95% CI: (2.0, 3.0) and +2.5 IQ points, 95% CI: (1.9, 3.0) per 1SD increase, respectively], after accounting for other growth parameters and potential confounders. A 1-SD delay in the timing of childhood growth spurt (age of acceleration of length/height velocity) was associated with lower mean cognitive scores [-2.2 IQ points, 95% CI: (-2.8, -1.7) at 6.5 years; -2.2 IQ points, 95% CI: (-2.7, -1.6) at 16 years]. Birth size and post-infancy growth velocity (but not growth in infancy) showed independent positive associations with cognitive scores at both ages. Associations of growth parameters with the change in cognitive scores were small and inconsistent across models. **Conclusion:** Amongst term-born children, the overall size and timing of the childhood growth spurt as well as birth size and post-infancy growth rate were important for cognitive development from early school age to adolescence.

MATERNAL HEPATITIS B OR C CARRIER STATUS AND THE LONG-TERM RISK FOR GASTRO-INTESTINAL MORBIDITY OF THE OFFSPRING: A POPULATION-BASED COHORT STUDY Israel Yoles, Tamar Wainstock, Eyal Sheiner, Naim Abu Freha (Soroka University Medical Center, Ben-Gurion University of the Negev, Beer-Sheva, Israel)

BACKGROUND Many women living with hepatitis B or C (HBV/HCV) are of childbearing age. While the risk of perinatal HBV/HCV has been well established, the long-term implications have been less studied. We aimed to evaluate the association between maternal HBV or HCV carrier status and long-term gastro-intestinal morbidities of the offspring. **METHODS:** A population-based cohort analysis compared the risk for long-term childhood gastro-intestinal diseases (GI) in children born to HBV/HCV carrier mothers vs. those that did not. Childhood GI were pre-defined based on ICD-9 codes, as recorded in the hospital medical files. Children with congenital malformations and multiple gestations were excluded from the analysis. Kaplan-Meier survival curve was constructed to compare cumulative gastro-intestinal morbidities over time, and a Cox proportional hazards model was used to control for confounders. **RESULTS:** During the study period (1991-2014), 242,342 newborns met the inclusion criteria: 771 (0.3%) born to HBV/HCV mothers and 241571 (99.7%) were not. Median follow -up was 10.5 years (0-18 years). Offspring to HBV/HCV mothers had higher incidence of GI diseases (9.3% vs. 5.4%, OR=1.82; 95%CI 1.43-2.32; Kaplan-Meier Log Rank = 0.001). The increased risk remained significant in the Cox proportional hazards models, adjusted for gestational age, mode of delivery and pregnancy complications (adjusted HR=2.26, 95% CI: 1.79- 2.85; p<0.001). **CONCLUSION** Maternal HBV or HCV carrier status is an independent risk factor for long-term GI morbidity of the offspring.

NEIGHBORHOOD SOCIOENVIRONMENTAL FACTORS ASSOCIATED WITH ASTHMA EMERGENCY DEPARTMENT VISIT DISPARITIES USING A SPACE-TIME MODEL: A CASE STUDY IN SOUTH CAROLINA

1999-2015 Matthew Bozigar, Andrew Lawson, Erik Svendsen, John Pearce, Kathryn Cristaldi, Allison Aiello (Medical University of South Carolina)

Long-term disparities in asthma, the leading chronic disease for children, are difficult to disentangle using existing data and methods. Limitations in previous studies using population-wide hospitalization data include inadequate control for confounders, especially when aggregated to spatial units for analysis. In this research, we employ geographic imputation, variable selection, and include numerous spatial and temporal random effects at multiple scales in a Bayesian framework to build a model of census tract risk for emergency department (ED) visits due to asthma among South Carolina children from 1999 to 2015. By reducing spatio-temporal confounding, this approach can both improve the precision of estimates of the effects of socioenvironmental factors (e.g., air pollutants, neighborhood qualities) and improve risk model fit, critical for accurately identifying disparities across numerous factors (e.g., rural/urban, race). In addition, by conducting the analysis at the census tract level, we leverage spatial units and measures devised by the US Census for homogenous population groups that further improve precision of neighborhood effects. We address potential effect modification that may occur in socioeconomically deprived neighborhoods via inclusion of interaction terms during the variable selection process. Results show that increased distance to a pharmacy and people per house were associated with increased asthma ED visit risk, and there were statistically significant air pollutant interactions with annual SO₂ concentrations including CO, NO₂, and O₃. Furthermore, several socioenvironmental factors typically associated with poor asthma outcomes were not significant including annual particulate matter (PM) concentrations, road density, and urban residence. Contrary to previous findings, these results indicate an overall asthma ED visit burden in rural areas in South Carolina, but that rurality itself is not a driver when disaggregated into its components.

**WEEKDAY BEDTIMES IN RELATION TO INCIDENT HYPERTENSION:
A PROSPECTIVE STUDY OF MEXICAN YOUTH**

Erica Jansen, Galit Dunietz, Amilcar Matos-Moreno, Maritsa Solano-Gonzalez, Eduardo Lazcano-Ponce, Luisa Maria Sanchez-Zamorano (University of Michigan School of Public Health)

Introduction: Hypertension affects up to 5% of children worldwide and predicts later cardiovascular morbidity. Associations of short sleep and hypertension have been reported in adults but less consistently in children. As a habitual and multi-dimensional behavior, sleep is plausibly linked to hypertension through pathways beyond its duration. This study aims to examine the role of sleep timing, a marker of disrupted circadian rhythms, on incident hypertension in a cohort of Mexican children. **Methods:** Participants included 2054 adolescents recruited from public schools in Morelos, Mexico who were free from hypertension (according to age and sex-based standards for blood pressure measurements). Approximately 1.2 years later, blood pressure was measured again to evaluate incidence of hypertension. Baseline habitual weekday bedtimes were abstracted from questionnaires to evaluate the association between bedtime and hypertension incidence. Sex-stratified risk ratios and 95% confidence intervals were estimated with log binomial models, adjusting for potential confounders. **Results:** Participants were 12.5 (SD=0.6) years old at baseline; 31% of boys and 36% of girls reported going to bed between 9 and 10 PM. At the follow-up visit which occurred 1.2 years later, 7.6% of the boys and 5.6% of the girls had developed hypertension. Compared to girls with a habitual bedtime between 9 and 10 PM, those with a bedtime 10 PM or later had a 3.2 times higher risk of developing hypertension over the follow-up period (95% CI 1.37 to 7.28; P=0.007), after accounting for age, menarche status, maternal education, screen time, alcohol use, and smoking. The association persisted after accounting for wake time. There was no association between bedtime and hypertension risk in boys. **Conclusion:** Later bedtime had a sex-specific association with hypertension risk. Behavioral modification targeting bedtime before 10 PM for adolescent girls may ameliorate hypertension risk.

A PROSPECTIVE STUDY OF CERVICAL INTRAEPITHELIAL NEOPLASIA, ITS TREATMENTS, AND FECUNDABILITY Lauren Wise, Alexandra Klann, Sydney Willis, Ellen Mikkelsen, Amelia Wesselink, Rebecca Perkins, Kristen Hahn, Kenneth Rothman, Elizabeth Hatch (Boston University School of Public Health)

Background: Treatments for cervical intraepithelial neoplasia (CIN) remove pre-cancerous cells from the cervix by excising or ablating the transformation zone. Most studies of CIN, its treatments, and fertility show no association. However, only two studies have examined time-to-pregnancy (TTP), both using retrospective study designs, with one showing a two-fold increased risk of infertility (TTP>12 months) following excisional or ablative treatments. **Methods:** We analyzed data from Pregnancy Study Online (PRESTO), a prospective cohort study of 6,368 North American pregnancy planners enrolled during 2013-2018. At baseline, women reported whether they ever had an abnormal Papanicolaou (Pap) test, the number of abnormal Paps, and their age at first abnormal Pap. They also reported whether they underwent diagnostic (colposcopy) or treatment (loop excision, cryosurgery, conization, laser ablation) procedures, and their age at each procedure. Analyses were restricted to women with ≤ 6 cycles of attempt time at study entry who reported a Pap test in the past 3 years. We estimated fecundability ratios (FR) and 95% CIs using proportional probabilities models adjusted for sociodemographics, smoking, number of sexual partners, history of sexually transmitted infections (STIs), and human papillomavirus vaccination (HPV). **Results:** History of abnormal Pap test, a proxy for CIN, showed little association with fecundability (FR=1.04, 95% CI: 0.97-1.11). Likewise, receipt of colposcopy, type of treatment, and time since diagnosis or treatment were not materially associated with fecundability. Results were similar when stratified by age, smoking status, history of STIs, or HPV vaccination. **Conclusion:** We observed no appreciable association of self-reported history of abnormal Pap test, colposcopy, treatments for CIN, or recency of diagnosis/treatment with fecundability. These results agree with most previous studies indicating no adverse fertility effects from CIN or its treatments.

DEPOT MEDROXYPROGESTERONE ACETATE CONTRACEPTIVE USE AND BLOOD LEAD CONCENTRATIONS Kristen Upson, Quaker Harmon, Ganesa Wegienka, Lauren Wise, Erik Tokar, Donna Baird (National Institute of Environmental Health Sciences, NIH)

Depot medroxyprogesterone acetate (DMPA) is a highly effective injectable contraceptive commonly used in the United States. The suppression of gonadotropins by DMPA produces a hypoestrogenic state that has been associated with a decrease in bone mineral density. Bone is the primary storage site for the toxic metal lead; increased bone resorption results in the release of bone lead to blood. To our knowledge, only one small study of 174 adolescent clinic patients has examined the association between current DMPA use and blood lead concentrations. We examined this relationship using enrollment data from the Study of Environment, Lifestyle & Fibroids (SELF), a cohort of 1693 African American women ages 23-35 years. Blood lead concentrations were measured in whole blood samples from 1548 participants (91% of the cohort) and data on DMPA use was collected by computer-adaptive telephone interview and questionnaire. We estimated the percent difference in blood lead concentrations and 95% confidence interval (CI) between current DMPA users and non-users using linear regression, adjusting for age, education, smoking, alcohol consumption, and recent birth/current lactation. At enrollment, 7% of participants (n=102) reported current DMPA use and the median blood lead concentration was 0.66 $\mu\text{g}/\text{dl}$ (interquartile range: 0.49-0.92). Current users of DMPA at enrollment had blood lead concentrations that were 18% higher than non-users (95% CI: 8, 29). We observed a similar association when we restricted the comparison group of non-users to those not using hormonal contraception (16% higher, 95% CI: 5, 27) and when we restricted the study population to never smokers (20% higher, 95% CI: 8, 33). Our results indicate that current DMPA use is associated with increased blood lead concentrations. Given the common use of DMPA among reproductive-age women and the potential health effects of blood lead concentrations, our observation warrants further investigation.

PROSPECTIVE ASSOCIATION OF AMBIENT TEMPERATURE AND HUMIDITY WITH RISK OF PREGNANCY LOSS Carrie Nobles, Pauline Mendola, Robert Silver, Keewan Kim, Sunni Mumford, Lindsey Sjaarda, Neil Perkins, Enrique Schisterman (National Institutes of Health, NICHD)

Introduction: Both extreme heat and cold have been associated with stillbirth and may have implications for other reproductive outcomes including pregnancy loss. Given the expected increase in extreme weather events and modifiable nature of ambient temperature exposure, we evaluated the relationship of ambient temperature and humidity with pregnancy loss in the EAGeR study. Methods: A total of 1,228 women from 4 temperate regions (Salt Lake City, Provo and Ogden, UT; Denver, CO; Buffalo, NY; Scranton, PA) were followed for up to 6 menstrual cycles attempting pregnancy and throughout pregnancy. Pregnancy loss occurred when an hCG-detected pregnancy was not confirmed on ultrasound or was followed by a clinically documented loss. Daily average temperature and humidity were abstracted from airport weather monitoring stations. Weighted log-binomial models estimated relative risk of pregnancy loss per 2-unit increase in degrees Celsius and humidity for gestational weeks 1 through 8, adjusting for ozone, fine particulate matter, study site and maternal characteristics. As both high and low temperature may increase risk, we evaluated the interaction of temperature and humidity with warm (April-September) versus cold (October-March) season. Results: Among 797 pregnancies, 188 losses (23.6%) were observed. During the warm season, higher humidity in gestational weeks 5 and 6 was associated with greater risk of loss (RR 1.04, 95% CI 1.01, 1.08 and RR 1.06, 95% CI 1.01, 1.08, respectively). While higher temperature appeared to be similarly associated with risk of loss, confidence intervals were wide. During the cold season, higher temperature in gestational week 6 was associated with a 15% lower risk of loss (95% CI 0.76, 0.96), with no associations observed for humidity. Conclusions: Early exposure to high humidity in the warm season and low temperature in the cold season appeared to increase pregnancy loss among prospectively followed women attempting pregnancy.

VAGINAL BLEEDING, CYCLE LENGTH, AND FOLLICULAR AND LUTEAL PHASE LENGTHS IN WOMEN WITHOUT KNOWN**SUBFERTILITY: A POOLED ANALYSIS OF 3 COHORTS** Shahpar

Najmabadi, Karen Cecilia Schliep (PhD, MSPH), Sara Ellis Simonsen (PhD, MSPH, CNM), Christina Porucznik (PhD, MSPH), Marlene J Egger (PhD), Joseph Stanford (MD, MSPH) (University of Utah)

Menstrual cycles (MC) are vital signs of women's reproductive health. Despite research indicating variability in MC parameters, there persists a common perception of a standard 28-day menstrual cycle with ovulation on day 14, and a 14-day luteal phase. We assessed MCs among 582 women who used a standardized protocol to observe, record and interpret vaginal bleeding and discharges, up to 1 year (3326 cycles). Women were ages 18–40, with no known subfertility, not currently taking any exogenous hormones. The peak day of cervical mucus was used to estimate the day of ovulation. We used linear and generalized linear mixed models to assess cycle and phase lengths, stratifying by age and parity. The majority of women were <30 years of age (75%), non-Hispanic white (89%), nulliparous (70%). The mean length of menses was 6.2 ± 1.5 days, median (M) 6, interquartile range (IQR) 5–7; cycle length 30.3 ± 6.7 days, M 29, IQR 27–32; follicular phase length 18.5 ± 6.5 days, M 17, IQR 15–20; luteal phase length 11.7 ± 2.8 days, M 12, IQR 10–13. The incidence of estimated ovulation on day 14, and luteal phase length of 14 days were 8.7% and 9.7%, respectively. The median estimated day of ovulation was 17 and the mode 15. Nulliparous women aged ≥ 30 years versus (<30 years) (RR 0.47 [CI 0.26, 0.84]), and a higher probability of >3 days variability in luteal phase length (RR 1.32 [CI 1.11, 1.58]). We found substantial variability in menstrual flow and cycle phase lengths in eumenorrheic women over the course of 1 year. Older nulliparous women had shorter cycles. These findings confirm previous work, and provide further evidence against a normative 28-day menstrual cycle with 14 days each for the follicular and luteal phases.

MULTIPLE GESTATIONS MEDIATE THE EFFECT OF IN VITRO FERTILIZATION ON ISCHEMIC PLACENTAL DISEASE

Anna Modest, Louisa Smith, Thomas Toth, Brett Young, Michele Hacker (Beth Israel Deaconess Medical Center)

Background: Ischemic placental disease (IPD) affects 16-23% of pregnancies in the United States. In vitro fertilization (IVF) is a risk factor for IPD, and the magnitude of the increase in risk is for women using donor oocytes (donor IVF) vs. their own oocytes (autologous IVF). In addition, multiple gestations, which are more common in IVF than non-IVF pregnancies, also are a risk factor for IPD. **Objective:** To determine the role of multiple gestations in the association between IVF and IPD. **Methods:** We identified deliveries at a tertiary hospital from January 1, 2000 to August 1, 2018 and IVF cycles from an affiliated IVF center using electronic medical records and state vital statistics data. IPD was defined as preeclampsia, placental abruption, small for gestational age (SGA), or an intrauterine fetal demise due to placental insufficiency. We used mediation analysis to decompose the total effect of IVF vs. non-IVF pregnancies on IPD into a direct effect and an indirect effect through multiple gestations. We repeated the analyses separately for donor and autologous IVF. All models were adjusted for maternal age, race, parity, insurance, and year of delivery. **Results:** Among the 86,514 deliveries, 281 resulted from donor IVF and 4,173 resulted from autologous IVF. IVF pregnancies had 2.1 times the risk of IPD compared to non-IVF pregnancies (95% CI 2.0-2.2) and 78% of this increased risk was mediated by multiple gestations. Autologous IVF pregnancies also had 2.1 times the risk of IPD compared to non-IVF pregnancies (95% CI 1.9-2.2) and the percentage mediated was 81%. Donor IVF pregnancies had 2.6 times the risk of IPD (95% CI 2.2-3.0) but the percentage mediated was 40%. **Conclusion:** The majority of the association between autologous IVF and IPD is mediated through multiple gestations; however, this is not the case in donor IVF pregnancies. This difference may highlight different mechanisms for the increased risk of IPD in donor and autologous pregnancies.

HOW IS THE RELATIONSHIP OF INFANT WEIGHT GAIN WITH CARDIO-METABOLIC DISEASE RISK MODIFIED BY FETAL GROWTH? ANALYSIS IN THE SOUTHAMPTON WOMEN'S SURVEY

Tom Norris, Sarah Crozier, Noel Cameron, Keith Godfrey, Hazel Inskip, William Johnson (Loughborough University)

Background: Rapid infant weight gain has been associated with several cardiometabolic outcomes in childhood. However much less is known about how this relationship differs by patterns of fetal growth. Aim: Explore how the associations between infant weight change and cardiometabolic outcomes in childhood are modified by patterns of fetal weight growth. Methods: We used data from 1203 children in the Southampton Women's Survey. Unconditional weight change (weight z-score at 2 years minus weight z-score at birth), was related to five cardiometabolic outcomes (body mass index, percent fat, trunk fat, systolic (SBP) and diastolic blood pressure), collected when the child was age 6 years. To see how fetal growth modified these associations, infant weight change was interacted with the random intercept and slope from a multilevel model of serial estimated fetal weight data. We adjusted for several putative confounders and used multiple imputation to account for missingness in the outcomes and covariates. Results: In both unadjusted and adjusted analyses, infant weight change was positively associated with the cardiometabolic outcomes. For example, going from the 10th-90th percentile of infant growth was associated with an increase in SBP of 3.06mmHg in those who were at the 10th percentile of fetal growth, compared to an increase of 1.2mmHg in those who were at the 90th percentile. However, the strength of evidence for the interaction term between fetal and infant growth was weak. Sensitivity analyses replacing continuous fetal growth with a categorical variable ('high', 'low', 'medium') yielded similar results. Conclusions: Infant growth was positively associated with a number of cardiometabolic outcomes in childhood. The finding that this relationship was not modified by fetal growth suggests that infant growth may act independently to increase the risk of adverse cardiometabolic outcomes, irrespective of whether growth was previously constrained in utero.

EVALUATION OF FETAL GROWTH CUSTOMIZATION METHODS IN THE NICHD FETAL GROWTH STUDIES -SINGLETONS Katherine Grantz, Lindsey Sjaarda, Stefanie Hinkle, Nicole Gerlanc, John Owen, Daniel Skupski, William Grobman, Karin Fuchs, Melissa Amyx, Yassaman Vafai, Cuilin Zhang, Anindya Roy (Eunice Kennedy Shriver National Institute of Child Health and Human Development)

Customized estimated fetal weight (EFW) percentile cutoffs as proposed by Gardosi empirically assumes the variance used for calculating the coefficient of variation (CV) and thus the percentiles (e.g. 10th) is proportional to the mean, although this assumption has never been formally tested. Our objective was to develop an expanded alternative method estimating both customized mean and variance using heteroscedastic regression. Using longitudinal sonographic biometric data (n=2288 pregnancies), we first examined empirical and Gardosi model-estimated variance with 6 customization characteristics (gestational age [GA], maternal prepregnancy weight, height, race, parity, infant sex) that predicted both the term optimal weight (TOW, 50th %ile) and the variance of TOW estimates used for determining %tile cutoffs. The variance had a non-constant behavior for many factors. The most pronounced sources of variability were seen with GA (linear, negative), pre-pregnancy weight (non-linear) and parity (linear, positive) with slight effects for race and sex. However, in the heteroscedastic model, only pre-pregnancy weight significantly affected the variance (linear term $\beta=0.0145$; $P<.0001$). To check cross sectional consistency of variance, the new model was repeated with EFW for pairs of weeks, i.e. 21-22, 22-23, etc. Though sporadic differences in variances were found by maternal weight and height, no systematic dependence on any particular factor was found across gestation. Importantly, in the expanded model, EFW 10th and 90th %iles were narrower across a range of maternal weights: 57kg, 64kg and 75kg for the 25th, 50th, and 75th %iles, respectively. For example, EFW 10th at 37-38 weeks for 57kg was 99g larger with customized variance (2571g heteroscedastic vs. 2472g Gardosi) while EFW 90th was 99g smaller. In summary, customization of the variance in addition to the mean may impact the threshold for determining abnormal fetal growth and warrants further investigation.

THE ASSOCIATION OF STILLBIRTH WITH PLACENTAL ABNORMALITIES IN GROWTH-RESTRICTED AND NORMALLY GROWN FETUSES Alexa Freedman, Carol Hogue, Robert Goldenberg, Carolyn Drews-Botsch (Northwestern University)

Background: Stillbirth, defined as fetal death ≥ 20 weeks' gestation, is often attributed to placental abnormalities, which, in turn, have been associated with abnormal fetal growth. Evaluating these interrelationships may improve our understanding of the underlying mechanisms for stillbirth. Methods: We used data from the Stillbirth Collaborative Research Network study, a population-based case-control study conducted from 2006-2008. Our analysis included 266 stillbirths and 1,135 live births. We evaluated associations of stillbirth with five types of placental characteristics (developmental disorders, maternal and fetal inflammatory responses, and maternal and fetal circulatory disorders) and examined mediation of these relationships by small for gestational age status (SGA). We also allowed for exposure-mediator interaction. Results: After adjustment for potential confounders, maternal inflammatory response (odds ratio [OR]: 2.58; 95% confidence interval [CI]: 1.77, 3.75), maternal circulatory disorders (OR: 4.14; 95% CI: 2.93, 5.84), and fetal circulatory disorders (OR: 4.58; 95% CI: 3.11, 6.74) were strongly associated with stillbirth, but the effect did not appear to be mediated by SGA status. Controlled direct effects for developmental disorders and fetal inflammatory response diverged for SGA and non-SGA births, and strong associations were only observed when SGA was not present. Natural indirect effects were all close to 1.0. Conclusions: Our results suggest that fetal growth does not mediate the relationships between placental abnormalities and stillbirth. The relationships of stillbirth with maternal and fetal circulatory disorders and maternal inflammatory response are independent of fetal growth, while developmental disorders and fetal inflammatory response likely interact with fetal growth to affect stillbirth risk.

GLOBAL INEQUITIES IN ASPIRIN USE FOR THE PREVENTION OF PREECLAMPSIA: FINDINGS FROM THE FACT TRIAL Katherine

Muldoon, Darine El-Chaâr, Natalie Rybak, Daniel Corsi, Amarjargal Dagvadorj, Yanfang Guo, Ruth Rennicks White, Alysha Harvey, Mark Walker, Shi-Wu Wen, Laura Gaudet (Ottawa Hospital Research Institute)

Background: Aspirin is a widely recommended treatment option for the prevention of preeclampsia (PE). However, many high-risk women do not receive this readily available treatment, and little is known about global variation in aspirin use for PE prophylaxis. This analysis is designed to investigate variation in aspirin use by country and indication. **Methods:** Secondary analyses of the Folic Acid Clinical Trial (FACT) (2011-2015), a double-blind, randomized controlled, trial investigating folic acid for the prevention of PE in high-risk pregnancies. The trial was conducted in 70 high-risk obstetrical centres in Canada, Argentina, Australia, Jamaica, and UK. Aspirin use is defined as taking a daily dose of aspirin (75-162mg per day) \geq 16 weeks gestation until delivery. Statistical associations were assessed using chi-square tests. **Results:** There were 2296 women with complete information on aspirin included in these analyses. The prevalence of PE was 14.1% and preterm PE (<37 weeks) was 6.1%. At baseline, all patients were at high-risk of PE and were eligible for aspirin prophylaxis, however only 660 (28.7%) were taking aspirin and 132/600 (20.0%) went on to develop PE. There was statistically significant variation in aspirin use between countries, with the highest rates found in the UK (34.8%), Australia (31.6%) and Canada (27.2%), and the lowest in Argentina (10.6%) and Jamaica (5.56%) ($p < 0.001$). The most common indications for aspirin use were for previous PE (50.3%), pre-existing hypertension (45.8%), and diabetes (24.1%). **Conclusion:** While aspirin is currently best practice for PE prevention, this study identified that <30% of women in this high-risk population were taking it, with significant variation between countries. Evaluation of individual national recommendations, including prescribing patterns and availability of aspirin in antenatal care settings, is warranted to ensure that all eligible women receive the best possible preventative care.

THE IMPORTANCE OF NON-TRADITIONAL RISK FACTORS FOR PREDICTION OF CARDIOVASCULAR DISEASE IN WOMEN OF REPRODUCTIVE AGE Sonia Grandi, Kristian B Filion, Jennifer A Hutcheon, Graeme N Smith, Robert W Platt (McGill University)

Introduction: Currently available risk prediction scores for cardiovascular disease (CVD) were developed in older populations which limits their ability to provide accurate estimates of risk in younger women. Moreover, these models do not incorporate pregnancy-related risk factors that have been shown to be associated with long-term risk of CVD. **Methods:** A cohort of 266,285 women aged 15-45 years with a recorded delivery (stillbirth or livebirth) from April 1999 to March 2018 in the United Kingdom's Clinical Practice Research Datalink database were created for this study. Women with a history of CVD, prior pregnancy, and <1 year of medical history prior to cohort entry were excluded. The primary outcome was CVD defined as myocardial infarction, cerebrovascular disease, coronary artery disease, peripheral vascular disease, coronary revascularization, unstable angina, or cardiovascular-related death. Missing predictor values were imputed using multiple imputation. An accelerated failure time model using the Adaptive Elastic Net method was used to determine the inclusion of predictors and to estimate the final model. Internal validation using bootstrapping resampling was used to correct for optimism in the measures of model performance. **Results:** A total of 1,001 women experienced a CVD event over a median follow-up of 3.82 (IQR: 1.51-7.90). Predictors in the final model included traditional CVD risk factors along with social deprivation, marital status, alcohol-related disorders, venous thromboembolism, polycystic ovary syndrome, renal disease, oral contraceptive use, depression, gestational diabetes, placental abruption, preterm birth, parity, history of pregnancy complications, and rheumatoid arthritis. The optimism-corrected model had good discrimination and calibration (C-statistic: 0.71, calibration slope: 0.89). **Conclusions:** The findings highlight the importance of non-traditional risk factors for the prediction of CVD risk in women of reproductive age.

ASSOCIATIONS OF MATERNAL TRAUMA EXPERIENCES WITH OFFSPRING BEHAVIORAL PROBLEMS: FINDINGS FROM THE PROMIS COHORT STUDY

Bizu Gelaye, Sixto Sanchez, Elizabeth Levey, Archana Basu, Marta Rondon, Michelle Williams (Harvard T. H. Chan School of Public Health)

Objective: Trauma tends to run across generations, with devastating consequences at individual, family and population levels. Available evidence, largely from developed countries, suggests that maternal exposure to interpersonal trauma negatively impacts child behavioral development. We sought to evaluate the extent to which maternal exposures to childhood abuse (CA) and intimate partner violence (IPV) are associated with behavioral problems among children in Peru. **Methods:** A total of 301 mother-child dyads, participants in the Pregnancy Outcomes, Maternal and Infant Study (PrOMIS) were included. The PrOMIS cohort is a longitudinal study aimed at understanding the intergenerational effects of trauma. In-person interviews were conducted to collect information regarding socio-demographic characteristics, history of CA, and IPV. The Child Behavior Checklist (CBCL) was used to identify externalizing and internalizing behaviors in children (2-5 years). Logistic regression was used to estimate adjusted odds ratios (aOR) and 95% confidence intervals (95%CI). **Results:** Approximately 46% and 54% of children had externalizing and internalizing problem behaviors, respectively (CBCL>70th percentile). Overall, children of mothers exposed to interpersonal trauma (any CA or IPV yes/no) were more likely to have externalizing (aOR=1.98, 95%CI:1.12-3.57 and aOR=1.55, 95%CI:0.96-2.52) and internalizing (aOR=1.66, 95%CI: 0.95-2.90 and aOR=1.66; 95%CI:1.02-2.72) problem behaviors as compared to children of non-exposed mothers. Children of mothers who experienced sexual and physical abuse as a child and as an adult had elevated risks of externalizing (aOR=2.34, 95%CI:1.1-8.0) and internalizing (aOR=2.14, 95%CI 1.07-15.9) problem behaviors as compared with children of non-exposed mothers. **Conclusion:** Maternal exposure to trauma has lasting effects on child behavior. Family focused trauma-informed programs aimed at promoting maternal and child well-being in LMICs are needed.

PRECONCEPTION MARIJUANA USE AND PREGNANCY OUTCOMES

Sunni Mumford, Kerry Flannagan, Jeannie Radoc, Torie Plowden, Keewan Kim, Alexandra Purdue-Smithe, Jessica Zolton, Lindsey Sjaarda, Neil Perkins, Josh Freeman, Zeina Alkhalaf, Victoria Andriessen, Robert Silver, Enrique Schisterman (NICHD)

Objective: Marijuana is the most widely used and fastest growing drug in the US, with legislation currently broadening legalization for both medical and recreational use. A few studies evaluating self-reported use suggest marijuana may not be harmful for pregnancy, yet there is concern for underreporting due to stigma as marijuana is not universally legalized. Our aim was to examine associations between preconception marijuana use, using both self-reported and urinary levels of tetrahydrocannabinol (THC), and fecundability, live birth, and pregnancy loss.

Methods: Women aged 18-40 years old (n=1212) enrolled in the EAGeR trial were screened for urinary THC up to 2 time points during preconception using a homogenous enzyme immunoassay (Randox Laboratories), and reported marijuana use during the past year at baseline. Women were followed for up to 6 months while attempting pregnancy. Cox proportional hazard regression was used to calculate fecundability odds ratios (FOR), and log-binomial regression to estimate risk ratios (RR) for live birth and pregnancy loss adjusting for age, race, BMI, education, smoking, alcohol, and detectable levels of opioids. Results: 33 (2.7%) women screened positive for THC, of which 14 self-reported use. 62 women (5.1%) screened positive or self-reported use. Women who screened positive for THC had reduced fecundability (FOR 0.50; 95% CI 0.25, 1.00), as well as women with self-report (FOR 0.54; 95% CI 0.31, 0.94), or using either urinary or self-report (FOR 0.53, 95% CI 0.33, 0.86). No associations were observed with live birth (RR 0.71; 95% CI 0.41, 1.22) or pregnancy loss (RR 0.78; 95% CI 0.28, 2.18). Conclusions: Women who screened positive for THC during preconception, or self-reported use during the past year had reduced fecundability, though no associations were observed with live birth or pregnancy loss. Further investigations are needed to determine what duration and dose of marijuana may negatively impact fecundability.

OPIOID PRESCRIPTION USE AFTER VAGINAL DELIVERY AND SUBSEQUENT PERSISTENT OPIOID USE AND MISUSE

Yanmin Zhu, Krista Huybrechts, Rishi Desai, Alexis Krumme, Loreen Straub, Raisa Levin, Helen Mogun, Sonia Hernandez-Diaz, Brian Bateman (Brigham and Women's Hospital and Harvard Medical School)

Prior studies have shown that 10-30% of women in the US fill an opioid prescription after vaginal delivery making this a common source of exposure to opioids in young women. Limited evidence is available regarding the impact of opioid use after vaginal delivery on the risk of subsequent persistent opioid use and misuse. We assembled a nationwide cohort of women without chronic opioid use, continuously enrolled in Medicaid from 90 days before to ≥ 365 days after vaginal delivery from 2009-2013. We ascertained opioid dispensings within 7 days of the date of delivery (DOD), as well as persistent opioid use (≥ 10 fills or > 120 days' supply, primary outcome) and opioid use disorder (secondary) between 30 to 365 days after DOD. We conducted logistic regression after propensity-score (PS) 1:1 matching and instrumental variable analysis (IVA) using a 2-stage least squares approach to control for potential confounding. Within each region, facilities were ranked according to their opioid dispensing rate after delivery and divided into deciles as the instrument. Among 226,995 vaginal deliveries, 29.9% had an opioid dispensing. Overall, 3,113 out of 67,954 (4.6%) exposed vs. 1,445 out of 159,041 (0.9%) unexposed had persistent opioid use during follow-up, for an unadjusted odds ratio (OR) of 5.2 (95% CI, 4.9 - 5.6) and a risk difference (RD) of 3.7% (3.5 - 3.8). After PS matching, the risk remained higher among the exposed, with an OR of 2.7 (2.5 - 3.0) and an RD of 2.4% (2.3- 2.6), confirmed by the IVA (pseudo R-squared=0.3, Figure 1). For opioid use disorder, the unadjusted OR of 2.4 (2.2 - 2.5) attenuated to 1.5 (1.4 - 1.6) after PS matching. The adjusted risk difference was 0.9% (0.7 - 1.0) after PS matching and 2.1% (1.8 - 2.4) using IVA. For every 83 women given opioids after vaginal deliveries, one became a persistent opioid user within one year postpartum. Given the observed risk, judicious opioid prescribing after vaginal deliveries is warranted.

EFFECT OF PRENATAL CANNABIS USE ON MATERNAL, PERINATAL AND NEONATAL OUTCOMES: A POPULATION-BASED STUDY OF 656,414 PREGNANCIES IN ONTARIO, CANADA Daniel J Corsi, Laura Walsh, Deborah Weiss, Helen Hsu, Darine El-Chaar, Steve Hawken, Mark Walker (Ottawa Hospital Research Institute/Institut de recherche de l'hôpital d'Ottawa)

Background: Cannabis use during pregnancy is increasing, although data about perinatal outcomes following in utero exposure remain limited. We examined associations between prenatal cannabis use and adverse maternal and perinatal outcomes in the Better Outcomes Registry & Network (BORN) Ontario registry. Methods: Population-based retrospective cohort study with self-reported cannabis use as the primary exposure. Primary outcome was preterm birth before 37 weeks' gestation. Secondary outcomes included preterm birth between 34-36 weeks, <32 weeks, <28 weeks, and adverse maternal, perinatal, and neonatal outcomes. Coarsened exact matching (CEM) techniques and Poisson regression models were used to estimate the relative risk associated with cannabis exposure and control for confounding. Results: A total of 9,422 (1.4%) women 15 years and older reported cannabis use in pregnancy. Imbalance in maternal obstetrical and sociodemographic characteristics between cannabis users and non-users across was removed using CEM (SMD <0.001), yielding a matched sample of 7,778 cannabis users and 256,262 non-users with a cannabis prevalence of 2.9%. In the matched cohort, the relative risk (RR) for preterm birth before 37 weeks' gestation was 1.5 (95% CI: 1.43-1.53, $p<0.001$) among cannabis users compared to non-users, and the RR increased to 2.6 (95% CI: 2.38-2.83, $p<0.001$) and 2.2 (95% CI: 1.94-2.54, $p<0.001$) for preterm birth before 32 and 28 weeks' gestation. Small for gestational age (SGA 3rd %ile, RR 1.54), placental abruption (RR 1.61), transfer to neonatal intensive care (RR 1.42), and 5-minute APGAR score <4 (RR 1.32) were all significantly related to preterm cannabis exposure in adjusted models in the matched cohort ($p<0.001$). Conclusion: Cannabis use in pregnancy was associated with increased risk of adverse perinatal and neonatal outcomes. Efforts to promote cannabis cessation in pregnancy may reduce the incidence of preterm birth and other adverse outcomes.

OPERATIONALIZING THE CONSTRUCT OF RESILIENCY DURING PREGNANCY: PATTERNS OF SOCIAL SUPPORT BY RACE/ETHNICITY AND SOCIOECONOMIC STATUS Yasamean Zamani-Hank, Claire E. Margerison, Claudia Holzman (Michigan State University)

Preterm birth (PTB) rates in the United States differ substantially by race/ethnicity and socioeconomic status (SES). In particular, the PTB rate for African-American (AA) women is 13.8% compared to 9.0% for white women (Martin et al., 2018). An increased burden of stress among disadvantaged women due to, for example, racial discrimination and/or stressful life events, may partially explain these disparities. Protective resources that promote resiliency processes may buffer against negative impacts of stressful experiences on pregnancy outcomes. Little research has explicitly operationalized the construct of resiliency resources during pregnancy or examined whether these resources differ by race/ethnicity and/or SES. To fill this gap, we will operationalize resiliency resources at the individual-, family-, and community-level using data on 1,371 pregnant women from the Pregnancy Outcomes and Community Health Study (POUCH, 1998-2004). Utilizing analysis of variance (ANOVA) to assess differences by race/ethnicity and SES, our preliminary results, focused on social support as one family-level measure of resiliency, showed that white women exhibited significantly higher mean levels of perceived (10.2 vs. 9.6, $p < 0.0001$), emotional (2.0 vs. 1.9, $p = 0.0014$), and instrumental social support (5.8 vs. 5.5, $p < 0.0001$) compared to AA women. High SES women also exhibited significantly higher mean levels of perceived, emotional, and instrumental social support compared to middle and low SES women. These results suggest that family-level measures of resiliency during pregnancy do in fact differ by race/ethnicity and SES. We are now investigating whether resiliency resources differ by race/ethnicity and SES at the individual and community level, and whether resiliency at multiple levels contributes to disparities in PTB.

JOINT IMPACT OF NEIGHBORHOOD EVICTIONS AND MARITAL/COHABITING STATUS ON RISK OF PRETERM BIRTH

AMONG AFRICAN AMERICAN WOMEN Shawnita Sealy-Jefferson, Brittney Butler, Shibani Chettri, Hikma Elmi, Allison Stevens, Chinenye Bosah, Dawn Misra (The Ohio State University)

Housing instability is an important determinant of health, but no studies have examined the spill-over effects of neighborhood eviction rates on risk of preterm birth (PTB) among African American (AA) women. We assessed whether living in a neighborhood with high eviction rates is associated with risk of PTB, and whether marital/cohabiting status modifies the association. We spatially linked survey, medical record, and current address data from the Life Influences on Fetal Environments Study (2009-2011, n=1387) of postpartum AA women from Metropolitan Detroit, MI, to publicly available data on block-group level rates of eviction filings and judgements. PTB was defined as birth before 37 completed weeks of gestation, and occurred in 16.3% of the sample (n=226). Eviction rate variables were rescaled by their interquartile ranges (75th versus 25th percentiles). Women reported whether they were married to or cohabiting with the father of their baby. We used Modified Poisson regression with robust error variance to estimate relative risks of PTB, associated with each eviction variable separately, and included an interaction term with marital/cohabiting status ($p < 0.10$ considered significant) in adjusted models. In the overall sample, neighborhood eviction filings and judgements did not predict PTB risk, but the associations were modified by marital/cohabiting status (p for interaction= 0.02, and 0.06, respectively). Among women who were married/cohabiting, those who lived in neighborhoods with high eviction filings (adjusted relative risk: 1.24, 95% confidence interval: 1.06, 1.47), and eviction judgements (adjusted relative risk: 1.18, 95% confidence interval: 1.05, 1.33) had higher risk of PTB than women who did not. No significant associations were observed for women who were not married/cohabiting. Future studies should examine the mechanisms of these associations, to better understand the unique stressors of this group and to identify intervention targets.

DELIVERY HOSPITAL AND RACIAL/ETHNIC DIFFERENCES IN SEVERE MATERNAL MORBIDITY IN THE STATE OF CALIFORNIA

Mahasin Mujahid, Peiyi Kan, Stephanie A. Leonard, Elleni Hailu, Elizabeth Wall-Wieler, Barbara Abrams, Elliot Main, Jochen Profit, Suzan Carmichael (University of California Berkeley, School of Public Health)

Hospital site of delivery has recently emerged as a potentially key determinant of racial/ethnic disparities in severe maternal morbidity (SMM) but investigations remain limited. We leveraged state-level data from California (2006-2012) to examine racial/ethnic differences in SMM and if these differences were explained by site of delivery. SMM was measured using the Centers for Disease Control and Prevention index of diagnoses and procedures. Mixed effects logistic regression models were used to compare racial/ethnic differences in SMM before and after adjustment for maternal, clinical, and hospital (teaching hospital, delivery volume, nursery level, hospital ownership) factors. We also estimated risk-standardized SMM rates for each hospital (N=245) and the percent reduction in SMM in each racial/ethnic group (African American=AA; US and foreign-born Hispanics=USH/FBH respectively; Asian/Pacific Islander=API) if women delivered at the same distribution of hospitals as non-Hispanic Whites (W). Of the 3,020,525 births, 3921 (1.3%) had SMM (2.2% AA; 1.3% USH; 1.4% FBH; 1.4% API, 1.1% W). Risk standardized rates of SMM ranged from 0.6 to 5.2 per 100 deliveries across hospitals. After adjusting for covariates, risk of SMM was greater among non-White deliveries compared to Whites (Odds Ratios and 95% Confidence Intervals; AA=1.25 (1.19-1.31), USH=1.25 (1.20-1.29), FBH=1.17 (1.11-1.24), API=1.26 (1.21-1.32). No hospital factors were associated with SMM in fully adjusted models. Although 33% of W delivered in hospitals with the highest tertile of SMM births compared to 56% of AA, site of delivery only accounted for 4.3% of the differences in SMM comparing AA and W; it actually increased the disparity in other groups (3.0-5.3% increase). In California, excess risk of SMM among racial/ethnic minorities was not explained by site of delivery. Future research should examine factors that may contribute to within-hospital differences in SMM across racial/ethnic groups.

THE EFFECT OF TIMING OF EARNED INCOME TAX CREDIT

REFUNDS ON PRETERM BIRTH Deborah Karasek, Akansha Batra, Rita Hamad, Rebecca Baer, Laura Jelliffe-Pawlowski (University of California, San Francisco)

Preterm birth occurs in nearly 10% of US births and increases the risk for adverse social and health outcomes. Socioeconomic and racial disparities in preterm birth are well established, and may be the result of economic insecurity and related stress. The earned income tax credit (EITC) is the largest US poverty alleviation program, providing tax refunds to low-income working families. Studies have shown that the EITC improves birthweight and gestational age. Using a quasi-experimental design, we examined whether the trimester of EITC receipt affects likelihood of preterm birth. We used a probabilistic algorithm to identify the EITC-eligible population. Assuming EITC refund receipt in February, we assigned California births during 2005-2011 (N=3,749,946) to trimester of EITC receipt based on date of birth and gestational age. We created a probabilistic algorithm to identify EITC-eligible births using the 2001-2015 waves of the Panel Study of Income Dynamics and applied it to the CA birth file. We compared this to a common method of using less than high school education as a proxy for EITC. We used difference-in-difference models, comparing outcomes among EITC-eligible women exposed to the EITC in different trimesters, while “differencing” out seasonal trends in outcomes among non-eligible women. Using a probabilistic algorithm to impute EITC eligibility revealed an increase in preterm birth when receiving the EITC refund in the first ($\beta=0.0010$, 95% CI 0.0002-0.0018) and second trimester ($\beta=0.0010$, 95% CI 0.0002-0.0018) relative to preconception. Using education as a proxy showed lower risk of preterm birth for each trimester relative to preconception. Differences in preterm birth by trimester of income receipt may reveal information about the stress pathway and identify points of intervention for social and economic policy. Prior studies that use simplistic methods to impute EITC eligibility may not accurately capture the exposed population.

EFFECT MEASURE MODIFICATION OF THE ASSOCIATION BETWEEN MATERNAL DIABETES AND BIRTH DEFECTS BY MATERNAL OBESITY, NATIONAL BIRTH DEFECTS PREVENTION STUDY, 1997-2011 Sarah C. Tinker, Suzanne M. Gilboa, Cynthia A. Moore, D. Kim Waller, Regina M. Simeone, Shin Y. Kim, Denise J. Jamieson, Lorenzo D. Botto, Jennita Reefhuis (Centers for Disease Control and Prevention)

Maternal pregestational diabetes and obesity (body mass index ≥ 30 kg/m²) are risk factors for several specific birth defects. Diabetes and obesity often occur together, and their pathophysiology overlaps in part. However, it is not clear to what extent their co-occurrence in pregnancy compounds birth defect risk. We used 1997-2011 data from the National Birth Defects Prevention Study, a multisite case-control study of selected structural birth defects, to assess for 39 defect categories, the independent and joint associations between pregestational obesity and diabetes (types 1 and 2), and the relative excess risk due to interaction (RERI, which is a measure of greater than additive effects). Pregestational diabetes, with or without obesity, was strongly associated with most birth defect categories (odds ratios [OR] range: 2.0 to 75.9), with the exception of spina bifida (association observed only among women with obesity). Among mothers with pregestational obesity but without diabetes, modest increased odds (OR range: 1.1 to 1.5) were observed for neural tube defects, anorectal atresia, renal agenesis/hypoplasia, omphalocele, and several congenital heart defects (CHDs). For most birth defect categories, the RERI was not elevated, with the exception of holoprosencephaly (18.3, 95% confidence interval [CI]: -3.7, 40.2), heterotaxia with CHD(s) (10.2; 95% CI: -2.4, 22.8), and double outlet right ventricle with transposition of the great arteries (12.3, 95%: -2.9, 27.5). We are planning additional analyses to further assess risk by different categorizations of body mass index. It is important to better understand these relationships because diabetes and elevated body mass index are common and potentially modifiable risk factors for many birth defects.

LOW-LEVEL CIGARETTE CONSUMPTION DURING PRECONCEPTION AND EARLY PREGNANCY IN RELATION TO RISK OF BIRTH DEFECTS: A LARGE POPULATION-BASED STUDY WITH 23 MILLION MOTHER-INFANT PAIRS Buyun Liu, Guifeng Xu, Yangbo Sun, Yongfu Yu, Linda Snetselaar, Wei Bao (University of Iowa)

Background: Prenatal exposure to high dose of tobacco smoke is teratogenic to developing fetuses. However, findings about the associations between low-level cigarette smoking and birth defects are inconsistent and controversial, especially for specific birth defects. This study aimed to examine the dose-response association of maternal periconceptional exposure to cigarette smoking with birth defects.

Methods: We used US nationwide birth certificate data from the National Vital Statistics System 2011-2017. Birth defects included anencephaly, meningomyelocele/spina bifida, cyanotic congenital heart disease, congenital diaphragmatic hernia, omphalocele, gastroschisis, limb reduction defect, cleft lip with or without cleft palate, cleft palate alone, Down syndrome, suspected chromosomal disorder, or hypospadias. We performed logistic regression analyses to estimate odds ratios (OR) of birth defects according to maternal smoking during preconception and the first trimester, adjusting for maternal age, race/ethnicity, parity, education, marital status, prepregnancy BMI, infant sex, and initiation of prenatal care. **Results:** This study included 23,583,372 live births, containing 72,838 with birth defects. Compared with women who never smoked, women who smoked, either before or during pregnancy, were at a higher risk of having a baby with birth defect. The OR (95% confidence interval [CI]) of birth defect was 1.11 (1.02-1.21), 1.20 (1.13-1.27), 1.07 (0.98-1.16), 1.18 (1.12-1.24), and 1.23 (1.17-1.30) for those who smoked 1-2, 3-5, 6-9, 10-19, and ≥ 20 cigarettes per day before pregnancy, respectively. The corresponding ORs for those who smoked during the first trimester were 1.04 (0.99-1.10), 1.07 (1.01-1.12), 1.04 (0.93-1.16), 1.09 (1.02-1.16), and 1.22 (1.08-1.39). Significant and positive associations were found for some types of birth defects. **Conclusion:** Periconceptional smoking, even as low as 1-2 cigarettes per day, may increase the risk of birth defects.

AN EVALUATION OF ZIKA BIRTH DEFECTS SURVEILLANCE: A MODEL FOR RAPID SURVEILLANCE OF BIRTH DEFECTS DURING AN EMERGENCY RESPONSE — UNITED STATES, 2018 Kathleen Krause, Elizabeth Ailes, Suzanne Gilboa, Van Tong, Janet Cragan, Augustina Delaney, Abbey Jones, John Nahabedian, Samantha Olson, Nicole Roth, Ashley Smoots, Tineka Yowe-Conley, Dana Meaney-Delman, Margaret Honein (CDC)

Background: Congenital Zika virus (ZIKV) infection can cause serious birth defects of the brain and eyes. During the ZIKV response, CDC funded 50 jurisdictions to conduct Zika Birth Defects Surveillance (ZBDS) to rapidly identify infants with birth defects potentially related to congenital ZIKV infection. Our evaluation assessed the attributes of the ZBDS system and whether ZBDS accomplished its purpose of documenting the prevalence of birth defects potentially related to congenital ZIKV infection. **Methods:** We evaluated the ZBDS system's attributes of timeliness, predictive value positive (PVP), data quality, and representativeness by interviewing six CDC and three jurisdictional stakeholders and performing descriptive analyses on key variables. **Results:** ZBDS was timely; case ascertainment, medical record abstraction, and clinical review occurred within six months of birth compared to two years for traditional birth defects surveillance. PVP was 78.4% and among ten key variables, missingness ranged from 0% to 5.3%. Staff maintained high data quality through clinical review of verbatim text abstracted from medical records, and pre- and postnatal imaging findings (when available), to determine whether every reported case met the surveillance definition. A 2018 Morbidity and Mortality Weekly Report used ZBDS data from 15 jurisdictions to estimate the prevalence of birth defects potentially related to congenital ZIKV infection, which was representative of areas with local transmission and high and low levels of confirmed, symptomatic travel-associated infection. **Conclusions:** ZBDS obtained timely, high-quality data during an emergency response, which provided representative prevalence estimates of the birth defects potentially related to congenital ZIKV infection. Successful implementation of ZBDS was predicated upon staff effort, which will be required for future emergency response in the absence of a national, standardized birth defects surveillance system.

ASSOCIATION OF DEMOGRAPHIC AND CLINICAL FACTORS WITH THE PRE-ZIKA TIME TREND OF MICROCEPHALY IN TEXAS, 1999-2014 Peter Langlois, Adrienne Hoyt, Mark Canfield (Senior Epidemiologist)

BACKGROUND In Texas, the birth prevalence of the birth defect microcephaly increased from 6.4 cases per 10,000 live births in 1999 to 16.7 cases in 2014. This preceded the Zika virus outbreak in the Americas. We tried using an objective statistical approach to identify which combination of factors might best explain this time trend. **METHODS** We used data from the Texas Birth Defects Registry and Texas birth certificates for deliveries to Texas residents in 1999 through 2014. Cases were included if they had a definite diagnosis of microcephaly or small head. Poisson regression was used to estimate the slope or annual percent change (APC) for year alone in crude models and together with covariates in two separate adjusted models. Covariates were entered into models both as main effects and interaction effects (year*covariate), and the most parsimonious model was sought beginning with a full model and using a change-in-estimate backwards selection approach for the year term. 'Explanatory' covariates were operationally defined those that most decreased the APC. **RESULTS** There were 7247 definite cases of microcephaly. The crude APC (with year as the only independent variable) was an average increase of 7.9% per year (95% CI 6.8, 9.0). The most explanatory combination of demographic factors was maternal race/ethnicity, maternal education, infant sex, and Texas health service region; this adjustment reduced the APC to 4.3% (1.9, 6.7). The most explanatory combination of clinical factors was severity of microcephaly, co-occurring exposures, and whether there were co-occurring birth defects, which combined brought the APC to 5.3% (0.8, 10.0). **DISCUSSION** This objective approach identified factors that might help explain some but not all of the time trend in microcephaly.

MATERNAL DIET AS A RISK FACTOR FOR PRIMARY CONGENITAL GLAUCOMA AND DEFECTS OF THE ANTERIOR SEGMENT OF THE EYE IN THE NATIONAL BIRTH DEFECTS PREVENTION STUDY. Kristin J. Voltzke, Suzan L. Carmichael, Nina E. Forestieri, Tania A. Desrosiers, Robert E. Meyer, Sharon F. Freedman, Kari E. North, Andrew F. Olshan (University of North Carolina at Chapel Hill)

Primary congenital glaucoma (PCG) and anterior segment defects of the eye (ASDs) are rare ocular malformations diagnosed early in life which can cause blindness. Mutations in several genes have been linked to these conditions in some families, but very little is known about non-genetic risk factors. In this study, we investigated maternal nutrition as a risk factor for PCG and ASDs in the National Birth Defects Prevention Study (NBDPS), a large population-based, multicenter case-control study of major birth defects in the United States. Mothers of cases (n=156) and control infants without a birth defect (n=8,978) completed a computer-assisted telephone interview about a range of demographic, clinical, and lifestyle factors, including a food frequency questionnaire capturing usual dietary intake in the year before pregnancy. We assessed maternal nutrition in three ways: examining individual nutrient intake [in quartiles (Q)]; calculating a Diet Quality Index for Pregnancy (DQI-P) score for each mother (also quartiles); and using latent class analysis to empirically derive 4 dietary patterns among women in our sample. We calculated adjusted odds ratios (aORs) and 95% confidence intervals (CI) using logistic regression and examined effect measure modification by periconceptional vitamin supplementation. The results for individual nutrients varied, with some having an inverse or U-shaped pattern of association with increasing nutrient intake. The DQI-P was not associated with risk of PCG and ASDs (aOR 0.9; CI 0.5-1.7, Q4 vs. Q1). In the dietary pattern analysis, those with a Prudent and Mexican dietary pattern suggested a decreased odds (aOR 0.8, 95% CI 0.5-1.3; aOR 0.8, 95% CI 0.4-1.8, respectively) compared to those in the Western dietary pattern. Results stratified by vitamin supplementation were similar. Consistent with previous work, we found that higher intake of some nutrients and certain dietary patterns may be inversely associated with PCG and ASDs.

**TREE-BASED MACHINE LEARNING IN BIRTH DEFECTS RESEARCH:
AN APPLICATION WITH GASTROSCHISIS** Julie Petersen, Samantha Parker,
Jaimie Gradus, Allen Mitchell, Martha Werler (Boston University School of Public
Health)

Machine learning may aid in epidemiologic surveillance and research. In this work, we evaluated replication of known associations, while generating new hypotheses, in the study of gastroschisis, an abdominal wall defect that has increased over time, most notably among young mothers. Data were from the case-control Slone Birth Defects Study (1998-2015). Mothers completed standardized interviews regarding pregnancy events and exposures. We restricted to cases affected by gastroschisis only (n=273) and frequency-matched controls by study center (n=2591). We used single classification trees to visualize data structure. After data reduction to avoid sparsity and overfit, we used random forest to identify predictors. To evaluate magnitude and direction of observed associations with gastroschisis, we estimated odds ratios with logistic regression. Lastly, we categorized the most important independent predictors and conducted stratified analyses using the above techniques. The random forest model demonstrated good discrimination (AUC=0.86). The strongest independent predictors were young parent age (OR=6.7, 95% CI 3.5,12.9) and being underweight (OR=4.4, 95% CI 1.9-10.2), controlling for the other factors recognized as important, including whether the parents were together, smoking, parity, and low monounsaturated fat. In stratified analyses, gastroschisis odds were stronger for 1st trimester maternal marijuana use among older parents (OR=5.7, 95% CI 2.4-13.5) and for daily fast food intake among mothers with BMI <25 kg/m² (OR=2.7, 95% CI 1.5-4.6). Parent education and family income were also strong predictors, but less so in subgroups due to high correlations with age. Machine learning recognized several factors previously identified using traditional analysis. Though estimates were imprecise, we identified new potentially modifiable behaviors (certain dietary factors, marijuana), which we hypothesize may increase gastroschisis risk and warrant further study.

EXOME SEQUENCING TO IDENTIFY NOVEL GENES UNDERLYING PRIMARY CONGENITAL GLAUCOMA IN THE NATIONAL BIRTH DEFECTS PREVENTION STUDY. Kristin J. Voltzke, Kari E. North, Tania A. Desrosiers, Robert E. Meyer, Suzan L. Carmichael, Janson J. White, Jessica X. Chong, Elizabeth E. Blue, Michael J. Bamshad, Debbie A. Nickerson, Mary M. Jenkins, Lynn L. Almli, James C. Mullikin, Andrew F. Olshan (University of North Carolina at Chapel Hill)

Primary congenital glaucoma (PCG) is a birth defect that, although rare, is a leading cause of blindness among children in the United States (US). PCG is typically inherited in an autosomal recessive manner, although variable expressivity and reduced penetrance have been reported, meaning that not everyone with the same mutation presents with the defect or does so in the same way. The most commonly mutated gene is CYP1B1, which is active in many tissues, including the eye, where it encodes an enzyme during development that metabolizes endogenous and exogenous compounds, such as retinoids. Mutations in this gene have been reported in as many as 90-100% of Slovakian Roma Gypsy families who have PCG; however, the prevalence in a recent study of US families was only 15%. This suggests that alternative genes or mechanisms may contribute to the condition. The purpose of this study was to utilize exome sequencing data to identify novel, rare variants in genes that have not previously been investigated for PCG. We used complete family trios of PCG cases (n=36) from the National Birth Defects Prevention Study (born 1997-2011), a population-based, multicenter case-control study of birth defects in the US. The trio design protects against spurious associations that arise because of population substructure, or differences in allele frequencies among different ethnic groups. Similar to previous findings, CYP1B1 variants were found in 16% (n=6) of families in our sample. Additionally, a number of case infants had potentially pathogenic variants in other genes not previously linked to PCG (e.g., CRYBB2, RXRA, GLI2), but are known to be important in eye development and/or to underlie similar Mendelian conditions with potential phenotypic overlap. These genes may help to explain the genetic underpinnings of PCG cases in the US.

EARLY CHILDHOOD ANTIBIOTICS USE AND THE RISK OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A POPULATION-BASED COHORT STUDY Amani Hamad, Silvia Alessi-Severini, Salah Mahmud, Marni Brownell, I fan Kuo (University of Manitoba)

Background: Early childhood antibiotic exposure induces changes in infants' gut microbiota composition reportedly associated with the development of Attention-Deficit/Hyperactivity Disorder (ADHD). In this study, we examined the association between antibiotic use in the first year of life and the risk of ADHD. Methods: This was a population-based cohort study utilizing the Manitoba Population Research Data Repository. The cohort included 187,605 children born in Manitoba, Canada between April 1, 1998 and March 31, 2017. Exposure was defined as having filled one or more antibiotic prescriptions during the first year of life. The outcome was ADHD diagnosis identified in hospital abstracts, physician visits or drug dispensations. Risk of developing ADHD was estimated using Cox proportional hazards regression models in a high dimensional propensity scores-matched cohort and a sibling cohort. Results: A total of 69,738 children were included in the matched-cohort. During follow-up, 6087 (8.7%) children received an ADHD diagnosis. ADHD risk was not found to be associated with antibiotic exposure in early life (HR 1.02, 95% CI 0.97-1.08). In secondary analyses, an association was observed in those receiving three or more antibiotic courses or for a duration longer than three weeks (HR 1.57, 95% CI 1.23-2.00 and HR 1.38, 95% CI 1.17-1.64, respectively). In the sibling cohort of 67,671 children, antibiotic exposure was not associated with the risk of ADHD (HR 0.96, 95% CI 0.89 - 1.03). No association was observed in any of the secondary analyses. Conclusions: Antibiotic use in the first year of life does not appear to pose an ADHD risk on a population level.

PARENTAL OBESITY AND OFFSPRING ADHD AND CONDUCT

PROBLEMS IN MIDDLE CHILDHOOD Sonia Robinson, Akhgar Ghassabian, Rajeshwari Sundaram, Tzu-Chun Lin, Mai-Han Trinh, Erin Bell, Edwina Yeung (Epidemiology Branch, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD)

Previous studies have observed an association between maternal pre-pregnancy obesity and offspring psychopathology. In utero exposure to obesity-related inflammation may impair development of the dopaminergic or serotonergic system in offspring. Shifts in epigenetic programming associated with obesity represent another potential mechanism. Despite potential epigenetic effects, few studies have investigated the association of paternal obesity with offspring behavior. We aimed to examine the relation of parental obesity with offspring behavior problems at 7-8 y in Upstate KIDS, a population-based birth cohort. Maternal body mass index (BMI) was calculated from pre-pregnancy height and weight provided in vital records or from self-report at baseline at 4 months post-partum. Baseline paternal height and weight were reported by mothers. At 7 or 8 y, mothers reported if their children had been diagnosed with attention deficit hyperactivity disorder (ADHD), anxiety, or conduct disorder (n=1909). In addition, children's behavior was measured with the Strengths and Difficulties Questionnaire (SDQ) at 7 y (n=1386). Based on the SDQ scores, we identified children with borderline behavior problems. Adjusted risk ratios (aRR) and 95% confidence intervals were estimated with multivariable Poisson regression. Compared with children of mothers with BMI<25, children whose mothers were overweight (BMI 25-30), obese class I (BMI 30-35) and obese class II/III (BMI≥35) had higher risks of reported ADHD (aRR 1.31 (0.87, 1.98); 2.01 (1.27, 3.16); 2.11 (1.37, 3.23), respectively). A similar trend was observed for higher risk of conduct disorder (aRR 1.36 (0.81, 2.27); 1.59 (0.82, 3.06); 2.05 (1.20, 3.51)) but not risk of anxiety disorder. Risks of behavior problems identified by the SDQ also increased with maternal BMI. Paternal BMI was not associated with any behavior outcomes. Our findings suggest that maternal, rather than paternal, obesity is associated with child psychopathology.

MARIJUANA AND MOMS: PREGNANT WOMEN'S KNOWLEDGE, ATTITUDES, AND EXPERIENCES WITH PRENATAL CAREGIVERS REGARDING MARIJUANA Mark Klebanoff, Sarah Keim, Lara McKenzie (The Ohio State University)

Marijuana (MJ) use is common in pregnancy and as laws are liberalized it may increase. This study explored pregnant women's beliefs, attitudes, and experiences regarding MJ. Focus groups were conducted within the Lifestyle and Early Achievement in Families study, an historical cohort. Children whose mothers were enrolled in pregnancy were followed at age 3.5-7 to estimate the association of in utero MJ and executive function and aggression. ~1/3 of mothers used MJ in pregnancy. 22 women participated in 4 focus groups, stratified by race and pregnancy MJ. Domains included risk perception of commonly-used substances, reasons for use in pregnancy, where pregnant women get health information, and providers' counseling about substances. Health literacy was assessed by the eHealth Literacy Scale (mean 31.4/40). Women preferred to get info from (>1 choice) providers (73%), internet (55%), social networking (41%), and online forums (36%). All women knew cigarettes were risky, although many smoked. However, many women said MJ was risky, but skepticism soon emerged. ("I circled risky for legality purposes. I don't think MJ's as detrimental as everybody says.") MJ was viewed as a plant, and thus natural ("MJ is not manmade. It's not a chemical like other drugs."), and was equally or less risky than prescription meds. The most common reason for MJ use was to gain weight/handle nausea ("I literally lost 37# in 2 wks because I couldn't hold anything down. The only way I could eat was to actually smoke"). Help sleeping was another reason for use. Doctors gave inconsistent information, even tacit encouragement, about MJ (" 'I can't tell you that you can't. Whatever you're doing, keep on doing it.' And I gained all my weight back"). Reports did not differ by race or MJ use in pregnancy. Regardless of use, participants had a benign attitude toward pregnancy MJ use, and caregivers gave mixed messages on use

PREECLAMPSIA AND RISK OF DEVELOPMENTAL DELAY: FINDINGS FROM DIFFERENT DATA SOURCES Edwina Yeung, Akhgar Ghassabian, Rajeshwari Sundaram, Germaine Buck Louis, Tzu-Chun Lin, Sonia Robinson, Erin Bell (NICHD)

We previously observed that maternal report of some pregnancy complications such as preeclampsia have low agreement with medical delivery ICD-9 codes. Preeclampsia is associated with increased risks of developmental delays. Here we assess whether the source of data impacts the estimates of risks. In Upstate KIDS, mothers reported their pregnancy complications at 4 months postpartum. New York State's Statewide Planning and Research Cooperative System (SPARCS) captured hospital ICD-9 codes over the pregnancy and delivery. Mothers were asked to complete the Ages and Stages Questionnaire (ASQ), a parental screening tool for developmental delay, at 4, 12, 18, 24, 30 and 36 months. Data were also linked to the State's Early Intervention Program to determine whether children received developmental services. 3902 singletons and 2132 twins were included. Adjusted odds ratios (95% confidence intervals) were estimated using generalized linear mixed models adjusting for sociodemographics, maternal smoking, parity, and pre-pregnancy BMI. Higher risk of failing any ASQ domain was observed among singletons regardless of data source (i.e., preeclampsia by self-report: 1.58 (0.96-2.60) vs. SPARCS: 2.42 (1.44-4.05) vs. any report: 1.53 (0.96-2.42) vs. both sources: 2.86 (1.63-5.03)). The same pattern emerged for all developmental domains but was stronger for gross motor (any report: 2.31; 1.05-5.07) and communication delays (any report: 2.33; 1.17-4.65) through 36 months of age. However, no associations were observed for twins. As the ASQ was not a diagnostic tool, increased risk for preeclampsia by linkage with Early Intervention was confirmed. In conclusion, preeclampsia remains a risk factor for developmental delay. Associations were slightly stronger when hospital administrative data was used to adjudicate exposure potentially due to minimizing measurement error arising from less familiarity among women for reporting on preeclampsia as a pregnancy complication.

ASSOCIATION OF OVARIAN VOLUME AND ESTRADIOL**CONCENTRATIONS DURING INFANCY** Helen Chin, Donna Baird, Margaret Adgent, David Umbach, Walter Rogan (NIEHS)

Estradiol production during early childhood is important for healthy brain and reproductive organ development. Estradiol is produced by maturing ovarian follicles; in infant girls, these growing follicles contribute to total ovarian volume. Using data from the Infant Feeding and Early Development Study, a longitudinal cohort study of estrogen-responsive outcomes in healthy term infants, we assessed whether total ovarian volume was predictive of estradiol concentrations at 4 (n=109), 8 (n=46), 16 (n=126), 24 (n=131), and 32 (n=120) weeks of age. We measured serum 17-beta estradiol (E2) using an isotope-dilution liquid-chromatography coupled with mass spectrometry method (limit of detection (LOD): 2.99 pg/ml). We used pelvic ultrasound to measure the dimensions of the ovary and identify visible follicles. The proportion of infants with detectable E2 concentrations peaked at 16 weeks (88%) and declined to a minimum of 60% at 32 weeks; values below the LOD were included as LOD/square root of 2. Median E2 concentration was highest at 16 weeks (6.9 pg/ml [interquartile range (IQR): 5.1, 10.1]). Median ovarian volume was highest at 8 (0.9 cm³; IQR: 0.5, 1.5) and 16 (0.9 cm³; IQR: 0.6, 1.2) weeks. Consistent with the peak in E2 and ovarian volume, the most follicles were visualized at 16 weeks with 43% of girls having greater than 3 follicles visible on both ovaries. We fit separate linear models that regressed log₂-transformed E2 on ovarian volume at each age and found a significant positive association for each. At 16 weeks, a 1 cm³ increase in ovarian volume corresponded to a 1.3-fold increase in E2 (p<0.01). This association did not change after adjustment for gestational age. Our results show that ovarian volume is predictive of E2 concentrations during infancy, suggesting ovarian volume may be an important predictor of estrogen-mediated neurologic and reproductive development. Studies that investigate determinants of ovarian growth during infancy may be warranted.

PRENATAL PBDE EXPOSURE AND NEURODEVELOPMENT IN CHILDREN SEVEN YEARS OLD OR YOUNGER: A SYSTEMATIC REVIEW AND META-ANALYSIS

Barbara Hudson-Hanley, Veronica Irvin, Brian Flay, Megan MacDonald, Molly Kile (Oregon State University)

Background: Prenatal PBDE exposure effects on neurodevelopment is controversial due to conflicting research results. Objective: Prenatal PBDE exposure effects on neurodevelopment summarized with systematic review, meta-analysis. Methods: Eligible birth cohort studies located through PubMed®, Web of Science® or Google Scholar®, reported PBDE concentration in cord blood, maternal blood or colostrum; assessed neurodevelopment at <7 years (Jan-1996-Feb-2017). Comprehensive Meta-Analysis (v.3.3.070, 20-Nov-2014) calculated summary effect. Covariates: age-category (< 2, 3-5, 6-7 years), region, latitude, time-period. Power and publication-bias calculated. Results: Six studies included in random effects comparison model. Prenatal PBDE exposure significantly correlated with decreased cognitive function (npooled=804; k=6; β =-0.237; [95%CI: -0.441, -0.010]; p=0.041), decreased motor function (npooled=794; k=5; β =-0.350; [95%CI: -0.610, -0.022]; p=0.037), and increased behavior problems (npooled=307; k=3; β =0.393; [95%CI: 0.133, 0.602]; p=0.004). Significant covariates: biomarker type, age category. Colostrum effect-size like cord blood; maternal blood effect-size smaller. Largest age-category effect-size: < 2 years (cognitive, motor function); 6-7 years (behavior problems). Number of studies needed to achieve 0.80 power: 23 (cognitive function), 19 (motor function), and 10 (behavior problems). Low likelihood of publication bias effect on result. Conclusion: Prenatal PBDE exposure adversely affected neurodevelopment. Pooled samples offset low power. Behavior studies used maternal blood only; effect-size may be underestimated.

NEONATAL THYROID STIMULATING HORMONE AND SUBSEQUENT DIAGNOSIS OF AUTISM SPECTRUM DISORDERS AND INTELLECTUAL DISABILITY

Jennifer Ames, Gayle Windham, Kristen Lyall, Michelle Pearl, Martin Kharrazi, Cathleen K. Yoshida, Judy Van de Water, Paul Ashwood, Lisa Croen (Kaiser Permanente Northern California)

Background: Hypothyroid conditions in early life, if left untreated, are associated with adverse neurodevelopment, including intellectual disability (ID). However, evidence addressing the role of neonatal thyroid hormones in autism spectrum disorders (ASD), particularly among its subtypes, is limited. **Methods:** We conducted a population-based, case-control study among a sample of 4.5-9-year-old children born during 2000-2003 in Southern California. We examined levels of neonatal thyroid-stimulating hormone (TSH) measured during routine newborn screening among children later diagnosed with ASD (n=518) or ID only (n=145) and general population (GP) controls (n=399). We further analyzed TSH in relation to ASD subtypes defined by intellectual ability and onset (early onset ASD vs. ASD with regression) ascertained by expert review of developmental services records. We modeled differences in TSH levels (continuously and as quartiles) between ASD or ID status vs. GP using odds ratios (ORs) obtained from multivariate logistic regression. **Results:** In adjusted models, we found no association between continuous neonatal TSH levels and ASD (adj-OR: 1.00, 95%CI: 0.79-1.26) nor ID (OR=0.97, 95%CI: 0.70-1.34). Among ASD subtypes, we observed an inverse trend between neonatal TSH and ASD with regression; ASD with regression was marginally associated with continuous TSH (adj-OR: 0.78, 95%CI: 0.55-1.09) and significantly associated with the highest TSH quartile (adj-OR: 0.51, 95%CI: 0.26-0.98). Odds of ASD without co-occurring ID were also inversely related to TSH but this relationship was more modest and not significant. **Conclusions:** While there was little evidence that neonatal TSH is related to overall risk of ASD, these findings suggest that neonatal TSH levels may be associated with subtypes of ASD defined by onset and co-occurring ID. Given that thyroid deficiencies at birth are amenable to therapy, the intersection of thyroid hormones and ASD subtypes warrants further scrutiny.

MATERNAL VITAMIN D AND ASSOCIATIONS WITH OFFSPRING BEHAVIOR AND SOCIOEMOTIONAL DEVELOPMENT

Ellen Francis, Elizabeth Charron, Brian Witrick, Liwei Chen, Rachel Mayo, Lior Rennert, Linda Butler (Clemson University)

Low maternal vitamin D during pregnancy is associated with risk of adverse child neurodevelopmental outcomes, but associations with offspring behavioral problems and social competence deficits are inconsistent. This study analyzed the association between maternal vitamin D during middle to late pregnancy and offspring behavioral problems and socioemotional competencies. This analysis included 126 maternal-offspring pairs from the National Children's Study. Pregnant women aged 18-49 years whose offspring had received a child development assessment were included. Total maternal vitamin D (calculated as the sum of plasma concentrations of 25-hydroxyergocalciferol and 25-hydroxycholecalciferol) were measured between 20-39 gestational weeks and dichotomized as above/below the 1st quartile. Linear regression models, adjusting for maternal age, race/ethnicity, education, and prepregnancy body mass index (kg/m²), estimated the beta coefficients and 95% confidence interval (CI) for the association between maternal vitamin D and offspring problem and competence scores on the Brief Infant-Toddler Social and Emotional Assessment (BITSEA). The mean (standard deviation) vitamin D concentration was 86.5 (27.8) nmol/L. The median (interquartile range) BITSEA problem score was 6.0 (4.0, 10.0) and competence score was 19.0 (17.0, 20.0). In multivariable models, offspring of women with vitamin D concentrations ≥ 71.5 nmol/L (1st quartile) had BITSEA problem scores that were on average -4.36 points (95% CI: -6.92, -1.80) lower compared to offspring of women with vitamin D below the 1st quartile. There were no significant associations between maternal vitamin D and BITSEA competence scores (β -0.05; 95% CI: -1.5, 1.5). Low maternal vitamin D in middle to late pregnancy was associated with increased offspring behavior problems during infancy. The association of maternal vitamin D and offspring development may depend on the specific component of development being investigated.

URINARY OXIDATIVE STRESS LEVELS AND REPRODUCTIVE OUTCOMES AMONG WOMEN UNDERGOING FERTILITY**TREATMENTS** Emma M. Rosen, Lidia Mínguez-Alarcón, John D. Meeker, Ginger L. Milne, Russ Hauser, Kelly K. Ferguson (NIEHS)

Background: Oxidative stress may contribute to adverse fertility outcomes in women and represents a potentially modifiable pathway. **Methods:** This analysis includes 481 women contributing 1001 cycles [n=575 intrauterine insemination (IUI) and n=426 in vitro fertilization (IVF) who enrolled in the Environment and Reproductive Health (EARTH), an ongoing prospective cohort study that enrolled women undergoing fertility treatments from 2004 onward. Urine samples were collected at each treatment cycle and analyzed for 2 oxidative stress [8-isoprostane-PGF2a (8-iso-PGF2a) and 8-isoprostane-PGF2a metabolite (F2-isoP-M)] and 1 inflammation [prostaglandin-F2a (PGF2a)] marker. Endpoints of interest included fertilization proportion for IVF (oocytes fertilized/mature oocytes retrieved), and proportion of cycles leading to implantation, clinical pregnancy, and live birth for IVF and IUI. Adjusted generalized linear mixed models were used to analyze associations between tertiles of oxidative stress and each outcome. **Results:** Overall, levels of F2-isoP-M in the 2nd tertile were associated with the most successful outcomes among women undergoing IVF as well as IUI, while the 3rd tertile was associated with the lowest success. Among IVF cycles, the adjusted mean percent of cycles leading to live birth was 38% (95% CI: 29%, 48%) for females in the upper tertile of F2-isoP-M as compared to 60% (95% CI: 50%, 68%) for those in the middle tertile. Similarly, among IUI cycles, the adjusted mean percent of cycles leading to live birth was 12% (95% CI: 7%, 19%) for females in the upper tertile of F2-isoP-M as compared to 24% (95% CI: 16%, 34%) for those in the middle tertile. No significant associations were found for other measured outcomes with 8-iso-PGF2a or PGF2a. **Conclusions:** In this population of women undergoing fertility treatments, there appears to be an inverse U-shaped relationship between urinary oxidative stress levels and reproductive success.

PRECONCEPTION SLEEP DURATION: PREDICTORS AND THE ASSOCIATION WITH TIME TO PREGNANCY IN A DIVERSE URBAN COHORT Linda Kahn, Akhgar Ghassabian, Sara Brubaker, Shilpi Mehta-Lee, Leonardo Trasande (New York University School of Medicine)

Background: Short sleep duration is associated with adverse pregnancy outcomes in women and poor semen quality in men. Yet little is known about women's preconception sleep and fecundity. Short sleep duration also has established links to stress and inflammation. We hypothesized that women with shorter sleep duration would have longer time to pregnancy (TTP), a measure of couple fecundity.

Methods: We examined self-reported sleep duration in the three months prior to pregnancy and TTP among the first 1000 participants in the New York University Children's Health and Environment Study birth cohort. Associations of health and demographic variables with sleep duration were assessed in bivariate analysis. Associations between sleep duration and TTP were assessed via Cox proportional hazards models.

Results: Sleep duration was normally distributed among 460 participants with valid sleep and TTP data, with a mean of 8.20 (SD 1.36) hours. Women who were Hispanic, were single/divorced, or had \leq high-school education had longer average sleep than others. Women who were older, consumed alcohol, or had body mass index (BMI) ≥ 35 kg/m² had shorter sleep. A prediction model including variables statistically significantly associated with sleep duration accounted for 15% of the variance in the data. Sleep duration was not associated with TTP (FOR 1.01; 95% CI 0.94, 1.08). Results were unaffected when we adjusted for covariates, restricted to women with TTP ≤ 12 months, or excluded those who conceived while using birth control (assigned TTP=1 month).

Conclusion: Demographic factors, BMI, and alcohol consumption do predict sleep duration; however, we did not find an association between preconception sleep duration and TTP. Our study was limited by lack of information on important potential confounders (e.g., physical activity and stress) and reliance on self-reported data. Future studies would benefit from prospective TTP data collection and objective sleep measurement.

PRECONCEPTION PSYCHOLOGICAL STRESS AND FECUNDABILITY AMONG CHINESE WOMEN

Lulu Zhang, Rong Huang, Wei Zhou, Rongrong Zhang, Xi Zhang, Yexuan Tao, Jun Zhang (Ministry of Education-Shanghai Key Laboratory of Children's Environmental Health, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China)

IMPORTANCE Previous studies have reported the association between psychological stress and fecundability in females, but the findings were inconsistent.

OBJECTIVE To determine whether preconception psychological stress affects fecundability in women who plan to be pregnant. **DESIGN** This was a prospective cohort study of 978 women who participated in the Shanghai Birth Cohort study, China. **PARTICIPANTS** From 2013 to 2015, a total of 1180 women who planned to be pregnant and came to visit two preconception care clinics were recruited. A telephone interview was conducted every two months to collect information on the status of conception during a follow-up period of 12 months. **EXPOSURES**

Psychological stress. **MAIN OUTCOMES** The main outcome was fecundability in women. Time to pregnancy was treated as the time variable in the Cox proportional hazard model. **RESULTS** 1134 women were finally identified with a successful follow-up proportion of 96% and 978 women were included in the final analyses. The median age of these women was 30 (interquartile range [IQR]: 28, 32) years old. Compared to the women with lowest quartile of stress score, those with the third and highest quartile had a lower probability of spontaneous conception after the adjustment for potential confounders, with Fecundability hazard ratios (FHRs) of 0.75 (95% confidence intervals [CI], 0.59-0.96) and 0.77 (95% CI, 0.60-0.99), respectively. In contrast, we didn't find significant association between women with the second quartile and probability of spontaneous conception (FHR, 0.89; 95% CI, 0.71-1.11). The probability of spontaneous conception decreased by 2% (95% CI, 0.5%-4%) for each one unit increase in female stress score. This trend was more prominent in women who had not experienced pregnancy and in women under 35. **CONCLUSIONS** Psychological stress decreases fecundability in reproductive age women. Our findings underlined the importance of preconception mental health for female fecundability.

PRECONCEPTION USE OF ASTHMA MEDICATION AND

FECUNDABILITY: A PROSPECTIVE STUDY Holly Crowe, Lauren Wise, Amelia Wesselink, Kenneth Rothman, Henrik Sørensen, Ellen Mikkelsen, Elizabeth Hatch (Boston University School of Public Health)

Asthma is a chronic inflammatory disease of the lungs. It has been associated with irregular menses and infertility in some studies, but there are limited data on the relation between asthma medication use and fecundability. We used data from Pregnancy Study Online (PRESTO), a North American preconception cohort study, to examine the association between asthma diagnosis and medication use with fecundability. During 2013-2018, we enrolled 6,868 female pregnancy planners who had been trying to conceive for ≤ 6 cycles at entry. Participants completed a baseline questionnaire and bimonthly follow-up questionnaires for up to 12 months or until pregnant. At baseline, participants reported if they had ever been diagnosed with asthma and their asthma medication use in the past four weeks. We used proportional probabilities models adjusted for factors such as socio-demographics and comorbidities to estimate fecundability ratios (FR) and 95% confidence intervals. The referent for all comparisons was women without an asthma diagnosis. Overall, 1,149 women (17%) reported an asthma diagnosis, of whom 395 (34%) reported use of asthma medication in the past four weeks. Of those who used asthma medication, 60% reported use when having symptoms, 22% reported daily use, and 18% reported daily use plus more when having symptoms. Overall, an asthma diagnosis had little association with fecundability (FR=0.98, 95% CI: 0.90-1.06). For women with asthma who reported medication use only when having symptoms, daily asthma medication use, daily asthma medication use with additional dosing for symptoms, or no medication use, FRs were 1.08 (95% CI: 0.91-1.28), 0.98 (95% CI 0.78-1.29), 0.79 (95% CI: 0.59-1.07), and 0.97 (95% CI 0.89-1.07), respectively. Despite the near-null findings overall, we found slightly reduced fecundability for the heaviest users of asthma medication, which might be a chance departure, confounding by asthma severity, or an effect of greater asthma medication use.

INTERVAL BETWEEN LIVE BIRTH AND INITIATION OF CURRENT PREGNANCY ATTEMPT AND FECUNDABILITY Sydney Willis, Elizabeth Hatch, Amelia Wesselink, Olivia Orta, Kenneth Rothman, Ellen Mikkelsen, Henrik Sorensen, Lauren Wise (Boston University School of Public Health)

The association between short interpregnancy interval and increased risk of adverse birth outcomes is well-documented. Possible mechanisms include maternal nutritional depletion and diminished vascularization from incomplete uterine tissue remodeling. Little is known about the optimal time between giving birth and attempting to conceive again (postpartum interval). We evaluated the association between the postpartum interval and fecundability in Pregnancy Study Online (PRESTO), a prospective preconception cohort of pregnancy planners. Eligible women were aged 21-45, residents of North America, attempting pregnancy, and not using fertility treatment. Women completed a baseline questionnaire to ascertain information on demographics, lifestyle, and reproductive history, including the gestational length of all prior pregnancies. They completed bi-monthly follow-up questionnaires to update pregnancy status over time. We restricted analyses to 1,238 women whose previous pregnancy resulted in a singleton live birth and who were attempting pregnancy for ≤ 6 months at study entry. We used proportional probabilities regression models to estimate fecundability ratios (FR) and 95% confidence intervals (CI), adjusted for age, partner's age, race/ethnicity, education, income, smoking history, breastfeeding, and weight gain during prior pregnancy. We defined the postpartum interval based on the time between the date of the prior live birth and the initiation of the current pregnancy attempt. Postpartum intervals ranged from 1-220 months. Relative to a 12-23 month postpartum interval, FRs for an interval of <12 , 24-27, and ≥ 48 months were 0.95 (CI: 0.79-1.13), 1.11 (CI: 0.94-1.31) and 0.85 (CI: 0.69-1.05), respectively. Results were similar after excluding time spent breastfeeding from the postpartum interval and when restricted to those without a history of infertility. These data indicate that postpartum intervals ≥ 48 months may be associated with reduced fecundability.

PROSPECTIVE COHORT STUDY OF PHYSICAL ACTIVITY, BICYCLING, AND SEMEN QUALITY Lauren Wise, Tanran Wang, Elizabeth Hatch, Greg Sommer, Kenneth Rothman, Michael Eisenberg (Boston University School of Public Health)

Objective: To assess the association between physical activity (PA) and semen quality. **Design:** Pregnancy Study Online (PRESTO) is a preconception cohort study of North American couples. **Methods:** After completing a baseline survey on socio-demographics, medical history, anthropometrics, and average PA levels in the last year, men attempting conception for ≤ 6 months at entry were invited to use Trak, an FDA-approved device for measuring sperm concentration and semen volume at home. We used generalized estimating equations to estimate risk ratios (RRs) and 95% confidence intervals (CIs) for the associations of vigorous PA (hours/week), moderate PA (hours/week), and bicycling (hours/week) with low semen volume (≤ 2 vs. > 2 ml), low sperm concentration (≤ 20 vs. > 20 million/ml), and low total sperm count (TSC, ≤ 50 vs. > 50 million). These models accounted for within-person correlation and adjusted for abstinence time, age, education, smoking, sleep duration, depressive symptoms, work hours/week, and BMI. **Results:** During 2015-2018, 186 men provided 313 semen samples (median time after entry: 3 weeks, interquartile range: 2-6 weeks). Nearly 14% ($n=43$) of samples had semen volume ≤ 2 ml, 19% ($n=60$) had sperm concentration ≤ 20 million/ml, and 14% had TSC ≤ 50 million. For a 1-hour/week increase in vigorous PA, moderate PA, and bicycling, the respective adjusted RRs (CIs) were 1.01 (0.92-1.12), 0.99 (0.92-1.06), and 0.92 (0.66-1.29) for low semen volume; 1.03 (0.95-1.12), 0.99 (0.93-1.06), and 1.20 (1.03-1.39) for low sperm concentration; and 0.96 (0.83-1.10), 0.98 (0.92-1.04), and 0.94 (0.69-1.28) for low TSC. **Conclusions:** In a geographically-diverse population of men not seeking fertility treatment, PA subtypes were not appreciably associated with semen volume, sperm concentration, or TSC, with the exception of a weak positive association between bicycling and low sperm concentration. Chance remains a plausible explanation of this association.

VEGF AND sFLT-1 ACROSS THE MENSTRUAL CYCLE IN HEALTHY REGULARLY MENSTRUATING WOMEN Jessica Zolton, Lindsey Sjaarda, Sunni Mumford, Kerry Flannagan, Elizabeth Devilbiss, Keewan Kim, Carrie Nobles, Alexandra Purdue-Smithe, Neil Perkins, Robert Silver, Micah Hill, Alan DeCherney, Enrique Schisterman (Eunice Kennedy Shriver National Institute of Child Health and Human Development)

Objective: Vascular endothelial growth factor (VEGF) and its receptor, sFLT-1, are angiogenic factors involved in endometrial remodeling and implantation and are implicated in development of preeclampsia and fetal growth restriction. However, it is unknown whether VEGF and sFLT-1 change over the menstrual cycle, which may have implications for understanding the pathogenesis of maternal-fetal complications. Our aim was to identify if changes in VEGF and sFLT-1 occur during the menstrual cycle. **Methods:** We measured VEGF and sFLT-1 in plasma, serum, and urine, and reproductive hormones 8 times during the cycle in healthy women (n=100 with ovulatory cycles) ages 18-44 enrolled in the BioCycle Study. Pearson correlation coefficients were used to compare concentrations in different specimens at each visit, and median concentrations were compared at each point. Harmonic models evaluated differences in the mean, amplitude, and phase shift of estradiol, progesterone, LH, and FSH by tertile of baseline VEGF and sFLT-1, adjusting for age and BMI. **Results:** Median (25th percentile, 75th percentile) concentrations of VEGF during the menstrual cycle were 32.2 pg/mL (24.1, 56.9) in plasma, 194.1 pg/mL (125.4, 350.2) in serum, and 101.7 pg/mL (64.2, 165.8) in urine. No variation in VEGF was detected over the menstrual cycle. Measurements in plasma and serum were correlated at each visit (range: 0.3 to 0.8), though measurements in urine with those in plasma/serum were not correlated (range: -0.2 to 0.1). VEGF was not associated with hormone concentrations, though higher plasma sFLT-1 was associated with higher estradiol amplitude (beta 0.16, 95% CI 0.03, 0.29; third versus first tertile). **Conclusions:** Lack of change in circulating and urine VEGF and sFLT-1 across the menstrual cycle makes it unlikely that they will be useful as peripheral biomarkers of endometrial remodeling. However, the receptor sFLT-1 may be positively associated with the degree of estradiol variation.

ORAL CONTRACEPTIVE USE AND INCIDENCE OF EARLY NATURAL MENOPAUSE Christine Langton, Brian Whitcomb, Alexandra Purdue-Smith, Susan Hankinson, JoAnn Manson, Bernard Rosner, Elizabeth Bertone-Johnson (University of Massachusetts)

Early menopause, the cessation of ovarian function before the age of 45, affects roughly 10% of women and is associated with increased risk of cognitive decline, osteoporosis, and cardiovascular disease. Oral contraceptives (OCs) may modify the rate of follicular atresia, preserve oocytes and suppress follicle-stimulating hormone and thus, may be associated with risk of early menopause. Most studies assessing this relationship have been cross-sectional and results have been conflicting. Our study included 108,813 participants in the prospective Nurses' Health Study II who were 25-42 years old and premenopausal in 1989. We assessed timing and duration of OC use using biennial questionnaires, following women through 2013. We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) adjusted for lifestyle, dietary, and reproductive factors including parity and infertility. During 1.7 million person-years of follow-up, 2,603 members of the analytic cohort experienced early natural menopause. In multivariable-adjusted models, current or past OC users had higher risk of early natural menopause compared to never users (HR=1.23, 95% CI: 1.03-1.46 and HR=1.24, 95% CI: 1.01-1.53, respectively). Duration of use was not linearly related to risk; for example, compared to never users, women reporting 120+ months of total use had an HR of 1.07 (95% CI: 0.90-1.27). Results were similar in sensitivity analyses considering age at first and last use to address possible reverse causality. However, analyses accounting for menstrual cycle length suggested that higher risk was limited to women with a history of very short (≤ 25 days) cycles. In this large prospective study, our results suggested that OC use was associated with modestly higher risk of early menopause in some women. Further analyses of timing of use and cycle length are needed to better understand the complex relationship between OC use and menopause timing.

REPRODUCTIVE GOALS IN AFRICAN AMERICAN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A PILOT STUDY Meghan Angley, Jessica B. Spencer, Cristina Drenkard, S. Sam Lim, Penelope P. Howards (Emory University)

Background: Women with systemic lupus erythematosus (SLE) tend to have smaller families than women without SLE. It has not been studied if disease activity and damage is associated with reproductive goals among women with SLE. **Methods:** African American (AA) women were enrolled from a cohort of validated SLE cases in Atlanta, Georgia. Women were ages 22-40, diagnosed after age 17, and had not had a hysterectomy. A comparison group of AA women ages 22-40 from the same area was also recruited. Both groups were asked about reproductive goals. In women with SLE, information on disease activity was collected with the Systemic Lupus Activity Questionnaire for Population Studies (SLAQ) and information on disease damage was collected with the Self-Administered Brief Index of Lupus Damage (BILD) over the past year. SLAQ and BILD scores were dichotomized at the median into low vs. high (SLAQ: 0-18 vs. ≥ 19 ; BILD: 0-1 vs. ≥ 2). **Results:** Average age at interview was 32.7 years in women with SLE and 35.2 in women without SLE. Average age at SLE diagnosis was 24.3 years. Only 3% of women with SLE stated they did not want to raise any children. Both SLE and non-SLE women wanted to raise a median of 2 children (IQR: 2-3). Similar proportions of SLE and non-SLE women who had not reached their goal family size stated that having a biologic child was important to them (83% and 79%) and that they would be disappointed if they found out they could not get pregnant again (57% and 63%). Among women with SLE, controlling for age, there was no difference between women with low vs. high disease activity (odds ratio [OR]: 1.19, 95% confidence interval [CI]: 0.46, 3.09) or low vs. high disease damage (OR: 0.84, 95% CI: 0.32, 2.22) in wanting to have a (or another) biologic child. **Conclusions:** Having biologic children is important to AA women with SLE, including those with high disease activity and damage. This may have implications for improved family planning as part of SLE clinical care.

TRICHOMONAS VAGINALIS, ENDOMETRITIS AND SEQUELAE AMONG WOMEN WITH CLINICALLY SUSPECTED PELVIC**INFLAMMATORY DISEASE** Ann Wiringa, Roberta Ness, Toni Darville, Richard Beigi, Catherine Haggerty (University of Pittsburgh)

Objective: To ascertain the prevalence of *Trichomonas vaginalis* and investigate associations between trichomoniasis, endometritis and long-term sequelae among women with pelvic inflammatory disease (PID). **Methods:** We assessed the prevalence of trichomoniasis identified via wet mount and its association with histologically confirmed endometritis, infertility and recurrent PID among 647 women in the PID Evaluation and Clinical Health (PEACH) study. Participants were treated for clinically suspected PID and followed for a mean of 84 months for incident sequelae. Analyses were adjusted for age, race, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Mycoplasma genitalium* and bacterial vaginosis. Additional adjustments were incorporated for history of infertility (models of pregnancy and infertility), history of PID (recurrent PID) and self-reported partner treatment and intercourse between baseline and 30-day follow-up (persistent endometritis). **Results:** *T. vaginalis* was present in the vagina of 12.8% of women. The odds of having endometritis at baseline were twice as high among women with trichomoniasis as compared to those without (adjusted odds ratio (AOR):1.9, 95% CI:1.0-3.3). Persistent endometritis was highly prevalent at 30 days (52.1%) and more common among women with baseline trichomoniasis (AOR:2.6, 95% CI:0.7-10.1), albeit non-significantly. Trends for increased infertility (AOR:1.6, 95% CI:0.9-3.0), recurrent PID (AOR:1.2, 95% CI:0.7-2.1) and decreased pregnancy (AOR:0.7, 95% CI:0.4-1.1) were observed following *T. vaginalis* infection. **Conclusions:** *T. vaginalis* was frequently isolated from the vagina of women with PID. Our findings of modest, albeit non-significant, prospective associations between trichomoniasis and persistent endometritis, infertility and recurrent PID are novel, underscoring the need for additional investigation into optimal treatment regimens and whether *T. vaginalis* may play an etiologic role in adverse reproductive and gynecologic outcomes.

VITAMIN D DEFICIENCY AND ITS IMPLICATIONS ON INTRAUTERINE GROWTH RESTRICTION (IUGR) Annalise Almdale, Casey Younkin, Elizabeth Unal, Kathleen Groesch, Teresa Wilson, Paula Diaz-Sylvester, (SIU-SOM)

Background: One billion people worldwide are estimated to be Vitamin D deficient. Current Vitamin D level deficiency cutoff is defined in a non-pregnant population; it is unknown if this requirement is the same in pregnancy. Incidence of Vitamin D deficiency in pregnancy is between 20-85% depending on study population. Vitamin D is important for a healthy pregnancy. Reports indicate an association between vitamin D deficiency and small for gestational age (SGA) and a possible linear relationship between birth weight and vitamin D intake. IUGR can lead to poor neonatal outcomes and have long term effect on infants including an increased risk of schizophrenia, diabetes and asthma. It is important to identify factors that contribute to IUGR to create new interventions that could prevent or reduce the incidence/severity. Methods: This is an ongoing case-control study. Nine singleton pregnancies with IUGR were enrolled between 32w-36w6d gestational age (GA) and control subjects were matched by GA, body mass index and phototype score. At delivery, Vitamin D was analyzed from maternal serum and umbilical cord blood. Results: Preliminary data indicates no significant difference in Vitamin D levels in either maternal or cord blood when comparing IUGR vs controls (p-value=0.79 & 0.73 respectively). Maternal levels significantly predicted fetal cord levels in IUGR patients (p=0.013); however, there was no significant relationship between maternal and fetal cord blood level in control subjects (p=0.197). Conclusion: These data show a positive correlation, however non-significant, between fetal and maternal levels of vitamin D in the IUGR population only. The data is limited by the size of the study, which may indicate that our study is underpowered to show significant correlation. Our goal is to establish vitamin D dosing recommendations, as there are no current recommendations during pregnancy.

FIVE COMPLICATIONS OF TERM PREGNANCIES THAT INCREASE THE RISK OF FUTURE PRETERM DELIVERY Liv Grimstvedt Kvalvik, Allen Wilcox, Rolv Skjærven, Truls Østbye, Quaker Harmon (University of Bergen, Norway)

Background. Women with a complication of pregnancy are at increased risk of recurrence of that complication in subsequent pregnancies. We explored whether poor outcomes in term pregnancies also predict preterm delivery in the next pregnancy. **Methods.** Using the population-based Medical Birth Registry of Norway (MBRN), we linked outcomes of women's first pregnancies with outcomes in their second for 785,540 women giving birth between 1967-2015. **Results.** Women with term pregnancies complicated by preeclampsia, placental abruption, stillbirth, neonatal death, or small-for-gestational-age were at increased risk of preterm delivery in the subsequent pregnancy. Relative risks for preterm delivery ranged from 1.7 to 2.8, with p-values all less than 0.001. An elevated preterm risk persisted after excluding recurrence of the specific complication. These associations were also seen in the reverse direction: preterm birth in the first pregnancy predicted the occurrence of pathological conditions in the second pregnancies delivered at term. **Discussion.** Complications of pregnancy at term apparently share underlying causes with preterm delivery. These likely reflect persistent conditions in the mother or her environment, possibly acting through placental pathology. **Conclusion.** Preterm delivery and complications of term pregnancy are not distinct entities. They share underlying pathological processes, to which some women are more susceptible.

ASSESSING THE VALIDITY OF BIRTH HOSPITAL DISCHARGE DATA IN IDENTIFYING PRETERM BIRTHS — MASSACHUSETTS, 2011–2015

Katja Gerhardt, Susan E Manning, Scott Grosse, Mahsa Yazdy, Rui Li, Norman Waitzman, Erin Stallings, Shanna Cox (BU School of Public Health)

Background: In Massachusetts (MA), preterm birth (PTB, <37 completed weeks of gestation) increased from 8.4% in 2015 to 8.9% in 2017, mirroring a similar national trend (from 9.6% in 2015 to 9.9% in 2017). Preterm infants have an increased risk of disability or death, and PTB imposes an economic burden to families, the health care system, and society as a whole. Administrative data are often used to estimate the burden of disease; however, the ability to accurately capture PTB in these data is not well understood. We used hospital discharge (HD) data linked with birth certificates (BC) to assess the validity of using administrative data for identifying PTB. **Methods:** Using the MA Pregnancy to Early Life Longitudinal data system, we linked BC and HD data for birth hospitalizations to resident mothers. PTB identified by the clinical estimate of gestational age on BCs was compared with PTB identified by ICD-9 CM coding (765.00 to 765.28) on HD data. Infants with birthweight <350 grams or gestational age 43 weeks were excluded. We calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), both overall and by individual week of gestational age. **Results:** The study sample included 318,107 infants born during January 1, 2011–September 30, 2015. Overall sensitivity and specificity were 87.3% and 99.1%, respectively. PPV was 89.7% and NPV was 98.9%. Levels of agreement differed by gestational age (sensitivity range 76.9–97.8%; specificity 92.3–100%). Sensitivity was lowest among infants born 35 (90.9%) or 36 weeks (76.9%). Among term births, specificity was lowest among infants born 37 weeks (92.3%). **Conclusions:** Agreement between PTB identification from birth HD and BC data was high. PTB classification on HD data was more specific than sensitive. These results from one state suggest that birth HD data can be used with a high degree of confidence to assess PTB for epidemiologic and health services research.

CEREBRAL TISSUE DESATURATION EVENTS ARE ASSOCIATED WITH GESTATIONAL AGE AMONG PRETERM NEONATES Michael Frasketi, Heather Hoffman, Mohamed Mohamed (Milken School of Public Health, George Washington University)

Several studies have correlated physiological and hemodynamic changes in cerebral tissue perfusion (SctO₂) of preterm neonates using near infrared spectroscopy (NIRS). Monitoring of cerebral tissue perfusion offers many benefits to avoid complications associated with oxygen therapy. Infants with gestational age of 34 weeks or less without diagnosed cerebral congenital anomalies were recruited. Monitoring equipment was applied on all participants at three timepoints between birth and discharge and data was collected electronically in two-second intervals. Desaturation events were defined as SctO₂ values below a defined threshold for more than 30 seconds and were considered resolved after two minutes at or above the defined threshold. Odds ratios were calculated with logistic regression and severity and duration associations with gestational age were calculated with linear regression. This analysis was performed on 70 infants, 45 (63.4%) of which experienced one or more SctO₂ desaturation events during NIRS monitoring. Overall, 457 SctO₂ desaturation events were observed with a median of 5.5 events per subject (IQR 9.0). Subjects consist of 28 (40%) males and 42 (60%) females (p-value=0.0943), mean gestational age was 28.2±2.5 weeks. Of 28 subjects born prior to 28 weeks, 25 (89.3%) experienced one or more SctO₂ desaturation events compared to 20 out of 42 (47.2%) born on or after 28 weeks. Resulting in a 9.2 (95% CI 2.4-35.1) higher odds of experiencing a desaturation event for subjects born prior to 28 weeks compared to subjects born on or after 28 weeks. Event duration and severity are also inversely correlated with gestational age (p=0.0095 and p=0.0008 respectively). Our results indicate that among preterm neonates, those born before 28 weeks are more likely to experience cerebral tissue desaturation events compared to infants born after 28 weeks. The implication of this is unclear on the long-term health outcomes and merits additional research.

HISTORY OF EARLY-LIFE CANCER AND RISK OF ADVERSE PREGNANCY AND NEONATAL OUTCOMES Leslie V. Farland, Judy E. Stern, Sunah Hwang, Chia Ling Liu, Howard Cabral, Richard Knowlton, Susan Gershman, Hafsatou Diop, Stacey A. Missmer (University of Arizona)

Background: As early-life cancer survivorship improves, there is increasing interest in the reproductive health of survivors. The goal of this study was to investigate the association between history of cancer, subsequent infertility, and perinatal outcomes. Methods: Deliveries from Massachusetts (MA) vital records for women >18 years old between 2004-2013 were linked to the Society for Assisted Reproductive Technology Clinic Outcome Reporting System, MA hospital stays and Cancer Registry. The relative risks (RR) and 95% confidence intervals of adverse outcomes (gestational diabetes (GDM), pregnancy induced hypertension (PIH), cesarean section (CS), small for gestational age (SGA), preterm birth (PTB), neonatal mortality, and prolonged neonatal hospital stay) were modeled with a log-link and a Poisson distribution. Generalized estimating equations accounted for women with >1 pregnancy. Models adjusted for maternal age, race/ethnicity, education, and delivery year. Effect modification by infertility history was examined. Results: Among 670,601 deliveries, 2,983 were to women with a history of cancer. The most common cancers were thyroid (21.2%), melanoma (17.8%), breast (10.7%), and cancers of the reproductive organs (23.1%). Deliveries to women with a history of cancer were not at greater risk of GDM, PIH, or CS. However, they were at greater risk of PTB (RR: 1.25 [1.12-1.41]), prolonged neonatal hospital stay (RR: 1.16 [1.01-1.33]), and neonatal mortality (RR: 1.64 [1.00-2.68]). There was heterogeneity in the relationship between history of cancer and SGA by infertility (p-value, test for heterogeneity: 0.02). Among deliveries with a history of infertility, those with a history of cancer had greater risk of SGA (RR: 1.33 [1.00-1.78]). Conclusions: Deliveries to women with a history of cancer had a greater risk of some adverse pregnancy and neonatal outcomes. The relation with SGA varied by infertility history, which warrants further investigation.

THE VAGINAL MICROBIOME IN PREGNANCY AND SPONTANEOUS PRETERM BIRTH Kimberly McKee, Christine Bassis, Sitara Murali, Jason Bell, Vincent Young (University of Michigan)

Preterm birth is the leading cause of infant morbidity and mortality. Although ~40% of preterm births may be infection-related, our understanding of urogenital pathogens and their interaction with the maternal host is limited. Culture-independent studies suggest vaginal microbiota, particularly *Lactobacillus* spp., may promote reproductive health. Our objective was to characterize the vaginal microbiota of women with preterm births compared to women who delivered at term and non-pregnant women. Methods: Vaginal swabs were collected longitudinally from 125 reproductive-aged women (80 pregnant women and 45 non-pregnant women) from Southeast Michigan clinics at 3 time points. Clinical, behavioral, demographic data were collected from surveys and medical records. Microbiota were analyzed using 16S rRNA gene amplicon sequencing. We assessed compositional differences between communities using θ YC distances and linear discriminant analysis effect size (LEfSe). Results: Mean age was 31.8 years (SD 4.3); 12.8% were African American. Among the pregnant sample, 16% had a preterm birth. Distinct vaginal microbiota signatures were evident in the first trimester of pregnancy. *Lactobacillus gasseri* was more abundant among pregnant women compared to non-pregnant women ($p=0.041$) whereas *Lactobacillus iners* and *Gardnerella vaginalis* were more enriched among non-pregnant women ($p=0.0003$ and 0.028 , respectively). Within the pregnant sample, the average θ YC distance within spontaneous preterm births was larger across time points in gestation compared to indicated preterm births and term deliveries. Conclusions: The first trimester may be a critical period of vaginal microbiota assembly for pregnancy maintenance. Less-stable vaginal microbiota across pregnancy may be associated with spontaneous PTB, but further investigation is warranted.

DOES HIV DISEASE PROGRESSION EXPLAIN THE ASSOCIATION BETWEEN PRECONCEPTION ANTIRETROVIRAL TREATMENT AND PRETERM BIRTH? Pamela Murnane, Moses Obimbo, Jared Mecha, Felix Matengo, Mercy Jelimo, Teddy Obonyo, Elizabeth Bukusi, Craig Cohen (University of California San Francisco)

Background: A recent meta-analysis found that initiation of antiretroviral treatment (ART) for HIV prior to conception was associated with an increased risk of preterm birth compared to initiation in pregnancy (risk ratio [RR] 1.41, 95% CI 1.22-1.63). This relationship may be confounded by indication, e.g. women with advanced HIV disease are more likely to initiate ART earlier and are more likely to deliver preterm. Prior studies have not adjusted for pre-ART nadir CD4 T-cell count, an important marker of HIV disease progression. We sought to explore the potential role of disease progression in the association between preconception ART and preterm birth in a retrospective cohort study in Nairobi, Kenya. **Methods:** We abstracted records from women with singleton live births who sought antenatal care at two hospitals in Nairobi between 2014-2016, and used Poisson regression with robust standard errors to estimate the association between preconception ART and preterm birth (<37 weeks). As CD4 counts were incomplete, we used time since diagnosis as a proxy for HIV disease progression. **Results:** Among 448 women with HIV diagnosis, ART initiation, and delivery dates, the median age was 31 years (range 17-43); 299 (67%) initiated ART preconception and 149 during pregnancy. Overall, 64 (14%) delivered preterm. Preconception ART was marginally associated with preterm birth (RR 1.49, 95% CI 0.88-2.54). Adjusting for age and parity attenuated the RR to 1.25, while further adjusting for time since diagnosis attenuated the RR to null (0.98, 95% CI 0.53-1.82). **Conclusion:** Our data suggest that HIV disease progression may be an important confounder of the association between preconception ART and preterm birth. Ongoing surveillance efforts should incorporate markers of HIV disease progression and inflammation in maternal records, such as pre-ART nadir CD4 count, to improve future observational analyses of the impact of ART regimens on preterm birth.

THE ASSOCIATION BETWEEN MATERNAL RESIDENTIAL NEIGHBOURHOOD INCOME AND CONCOMITANT PRETERM BIRTH AND SEVERE SMALL-FOR-GESTATIONAL AGE BIRTHWEIGHT

Jennifer Jairam, Simone Vigod, Patricia O'Campo, Alison Park, Arjumand Siddiqi, Joel Ray (University of Toronto)

Background: Socioeconomic position gradients have been individually demonstrated for preterm birth (PTB) at < 37 weeks' gestation and severe small for gestational age birthweight at < 5th percentile (SGA). It is not known how neighbourhood income is related to the combination of PTB-severe SGA, a state reflective of greater placental dysfunction and higher risk of neonatal morbidity and mortality than PTB or severe SGA alone. **Methods:** This population-based study used Vital Statistics data and comprised all 1,367,656 singleton livebirths in Ontario, Canada, 2002-2011.

Multinomial logistic regression was used to estimate the odds of PTB-severe SGA, PTB without severe SGA, and severe SGA without PTB, compared to neither PTB nor severe SGA, in relation to maternal neighbourhood income quintile (Q). The highest income quintile, Q5, served as the exposure referent. Odds ratios (aOR) were adjusted for maternal age at delivery, parity, marital status and world region of birth. **Results:** Relative to women residing in Q5 (2.3 per 1000), the rate of PTB-severe SGA was highest among those in Q1 (3.6 per 1000) – an aOR of 1.34 (95% CI 1.20-1.50). The corresponding aORs were 1.23 (95% CI 1.09-1.37) for Q2, 1.14 (95% CI 1.02-1.28) for Q3 and 1.06 (95% CI 0.95-1.20) for Q4. Less pronounced aORs were seen for each individual outcome of PTB and severe SGA. **Conclusion:** Women residing in the lowest income areas are at highest risk of having a fetus born too small and too soon. Future research should focus on identifying those women most predisposed to PTB-severe SGA.

**PLASMA PHOSPHOLIPID POLYUNSATURATED FATTY ACIDS
ACROSS PREGNANCY IN RELATION TO NEONATAL SIZE AND BODY
COMPOSITION: A LONGITUDINAL STUDY WITHIN THE NICHD**

FETAL GROWTH STUDIES Yeyi Zhu, Mengying Li, Stefanie Hinkle, Qi Sun, Jing Wu, Mohammad Rahman, Michael Tsai, Cuilin Zhang (Kaiser Permanente Northern California Division of Research & University of California, San Francisco)

Objective: Polyunsaturated fatty acids (PUFAs) are essential for fetal growth and development, yet longitudinal data on objectively measured maternal PUFAs in relation to fetal growth remain elusive. We prospectively and longitudinally investigated plasma phospholipid PUFAs in pregnancy in relation to neonatal size and body composition. **Methods:** Within the NICHD Fetal Growth Studies-Singleton Cohort (n=2802), individual plasma phospholipid PUFAs were measured in blood samples collected at gestational weeks (GW) 10-14, 15-26, 23-31, and 33-39 in a subset of 321 women. Birthweight (BW) was abstracted from medical records. Neonatal length and skinfolds were measured and fat mass (FM) and % body fat (BF) were estimated by Catalano's formula. We used linear regression models with robust variance and inverse probability weighting to standardize the sample. **Results:** In late pregnancy at GW 33-39, after adjusting for covariates including prepregnancy BMI, per unit increase (PUI) in 22:6n-3 was related to a 95.3 g (95% CI 33.6, 157.0) greater BW, 0.49 cm (0.09, 0.90) longer neonatal length, 41.2 g (13.6, 68.9) greater FM, and 0.79% (0.21, 1.37) higher BF. As for n-6 PUFA, at GW 33-39, 20:4n-6 PUI was associated with 41.7 g (5.22, 78.3) greater BW and 22:4n-6 PUI was related to 462.3g (98.0, 826.6) and 145.5 g (12.1, 278.9) greater BW and FM, respectively. The PUFA n-6/n-3 ratio PUI at GW 33-39 was significantly related to 14.6g (-29.2, -0.04) lower FM. Further, associations of n-3 PUFA with neonatal adiposity varied by prepregnancy obesity and exposure window. Total n-3 PUFA PUI at GW 23-31 and 33-39 was associated with 0.68-0.78% greater neonatal BF among women without obesity, whereas at GW 10-14 and 15-26 it was associated with 1.07-1.36% lower BF among women with obesity (P-interaction <0.001). **Conclusions:** Our data suggest that maternal plasma phospholipid PUFAs are implicated in fetal growth and their roles may vary by prepregnancy obesity and timing in pregnancy.

ADVERSE PREGNANCY OUTCOMES AMONG AMERICAN INDIAN / ALASKAN NATIVE WOMEN – GOING FROM BAD TO WORSE Lynne Messer, Zoe Watson (OHSU-PSU School of Public Health)

Background: The health of American Indian/Alaskan Native (AIAN) women and their offspring is rarely considered in most reproductive health research, owing to their low numbers. Further, the heterogeneity of risk factors across urban and rural residence is under-explored. Yet the prevalence of adverse pregnancy outcomes among AIAN women is large and appears to be increasing. **Methods:** We used 2010-2014 vital records data to construct a geographically-defined cohort in one tri-county area of the Pacific Northwest. In logistic regression, adjusted for confounders (continuous and quadratic maternal age, categorical education and payment, dichotomous marital status), we modeled preterm birth (PTB), low birthweight (LBW)) and gestational diabetes (GDM), defined using standard definitions. We further calculated the annual PTB percentages and disparity-difference (AIAN PTB-white PTB) over time. **Results:** Of the 97,578 women included in the cohort, 65.3% were white non-Hispanic, 4.7% were black non-Hispanic, 17.8% were Hispanic, 10.2% were Asian and 1924 (2%) were AIAN. Many AIAN women lacked typical risk factors for poor pregnancy outcomes: 44% of AIAN women were partnered, 60% had more than a high school education, and 51% paid for their deliveries with private insurance. Despite these favorable profiles, in adjusted models, AIAN women were at increased odds of PTB (odds ratio (OR))=1.3; 95% confidence intervals (95%CI): 1.1, 1.6, LBW (OR=1.3; 95%CI: 1.0, 1.6), and GDM (OR=1.3; 95%CI: 1.1, 1.6), compared with white non-Hispanic women. The AIAN PTB percentages were 7.1, 8.0, 6.2, 7.0 and 9.0 while the PTB differences were 1.9, 3.3, 1.1, 2.3 and 4.1 for each of the years 2010-2014, respectively. **Conclusion:** In the United States west, AIAN women experience worse adverse pregnancy outcomes than any other group, including black non-Hispanic women, and the disparity is greater at most every point in time. The etiology of these poor outcomes is unknown and requires more attention.

RACIAL/ETHNIC DIFFERENCES IN THE CONTRIBUTION OF PRE-PREGNANCY OBESITY AND EXCESSIVE GESTATIONAL WEIGHT GAIN ON LARGE-FOR-GESTATIONAL-AGE NEONATES: A POPULATION RETROSPECTIVE STUDY IN CANADA Yanfang Guo, Qun Miao, Tianhua Huang, Deshayne Fell, Katherine Muldoon, Shi Wu Wen, Mark Walker, Laura Gaudet (Children's Hospital of Eastern of Ontario)

Objective: To examine the racial/ethnic differences in the contribution of pre-pregnancy obesity and excessive gestational weight gain to large-for-gestational-age (LGA) neonates. **Methods:** We conducted a population-based retrospective cohort study among all women who had prenatal screening and had a singleton live birth in an Ontario hospital (April 1st, 2016 - March 31st, 2017) using data from the Ontario birth registry. We used multivariable log-binomial regression models to estimate the risk ratio (RR) and population attributable fraction of obesity and excessive gestational weight gain to LGA neonates. All models were stratified by race/ethnicity (White, Asian and Black). **Results:** Of the 70,357 eligible women, the prevalence of LGA neonates varied from 11.4% for Whites, 5.5% for Asians to 8.0% for Blacks. Compared to normal weight women, adjusted RR of obesity for LGA neonates was 2.18 [95% confidence interval (CI): 2.04-2.32], 2.81 [95% CI: 2.38-3.32], 2.40 [95% CI: 1.87-3.09] for White, Asian and Black women, respectively. Compared to adequate gestational weight gain women, adjusted RR of excessive gestational weight gain for LGA neonates was 1.87 (95% CI: 1.72-2.03), 1.98 (95% CI: 1.68-2.34), 1.52 (95% CI: 1.15-2.00) for White, Asian and Black women, respectively. 18.0%, 12.1% and 25.8% of LGA neonates were attributable to obesity, and 34.3%, 32.8% and 22.3% of LGA neonates were attributable to excessive GWG for White, Asian and Black women, respectively. **Conclusion:** Both pre-pregnancy obesity and excessive gestational weight gain play strong roles in the development of LGA neonates, with variable magnitude by race/ethnicity. Excessive gestational weight gain contributes more to LGA neonates than pre-pregnancy obesity among White and Asian women, while pre-pregnancy obesity and excessive GWG almost equally contribute to LGA among Black women.

URINARY TRACE METALS INDIVIDUALLY AND IN MIXTURES IN ASSOCIATION WITH ULTRASOUND MEASURES DURING**PREGNANCY** Stephani Kim, John Meeker, Alexander Keil, David Cantonwine, Thomas McElrath, Kelly Ferguson (NIEHS)

Toxic metals, such as lead and cadmium, are associated with lower birth weight while essential metals, such as selenium (Se) and zinc (Zn), are associated with higher birth weight, but evidence for other metals are inconsistent or understudied. This is one of the first studies to examine a mixture of metals during pregnancy. We examined the association between a panel of 17 urinary trace metals, individually and as a mixture, in association with fetal growth measures across gestation in the LIFECODES birth cohort. Ultrasound was used to measure abdominal circumference, head circumference, and femur length and measures were used to calculate estimated fetal weight (EFW) at ~26 and ~35 weeks of gestation. We calculated the z-score based on gestational age at scan for all measures, and EFW was combined with birth weight z-score (BWZ) for longitudinal analyses. Urinary trace metals were measured in samples collected at ~26 weeks gestation using mass spectrometry. We used linear mixed effects (LME) models to examine associations between individual trace metals and repeated measures of each outcome, controlling for covariates. We also used principal components analysis (PCA) to highlight salient features of exposure. Our results demonstrate an association between shorter femur length and higher Se (-0.60 [95% confidence interval, CI]: -1.00, -0.20). Se was also inversely associated with other outcomes. Zinc was associated with longer femur length (0.37 [95% CI 0.10, 0.60]). PCA yielded 3 primary components, though these were not associated with the fetal growth outcomes. In conclusion, we observed that essential metals were associated with skeletal growth but in different directions, whereas toxic metals did not demonstrate associations in these data.

MATERNAL IRON INTAKE THROUGH CONSUMPTION OF LEAFY VEGETABLES AND BIRTH OUTCOMES IN AN ENVIRONMENTAL EPIDEMIOLOGY PREGNANT WOMEN COHORT IN SURINAME Firoz Abdoel Wahid, Ashna Hindori-Mohangoo, Emily Harville, Carlo Basilio, Cornelis Zijlmans, Maureen Lichtveld (Scientific Research Center Suriname / Academic Hospital Paramaribo, Paramaribo, Suriname)

In Suriname, a middle-income Caribbean country, one in five pregnancies ends in at least one adverse birth outcome. Low maternal iron (Fe) intake is associated with adverse birth outcomes, especially low birth weight. This research represents the first environmental epidemiological investigation in Suriname designed to assess the relationship between maternal intake of Fe, based on the three most frequently consumed leafy vegetables, and birth outcomes. This study is embedded in the Caribbean Consortium for Research in Environmental and Occupational Health, an environmental epidemiology cohort study that examines associations between environmental exposures and birth outcomes in Surinamese mother-child dyads (n=1150). Intake rates of the three most consumed vegetables were identified through a dietary survey of 1038 participants. Fe intake rates were calculated by using the intake rates and the Fe contents of these three vegetables. Low Fe intake rate (intake rate <25th percentile), was the main determinant. Associations with adverse birth outcomes low birth weight (LBW), preterm birth (PTB), and 5 minutes Apgar score <7 were examined using the Chi-square test (birth outcomes' n=491). The top three most consumed were *Xanthosoma brasiliense* (tannia), *Cestrum latifolium* (bitter greens) and *Amaranthus dubius* (spleen amaranth) of which low Fe intake rates were defined as <0.17 mg/day, <0.45 mg/day and <0.33 mg/day respectively. Women with low Fe intake rates related to tannia consumption had higher proportions of adverse birth outcomes (28.0 vs. 22.3%; p=0.298), more PTB (20.8 vs. 17.6%; p=0.514), more low Apgar score babies (6.8 vs. 4.3%; p=0.351) and significantly more LBWs (20.8 vs 11.8%; p=0.039). No significant associations were found between low Fe intake rates related to consumption of bitter greens and spleen amaranth and adverse birth outcomes. Studies are needed to examine the role of other nutrients and chemicals in Surinamese vegetables in birth outcomes.

MATERNAL EXPOSURE TO ARSENIC IN DRINKING WATER AND RISK OF PRETERM BIRTH AND SMALL-FOR- GESTATIONAL AGE BIRTH IN MICHIGAN Tengfei Ma, kyle Redican, Nigel Paneth (Michigan State University)

Background Michigan is a state with high arsenic concentrations in groundwater. Our study was aimed at exploring the relationships between arsenic concentrations in drinking water and pregnancy outcomes in a pregnancy cohort (534 participants) recruited 2008-2016 in three prenatal clinics in Ingham County, MI. Methods Using birth certificates, we categorized preterm as birth 10 ug/L throughout pregnancy and 93 women had high arsenic exposure during at least one trimester. High arsenic exposure in the first trimester was associated with an increased risk of small for gestational age (SGA) after adjustment for several covariates (Adjusted odds ratio 3.8, 95% CI 1.9 to 7.6). Arsenic levels during second trimester, third trimester and the pregnancy overall were not associated with SGA. No significant association of high arsenic levels and preterm birth was found (Adjusted odds ratio 0.5, 95% CI 0.1 to 3.6, for whole pregnancy exposure). Conclusions High arsenic exposure in the first trimester may be associated with having a small for gestational age infant.

THE ROLE OF PLACENTAL HUMAN CHORIONIC GONADOTROPIN IN THE RELATIONSHIP BETWEEN MATERNAL FIRST TRIMESTER BODY MASS INDEX AND BIRTHWEIGHT

Xiaoshuang Xun, Shyamal Peddada, Qing Yin, Shanna Swan, Emily Barrett, Nicole Bush, Sheela Sathyanarayana, Jennifer Adibi (University of Pittsburgh)

Birthweight (BW) is a crucial indicator of fetal development, yet the early pregnancy determinants of BW are not well understood. The first trimester is critical for placental and fetal growth. First trimester body mass index (T1-BMI) has a positive relationship with BW. The placental hormone human chorionic gonadotropin (hCG) is also associated with BW. The aim of this study was to examine the role of hCG in the relationship between T1-BMI and BW. Study subjects were 525 women recruited into The Infant Development and Environment Study (TIDES) in 4 U.S. cities. Subjects' information was collected using T1 questionnaires and birth records. T1-serum hCG levels were obtained from clinical laboratories and z-score transformed to normalize across sites. BW was modeled as a z-score to normalize for gestational age at delivery and fetal sex. Multivariate linear regression models were used to estimate associations between all key variables. A four-way decomposition of the total effect (TE) was used to compare the TE and the controlled direct effect (CDE), and to identify mediation and/or interaction effects. Maternal T1-BMI was positively associated with BW. This association was stronger in women carrying males. The data suggested that the association between T1-hCG and BW varied by fetal sex, being negative for women carrying males ($\beta = -0.20$, 95% CI: -0.39, -0.01) and positive for women carrying females ($\beta = 0.08$, 95% CI: -0.06, 0.22). In women carrying males, there was no difference between the TE and CDE. However, in women carrying females, the TE ($\beta = 0.09$, 95% CI: -0.13, 0.31) was smaller than the CDE ($\beta = 0.15$, 95% CI: -0.07, 0.38). Most of this difference was due to the indirect effect of hCG ($\beta = -0.09$, 95% CI: -0.18, -0.01). The association between T1-BMI and BW was partially mediated by the T1-hCG only in women carrying females. This finding provides evidence for a sex-specific placental mechanism in the pathway between maternal BMI and BW.

OMEGA-3 POLYUNSATURATED FATTY ACID INTAKE NORMS AND PRETERM BIRTH RATE: A CROSS-SECTIONAL ANALYSIS OF 184 COUNTRIES Timothy Ciesielski, Jacqueline Bartlett, Scott Williams (Case Western Reserve University)

Background: Thirty years ago epidemiologic observations suggested that high dietary intake of fish oils (long-chain omega-3 polyunsaturated fatty acids) could reduce the risk of Preterm Birth (PTB), but the initial follow-up studies were inconsistent. The preponderance of evidence now confirms this discovery but the design of preventative interventions requires us to understand why the findings varied. We probed the reasons for this heterogeneity across studies using country level data. **Methods:** We analyzed the relationship between national PTB rates (<37 weeks gestation) and omega-3 PUFA intake norms from 184 countries for the year 2010. To estimate the total LC omega-3 PUFA levels (eicosapentaenoic acid and docosahexaenoic acid: EPA/DHA) that these norms produce we utilized a metric that accounts for: 1) seafood based omega-3 intake (EPA/DHA), and 2) plant based omega-3 intake (alpha linolenic acid: ALA), approximately 20% of which is converted to EPA/DHA in vivo in females. We then assessed the shape of the omega3-PTB relationship with a penalized spline and conducted linear regression analyses within the linear sections of the relationship. **Results:** Penalized spline analyses indicated that PTB rates decrease linearly with increasing omega-3 levels up to ~600 mg/day. Unadjusted linear regression analysis among the countries in this exposure range indicated that the number of preterm births per 100 live births decreases by 2.9 (95% CI: 4.2, 1.6) for each 1 standard deviation increase in omega-3 intake norms (383 mg/day). After adjusting for country income the association remained significant (1.5, 95%CI: 2.8, 0.3). **Conclusions:** Taken with prior evidence for a causal association on the individual level, our findings indicate that omega-3 PUFA deficiency may be a widespread contributing factor in PTB risk. Consideration of baseline omega-3 PUFA levels is critical in the design of future interventions.

OIL AND GAS DRILLING AND RISK OF PRETERM BIRTH IN THE SAN JOAQUIN VALLEY, CALIFORNIA David Gonzalez, Allison Sherris, Wei Yang, Mark Cullen, Gary Shaw (Stanford University)

A few studies have observed an association between adverse birth outcomes, including preterm birth, and maternal residential proximity to oil and gas wells. Attention has focused on unconventional (hydraulic fracturing) natural gas developments, with little attention to conventional oil and gas extraction. Our objective was to determine whether maternal residence proximity to oil and gas extraction increased odds of preterm birth. We conducted a case-control study using data from 27,913 preterm births and 197,461 term births between 1998 and 2011 in the San Joaquin Valley, California. We obtained births data from the Office of Statewide Health Planning and Development and wells data from the California Department of Conservation. For each birth, we computed an exposure index by taking the sum of the inverse distance to all oil and gas drilling activity within a 15 km radius of the maternal residence. We defined three preterm birth categories based on gestational length (in weeks): 20-27, 28-31, and 32-36. We estimated crude and adjusted odds ratios (ORs) for each category using logistic regression. Exposure to oil and gas drilling activity was associated with a small but significant increase in the odds of preterm birth, with adjusted ORs for each preterm birth and gestational month stratum ranging from 0.12 to 0.36. Risk was highest for the 32 to 36-week preterm birth category, with exposure throughout gestation associated with increased risk for this group.

(1) PRENATAL MARIJUANA USE AND PSYCHOLOGICAL HEALTH IN PREGNANT BLACK WOMEN IN THE BIOSOCIAL IMPACTS ON BLACK BIRTHS (BIBB) STUDY Rhonda Dailey, Liying Zhang, Heather Frey, Mercedes Price, Dawn Misra, Carmen Giurgescu (Wayne State University School of Medicine)

The possible influence of marijuana use on psychological health in pregnant Black women has not been well studied. This study aimed to identify the prevalence of marijuana use and its associations with psychological health among pregnant Black women. A sample of 203 Black women with 8-29 weeks gestation from metropolitan Detroit, MI and Columbus, OH completed questionnaires. Data were collected in 2018 prior to legalization of recreational marijuana in Michigan and Ohio. Participants were asked about a range of health behaviors including use of marijuana before and during the pregnancy. Questionnaires included scales for depressive symptoms, perceived stress and psychological well-being. Marijuana was the most prevalent substance used. The proportions of marijuana use were 40.5% before pregnancy and 16.7% during pregnancy. Results from multiple linear regression analysis models predicting each psychological factor indicated that marijuana use was associated with higher levels of depressive symptoms ($\beta=5.81$, $p=0.003$), higher levels of perceived stress ($\beta=3.08$, $p=0.010$), and lower levels of psychological well-being ($\beta=-10.69$, $p=0.001$). Each of these three models controlled for maternal age, gestational age at baseline survey, levels of education, and marital status. Marijuana use during pregnancy may be a marker of increased risk of psychological distress. Although the proportion of marijuana use was lower during pregnancy compared with the proportion of marijuana use before pregnancy, marijuana use remains prevalent in this population (~17%). This health behavior was significantly associated with indicators of psychological distress during pregnancy, factors which may increase risk of adverse birth outcomes (e.g., preterm birth). Recent changes in legalization of marijuana may lead to even higher rates of use during pregnancy. More research is needed to understand the relationships between marijuana use and psychological health during pregnancy.

(3) FAMILY PRENATAL INVOLVEMENT AND MATERNAL PSYCHOLOGICAL HEALTH IN PREGNANT BLACK WOMEN IN THE BIOSOCIAL IMPACTS ON BLACK BIRTHS (BIBB) STUDY Dawn Misra, Liying Zhang, Rhonda Dailey, Mercedes Price, Carmen Giurgescu (Wayne State University School of Medicine)

Family prenatal involvement, particularly paternal involvement plays a critical role in positive maternal and infant outcomes. To date, limited research has examined the associations between family prenatal involvement and psychological health in pregnant Black women. This study is to examine the association between family prenatal involvement and maternal psychological health. We used baseline data of a longitudinal study in 203 Black women from metropolitan Detroit, MI and Columbus, OH recruited between 8-29 weeks gestation. Family prenatal involvement was assessed using three questions that were related to the frequency of time that family members (i.e., father of this baby, paternal family members, and maternal family members) spent with the pregnant woman during her pregnancy with a 5-point Likert response (1= “none of the time” to 5=“all of the time”). A composite score was obtained by summing scores for 3 items, with a higher score indicating a higher family prenatal involvement (range 3-15, Cronbach’s $\alpha=0.74$). Questionnaires also included scales for depressive symptoms (20 items, Cronbach’s $\alpha=0.89$); pregnancy-related anxiety (10 items, Cronbach’s $\alpha=0.87$); perceived stress (10 items, Cronbach’s $\alpha=0.80$); and psychological general well-being (22 items, Cronbach’s $\alpha=0.90$). Results from multiple linear regression analysis models predicting each psychological factor indicated that composite family prenatal involvement was associated with lower levels of depressive symptoms ($\beta=-1.25$, $p<0.001$); lower level of pregnancy-related anxiety ($b=-0.39$, $p=0.006$); lower level of perceived stress ($\beta=-0.78$, $p<0.001$); and higher level of psychological well-being ($\beta=2.19$, $p<0.001$), after controlling for maternal age, gestational age at data collection, level of education, and marital status. The results from the current study could inform the future interventions to increase family prenatal involvement to benefit maternal psychological health.

(2) INTIMATE PARTNER VIOLENCE AND PSYCHOLOGICAL HEALTH IN PREGNANT BLACK WOMEN IN THE BIOSOCIAL IMPACTS ON BLACK BIRTHS (BIBB) STUDY Liying Zhang, Rhonda Dailey, Mercedes Price, Dawn Misra, Carmen Giurgescu (Wayne State University School of Medicine)

Intimate partner violence (IPV) against women is a global public health issue and it is significantly associated with lower levels of psychological well-being. Data on associations between IPV and psychological health in pregnant Black women are limited. The purpose of this study was to examine the association of IPV with psychological health among pregnant Black women. A sample of 203 Black women from metropolitan Detroit, MI and Columbus, OH were recruited between 8-29 weeks gestation. Participants were asked “While you are pregnant this time, has your husband or partner hit, pushed, slapped, kicked, choked, or threatened your safety in any other way?” Questionnaire data also included scales for depressive symptoms (20 items, Cronbach’s $\alpha=0.89$); perceived stress (10 items, Cronbach’s $\alpha=0.80$); and psychological well-being (22 items, Cronbach’s $\alpha=0.90$). Results indicated that 5.6% of participants reported IPV during their pregnancy. Results from multiple linear regression analysis models predicting each psychological factor indicated that IPV was associated with higher levels of depressive symptoms ($\beta=5.41$, $p=0.050$) and higher levels of perceived stress ($\beta=4.26$, $p=0.012$). The associations of IPV with psychological well-being did not show statistical significance. Each of these 3 models controlled for maternal age, gestational age at data collection, level of education, and marital status. Research shows that IPV, depressive symptoms and perceived stress have been related to adverse birth outcomes (i.e., preterm birth, low birthweight infants). Our results suggest the need for interventions to address IPV in order to improve psychological health of pregnant Black women and potentially reduce adverse birth outcomes for these women.

FIRST TRIMESTER LOW FETAL HEART RATE AND SMALL CROWN-RUMP LENGTH PREDICT PREGNANCY LOSS AMONG WOMEN WITH HISTORY OF PREGNANCY LOSS

Elizabeth DeVilbiss, Sunni Mumford, Lindsey Sjaarda, Matt Connell, Torie Plowden, Victoria Andriessen, Neil Perkins, Micah Hill, Bob Silver, Enrique Schisterman (NICHD)

Objective: Identify characteristics of the early first trimester ultrasound, and their gestational age specific cut-points, most predictive of subsequent pregnancy loss. **Methods:** Cohort nested within the Effects of Aspirin in Gestation and Reproduction (EAGeR) trial, a double-blind, randomized controlled trial, conducted at 4 clinical sites in the United States in 2006-2012; women had 1-2 previous pregnancy losses and no documented infertility. 638 pregnant women each had a single ultrasound between 6w 0d and 8w 6d. Cut-points for low fetal heart rate and small crown-rump length were separately defined for gestational weeks 6, 7, and 8 respectively, using the Youden index. Abnormal yolk sac diameter was defined as 6.5 mm. Identity and log-binomial regression models estimated absolute and relative risks (RRs), respectively, and 95% confidence intervals (CI) between clinical pregnancy loss and jointly categorized fetal heart rate and crown-rump length. Adjusted models accounted for gestational age and maternal age. Missing data were addressed using multiple imputation. **Results:** 85 women experienced a clinical pregnancy loss (13.3%), 6 were lost to follow-up (1.0%), and 547 (85.7%) women had a live birth. Low fetal heart rate and small crown-rump length (≤ 119 , 142, and 158 bpm; ≤ 6.8 , 8.2, and 13.6 mm for gestational weeks 6, 7, and 8 respectively) were independent predictors of clinical pregnancy loss. Greatest risks were observed for pregnancies having both characteristics (RR 5.76 [95% CI: 2.60 to 8.93]), corresponding to a 25% [95% CI: 17 to 31%] adjusted absolute increase in risk, from 5% [3 to 8%] to 30% [23 to 38%]. Neither subchorionic hemorrhage nor yolk sac diameter further improved prediction. **Conclusions:** We identify gestational age-specific cut-points for low fetal heart rate and small crown rump length most predictive of subsequent risk of pregnancy loss, which can be used to inform clinical counseling and monitoring.

**PRE-PREGNANCY ADMINISTRATION OF ANTINEOPLASTIC DRUGS,
USE OF PROTECTIVE CLOTHING, AND RISK OF SPONTANEOUS****ABORTION IN FEMALE NURSES** Feiby Nassan, Jorge Chavarro, Candice Johnson, James Boiano, Carissa Rocheleau, Janet Rich-Edwards, Christina Lawson (Harvard T. H. Chan School of Public Health)

Objective:To examine prospectively the association between pre-pregnancy administration of antineoplastic drugs (AD) and risk of spontaneous abortion (SA). **Methods:** Women in the Nurses' Health Study 3 self-reported AD administration and use of protective clothing (i.e., gloves and gowns) at baseline. Nurses whose self-reported pregnancies occurred after baseline were included in this analysis; SAs (<20 weeks of gestation) were compared to pregnancies ending in live birth (LB) or stillbirth. We estimated the relative risk (RR) of SA in relation to AD administration using multivariable log-binomial regression using generalized estimating equations with an exchangeable working correlation structure to account for the within-woman correlation between pregnancies. **Results:**Among 2,656 nurses, 3,656 pregnancies were reported with median of 3 years after baseline (range: 1-8) years. 598 (16.4%) of these pregnancies ended in SA, 13 in stillbirth, and 3,151 in LB. Mean (standard deviation) age was 29.8 years (4.2). Of those nurses, 40% reported ever administering AD (29% only in the past and 11% at baseline). Compared to nurses who reported never administering AD, nurses administering AD formerly had a RR of SA of 1.08 (95%CI: 0.91, 1.27), nurses administering AD at baseline had a RR of SA of 1.26 (95%CI: 1.00, 1.58), after adjusting for age, body mass index, and smoking. Among those who administered AD at baseline, the risk was highest among nurses who did not always use gloves [RR: 1.54 (1.03, 2.31)], and 1.18 (0.91, 1.53) for nurses who always used gloves. Similarly, nurses who did not always use gowns had a RR: 1.33 (1.01, 1.76) compared to 1.16 (0.83, 1.63) for nurses who always used gowns. Results were similar when we restricted the data to pregnancies that ended within 2 years after baseline. **Conclusions:**AD administration was associated with increased risk of spontaneous abortion, particularly if protective clothing such as gloves and gowns were not always used.

THE EFFECT OF INTERPREGNANCY INTERVAL ON SUBSEQUENT STILLBIRTH: A CAUSAL ANALYSIS OF 357,857 BIRTHS FROM 52 LOW AND MIDDLE-INCOME COUNTRIES

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Background: Approximately 3 million stillbirths occur each year, and 98% occur in low and middle-income countries. Interpregnancy interval is a key potential risk factor of interest, because it is possible to modify. **Methods:** We studied 357,857 births from 52 low and middle-income countries. We combined two analytic approaches: one that considers all births as independent, and another that analyzes intervals within mothers. We controlled for several covariates, including all past birth outcomes and intervals in a 5-year period, and also report stratified estimates for the 1st, 2nd and 3rd intervals. We also explore effect heterogeneity across key cohort subgroups. **Findings:** Intervals <12 months were significantly associated with a higher risk of stillbirth in the independent birth models when considering the first (additional 69 stillbirths per 1000 births, 95% CI: 56, 82) or all (additional 53 stillbirths per 1000 births, 95% CI: 41, 65) intervals. When only considering the 2nd or 3rd intervals, no significant associations were observed. Within-mother modeling also yielded no significant estimates. **Interpretation:** Although shorter intervals were associated with higher risk of stillbirth in the independent model, there was insufficient evidence of a causal relationship between interpregnancy interval and stillbirth across all models. Therefore, it may be unnecessary to advise couples to delay pregnancy after a recent delivery or abortion. Future studies should use generalizable cohorts with longitudinal data, and report estimates stratified by interval.

EXPOSURE TO PERFLUOROALKYL SUBSTANCES AND RISKS FOR SPONTANEOUS ABORTIONS Zeyan Liew, Jiajun Luo, Ellen Nohr, Rossana Bossi, Onyebuchi Arah, Jørn Olsen (Yale School of Public Health)

BACKGROUND: Perfluoroalkyl substances (PFASs) are widespread persistent organic pollutants and endocrine disruptors. Two smaller epidemiological studies have previously suggested PFASs exposure may increase the risks for miscarriage; while these findings raised concerns replication in a larger study is needed.

METHODS: We conducted a nested case-control study in the Danish National Birth Cohort (DNBC;1996-2002) comparing 220 pregnancies ended in spontaneous abortion occurred during week 12-24 of gestations with 218 pregnancies resulted in live births. Seven types of PFASs (PFOS, PFOA, PFHxS, PFHpS, PFNA, PFDA, and PFOSA) were examined based on first-trimester maternal plasma collected around gestational week 8. We estimated the odds ratios (OR) and 95% confidence intervals (CI) for spontaneous abortion according to PFAS quartile, controlling for a range of potential confounders including age, parity, socio-economic status, BMI, gestational week of blood sampling, and maternal history of miscarriage. **RESULTS:** We found linear dose-response relationships between first trimester PFOA and PFHpS concentrations and risks for abortion ($p < 0.05$ for linear trend, and nearly two-fold higher risks compared the highest to the lowest exposure quartile). The estimated ORs were also elevated for the first or second quartile of PFHxS or PFOS but no consistent exposure-response pattern was observed. **CONCLUSION:** Maternal exposure to PFASs, particularly PFOA and PFHpS, were associated with risks for spontaneous abortions.

PARTICIPATION IN SURVEY RESEARCH AMONG WOMEN WITH A RECENT LIVE BIRTH: A COMPARISON OF MOTHERS WITH LIVING VERSUS DECEASED INFANTS — PREGNANCY RISK ASSESSMENT MONITORING SYSTEM (PRAMS), 2012-2016 Lee Warner, Katherine

Kortsmit, Holly Shulman, Carrie Shapiro-Mendoza, Shanna Cox, Suzanne Folger, Maura Whiteman, Ruben Smith, Leslie Harrison, Lauren Christiansen-Lindquist, Wanda Barfield (Centers for Disease Control and Prevention)

Despite high infant mortality rates in the United States relative to other developed countries, little is known about survey participation among mothers of deceased infants. We analyzed 2012-2016 data for 41 sites from PRAMS, a site-specific, population-based surveillance system of mothers with a recent live birth.

Participants are sampled from birth certificates and PRAMS surveys are mailed at 2-4 months after birth. We assessed differences in survey participation for mothers of deceased and living infants at time of survey mailing. We calculated the proportion who participated among sampled women (response rate) and among contacted women (cooperation rate). We calculated adjusted weighted response rates by maternal and infant characteristics, adjusting for all assessed characteristics, region and year. Among sampled mothers, 99.7%(n=371,097) of infants were alive and 0.3%(n=4,813) had died by the time the survey was mailed. Mothers of deceased infants had significantly lower weighted response(49% vs 60%) and cooperation rates(75% vs 83%) than mothers of living infants. Among mothers of deceased infants, response rates were significantly higher for those who were ≥ 35 years(58% vs 49%), non-Hispanic white(56% vs 46%), married(56% vs 45%), WIC participants(60% vs 44%) and had >12 years of education(56% vs 45%) compared to their counterparts. Among mothers with living infants, differences in response rates were similar to mothers of deceased infants; mothers of living term infants(60% vs 58%) were significantly more likely to respond than mothers of living preterm infants. These findings indicate survey participation is lower for mothers of deceased infants than mothers of living infants. Strategies to increase PRAMS participation for mothers of deceased infants could inform knowledge about experiences and behaviors before, during, and after pregnancy to help reduce infant mortality and better understand the needs of mothers of deceased infants.

THE EFFECT OF BECOMING PREPREGNANCY OBESITY ON STILLBIRTH AND INFANT MORTALITY IN A COHORT OF**MULTIPAROUS WOMEN** Ya-Hui Yu, Lisa Bodnar, Katherine Hime, Maria Brooks, Ashley Naimi (McGill University)

Little is known regarding the timing of obesity onset relative to pregnancy outcomes. Therefore, we evaluated the relation between newly-developed pre-pregnancy overweight and obesity and stillbirth and infant mortality. We studied subsequent pregnancies of mothers who were normal weight at conception of their first pregnancy, from a population-based cohort that linked the birth registry with death records in Pennsylvania, 2003-2013. Newly-developed overweight and obese pregnancies were identified from women whose prepregnancy body mass index (BMI) at second pregnancy was ≥ 25 kg/m² to ≤ 30 kg/m². Our outcomes of interest were stillbirth defined as in-utero death ≥ 20 weeks of gestation and infant mortality: death < 365 days after birth. Adjusted associations of both prepregnancy BMI categories and continuous BMI unit changes with each outcome were estimated by nonparametric targeted minimum loss-based estimation and inverse-probability weighted dose-response curves, respectively. Compared with women who stayed normal weight in their second pregnancies, those becoming overweight had 1.4 (95% confidence interval [CI]: 0.6, 2.2) excess stillbirths per 1,000 pregnancies. Mothers who became obese had 4.0 (95% CI: 1.4, 6.6) excess stillbirths per 1,000 pregnancies and 2.3 (95% CI: 0.1, 4.5) excess neonatal deaths per 1,000 livebirths. There was a dose-response relationship between a prepregnancy BMI increase of more than 2 units and increased risk of stillbirth and infant mortality. Our results suggest that transitioning from normal weight to overweight or obese between the first and second pregnancy increases risk of stillbirth and neonatal mortality. Health care providers should monitor and provide weight counseling about proper gestation weight gain during pregnancy or postpartum weight loss for pregnant women to minimize risk of adverse outcomes for future pregnancies.

MATERNAL BLOOD PRESSURE AND DIFFERENTIAL PLACENTAL DNA METHYLATION Tsegaselassie Workalemahu, Xuehuo Zeng, Deepika Shrestha, Marion Ouidir, Katherine Grantz, Fasil Tekola-Ayele (The National Institute of Child Health and Human Development (NICHD))

DNA methylation is a potential regulatory pathway through which maternal blood pressure (BP) may influence placental development. However, specific methylated sites in the placenta associated with BP have not been identified. We examined the associations of maternal systolic blood pressure (SBP) and diastolic blood pressure (DBP) with epigenome-wide placental DNA methylation. This study included 301 mothers that provided placenta at delivery as part of the NICHD Fetal Growth Studies. Genome-wide placental CpG methylation was measured using HumanMethylation450BeadChip. Trimester specific (TM1, TM2, TM3) SBP/DBP measurements were abstracted from medical records. Epigenome-wide analysis that adjusted for race/ethnicity and fetal sex was used to estimate percent methylation change per mmHg increase in DBP/SBP. The biological functions of the genes near the top epigenome-wide signals ($p < 1e-5$) associated with SBP/DBP were evaluated using pathway analysis. Although none reached genome-wide significance, top CpGs associated with 1 mmHg increase in DBP and SBP during TM1 include, 1.1% ($p = 2.8e-6$) and 0.8% ($p = 2.4e-6$) higher methylation of cg11480264 near ANKRD31, respectively. In TM2, 1.6% ($p = 8.8e-7$) higher methylation of cg02955114 near ERC2 and 0.5% ($p = 3.3e-6$) lower methylation of cg05412396 near ISL2 were observed for 1 mmHg increase in DBP and SBP, respectively. In TM3, 0.1% ($p = 2.3e-6$) higher methylation of cg00563678 near RNF150 and 0.1% ($p = 1.1e-6$) higher methylation of cg04237822 near PTPRN2 for 1 mmHg increase in DBP and SBP, respectively. Notably, the genes near our top signals were significantly enriched in cardiac dysfunction/cardiovascular disease functions. The present study provides the first evidence that higher maternal BP may alter placental DNA methylation at genes implicated in cardiovascular diseases. Future studies with larger samples may facilitate identification of biomarkers and drug targets for BP regulation.

TIMING OF PREECLAMPSIA ONSET AND TIME BETWEEN ONSET AND DELIVERY Quaker Harmon, Kari Klungsøyr, Allen Wilcox, Stephanie Engel (NIEHS)

Background: National registries routinely record preeclampsia at the time of birth. There is limited published data on the timing of preeclampsia onset, which frequently precedes delivery. Timing of onset is a clinical marker of disease severity and is relevant for causal inference in epidemiologic studies. Methods: We reviewed antenatal charts from 3091 Norwegian women with preeclampsia who delivered between 1999-2008. Onset was defined as the first prenatal visit with hypertension (SBP>140 mmHg or DBP>90mmHg) and proteinuria. We describe the timing of onset overall and by maternal factors (parity, smoking, body mass index (BMI), chronic hypertension). Results: Women had mean age of 30.1 years at delivery (SD 4.9). The majority were nulliparous (64%), with normal pre-pregnancy BMI (49%); 5% were daily smokers in the first trimester and 12% had chronic hypertension. 21% of preeclamptic pregnancies delivered preterm (before 37 weeks; a common surrogate for severe disease), while 37% had preterm onset of preeclampsia (15% before 34 weeks). Diagnosis before 34 weeks was more common among smokers (26%) and those with obesity (20%) or chronic hypertension (30%). Delivery occurred within a week of onset for 50%, while 11% had 4 or more weeks between onset and delivery. Even though preeclampsia is a threat to the mother and fetus, clinical practice is to delay delivery until 34 weeks when possible. We observed that pregnancies with onset before 34 weeks were more likely to have longer intervals between onset and delivery. Conclusion: Preeclampsia can emerge more than a month before delivery. Even though preeclampsia is generally more severe when diagnosed before 34 weeks, the interval between diagnosis and delivery was on average longer for these cases, presumably to avoid delivery of an immature fetus. Prevalence of preeclampsia at the time of birth misses variability in the timing of disease onset and is not necessarily the best surrogate for disease severity.

CHARACTERISTICS OF WOMEN WITH HYPERTENSIVE DISORDERS OF PREGNANCY AND FUTURE CARDIOVASCULAR DISEASES

Ugochinyere Vivian Ukah, Natalie Dayan, Nathalie Auger, Robert Platt (McGill University)

Background: Hypertensive disorders of pregnancies (HDP) complicate 5-10% of pregnancies and are associated with severe maternal and perinatal outcomes. HDPs increase the risk of developing future cardiovascular diseases (CVD). Certain factors may contribute to the increased risks of CVD in women with HDP.

Therefore, we sought to describe the characteristics of women with a history of HDP according to their future CVD status. **Method:** MED-ECHO dataset, consisting of all women who delivered in hospitals in the Quebec province of Canada between 1989 and 2016, was used. The analyses were restricted to women who had a history of HDP in any pregnancy and no pre-existing CVD. HDPs were defined as chronic hypertension, gestational hypertension, pre-eclampsia/eclampsia, and superimposed pre-eclampsia, using International Classification of Diseases (ICD) codes. Outcomes were CVD outcomes also identified using ICD codes which included heart diseases e.g. heart failure, cerebrovascular diseases e.g. stroke pulmonary heart diseases, procedures involving the heart and blood vessels, and coronary care unit admission. The demographics and characteristics of women with and without CVD were presented. **Results:** Of 2,197,124 pregnancies admitted for hospital delivery, HDP occurred in n=60,850 (5.2%), with the majority (69.7%) occurring in first births. Among women with HDP, the rate of CVD was 9.8%. Women who developed CVDs were more likely to be older, have had substance abuse during pregnancy, pre-existing diabetes, and socio-economic disadvantage compared with women without CVD. Women with CVD were also more likely to have a history of gestational diabetes and adverse perinatal outcomes such as preterm delivery and stillbirth. **Conclusion:** Future studies should investigate whether these identified factors e.g. substance abuse, diabetes, socio-economic disadvantage, preterm delivery and stillbirth, can be used to predict the risk of future CVD in women with a history of HDP.

WHAT ARE THE GREATEST RISK FACTORS FOR PREECLAMPSIA AMONG HIGH-RISK PREGNANCIES ALREADY USING ASPIRIN?

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Background: Recent studies have shown that the incidence of preeclampsia (PE) among high risk women can be reduced by daily aspirin use. However, there is limited information on the cases that develop PE despite taking the recommended aspirin regimen. This study has been designed to investigate PE risk factors that persist in high-risk pregnancies already using aspirin. **Methods:** This is a cohort study using data from the FACT Trial, a multi-country randomized control trial investigating the role of folic acid on the prevention of pre-eclampsia among high risk pregnancies. The sample was restricted to women taking aspirin before 16 weeks of gestation. Descriptive statistics characterize the sample and bivariable/multivariable logistic regressions assessed factors significantly associated with any PE and preterm-PE (<37 weeks) using odds ratios (OR) and 95% confidence intervals (CI). **Results:** Out of 2301 FACT trial participants, there were 660 (28.63%) taking aspirin and included in this analysis. The prevalence of PE was 20.00% (95% CI: 16.95-23.05%) and preterm PE was 9.09% (95%CI:7.01-11.55%). Among the 132 PE cases, 77 (58.33%) had a previous history of PE, 50 (37.88%) had existing hypertension, 47 (35.61%) had obesity (BMI 35+), and 21 (15.91%) were carrying twins. The odds of PE were highest for hypertension (AOR:2.76, 95% CI: 1.71-4.47), twins (AOR:3.66, 95% CI: 1.89-7.07) and history of PE (AOR:3.53, 95% CI: 2.19-5.69). Similar trends were found for preterm PE, with elevated odds found for hypertension (AOR:2.63, 95% CI:1.37-5.06), twins (AOR:5.09, 95% CI:2.21-11.72), and history of PE (AOR:3.51, 95% CI: 1.82-6.75). **Conclusion:** While aspirin continues to be the best course of treatment in the prevention of PE among high risk women, 20% and 9% developed PE and preterm PE, respectively, in this cohort of aspirin users. In addition to aspirin use, patients with hypertension, twin pregnancies and history of PE should be carefully monitored.

EXPOSOME ANALYSIS OF 1ST TRIMESTER BLOOD FOR BIOMARKERS AND CAUSAL MECHANISMS OF HYPERTENSIVE DISORDERS OF PREGNANCY Ke Pan, Susan Sumner, Susan McRitchie, Yan Li, Emily Harville (Tulane University)

Objective: This study aims to identify biomarkers in the 1st trimester serum that predict gestational hypertension disorder (gestational hypertension and pre-eclampsia) and inform causal mechanisms for the development of intervention strategies. **Methods:** Serum specimens and questionnaires from 159 pregnant women (52 cases of hypertensive disorders, either pre-eclampsia or gestational hypertension, and 107 controls) were obtained from the Global Alliance to Prevent Prematurity and Stillbirth (GAPPS) repository. Blood specimens were collected during the first trimester of pregnancy. Questionnaires regarding women's health history, dietary assessment, home and work environment were conducted multiple times throughout pregnancy. Metabotyping of the serum specimens was conducted using a UPLC coupled to a Q-Exactive HFX Orbitrap Mass Spectrometer. Stepwise multiple logistic regression modeling was used to identify metabolites that predicted hypertensive disorders of pregnancy, with control for covariates. **Result:** Univariate analyses for data from baseline questionnaires indicated that hypertensive disorders were associated with obesity, previous pregnancy complications, smoking, secondhand smoke exposure, substance abuse, dietary patterns, exercise, and work environment. Over 100 exogenous metabolites of common environmentally relevant chemicals were assigned (identified/annotated) using Mass, or MS/MS, and RT of standards (as possible) in maternal serum. Nine were significantly ($p < 0.1$) different between the groups. In multiple logistic regression analyses, hypertensive disorders were significantly predicted by obesity and eating doughnuts frequently. After controlling for these factors, possible metabolites of insecticides and tea remained associated with gestational hypertensive disorders. **Conclusion:** Exposome analysis of first-trimester maternal serum shows potential for revealing biomarkers of hypertensive disorders of pregnancy and inferring causal mechanisms.

BREASTFEEDING AFTER HYPERTENSION IN PREGNANCY: A SNAPSHOT FROM THE MICHIGAN WIC PROGRAM

Elizabeth MacQuillan, Leila Alattar (Grand Valley State University)

Introduction: Hypertension (HTN) is a common complication during pregnancy, affecting about 10% of pregnant women. Yet the relationship between HTN and breastfeeding rates is not well-established. This study aimed to understand factors affecting breastfeeding in Michigan WIC participants with HTN. **Methods:** This retrospective, cross-sectional study examined data from the 49,370 women enrolled in the Michigan WIC program in the year 2016. **Results:** From the total sample, 5.7% of women (n= 5,387) had HTN during their pregnancy. There was a significant difference in breastfeeding rate by HTN status; 65.8% (n = 28,697) of WIC participants who did not have HTN during pregnancy were breastfeeding, while 63.6 % (n = 3 424) of WIC participants who had HTN were breastfeeding ($X^2 = 10.48$, $p = 0.001$). Logistic regression showed that maternal education level significantly affected the breastfeeding rate of WIC participants with HTN, however, preterm birth had no significant effect. Between three and six months post-partum, the percent of mothers breastfeeding dropped by half, from 12% to 6%, and by 9 months fewer than 1% of all mothers reported breastfeeding. **Conclusion:** WIC participants with HTN were less likely to breastfeed. Compared to mothers with a high school diploma, those with less education were less likely to breastfeed. Another important finding of this study was the short breastfeeding duration among WIC participants, regardless of HTN status. Emphasizing effective education and breastfeeding support for WIC participants, particularly aimed at increasing breastfeeding duration, should be a priority of efforts to promote breastfeeding to WIC-enrolled mothers.

DOCUMENTATION STATUS AND ADVERSE PREGNANCY OUTCOMES AMONG WOMEN OF MEXICAN ETHNICITY Lynne Messer, Dawn Richardson, Sarah Andrea, Betty Izumi (OHSU-PSU School of Public Health)

Background: Mexican women in the United States (US) have better birth outcomes than might be predicted given their educational and income status but other pregnancy outcomes such as gestational diabetes (GDM) or pregnancy-induced hypertension (PIH) are rarely assessed. Further, being undocumented in the US may offset protective effects by limiting prenatal care access or increasing fear of discrimination or deportation. Methods: We used 2010-2014 data representing 17,625 Hispanic women (14,822 of Mexican ethnicity) delivering in one US county offering emergency medical coverage for non-citizens not meeting Medicaid immigration status requirements; >95% of pregnant Latinas delivering under this program are undocumented. In logistic regression adjusted for confounders (continuous and quadratic maternal age, categorical education, marital status) we modeled pregnancy outcomes (GDM, PIH, eclampsia) as a function of ethnicity (Mexican, non-Mexican Hispanic); then for Mexican births, modeled the role of documentation status (proxied by payment type (emergency medical vs. private, Medicaid, other)). Results: Only 3% of births to Mexican women were undocumented. Mexican women had greater odds of GDM (odds ratio (OR)=1.2; 95% confidence interval (95%CI: 1.0, 1.4) and eclampsia (OR=1.5; 95% CI 1.1, 2.4) but lower odds of PIH (OR=0.9; 95% CI: 0.7, 1.0) compared with non-Mexican women. Among Mexican women, being undocumented was neither positively nor negatively associated with GDM, was associated with lower odds of PIH (OR=0.4; 95% CI: 0.2, 0.8) and higher odds of eclampsia (OR=9.2; 95% CI: 4.8, 17.8), compared with documented Mexican women. Conclusion: Findings, which preceded calls for a Mexican border wall, suggest that undocumented Mexican women do not equally benefit from the Latina Paradox and are at increased risk for adverse pregnancy outcomes. Addressing documentation status is a critical public health intervention with maternal and child health equity implications.

OBTAINING A PRENATAL CARE CLINIC-BASED PROBABILITY SAMPLE OF MICHIGAN BIRTHS: THE MARCH STUDY Michael Elliott, Tracy Thompson, Alexa Krueger, Gwendolyn Norman, Charles Barone, Terri Ridenour, Eva Leissou, Jean Kerver, Nigel Paneth (University of Michigan)

Despite some criticism in research years (Rothman et al. 2013), use of probability sampling remains an important tool in the epidemiological research toolbox, both for estimation of population descriptors and deeper understandings of health mechanisms (Keiding and Louis 2016). Obtaining a probability sample of pregnancies is an extremely challenging undertaking, as shown by the struggles of the National Children's Study (NCS), where traditional face-to-face sampling proved infeasible (Wadman 2012). However, the NCS also suggested that recruitment methods through prenatal care clinics could be successful, given the context and support provided in that setting (Kerver et al. 2013, Robbins et al. 2015). The key insight in this presentation is the ability to marry clinic recruitment with probability sampling through the use of birth certificate (BC) records. BCs identify the hospital in which the birth occurs and the name of the provider associated with the delivery, creating a natural sampling frame from which a probability-proportional-to-size (PPS) sample of hospitals can be obtained. Further investigation of providers in sampled hospitals allows creation of a second-stage frame of prenatal clinics, which can also be PPS-sampled, and approximately equal numbers of pregnant women recruited at each clinic to approximate equal probabilities of selection. BCs also provide information about the demographics of the birth mother, allowing stratification by socioeconomic factors as well as region. We describe a sample design of 10 hospitals, 20 clinics, and 50 women per clinic for the State of Michigan, for a total sample size of 1,000. We also discuss critical issues relevant to successful onboarding of hospitals and clinics, and to recruitment, as well as complexities that arise during prenatal and postnatal follow-up. Data collection is ongoing, but we will present preliminary results of our recruitment efforts, highlighting both successes and struggles thus far.

DO COMPETING RISKS MATTER? THE CASE OF CHRONIC HYPERTENSION AND THE INCIDENCE OF SEVERE PREECLAMPSIA.

Sarka Lisonkova, (University of British Columbia)

Background: Chronic hypertension (CH) is a known risk factor for severe preeclampsia. However, CH is also strongly associated with obstetric intervention (labour induction or pre-labour caesarean), which is a competing risk for severe preeclampsia. The effect of CH on the incidence of severe preeclampsia in the presence of a competing risk has not been examined. **Objective:** To examine incidence of severe preeclampsia among women with and without CH and to estimate the effect of obstetric intervention at preterm (20-36 weeks) and term (≥ 37 weeks) gestation. **Methods:** All singleton hospital births at ≥ 20 weeks gestation in Washington State, 2003-2013, were included (N=734,661) with data obtained from birth certificates and delivery hospitalizations. The Cox model was used to obtain cause-specific hazard ratios (HR) and 95% confidence intervals (CI) at preterm and term gestation. The Fine and Gray model was used to estimate the sub-distribution HRs, taking into account obstetric interventions. **Results:** In women with CH, gestational age-specific rates of severe preeclampsia increased from 0.9 at 20 weeks to 679.8 per 10000 ongoing pregnancies at ≥ 40 weeks; in those without CH, the increase rose from 0.0 to 32.3 per 10000, respectively. The cause specific HR for severe preeclampsia was 15.7 (CI 14.7-16.9) at preterm and 25.6 (CI 23.8-27.6) at term. The sub-distribution HR was 15.5 (CI 14.5-16.6) at preterm and HR=21.5 (CI 20.0-23.1) at term. Results were similar when adjusted for other covariates (eg, maternal age, BMI, etc.). **Conclusion:** In the presence of competing risks, the Cox model is not appropriate for predicting incidence. This example suggests that while the risk of severe preeclampsia is substantially increased at each gestation among hypertensive women with ongoing pregnancy, the relative difference in the incidence (prognosis) of severe preeclampsia between women with and without CH is smaller at term gestation due to obstetric interventions.

INTERRUPTED TIME SERIES ANALYSIS TO ASSESS PRESCRIPTION FILLING AROUND CONCEPTION AND IMPLICATIONS FOR MISCLASSIFICATION OF MEDICATION USE IN PREGNANCY

Jacqueline Cohen, Randi Selmer, Kari Furu, Øystein Karlstad (Norwegian Institute of Public Health)

Medication exposures are often defined by one or more prescription fills in pregnancy. Harmful effects could be underestimated if there is rapid discontinuation of use after pregnancy recognition. We hypothesized that prescription fills for some psychotropic drugs may decrease rapidly after conception, due to a preference for avoidance of use in pregnancy. Few studies have used a critical biological period as an intervention for interrupted time series analysis (ITSA). Using data from the Norwegian Prescription Database linked the Medical Birth Registry (2005-2015), we linearly modeled the number of prescription fills in the each of 12 weeks before and after conception with ITSA. The “intervention” was the earliest date of pregnancy recognition, i.e. 2 weeks after conception. We examined psychostimulants, antidepressants, antipsychotics and antiepileptic drugs (AEDs; separated by use for epilepsy or other indication). We used relative measures (%) to compare the model coefficients. We observed similar patterns for psychostimulants, antidepressants, and AEDs (other indication): a sudden decline in prescription fills from 2 weeks after conception (-47, -30, and -23%) and decreasing fills thereafter (-10, -6.9, and -4.2% per week). We also saw similar patterns for antipsychotics and AEDs (epilepsy): The intercept-only model fit the data better with a trend toward a slight increase in prescription fills during the first trimester. We also compared the number of pregnancies defined as exposed when the earliest fill was 30 days before the last menstrual period (LMP), LMP, or conception (LMP+14 days). Only 77% of pregnancies with fills for psychostimulants from LMP and 58% with fills from LMP-30 days had fills from conception. Similar figures for AEDs (epilepsy) were 99% and 96%. This application shows that ITSA can help researchers understand rapid changes in patient behavior around conception that has consequences for exposure misclassification in pregnancy studies.

PRECONCEPTION INFLUENCES ON PREGNANCY AND BEYOND: THE PREPARED CONSORTIUM Emily Harville, Gita Mishra, Lydia Bazzano, Danielle Downs, Deborah Ehrenthal, Erica Gunderson, Alysha Harvey, Lauren Wise (Tulane University)

Additional authors: EE Hatch, H Jiang, AM Jukic, SL Mumford, C Porucznik, EF Schisterman, J Stanford, DA Santillan, M Santillan, D Sotres-Alvarez, SW Wen, J Woo, C Yajnik, E Yeung The preconception period is a critical but often neglected time in the life cycle for understanding determinants of women's and offspring health across the life course. Few studies have collected data on both preconception and during-pregnancy risk factors. Pregnancy cohorts usually have information only on diagnosed preconception conditions among women who successfully conceive, while general longitudinal cohort studies tend to focus on older populations and often exclude pregnant women. Cohorts that focus on women attempting to conceive may be unrepresentative, due to unplanned pregnancies. In addition, individual cohorts often lack power to examine less common complications, and effect modifiers such as age, race, and parity. To address these gaps, we have formed the PrePARED consortium (Preconception Period Analysis of Risks and Exposures Influencing Development and Disease) of preconception and life course studies. A study is eligible to participate if it a) has data measured in the preconception period, b) has a minimum set of covariate data, and c) is open to collaboration and data harmonization. The member cohorts are diverse in their populations and study design, and have extensive measures of cardiometabolic risk, diet, fertility, biosamples and/or environmental factors. Current consortium-related work involves determining details of existing data, setting up data use agreements, and initiating harmonization efforts. Initial areas of focus for the cohort include nutrition and obesity; mental health; substance use; and effects of male partner exposures. Additional cohorts may join this open consortium which will serve as a resource identifying the factors with perinatal and potentially inter-generational influences, with implications for science, practice, and policy.

DEVELOPMENT OF A PUBLIC HEALTH SURVEILLANCE SYSTEM FOR NEW FATHERS: ADAPTATION OF THE PREGNANCY RISK ASSESSMENT MONITORING SYSTEM (PRAMS)

Lee Warner, Clarissa Simon, Katherine Kortsmit, Ada Dieke, Letitia Williams, Michael Bryan, Florence Kanu, Patricia Castro, Michele Mindlin, Christopher Harrison, Craig Garfield (Centers for Disease Control and Prevention)

Over the past 30 years, PRAMS, a site-specific and population-based surveillance system, has collected data from mothers with a recent live birth to assess maternal experiences and behaviors before, during and shortly after delivery. While fathers play key roles in the health and development of their families, research on fathers is limited and there is no ongoing state-based, surveillance system examining men's experiences during the perinatal period. This presentation summarizes: 1) findings from formative research used to inform development of "PRAMS for Dads," a novel public health surveillance system for fathers, 2) the design and proposed study outcomes of a pilot evaluation of PRAMS for Dads, and 3) preliminary results of initial implementation efforts. In Spring 2014, focus groups (n=4) were conducted with fathers (n=2) and mothers (n=2) to assess how to most effectively reach fathers and to guide development of PRAMS for Dads. Two methodological approaches were identified for reaching fathers: "Mothers-as-Gatekeepers" and "Direct-to-Dads." An ongoing pilot study is comparing which method is the most effective approach for reaching fathers and assessing differences in the proportion of fathers who completed an online versus traditional mailed paper survey. PRAMS for Dads follows the general PRAMS protocol for new mothers, aims to reach over 550 fathers, and was launched in the field in one state [Georgia] in October, 2018. To date, 378 fathers have been randomized to one of the two approaches [189 Mother as Gatekeeper; 189 Direct to Dads] and invited to participate. PRAMS for Dads provides a framework for states to implement a public health surveillance system for new fathers. Implementation of such a system provides population-based estimates on the health and behaviors of fathers before, during and shortly after pregnancy which may better inform efforts to improve the health and well-being of fathers and their families.

ASSOCIATION OF NEWBORN APGAR SCORE WITH MATERNAL ADMISSION TO THE INTENSIVE CARE UNIT (MADICU) Jagjit Singh Teji, (Ann and Robert H. Lurie Children's Hospital)

Background It is well known that the maternal mortality is increasing in the USA every year in spite of all efforts to reduce it. There are a few reports in the literature on the MADICU and its inverse relationship with apgar score at 5 minutes (APG5). Predictability of severe maternal morbidity (SMM) is reflected by low APG5.

Objective To determine the association of MADICU with APG5 in the births in the USA. **Methods** NCHS Natality file for the year 2015 was used for the analysis.

Logistical regression analysis was performed on the APG5 as independent variable and MADICU as the dependent variable, controlling for maternal age, educations risks due to hypertension and diabetes, marital status, body mass index (BMI) and exposure to tobacco, delivery mode, and maternal race. STATA 14.0 and EXCEL 2016 were used. **Results** Total deliveries in 2015 were 3,967,866 that were usable for analysis out of 3,988,733. Incidence of MADICU 1.56 per 1000 live births.

MADICU for APG5=0 to 3, OR 12.34 (95% cf: 11.03-13.81); APG5=4 to 6, OR 7.90 (95% cf: 7.25-8.62) compared to APG5=7-10, OR 1. Additionally significant variables that were independently predictable for MADICU were newborn NICU admission, higher BMI, tobacco exposure, higher maternal age, pregnancy diabetes and hypertension and gestational hypertension and slightly higher for non-college educated mothers. **Conclusion** 1. This is the largest population analysis inversely relating low APG5 with MADICU. 2. Low APG5 for the newborns should be a warning sign for the providers be more vigilant when taking care of the mothers for possible MADICU. **Reference:** Ray JG, Medcalf KE, Park AL Association of Newborn Apgar Score With Maternal Admission to the Intensive Care Unit. JAMA Pediatr. 2016 Jan;170(1):88-9.

PREGNANCY PER- AND POLYFLUOROALKYL SUBSTANCE EXPOSURE, GESTATIONAL WEIGHT GAIN, AND POSTPARTUM WEIGHT RETENTION IN PROJECT VIVA Susanna D. Mitro, Sharon K. Sagiv, Sheryl L. Rifas-Shiman, Abby F. Fleisch, Lindsay M. Jaacks, Paige L. Williams, Emily Oken, Tamarra M. James-Todd (Harvard University)

Background: Per- and polyfluoroalkyl substances (PFAS) are synthetic chemicals previously associated with gestational weight gain (GWG), though associations with postpartum weight retention (PPWR) are unknown. Methods: We studied 1631 women recruited 1999-2002 in the Project Viva cohort with early pregnancy (median 9.7 weeks) plasma measurements of 6 PFAS, including perfluorooctanesulfonic acid (PFOS), perfluorooctanoic acid (PFOA), and 2-(N-ethyl-perfluorooctane sulfonamido) acetic acid (Et-PFOSA-AcOH). We defined GWG as the difference between last pregnancy weight and pre-pregnancy weight, and PPWR as the difference between weight at 1 or 3 years postpartum and pre-pregnancy weight. We used multivariable regression adjusted for age, pre-pregnancy body mass index, marital status, race/ethnicity, education, income, smoking, and parity. Postpartum models were adjusted for differential loss to follow up using inverse probability of censoring weights (sample sizes in adjusted models: GWG n=1404; 1-year PPWR n=793; 3-year PPWR n=526). Results: Mean GWG was 15.7 kilograms (kg) (standard deviation (SD)=5.7). Mean 1-year PPWR was 0.7 kg (SD=4.8); 12.7% of women had substantial PPWR (≥ 5 kg). Each doubling of PFOA was associated with 0.33 kg (95% confidence interval (CI): -0.09, 0.76) greater GWG, 0.53 kg (95%CI: 0.07, 0.99) greater 1-year PPWR, and 1.07 kg (95%CI: 0.27, 1.87) greater 3-year PPWR. Each doubling of Et-PFOSA-AcOH was associated with 0.36 kg (95%CI: 0.10, 0.63) greater GWG, 0.27 kg (95%CI: -0.06, 0.61) greater 1-year PPWR, and 0.43 kg (95%CI: -0.17, 1.03) greater 3-year PPWR. The odds ratio for substantial 1-year PPWR was 1.29 (95%CI: 0.94, 1.78) per doubling of PFOS, 1.63 (95%CI: 1.15, 2.32) per doubling of PFOA, and 1.18 (95%CI: 0.95, 1.48) per doubling of Et-PFOSA-AcOH. Conclusion: Our study adds to the evidence linking PFAS to GWG and is the first to show that early pregnancy PFAS exposure may also increase PPWR, a risk factor for poor long-term health.

BRANCHED CHAIN AMINO ACIDS, HISTORY OF GESTATIONAL DIABETES, AND LACTATION Emily Harville, Lydia Bazzano, Lu Qi, Jiang He, Kirsten Dorans, Tanika Kelly (Tulane University)

Background: Branch chain amino acids (BCAA; leucine, isoleucine, and valine) and their metabolites have been associated with diabetes. At least one in four women who develop gestational diabetes (GDM) will progress to type 2 diabetes, while breastfeeding is protective. We examine the associations between history of GDM and lactation with BCAA and their metabolites in later life in a biracial, semi-rural cohort. **Methods:** 630 women (mean age 48.0 y) who had participated in the Bogalusa Heart Study had untargeted, ultrahigh performance liquid chromatography-tandem mass spectroscopy conducted by Metabolon© on serum samples.

Metabolites were identified that were BCAA or associated with BCAA metabolic pathways. History of GDM at any pregnancy (self-reported, confirmed with medical records when possible) as well as breastfeeding were examined as predictors using linear models, controlling for age, race, BMI, and menopausal status. **Results:** Each of the BCAA was higher in women with a history of GDM, but not statistically significant. Isoleucine was lower in women with a history of breastfeeding. No interactions were found between the two. Of the 31 metabolites on the leucine, isoleucine and valine metabolism subpathway, 1-carboxyethylleucine, 1-carboxyethylvaline, N-acetylleucine, 3-methyl-2-oxovalerate, 3-hydroxy-2-ethylpropionate, 4-methyl-2-oxopentanoate, alpha-hydroxyisocaproate, and 3-methylglutaconate were all higher in women with a history of GDM. In women with a history of breastfeeding, 1-carboxyethylleucine, 1-carboxyethylisoleucine, 1-carboxyethylvaline, 2-hydroxy-3-methylvalerate, and alpha-hydroxyisovalerate were lower, while 3-hydroxyisobutyrate, ethylmalonate, and 3-hydroxy-2-ethylpropionate were higher. **Conclusions:** Lactation may be associated with long-term changes in BCAA levels and related metabolites. GDM and lactation are associated in opposite directions with several metabolites on the BCAA metabolic pathway.

A POPULATION-BASED STUDY OF THE ASSOCIATION BETWEEN AUTOIMMUNE DISEASE AND PERINATAL MENTAL ILLNESS Hilary Brown, Andrew Wilton, Joel Ray, Cindy-Lee Dennis, Astrid Guttman, Simone Vigod (University of Toronto)

Perinatal mental illness is the most common complication of childbirth. Universal prevention efforts have not reduced its incidence, making identification of high-risk groups important for developing targeted interventions. Outside pregnancy, autoimmune disease (AD) increases the risk of mental illness, possibly due to inflammation. We examined the association between AD and perinatal mental illness overall and according to whether AD was associated with brain-reactive antibodies that impact neurological function. We undertook a population-based study in Ontario, Canada (2005-2015) of 15- to 49-year-old women with AD with brain-reactive antibodies (n=4,483), other AD (n=7,524), and no AD (n=846,166), all who had a singleton livebirth and no mental illness history ≤ 2 years before conception. Modified Poisson regression was used to estimate risk for mental illness, addiction, or self-harm between conception and 365 days postpartum, adjusting for age, parity, income, rurality, and other chronic disease. Analyses were stratified by remote history of mental illness > 2 years before conception. In women with remote history of mental illness, perinatal mental illness risk was increased in those with vs. without AD (22.5% vs. 20.6%; adjusted relative risk [aRR] 1.10, 95% CI 1.05-1.15), with greater risk in AD with brain-reactive antibodies (23.3% vs. 20.6%; aRR 1.13, 95% CI 1.06-1.21) than other AD (22.0% vs. 20.6%; aRR 1.07, 95% CI 1.01-1.13). In women with no remote history of mental illness, risk was elevated but non-significant for AD overall and for AD with and without brain-reactive antibodies separately. Autoimmune diseases, especially those with inflammatory mechanisms that affect the brain, increase risk for mental illness relapse, but not new-onset mental illness, perinatally. Preventive mental health interventions should be initiated preconceptionally in women with AD with a remote history of mental illness, with screening in pregnancy also being warranted.

PREGNANCY COMPLICATIONS AND TOTAL AND CAUSE-SPECIFIC MORTALITY AMONG WOMEN IN A LARGE HISTORIC U.S. COHORT

Cuilin Zhang, Stefanie Hinkle, Anna Pollack, Danping Liu, Edwina Yeung, Sunni Mumford, Katherine Grantz, Fasil Tekola Ayele, Neil Perkins, Lindsey Sjaarda, James Mills, Pauline Mendola, Enrique Schisterman (NICHD, National Institutes of Health)

OBJECTIVE: Evidence suggests that women with pregnancy complications such as hypertension, gestational diabetes, and preterm delivery have an increased risk of mortality from later cardiometabolic diseases. Long-term follow-up data are scarce in the U.S. **METHODS:** We examined associations of gravid complications (gestational hypertension, preeclampsia, glucose intolerance in pregnancy [gestational diabetes/impaired glucose tolerance], and preterm delivery from the Collaborative Perinatal Project (CPP; 1959-1966; n=46,474 women) with total and underlying cause-specific mortality through 2016. Vital status was determined by linkage to the National Death Index (NDI). Hazard ratios (HR) were estimated using Cox models adjusted for race, age, pre-pregnancy body mass index, smoking, parity, marital status, socioeconomic status, prior chronic conditions, site, and year of last CPP pregnancy. **RESULTS:** The mortality rate was 37% (n=17,004) and higher among women with gestational hypertension (adjusted HR: 1.1 [95% CI 1.0, 1.2]) and preeclampsia (1.2 [1.0, 1.3]) compared to normotensive women; women with glucose intolerance in pregnancy (1.2 [1.0, 1.3]) compared to normoglycemic women; and women with a spontaneous (1.1 [1.0, 1.1]) or indicated (1.3 [1.1, 1.5]) preterm compared to term delivery. Women with indicated preterm had a 2.5 (1.2, 5.4), 2.1 (1.2, 3.6), and 1.4 (1.1, 1.9) fold increased hazard of kidney disease, diabetes, and CVD mortality, respectively, whereas women with a spontaneous preterm had a 1.2 (1.1, 1.3) fold increased hazard of CVD mortality. Preeclampsia was related to diabetes, kidney disease, and CVD mortality. Glucose intolerance in pregnancy was related to diabetes and kidney disease mortality. **CONCLUSION:** Our study, the largest with longest follow-up in the U.S., confirms that gravid complications were associated with later mortality, further suggesting that gravid health may act as a vital sign for future health.

CHARACTERIZING PSYCHOLOGICAL MORBIDITIES, MITIGATING FACTORS, AND STRESSFUL LIFE EVENTS IN PREGNANCY Miriam Haviland, Heather Burris, Howard Cabral, Lauren Wise, Yael Nillni, Matthew Fox, Michele Hacker (BUSPH)

Background: While depression and anxiety during pregnancy are associated with preterm delivery, the strength of these associations varies across studies. Characterizing depression and anxiety as a multidimensional characteristic could improve our understanding of these associations, as well as the role of mitigating factors such as resilience. Methods: Spontaneous Prematurity and Epigenetics of the Cervix (SPEC) is an ongoing prospective cohort study of pregnant women. In this analysis, we included women who enrolled after August 24, 2014 and delivered by April 20, 2018. We used latent profile analysis to identify distinct groups of women based on their responses to measures assessing depression, perceived stress, anxiety (pregnancy-related and generalized), stressful life events, resilience, and social support (partner and friend/family). We used multinomial logistic regression to identify predictors of profile membership and linear regression to compare mean gestational age at delivery among profiles. Results: We included 672 eligible women. We identified four profiles of psychosocial stress: women in profile 1 had average scores on all measures; those in profile 2 had above average depression and anxiety scores, those in profile 3 had below average resilience and above average depression, anxiety, social support, and stressful life events scores, and those in profile 4 had above average social support scores. Compared with women in profile 1, women were more likely to be classified as profile 2 (1.9; 95% CI: 1.1, 3.5) or profile 3 (8.3; 95% CI: 2.7, 25.9) if they reported symptoms of anxiety or depression before pregnancy. Mean gestational age at delivery was lower among women in profile 3 (-0.36; 95% CI: -1.0, 0.28) and profile 4 (-0.59; 95% CI: -1.1, -0.1), compared to those in profile 1. Conclusions: We identified distinct profiles of psychosocial stress during pregnancy that may be associated with the length of gestation.

URINARY TRACT INFECTION IN PREGNANCY: RISK FACTORS AND PREVALENCE IN THE NATIONAL BIRTH DEFECTS PREVENTION STUDY Candice Johnson, Carissa Rocheleau, Meredith Howley, Elizabeth Ailes (CDC/NIOSH)

Background: Urinary tract infection (UTI) is the most common medical complication of pregnancy. Because it can result in kidney infection and preterm birth, women are screened for UTI early in pregnancy and treated with antibiotics if UTI is found. Prevention of UTI in pregnancy is an opportunity to reduce both maternal morbidity and antibiotic use in pregnancy; unfortunately, prevention is currently infeasible because so little is known about UTI epidemiology. Our objective was to identify risk factors for UTI in pregnancy in a large, population-based study. **Methods.** We included control mothers participating in the National Birth Defects Prevention Study — a case-control study of birth defects in 10 U.S. states — who had live births during 1997–2011. Mothers self-reported UTI, sociodemographics, and health behaviors. We estimated prevalence ratios (PRs) and 95% confidence intervals (CIs) for associations between maternal characteristics and UTI in pregnancy. Log-binomial models were adjusted for study design variables and sociodemographic characteristics. **Results:** Among 11,655 participating mothers, 17% reported UTI in pregnancy. However, there were marked geographic differences, with 9% of Massachusetts mothers reporting UTI compared to 25% in Arkansas. Maternal age was also a predictor: the prevalence was 29% among mothers aged <20 years, but 11% among mothers aged ≥35 years. In adjusted analyses, a wide variety of maternal characteristics was associated with higher UTI prevalence, including race/ethnicity (PR 3.19, CI: 2.15–4.71 for Hispanic vs. Asian/Pacific Islander mothers), low income (PR 1.47, CI: 1.23–1.76 for <\$10,000 vs. ≥\$50,000), and high caffeine intake (p-trend <0.001), among others. **Conclusions:** One in six women reported UTI in pregnancy. Geographic and socioeconomic gradients in risk suggest the existence of modifiable risk factors that could lead to interventions to prevent UTI and decrease antibiotic use in pregnancy.

DEPRESSIVE SYMPTOMS, PERCEIVED STRESS, AND PRETERM BIRTH: ASSESSING MEDIATION BY PSYCHOTROPIC MEDICATION USE

Miriam Haviland, Yael Nillni, Matthew Fox, Michele Hacker, Elizabeth Hatch, Kenneth Rothman, Lauren Wise (BUSPH)

Background: High levels of depressive symptoms and stress are associated with a greater risk of preterm birth (<37 weeks' gestation). The extent to which psychotropic medication use mediates these associations is unclear. **Methods:** Boston University Pregnancy Study Online (PRESTO) is a North American prospective cohort study of female pregnancy planners aged 21-45 years, who enrolled during the preconception period. At enrollment, participants completed a survey with questions on socio-demographics and medical history, including the Major Depressive Inventory (MDI) and the 10-item Perceived Stress Scale (PSS). In follow-up questionnaires completed in early (8-12 weeks) and late (~32 weeks) pregnancy, women reported on psychotropic medication use. Data on gestational age at birth were abstracted from birth registries and the postpartum questionnaire (completed ~6 months post-delivery). We analyzed data from 2,780 women who reported a conception from 6/2013-12/2017, after excluding women with pregnancy loss ≤ 20 weeks' gestation. We used Cox regression to compare time to preterm birth between women with moderate or severe depressive symptoms ($MDI \geq 25$) vs. others ($MDI < 25$), and those with PSS scores ≥ 20 vs < 20 . We used causal mediation analysis to quantify mediation by psychotropic medication use. **Results:** The hazard ratio (HR) for moderate or severe depressive symptoms compared with none or milder symptoms was 0.94 (95% CI: 0.53-1.66). PSS scores ≥ 20 were associated with a higher incidence of preterm birth than scores < 20 (HR=1.25; 95% CI: 0.93-1.67), as was use of psychotropic medications compared to no use (HR=1.34; 95% CI: 0.81-2.23). The proportion of the association between PSS and preterm birth mediated by psychotropic medication use was zero. **Conclusions:** Higher levels of perceived stress, but not depressive symptoms, was positively associated with preterm birth. Psychotropic medication use did not appear to mediate this association.

CHILD MARRIAGE AND PERINATAL HEALTH IN THE UNITED STATES Marcelo Urquia, Kathleen Kenny (University of Manitoba)

Background. Marriage has been linked with favorable reproductive health outcomes. Child marriage (<18 years) is a notorious exception observed in low and middle-income countries but understudied in high-income countries. We assessed the association between marital status and perinatal health among minors in the United States, and if it differs by Foreign-born (FB) status and race/ethnicity. **Methods.** We used the Natality Public Use Files 2014-2017 of the National Center for Health Statistics to extract singleton births with complete information on maternal age, marital status, nativity and race/ethnicity. We used logistic regression to assess associations with adverse outcomes. **Results.** There were 14.4 million singleton births. The proportion of births to married mothers was 59.7% overall, 11.1% among teenagers and 3.9% among minors (US-born = 3.3% and FB = 8.1%). In analyses restricted to mothers <18 years, marriage rates varied substantially according to nativity and race/ethnicity, from 0.4% among US-born Non-Hispanic Blacks to 34% among FB Non-Hispanic Whites. Married girls had lower odds of late prenatal care entry, pregnancy smoking, low Apgar and sexually transmitted infections but higher odds of a repeat birth or pregnancy termination. Preterm birth (PTB) (<37 weeks gestation) rates were slightly lower among married (8.6%) than among unmarried minors (9.6%). Marriage was associated with lower PTB rates among FB girls [adjusted odds ratio (AOR): 0.70; 95% confidence interval (CI): 0.59, 0.83] but not among the US-born [AOR: 0.96; 95% CI: 0.88, 1.04] (p-value for interaction <0.001). Lower odds were observed across all FB ethnoracial groups, particularly among Non-Hispanic Whites [AOR: 0.56; 95% CI: 0.35, 0.90]. **Discussion.** Immigrants to the United States have higher child marriage rates than their US-born counterparts but more favorable perinatal outcomes. Yet, all minors, irrespective of marital status, have less favorable outcomes than older mothers.

ASSESSING THE EVIDENCE FOR THE MATERNAL FOLATE DEPLETION HYPOTHESIS IN THE UNITED STATES Catherine Vladutiu, Veni Kandasamy, Katherine Ahrens (HRSA/MCHB)

The maternal folate depletion hypothesis posits that serum folate levels are lower in the postpartum period, thus increasing the risk of adverse pregnancy outcomes for women who become pregnant after short interpregnancy intervals. We sought to assess the evidence for this hypothesis in the US, a country with folic acid fortification of grain products and common use of folic acid supplementation in pregnancy. We examined serum folate levels by time since last live birth among a nationally representative sample of non-pregnant US women, ages 20-44 years, in the National Health and Nutrition Examination Survey during 2007-2010 (2011-2014 data pending release). Red blood cell folate was measured using a microbiological assay on whole blood samples. Low folate was defined as 12 months but <3 years ago (“mothers of toddlers”; 11%), or ≥3 years ago (“mothers of older children”; 48%); 35% were nulliparous. Mean (\pm standard error) serum folate levels were, respectively: 536 ± 22 , 483 ± 16 , 481 ± 9 , and 466 ± 10 ng/mL. Mothers of infants had the lowest prevalence of low folate (30%) compared with mothers of toddlers (37%), mothers of older children (38%), and nulliparous women (41%) (pairwise comparisons, $p=0.23$, $p<0.01$, and $p<0.01$). Our findings indicate that serum folate levels are highest in non-pregnant reproductive age US women during their first year postpartum compared with other stages of life. This evidence does not support the hypothesis of postpartum folate insufficiency as the biological mechanism for explaining the association between short interpregnancy intervals and adverse pregnancy outcomes in the US.

RELATIONS AMONG PRENATAL MATERNAL ANXIETY/DEPRESSION AND POSTNATAL MATERNAL-INFANT HEALTH Jessica Riedstra, Nicki Aubuchon-Endsley, Jennifer Hambleton (Idaho State University)

Roughly 10% of pregnant women meet criteria for a mental disorder, most commonly depression and anxiety. Extant research suggests that obstetric mental health has implications for physical health outcomes in both mothers and infants. However, more research is needed to explore these relationships later in the postnatal period to determine the duration of these effects. Additionally, more studies are needed with understudied rural samples at greater risk of mental health concerns with more limited access to care. Therefore, the current study sampled from a rural southeastern Idaho community. Data were drawn from 96 expectant mothers at 33-37 weeks gestation and 6 months postpartum participating in the Infant Development and Healthy Outcomes in Mothers study. It was hypothesized that both prenatal anxiety (Perinatal Anxiety Screening Scale) and depression (Edinburgh Postnatal Depression Scale-Prenatal Version) would be significantly correlated with maternal (e.g., gestational/Type 2 diabetes, high blood pressure, pre-eclampsia, toxemia, hyper/hypothyroidism, group B strep, anemia, asthma, and infection) and infant (e.g., fever, ear infection, colic, reflux, diarrhea, vomiting, fussy/irritable, jaundice, cold, respiratory syncytial virus, cough or wheeze, asthma, food allergy, eczema, thrush, and teething) physical health. Results revealed a significant relationship between prenatal anxiety and maternal 6-month health ($r=.222$, $p<.05$). Future research should examine prospective mediators and mechanisms that may account for relations between prenatal anxiety and postnatal maternal health in order to highlight potential targets for perinatal prevention.

KNOWLEDGE OF FOODBORNE RISKS AND PRENATAL DIETARY CHANGES AMONG PREGNANT WOMEN Marni Jacobs, Karen Robbins, Ashley Ramos, Linda Herbert (Children's National Health System)

Though prenatal dietary guidelines have been developed to minimize foodborne risk, the extent to which women change their diet due to perceived risk and the ways by which they acquire information to inform these changes are unclear. Using data from the Food and Drug Administration and Center for Disease Control's Infant Feeding Practices Study II, risk-reduction related prenatal dietary changes, including reasons for change, knowledge of food risks, and sources of information, were assessed via a prenatal survey. Of 4,899 respondents, 36% reported avoiding specific foods due to perceived harm to the baby; various fish (11%-19%) and lunchmeats (16%) were the most commonly avoided. Women who avoided specific foods tended to be older, nulliparous, and have higher income and education (all $p < 0.0001$), regardless of whether the foods fell under published guidelines. Most women had heard of problems related to mercury (68%), though fewer had heard of listeria (33%) or dioxins (23%). A minority correctly identified all foods associated with mercury (37%), listeria (10%), or dioxins (11%), and a similar number incorrectly identified an at risk food (27%, 4%, and 12%, respectively). Most women (81%) received dietary information from a health professional, though 70% sought additional sources. Women who sought external information were more likely to report diet change ($p < 0.0001$), and women who received dietary information from medical professionals or external sources only were more likely to be unsure about foods that should be avoided versus women who received information from both sources ($p < 0.0001$). Findings suggest women are not following published prenatal diet guidelines and frequently seek non-medical sources to guide decisions, suggesting uncertainty or confusion about which foods should be avoided. This research highlights a need to better address prenatal diet uncertainty among pregnant women and understand the sources of information that inform their choices.

PRENATAL MEDICATION AND DIETARY SUPPLEMENT USE IN THE NICHD FETAL GROWTH STUDIES-SINGLETON COHORT BY OBESITY STATUS

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Limited research from administrative data has shown that maternal body mass index (BMI) ≥ 30 kg/m² is associated with increased medication use. We examined the differences between the quantity and types of medications and supplements used, by obesity status in 2186 low risk pregnant women with no prepregnancy high risk chronic conditions such as diabetes, or hypertension requiring multiple medications (1750 non-obese, and 436 obese) in the NICHD Fetal Growth Studies-Singleton cohort. Women of Asian ethnicity were excluded due to few numbers (n=6 obese). Free text data on supplement and medication use was self-reported at each study visit and abstracted from medical records. Data were mapped to active ingredients and classes using the Slone Drug Dictionary. Differences in the overall and by trimester in the quantity and types of medications between women with and without obesity were examined adjusting for race/ethnicity, sociodemographics and smoking status. Nearly all women (98% both groups) took at least 1 dietary supplement during pregnancy. Overall medication use did not vary by obesity status ($p=0.91$): 23% of women with versus 27% without obesity took no medication, 24% vs. 23% took 1, 20% vs. 19% took 2, and 33% vs. 31% took ≥ 3 . The use of medications increased from the 1st to 3rd trimester for both the obese (51% to 61%) and the non-obese (46% to 57%) groups. Both groups reported taking the same top 3 medication classes at similar proportions: 1) central nervous system agents including pain killers, opioids, narcotics, and antidepressants (50% obese vs. 46% non-obesity, $p=0.32$); 2) gastrointestinal drugs (43% vs. 40%, $p=0.64$); and 3) anti-infective agents (23% vs. 21%, $p=0.98$) respectively. Although most women took medications during pregnancy, use did not differ by obesity status. Given the healthier status of women in this cohort, our findings suggest that any increased use of medication by obese women may be due to potential comorbidities.

DOUCHING, PERINEAL TALC USE AND FIBROIDS Maya Wright, Helen Chin, Kristen Moore, Kristen Upson, Donna Baird (University of North Carolina at Chapel Hill)

Background: Uterine fibroids are very common benign smooth-muscle tumors. Black women are at an increased risk of developing fibroids, but the cause is unclear. Douching and perineal talc use are common lifestyle exposures among Black women, and may be risk factors for fibroid development. **Methods:** The Study of Environment, Lifestyle and Fibroids (SELF) is a prospective cohort study of young African American women aged 23 to 35 in the metropolitan Detroit area (n=1,693) without prior diagnoses of fibroids and intact uteri. The two exposures were defined as greater than 10 self-reported douching events to date (yes/no) and any perineal talc use (ever/never). Prevalent fibroids were measured at baseline using transvaginal ultrasound. We used log binomial regression to estimate prevalence ratios (PR) and 95% confidence intervals (CI) for fibroid prevalence (yes/no) and multinomial logistic regression to estimate odds ratios and CI for total fibroid volume, categorized as no fibroids, \geq median total volume in this cohort (1.88cm³) and $<$ median total volume. **Results:** Forty-three percent of women reported ever douching, 15% reported ever perineal talc use, and 9% reported using both. Fibroid prevalence was 23%. Women who douched were no more likely than women who did not to have prevalent fibroids (PR 1.05; CI=0.89,1.23), nor have fibroid volumes $<1.88\text{cm}^3$ or $\geq 1.88\text{cm}^3$ when compared to no fibroids (OR $<1.88\text{cm}^3$:1.04; CI= 0.66,1.42; OR $\geq 1.88\text{cm}^3$:1.06; CI=0.77,1.44). Women who used perineal talc had marginally increased prevalence of fibroids (PR 1.19; CI=0.97,1.46). Perineal talc use was also marginally associated with fibroid volumes $\geq 1.88\text{cm}^3$ (OR 1.39; CI=0.93 ,2.09) but not volumes $<1.88\text{cm}^3$ (OR 1.04; CI=0.66,1.42) when compared to women without fibroids. **Conclusions:** Our results suggest perineal talc may be a uterine irritant that could increase the risk of fibroids. Continued research is needed exploring behavioral exposures and their effects on fibroid development.

**GEOGRAPHIC PATTERNS OF PREGNANCY-RELATED MORTALITY
USING DIFFERENT DENOMINATORS TO REPRESENT POPULATION
AT RISK** Jessica Preslar, Michael Kramer, David Goodman, Dabo Brantley, Nicole
Davis (Emory University)

Maternal mortality continues to be unacceptably high in the United States, with stark disparities by race and socioeconomic status that could be due in part to prepregnancy health. Estimates of maternal mortality are conventionally presented as ratios of maternal deaths to live births. While live births is a proxy for women at risk of dying from pregnancy-related complications, it does not take into account drivers of the incidence of pregnancy itself, which may be more informative for studies of prepregnancy health and maternal mortality. An alternative measure is a rate, which uses women of reproductive age as the denominator. To describe how geographic variation in maternal mortality change under each definition of the population at risk, we compared pregnancy-related mortality rates and ratios between states and counties. We used pregnancy-related deaths (death while pregnant or within one year as a causal result of pregnancy or birth) from the Maternal Mortality Review Information Application (MMRIA), encompassing data shared by Maternal Mortality Review Committees in 10 states. Deaths are linked to their last county of residence in MMRIA; county level denominator data were assessed for live births (National Center for Health Statistics) and women of reproductive age (American Community Survey). Using 368 pregnancy-related deaths across 146 counties, we modelled pregnancy-related mortality ratios and rates at the state and county levels using Bayesian methods. Preliminary results at the state level show a coefficient of variation for pregnancy-related mortality of 48.0 using live births and 52.6 using women of reproductive age. These results may inform new approaches to studying the effects of prepregnancy health on maternal mortality.

SOCIOCULTURAL FACTORS ASSOCIATED WITH EXCESSIVE GESTATIONAL WEIGHT GAIN AND POSTPARTUM WEIGHT RETENTION IN THE HISPANIC COMMUNITY HEALTH STUDY/STUDY OF LATINOS Christina Cordero, Maria Llabre, Michelle Kominiarek, Anna Maria Siega-Riz, Catherine Vladutiu, Krista Perreira, Kelly Evenson, Lindsay Fernandez-Rhodes, Linda Gallo, Carmen Isasi, Melissa Simon, Neil Schneiderman (University of Miami)

Excessive gestational weight gain (GWG) and postpartum weight retention (PPWR) are associated with poor health outcomes. Hispanic/Latina women are less likely to meet recommendations for GWG and PPWR compared to non-Hispanic white women. Data on GWG and PPWR by Hispanic/Latina background and sociocultural factors are lacking. We evaluated associations between sociocultural factors (socioeconomic status, family support, acculturation, and psychosocial status) and GWG and PPWR among 491 Hispanic/Latina women participating in the Hispanic Community Health Study/Study of Latinos, a multi-site prospective study in the US with baseline (2008-11) and Visit 2 (2014-17) data. At Visit 2, women reported pregnancies since baseline. GWG was self-reported from the first singleton pregnancy after baseline. PPWR was the weight measured at Visit 2 from women with only one singleton pregnancy since baseline and ≥ 6 months postpartum ($n=359$). We defined excessive GWG based on Institute of Medicine guidelines and PPWR as >10 lbs. We used survey linear regression to model associations with GWG and PPWR, and survey logistic regression with indicators for GWG and PPWR. Models were adjusted for maternal age, BMI, length of gestation, study site, Hispanic/Latina background, and time lapse from baseline for GWG or to Visit 2 for PPWR. Mean GWG was 29.3 lbs (SE=1.2) with women of Mexican origin having the lowest GWG (mean=26.3, SE=1.0). Mean PPWR was 10.3 lbs (SE=1.2) with women of Cuban origin having the highest PPWR (mean=18.1, SE=3.5). Being married was associated with inadequate GWG (Odds ratio (OR)=0.52; 95% CI 0.28, 0.98) and excessive PPWR (OR=0.41; 95% CI 0.22, 0.75), as was having contact with parents associated with inadequate GWG (OR=0.07; 95% CI 0.02, 0.31) and contact with 1-3 relatives (reference=none) with excessive PPWR (OR=0.21; 95% CI 0.07, 0.62). Findings suggest that family support may be important in reducing PPWR and obtaining adequate GWG among Hispanic/Latina women.

**TO SCREEN OR NOT TO SCREEN: LESSONS LEARNT FROM
GLUCOSE CHALLENGE TEST IN CONSECUTIVE PREGNANCIES** Israel
Yoles, Tamar Wainstock (Clalit Health Services)

Objective: A 1-hour 50-gram glucose challenge test (GCT) is the first step in the screening for gestational diabetes mellitus (GDM). Today, abnormal GCT in index pregnancy is not an indication for a 100-gram glucose challenge test (OGTT) in consecutive pregnancies. The aim of this study was to evaluate GCT results in serial pregnancies in a large cohort. **Design:** This cohort study included all pregnant women who underwent GCT between the years 2005 to 2018 at the Central District of Clalit Health Services, the largest health maintenance organization in Israel. Data on were collected from the computerized database and analyzed. Abnormal GCT results were defined as >140 mg/dl. Multivariable logistic model was used to study the association between abnormal GCT results and a history of a previous abnormal GCT result, while adjusting for maternal age and inter- pregnancy interval. Results 66,860 women performed 117,435 GCTs during the study period. 32,677 women performed at least two GCT's in consecutive pregnancies. Abnormal results were detected in 4,019 (12.3%) first tests, and 4,640 (14.2%) in the consecutive pregnancy. Women with history of abnormal GCT were more likely to have an additional abnormal result (10.7% vs. 39.2%, among women with history of normal vs. abnormal results, respectively, (OR)=5.38, 95%CI 5.0-5.8) (Figure). Adjustment for maternal age and inter-pregnancy interval did not change the results (adjusted OR=5.15; 95%CI 4. 8-5.5). Among women with inter-pregnancy interval greater than 5 years, incidence rates were 16.1% and 49.3%, for women with history of normal vs. abnormal results, respectively (OR=5.05, 95%CI 4.2-6.1). **Conclusions** Women with a history of abnormal GCT are at increased risk for abnormal GCT in consecutive pregnancies. This risk increases if inter-pregnancy interval is greater than 5 years. OGTT instead of 50 gr GCT screening should be considered in women with a history of abnormal GCT results in previous pregnancies.

PRENATAL SURGERIES, PREGNANCY OUTCOMES AND LONG TERM PEDIATRIC MORBIDITIES: A POPULATION BASED COHORT STUDY

Israel Yoles, Tamar Wainstock, Asnat Walfisch, Eyal Sheiner (Clalit Health Services)

Introduction: Prenatal surgeries are rare and are usually performed as an emergency and usually under general anesthesia. Main indications are appendicitis, ovarian torsion or cholecystitis. There is limited information on the association between prenatal surgeries and pregnancy outcomes. We aimed to evaluate these associations in a large population-based cohort. **Study design:** A prospective cohort study was performed comparing pregnancy and newborn outcomes of mothers who underwent surgeries during pregnancies (Exposed offspring), as compared to those who did not (Unexposed). Data was collected from the perinatal and pediatric databases of a single large tertiary center between the years 1991-2013. Propensity score analysis and multivariable logistic models were used to address confounding characteristics of the association between the defined exposure and outcomes, such as maternal age, and Kaplan-Meier survival curves compared the cumulative hospitalization rates between the study groups. **Results:** 243,682 newborns met the inclusion criteria, 91 (0.04%) were born to mothers who had surgeries during their pregnancies. Mothers who underwent prenatal surgeries as compared to those who did not, were more likely to have cesarean sections (31.9% vs. 13.5%; adjusted OR= 2.39; 95%CI 1.62- 3.52) preterm delivery (gestational age < 37; 16.5% vs. 6.9%, adjusted OR= 2.55; 95%CI 1.49- 4.36) and low birthweight newborns (<2,500 gr. 6.7% vs. 22.0%; adjusted OR=3.91; 95%CI 1.73- 4.66). Hospitalizations rates due to neurological, infectious or respiratory morbidities, were higher among offspring exposed to maternal surgeries. **Conclusions:** Prenatal maternal surgeries are associated with increased risk for preterm deliveries, low birthweight and cesarean sections. Offspring were also at increased risk for selected childhood morbidities. Exposure to general anesthesia and surgery during pregnancy may compromise fetal environment and affect offspring health.

PARTICIPANT CHARACTERISTICS AND ATTENDANCE PATTERNS OF A COMMUNITY-BASED PREGNANCY SUPPORT PROGRAM IN URBAN AREAS AT HIGH RISK OF INFANT MORTALITY

Rachel M. Smith, Jason Benedict, Erinn M. Hade, Courtney D. Lynch, Patricia T. Gabbe (The Ohio State University Wexner Medical Center)

Moms2B is a community-based pregnancy support program designed to mitigate poor pregnancy outcomes in Columbus, Ohio. The Moms2B program recruited from 4 high risk infant mortality areas in 2014-2016 and from an additional 4 areas in 2017. We compared Moms2B participant demographics to vital records data from these target areas. Women were considered Moms2B participants if they initiated prenatally in the program (N=1,093). The target population was established from vital records data from mothers who resided in one of the target zip codes served by Moms2B (N=12,292). Moms2B participants attended a median of 7 prenatal sessions (range: 1-33), with 89% attending two or more. Participants had a median age of 25 (range: 13-53), compared to 27 in the target population (range: 12-51). Almost half of Moms2B moms resided in a target zip code (49%). Participants were less educated compared to mothers in the population (at least some college education: 29%, 95% CI: 27%, 32% vs. 41%). The majority of participants identified as non-Hispanic black (55%, 95% CI: 52%, 58%), compared to 44% of the population; 6% of participants identified as Hispanic (95% CI: 5%, 8%), slightly lower than the population (9%). 83% of Mom2B participants had Medicaid (95% CI: 81%, 86%) compared to 65% of those who gave birth in the target population. 37% of women who attended two or more Moms2B sessions had at least some college education (95% CI: 32%, 42%) compared to 21% of moms who only attended one session (95% CI: 10%, 35%). Of women who only attended one session, 16% were Hispanic (95% CI: 7%, 30%) compared to 6% of moms who attended two or more sessions (95% CI: 4%, 9%). Moms2B has been successful in enrolling women at highest risk of infant mortality, Non-Hispanic black women with low educational attainment. Attendance rates are encouraging despite the barriers this population faces.

FEASIBILITY OF A DUAL INTERVENTION TO SUPPORT BREASTFEEDING AND WEIGHT MANAGEMENT IN URBAN AFRICAN AMERICAN WOMEN Jean Kerver, Gayle Shipp, Gwendolyn Norman, Kathryn Brogan-Hartlieb, Joseph Gardiner, Charles Barone, Steven Ondersma, Nigel Paneth, Robert Sokol, Gwen Alexander (Michigan State University)

Maternal diet and infant feeding practices are important for maternal and infant health but are notoriously subject to confounding and many unanswered causality questions remain. Our goal was to assess feasibility of a randomized controlled trial (RCT) in an underserved population with a peer-support intervention (INT) to increase breastfeeding duration and reduce postpartum (PP) weight retention. Employing a 2-arm RCT, we recruited African-American women intending to “try breastfeeding” (n=53) in mid-pregnancy from a prenatal care clinic in Detroit, MI, randomized participants to the INT (n=28) or to usual care (UC) (n=25), and followed to 20 wks PP. Data were collected at enrollment (T1), 6 (T2) and 20 wks PP (T3) and included surveys, measured weight, and maternal blood and urine at T1 and T2. The INT included 3 in-person visits (prenatal, 3 d and 6 wks PP) from a peer counselor with phone/text follow-up. Mean age (SD) was 28.3 (6.4) y; mean pre-pregnancy BMI (SD) (per medical record) was 31.9 (9.9) kg/m². Participant retention was 68% at T3; however, after extensive changes mid-study, subgroup analyses show participant retention improved to 87% at T3 for the last 30 women enrolled. There were no significant differences in breastfeeding duration or weight retention between the INT and UC groups at T3, however, breastfeeding rates were high with 47% in each study arm breastfeeding at T3, a likely reflection of the delivery hospital’s newly acquired “Baby-Friendly” status. Results on weight retention (weight at T3 – pre-pregnancy weight) favored the INT (mean [SD] weight retention=1.5 [19.2] lbs for INT vs. 11.7 [21.6] lbs for UC, p=0.167). Survey results revealed important insights on moderating factors (e.g., depression, sleep, self-efficacy, social support, diet, physical activity), allowing this pilot trial to inform INT refinement for use in a larger, longer study to test INT effects on a variety of obstetric and pediatric health outcomes.

ASSOCIATION BETWEEN NEIGHBORHOOD ETHNIC DENSITY AND MATERNAL AND NEONATAL HEALTH CONDITIONS: A SYSTEMATIC REVIEW Marzieh Ghiasi, Claire Margerison (Michigan State University)

Purpose: Disparities in adverse pregnancy and perinatal conditions have been linked with aggregation of co-ethnic populations, characterized as neighborhood ethnic density. However, there exists no comprehensive synthesis of the evidence examining maternal and neonatal health in non-white/non-black high ethnic density neighborhoods. In this systematic review we examined this association and explored the impact of factors such as foreign-born concentration. **Methods:** Studies published up to October 26, 2018 were systematically identified through a search of PubMed, Web of Knowledge and Scopus, and manually through references of articles, reviews and books. We selected articles based on inclusion criteria including peer-reviewed English language, quantifiable measures of exposures and outcomes for populations and conditions of interest. Study characteristics and effect estimates were extracted for articles and synthesized, focusing on emergent themes. **Results:** In total, we screened 832 citations for titles and abstracts. The full text of 67 articles was retrieved and reviewed, and 18 studies met the inclusion criteria. Four outcome categories emerged from the literature. Neighborhood ethnic density was adversely associated with maternal gestational diabetes. However, in studies where an association was observed between high neighborhood ethnic density and infant mortality, pre-term birth (<32 weeks), and low birth weight (<2500g), we found both adverse and protective associations. Foreign-born density was not a protective factor for the outcomes under consideration. **Discussion:** Associations between ethnic density and outcomes of interest were mixed. We found high heterogeneity in the operationalization of neighborhood ethnic density as an exposure. Future research should focus on elucidation of pathways by which ethnic enclaves exert their effects on maternal and neonatal health outcomes of the residents, specifically focusing on acculturation and health behaviors.

PREDICTORS OF BREASTFEEDING IN THE NATIONAL IMMUNIZATION SURVEY-CHILD Erika Fuchs, (University of Texas Medical Branch)

Background: The American Academy of Pediatrics (AAP) recommends exclusive breastfeeding for the first 6 months of an infant's life followed by breastfeeding and complementary feeding for at least 1 year. Despite recent improvements in breastfeeding initiation in the United States, the proportion of children who receive any infant formula remains high. The aim of this study was to identify demographic predictors of initiation of and continued breastfeeding in a nationwide sample.

Methods: Predictors of breastfeeding were examined using data from the 2017 National Immunization Survey (NIS) – Child. Participants were included if they had adequate provider data (n=15,333). Demographic variables in adjusted models included: child's age, sex, race/ethnicity, census region, whether child was the firstborn, household income, Women, Infants, and Children (WIC) participation, language, insurance, and maternal age, education, and marital status. Probabilities of breastfeeding were estimated from predictive margins after weighted unadjusted and adjusted logistic regression models using Stata SE version 15.1.

Results: Most (84.4%) children had ever been breastfed. By 3 and 6 months, 66.1% and 34.7% of children were exclusively breastfed, respectively. At 12 months, 32.0% were still breastfed with no supplemental formula. After adjustment, participation in WIC was consistently associated with breastfeeding outcomes at each time point. Ever participating in WIC was associated with lower rates of breastfeeding ever (-9.2%, 95% confidence interval (CI) -13.1, -5.2), exclusive breastfeeding at 3 months (-7.2% 95% CI -13.2, -1.2) and 6 months (-8.2%, 95% CI -13.5, -2.5), and still breastfeeding at 12 months (-13.3%, 95% CI -18.3, -8.2).

Conclusion: Though breastfeeding initiation is high, breastfeeding according to AAP guidelines falls throughout infancy. It is likely that barriers to breastfeeding remain among all women and especially those participating in the WIC program.

SURGICAL REMOVAL OF TONSILS AND ADENOIDS IN CHILDREN: USING POPULATION DATA TO EVALUATE IMPACT OF TIMING OF SURGERY AND POST-OPERATIVE OUTCOMES Francisco Schneuer, Chris Dalton, Susan Adams, Leslie White, Adam Elshaug, Natasha Nassar (The University of Sydney)

Background: Adenotonsillectomy (ADT), tonsillectomy (TS) and adenoidectomy (AD) are the most common surgeries performed in children. We aimed to determine the burden of ADT, TS and AD on child health and evaluate their post-operative outcomes. Methods: We included all children aged <16 years undergoing ADT, TS or AD in New South Wales, Australia, 2001-2014. Health information was obtained from administrative hospitalization data. The association between age and outcomes including post-operative complications and re-operation were evaluated using generalized estimating equations and Kaplan-Meier methods, respectively. Results: A total of 101,138 children had ADT, 21,426 TS and 45,215 AD. Population rates of ADT doubled in 2001-2014 (34 to 68 per 10,000 children), TS rates decreased from 13 to 8 per 10,000 children and AD increased from 20 to 28 per 10,000. Overall, 5,967 (5.9%), 1,422 (6.6%) and 1,198 (2.9%) had post-operative complications (mostly hemorrhage) following ADT, TS and AD, respectively, while 2,229 (2.2%), 481 (2.2%) and 4,866 (10.4%) children required re-operation. Compared to children aged 2-3 years (lowest risk), children 0-1 years undergoing ADT and TS had 1.8-fold (95%CI: 1.58-2.04) and 2.3-fold (95%CI: 1.68-3.11) increased risk of post-operative complication, respectively. This risk increased with age. Five-year re-operation rates following ADT, TS and AD were highest for children aged 0-1 years at index surgery at 10.3%, 15.6% and 32.1%, respectively, and steadily decreased with age to 0.9%, 1.4% and 4.7% for 8-9 year olds. Conclusions: Surgical removal of tonsil and adenoids in children have significantly increased in the last decade with 1 in 150 children undergoing surgery in 2014. These findings highlight surgery is not without risk and with highest re-operation rates in children having surgery at youngest ages. More judicious use of surgery and treatment with conservative measures should be first line of management.

PREDICTORS OF BREASTFEEDING DURATION IN THE NEW HAMPSHIRE BIRTH COHORT STUDY Kathryn Crawford, Lisa Gallagher, Margaret Karagas, Megan Romano (Dartmouth College, Geisel School of Medicine)

Breastfeeding has significant health benefits for infants and mothers, including optimal nutrition, improved postpartum health and reduced risk of chronic disease. The American Academy of Pediatrics recommends infants be exclusively breastfed for the first 6 months (mo) of life, and as a supplement to solid foods until 1 year (yr). However, studies consistently identify lower breastfeeding rates among U.S. infants. Sociodemographics and maternal health are among factors known to influence breastfeeding outcomes, yet specific factors tend to vary regionally and demographically. In this study, we examined breastfeeding in mother-infant pairs enrolled in the New Hampshire Birth Cohort Study between 2010-2018 (n=1773). Pregnant women 18-45 years old were enrolled during prenatal care visits in New Hampshire at ~24-28 weeks gestation and have been followed since enrollment. Breastfeeding status was obtained from postpartum questionnaires and covariates related to maternal and infant health and sociodemographics were abstracted from medical records and prenatal and postpartum questionnaires. 95% of infants were breastfed at least once, yet only 29% were exclusively breastfed at 6mo and 28% were at least sometimes breastfed at 1yr. We evaluated the effects of maternal age, race, education, relationship status, body mass index (BMI), smoking and parity, as well as infant sex, ponderal index, gestational age and delivery mode on breastfeeding duration (mo) using multiple linear regression. Maternal age ($\beta=0.17$, 95% confidence interval (CI)=0.05, 0.28), parity ($\beta=2.35$, 95% CI=0.90, 3.81) and education ($\beta=0.96$, 95% CI=0.40, 1.53) were positively associated with any breastfeeding duration (mo). BMI was significantly negatively associated ($\beta=-0.18$, 95% CI=-0.26, -0.09). These findings are consistent with prior studies. Given the public health importance of breastfeeding for infants and mothers, interventions are needed to support women to extend their breastfeeding duration.

PERINATAL RISK FACTORS AND THEIR ASSOCIATION WITH FALSE POSITIVE NEONATAL HEARING SCREENING RESULTS Nicole Talge, Melanie Adkins, , (Michigan State University)

Neonatal hearing screening programs facilitate the detection of hearing loss and access to time-sensitive interventions. However, there is speculation that neonatal hearing screening failure in absence of diagnosed hearing loss may reflect risk for neurodevelopmental disorders. We aim to investigate whether male sex and preterm delivery, two replicable risk factors for neurodevelopmental disorders, are associated with false positive results at initial screening. To do this, we linked birth certificate and Early Hearing Detection and Intervention data maintained by the Michigan Department of Health and Human Services. Singleton births (2007-2015) with available hearing screening data were eligible for analysis (n=863,589). We then excluded children with conductive, sensorineural, or mixed hearing loss to yield our analytic sample (n=856,928). False positive findings included newborns with “refer” results (right or left ear) at the initial screen. We obtained sex and preterm delivery (early: <34 weeks; late: 34-36 weeks) information from birth certificates, the latter of which was based upon obstetric estimates of gestational age. Approximately 4% of newborns obtained “refer” results in the absence of hearing loss. Male newborns were more likely to obtain these false positive findings (OR=1.2, 95% CI: 1.2, 1.3), along with children born early and late preterm (OR=1.3, 95% CI: 1.4, 1.5; OR=1.4, 95% CI: 1.1, 1.4, respectively). Findings persisted following adjustment for socio-demographics, congenital anomalies, and age at screening, except for the early preterm finding which attenuated to non-significance. Perinatal risk factors linked to neurodevelopmental disorders are associated with a small, but significantly greater likelihood of false positive neonatal hearing screening results. Future research is needed to examine the factors underlying these findings and whether false positive results are associated with neurodevelopmental disorder diagnoses.

EFFECTS OF INTEGRATED POSTPARTUM MATERNAL ANTIRETROVIRAL TREATMENT AND INFANT CARE (MCH-ART) ON GROWTH AND MORBIDITY OF HIV-EXPOSED INFANTS IN SOUTH AFRICA: A RANDOMIZED TRIAL Ayesha Sania, Stanzi le Roux, Kirsty Brittain, Tamsin Phillips, Allison Zerbe, Agnes Ronan, Landon Myer (Columbia University)

Background: Integration of maternal antiretroviral treatment (ART) and HIV-exposed infant (HEI) follow-up into maternal-child health (MCH) services is hypothesized to improve HEI health. We evaluated the effects of integrating MCH and ART care on undernutrition and infectious morbidity in South African HEIs. **Methods:** Using a randomized trial, we compared an integrated MCH-ART service to standard of postpartum care (SOC, general ART services for mothers and separate HEI follow-up at well-baby clinics). All women received general antenatal and HIV care at a primary care centre. Eligible, mother-infant pairs were randomized in the neonatal period. Data on infant anthropometry and morbidity were collected at 6 weeks, and 3-monthly from 3 to 12 months postnatal. Mixed effects models evaluated intervention effects on weight-for-age (WAZ) and length-for-age (LAZ) z scores. Mean weight- and length-velocity-for-age z scores were compared using T-tests. Incidence and prevalence of diarrheal and respiratory morbidity were compared using Poisson models. **Results:** Of 471 mother-infant pairs randomized between March 2013 and June 2014, 441 (MCH-ART, n=218; SOC, n=223) were eligible for this study. During 403 child-years of follow-up, compared with the World Health Organization (WHO) standards mean WAZ increased over time; LAZ slowly increased during the first 8 months and declined thereafter. Comparing MCH-ART to SOC, there were no differences in mean WAZ ($\beta = -0.14$, 95% confidence interval, CI: -0.35, 0.07) or LAZ ($\beta = -0.05$, 95% CI: -0.27, 0.17). Incidence of diarrhoea was similar between study arms (MCH-ART vs SOC: risk ratio, RR: 1.01 95% CI: 0.78, 1.31); incidence of respiratory infection was slightly elevated in the MCH-ART arm (RR: 1.19, 95% CI: 1.01, 1.40). **Conclusion:** In a setting with good primary care ART and child health services, our findings suggest no beneficial effect of an integrated MCH-ART service on the early growth and morbidity of breastfed infants.

PRESCRIPTION OPIOID USE IN CHILDREN AND ADOLESCENTS IN AUSTRALIA, 2013-2017: A NATIONAL POPULATION-BASED STUDY

Jane Bell, Timothy Nielsen, Simon Paget, John Collins, Nicholas Buckley, Sallie Pearson, Natasha Nassar (University of Sydney)

Background There are few population-based studies of paediatric opioid use; most research has focussed on specific populations or health settings. We investigated rates of opioid dispensing to Australian children and young people. **Methods** Using a 15% random sample of children and young people in Australia, and their dispensing history, we identified a cohort from birth to <18 years who were dispensed at least one opioid in 2013-2017. We calculated annual prevalence rates in opioid use by age group (all, <1, 1-4, 5-12, 13-17 years) and opioid characteristics (weaker/stronger, short/long acting) and determined trend using Poisson regression. We identified those with new use (no opioid dispensing in previous 90 days) and quantified the number of dispensings in the year following. **Results** Over 2013-2017, prevalence of opioid use fell from 148 to 135/10,000. Rates increased for 1-4 year olds (29 to 32/10,000), were stable in those aged 5-12 years (~49/10,000) and fell in adolescents (440 to 405/10,000). Use of stronger opioids (mainly oxycodone) increased in every age group; weaker opioids (mainly codeine) declined in all except infants. Annual prevalence of short acting opioids decreased; use of long acting opioids increased. Of children and adolescents with a new course of treatment, 80.2% had one dispensing only, 18.0% had 2-4 and 1.8% ≥ 5 dispensings in the year following. Primary care physicians prescribed 47.6% of dispensings, medical specialists 28.4% and others 22.4%. **Conclusion** One in 74 Australian children was dispensed an opioid and rates fell over time. Rates were highest in adolescents (1 in 25), but 4-9 times lower than the USA, possibly due to restrictions and regulations on marketing and prescribing in Australia. We saw a trend in prescribing of weaker to stronger opioids, and increased prescribing of longer-acting opioids, but this was low. Few received ≥ 5 dispensings in the year following new use. Real-time monitoring may reduce potential misuse.

ADDRESSING THE RISE OF CONGENITAL SYPHILIS IN CALIFORNIA AND LOUISIANA: WORKING TOWARD SETTING-SPECIFIC SOLUTIONS AMONG HIGH-RISK PREGNANT WOMEN Emily Harville, Pierre Buekens, Gloria Giarratano, Eunhee Park, Jennifer Wagman (Tulane University)

Congenital syphilis is completely preventable through effective antenatal screening and treatment, but has been rising in recent years in the United States. Kern County, CA and East Baton Rouge Parish, LA are two of the highest congenital syphilis frequency jurisdictions. The objective of this study was to assess the knowledge, attitudes, and factors that influence decision-making and behavioral practices surrounding congenital syphilis among high-risk pregnant women and prenatal care providers. 20 in-depth interviews were conducted with health care providers at the two sites, and 7 focus groups were held with high-risk pregnant and postpartum women. A transcript of each interview and focus group was imported into QSR NVivo and coded, and text extracted and organized to identify emergent themes. Most providers were aware that the rates of congenital syphilis were higher in their regions. For treatment, most referenced guidelines by the American Congress of Obstetricians and the Center for Disease Control. Most women were aware that syphilis was a sexually transmitted disease and the basic precautions necessary to prevent it, though were not necessarily knowledgeable about the details of the effects of congenital syphilis. Providers and women agreed that gaps in prevention and treatment included delays in entering prenatal care, delays in receiving treatment, lack of a rapid test meaning that results required 24-48 hours, and lack of partner testing and treatment. High-risk women often had multiple risk factors, including homelessness and substance use, which limited their ability to access care and made them wary of providers. Women also mentioned difficulties in being approved for Medicaid and finding a provider who would take their Medicaid plan, as well as transportation to the clinic. Interventions at the policy, community, social network, and individual level may be necessary to reverse the trends in congenital syphilis.

DOES BIRTH ANTHROPOMETRY MEDIATE THE ASSOCIATION BETWEEN MATERNAL PRE-PREGNANCY OVERWEIGHT/OBESITY AND CHILDHOOD OVERWEIGHT/OBESITY IN A COHORT OF AFRICAN AMERICAN CHILDREN? Danielle Stevens, Sarah Taylor, Roger Newman, John Vena, James Roberts, Brian Neelon, Kelly Hunt (Medical University of South Carolina)

Objective: To examine to what extent the association between in utero exposure to maternal adiposity and childhood adiposity is mediated by birth anthropometry in a cohort of African Americans. **Study Design:** 1,023 African Americans from one southeastern hospital system were included in analyses. Logistic regression provided odds ratios and 95% confidence intervals (OR [95% CI]) for the association between maternal pre-pregnancy BMI category (overweight/obese vs normal weight) and offspring overweight/obesity in childhood. Models adjusted for maternal and child sociodemographics (model 1) and additionally for gestational cardiometabolic disorders (model 2). A natural effects model framework was used to estimate the natural direct effect and natural indirect effect of weight, length, head circumference, and ponderal index at birth for this association. **Secondary analyses** assessed moderation of these effects by child's sex. **Results:** Children exposed to maternal pre-pregnancy overweight/obesity had significantly increased odds of being overweight/obese as opposed to those with normal weight mothers (Model 1 OR: 1.82 [1.34, 2.48], Model 2 OR: 1.89 [1.38, 2.59]). The natural indirect effect of maternal pre-pregnancy overweight/obesity on child's odds of overweight/obesity was significant for the child's weight at birth (Model 1 OR: 1.08 [1.02, 1.13], Model 2 OR: 1.09 [1.02, 1.13]), but not for child's birth length, head circumference, or ponderal index. There was no significant moderation of the natural direct or indirect effect by sex for any of the measures of birth anthropometry. **Conclusions:** Our study suggests that birth weight plays a small role in mediating the association between maternal pre-pregnancy overweight/obesity and offspring overweight/obesity and childhood, but most of this association takes place via a direct effect. Future studies should assess alternative pathways of interest to identify other mediating factors of this association.

FOLIC ACID ANTAGONIST USE DURING PREGNANCY Stephen Kerr,
Samantha Parker, Martha Werler, Allen Mitchell (Slone Epidemiology Center)

Background: Evidence that folic acid (FA) intake reduces risk of neural tube defects (NTDs) is clear; for oral clefts, urinary defects and cardiac defects, it is suggestive. We previously found increased NTD odds ratios for use of dihydrofolate reductase inhibiting (DHFRI) medications and anti-epileptic drugs (AEDs), both of which affect folate metabolism. FA supplementation attenuated the risks associated with use of DHFRIs, but not AEDs. **Methods:** We re-examined DHFRI and AED use using recently-collected data from the Slone Birth Defects Study. The relevant exposure periods were periconception for NTDs and 1st trimester for oral clefts, urinary defects and cardiac defects. Odds ratios (aORs) and 95% confidence intervals (CIs) were estimated with multivariable logistic regression. Intake of >400 mcg FA was explored as an effect modifier. **Results:** The aOR for AEDs and NTDs was 2.8 (1.2,6.4); no cases were exposed to DHFRIs. AORs for AED use were also increased for oral clefts (1.9 (1.1,3.5)), urinary defects (1.5 (0.9,2.5)), and cardiac defects (1.4 (0.9,2.1)). No attenuation by FA intake was observed. DHFRI use was not associated with oral clefts or cardiac defects, but the aOR for urinary defects was 1.5 (0.7,3.1). **Conclusions:** Similar to our previous work, we found an association between AED use and NTDs that was not attenuated by FA intake. In contrast, we found aORs for DHFRI exposure were not associated with increased risks of NTDs, oral clefts, and cardiac defects, and possibly slightly elevated for urinary defects, with no clear evidence of FA effect modification. Our observed null results for DHFRI use may reflect moderated risks from higher serum FA levels resulting from increased exposure to folate through food fortification. However, the persistent risk among AED-exposed mothers with adequate FA intake supports a folate-independent ‘direct toxic effect’ of these medications.

ASSOCIATIONS BETWEEN CUMULATIVE ENVIRONMENTAL QUALITY AND ORAL CLEFT BIRTH DEFECTS Alison Krajewski, Kristen Rappazzo, Peter Langlois, Lynne Messer, Danelle Lobdell (ORISE/US EPA)

The etiology of most birth defects are unknown. While genetics, maternal factors (age, smoking) and environmental exposures have all been linked to birth defects such as oral cleft (OC), cleft palate (CP), and cleft lip with and without cleft palate (CL \pm CP), cumulative environmental quality (EQ) may also contribute to these associations. The Environmental Quality Index (EQI), a county-level measure of cumulative environmental exposure from 2000-2005, was used to explore potential associations with Texas Birth Defects Registry and birth records for OC, CP, and CL \pm CP births between 2000 through 2006 among Texas counties. Poisson regression models estimated the prevalence ratio (PR) and 95% CI for associations between increasing percentile (%) categories (75%) of overall and domain-specific EQI (air, water, land, sociodemographic (SD), built) and OC, CP, and CL \pm CP defects, adjusted for potential confounders. Comparing highest % category (worst EQ) to lowest % category (better EQ) for overall EQI, the PRs were 1.01 (95% CI: 0.93,1.10) for OC, 1.04 (0.96,1.14) for CP, and 0.99 (0.91,1.08) for CL \pm CP. In domain specific analyses, the strongest associations for all three defects were seen with the SD domain. The PRs for OC were 1.74 (1.32, 2.26) and 1.35 (1.22,1.50) for mid EQ and better EQ compared to the worst EQ. The PRs for CP were 1.45 (1.08,1.90) and 1.18 (1.05,1.32) for mid EQ and better EQ compared to the worst EQ. The PRs for CL \pm CP were 1.87 (1.43, 2.41) and 1.42 (1.28,1.57) for mid EQ and better EQ compared to the worst EQ. The results suggest that SD factors may contribute to the associations between OC, CP, and CL \pm CP birth defects, as observed in the SD domain. This abstract does not reflect EPA policy.

NON-GENETIC MATERNAL RISK FACTORS FOR THE VACTERL ASSOCIATION: A EUROCAT CASE-CONTROL STUDY Romy van de Putte, Iris van Rooij, Cynthia Haanappel, Maria Loane, Ingeborg Barisic, Hermien de Walle, Nel Roeleveld, Jorieke Bergman (Radboudumc)

INTRODUCTION: The VACTERL association is the non-random occurrence of at least three of these birth defects: vertebral, anal, cardiac, tracheo-esophageal, renal, and limb defects. Other than indications for several risk factors, such as pregestational diabetes and assisted reproductive techniques (ART) from case-reports and small studies, the etiology remains largely unknown. It is hypothesized that VACTERL has a multifactorial etiology in which genetic and non-genetic risk factors play a role. Our study aim was to identify non-genetic maternal risk factors for the VACTERL association in offspring. **METHODS:** A case-control study was performed using data from 25 EUROCAT registries over the period 1997–2015, ascertained through hospital records, birth and death certificates, questionnaires and/or post mortem examinations. We included 378 VACTERL cases and 43,583 controls with recognized syndromes or chromosomal abnormalities. Some registries were excluded from the analyses of specific maternal risk factors as they did not collect this information. Multivariable logistic regression analyses were performed to estimate maternal age and other confounder adjusted odds ratios (ORa) and 95% confidence intervals (95%CI). **PRELIMINARY RESULTS:** VACTERL patients were more often born from a first pregnancy than controls (ORa 1.5 [95%CI 1.1-1.9]). For couples who used ART, we found an increased risk of VACTERL (2.9 [1.8-4.6]) in offspring. This risk was higher when non-invasive ART (artificial insemination or hormonal treatment) was used (4.0 [2.1-7.6]). Maternal chronic illnesses, such as pregestational diabetes (3.0 [1.4-6.2]) and chronic lower obstructive pulmonary diseases (3.6 [2.3-5.6]) also increased the risk of having a child with VACTERL. Twin pregnancies were not associated with VACTERL (0.9 [0.4-1.8]). **CONCLUSION:** In this large case-control study, we identified several maternal non-genetic risk factors for VACTERL in offspring, which fits a multifactorial etiology.

HOSPITAL REVISIT RATES AFTER OUTPATIENT REPAIR OF DISTAL HYPOSPADIAS IN A LARGE, MULTI-STATE COHORT Yuri Sebastiao, Daryl McLeod, Jennifer Cooper, Christopher Brown, Daniel DaJusta (Nationwide Children's Hospital)

Background: Hypospadias is a common birth defect that occurs in 0.4% of U.S. boys. Surgical repair of distal hypospadias is usually an elective, outpatient procedure. While it has been reported that 7% of patients eventually need reoperations, short-term complications after distal hypospadias repair have not been reported in a representative population. We 1) examined the risk of unplanned hospital revisits following distal hypospadias repair 2) characterized reasons for surgery-related revisits and 3) identified risk factors for revisits. **Methods:** Patients aged 0-18 years who underwent outpatient, single-stage repair of distal hypospadias in 2010-2015 were identified using Current Procedural Terminology codes in the State Ambulatory Surgery Databases from 9 states. Hospital revisits occurring within 30 days after surgery were tracked after linkage with State Emergency Department and Inpatient Databases. Reasons for unplanned surgery-related revisits were identified by reviewing all available discharge diagnoses. Log-binomial regression with generalized estimating equations was performed to identify risk factors for unplanned revisits. **Results:** Among 4745 boys who had an initial distal hypospadias repair, 112 (2.4%) had an unplanned, surgery-related revisit within 30 days, 20 of whom required inpatient readmission. Patients aged ≥ 2 years at repair had an approximately twofold increased risk of revisit compared to infants aged < 1 (3.7% vs. 1.8%; RR: 1.9; 95% CI: 1.1-3.5). Postoperative pain and dysuria accounted for 28% of revisits among patients aged ≥ 2 years vs. 11% among infants. **Conclusions:** Over 2% of children undergoing a distal hypospadias repair have an unplanned surgery-related hospital revisit within 30 days. Patients aged ≥ 2 years at repair have a higher risk of revisit, suggesting potential advantages to early surgical repair. Our results can inform expectations and help guide the improvement of short-term outcomes from distal hypospadias repair.

PATIENT AND INFERTILITY TREATMENT CONTRIBUTORS TO CONGENITAL HEART DEFECTS AFTER INFERTILITY TREATMENT

Michael Davies, Kristyn Willson, Renae Fernandez, Alice Rumbold, Vivienne Moore (University of Adelaide)

Congenital Heart (CH) defects are a leading cause of death in the first year of life, and occur in around 8 per 1,000 births, but 16 per 1,000 after infertility treatment. There is a need to consider specific defect types by mode of treatment, together with a range of patient characteristics, in a representative sample. Participants, methods: The South Australian Birth Cohort is a census of all registrations of all births (n=302,811) and terminations of pregnancy for Jan 1986-Dec 2002, linked to all cycles of assisted reproductive technology (ART), and to all congenital anomalies notified to the 5th birthday (ICD-9 British Paediatric Association codes). Logistic regression was used to investigate associations between parental factors, treatment modality and the presence of CH defects. Results: Maternal age, nulliparity, and a history of miscarriage, pre-existing diabetes, gestational diabetes and hypertension, twins and higher order multiples, female baby sex each increased the risk of CH defects. Compared to the fertile population, after adjustment: a) Cardiac Septal Closure anomalies (BPA 74500-74599) did not vary by ART treatment, but were increased after infertility consultations conducted outside an ART clinic. b) A two-fold increase in Other Congenital Heart anomalies (BPA 74600-74699) was observed for OI, IVF fresh, IUI, and 'natural' conceptions to ART patients. c) A two-fold increase in Other Congenital Circulatory System anomalies (BPA 74700-74799) was observed for fresh IVF, IUI, and conceptions after infertility consultation outside an ART clinic; a four-fold increase for ICSI frozen. CH defects were related to maternal factors, mode of fertilization, gamete source, cryopreservation, and non-ART infertility care – most likely ovulation induction. Cryopreservation did not reduce the excess risk of cardiac defects. Further epidemiological and basic research is therefore required urgently.

IS THERE A PATERNAL OR GRANDMATERNAL AGE EFFECT ON PROBABILITY OF DOWN SYNDROME? A POPULATION-BASED, MATCHED CASE-CONTROL STUDY. Karen Schliep, Katherine Panushka, Michael Varner, Marcia Feldkamp, Heidi Hanson, Mike Hollinghaus, Alison Fraser, Ken Smith (University of Utah)

Background: Although fetal aneuploidy risk increases with maternal age, the majority of pregnancies complicated by Down Syndrome (DS) occur in younger women. It has been suggested that the age of the mother's mother at the time she delivered the fetuses' mother as well as paternal age may also play a role in DS risk. **Methods:** All DS cases in a statewide birth defects surveillance system (Utah, 1995–2010) who were members of 3-generation matrilineal pedigrees were included (n=566). Ten sex/birth year-matched controls were selected for each DS case. Maternal, grandmaternal, and paternal ages were categorized by 5-year intervals. Conditional logistic regression was used to model the association between maternal, grandmaternal and paternal age and DS. Effect modification by grandmaternal and paternal age was explored when looking at the association between maternal age and DS. **Results:** Mothers aged 35–39 years had a 3.8 adjusted odds ratio (aOR) (95% CI: 2.7, 5.2) and women ≥ 40 had a 15.7 aOR (95% CI: 9.6, 25.7) of having offspring with DS compared to women 25–29 (the modal maternal age group) after taking into account maternal race/ethnicity and grandmaternal age and race/ethnicity. No associations between grandmaternal age and DS were detected, whether assessed continuously (aOR: 1.01; 95% CI: 0.99, 1.03) or categorically. Effect modification by paternal (but not grandmaternal) age was observed in the association between maternal age and DS (likelihood ratio test, $P < 0.001$). Mothers < 25 years of age partnered with fathers ≥ 30 had a 1.8 higher odds (95% CI: 1.0, 3.2) of having offspring with DS compared to mothers < 25 years partnered with fathers < 30 years. **Conclusion:** While we find no association between grandmaternal age and DS risk in matrilineal grandchildren, our finding that paternal age independently increases risk of having DS offspring suggests that mother's age should not be the sole age-based consideration when assessing a couple's risk.

EVALUATION OF A PARENT-REPORTED ADHD SEVERITY**INDICATOR USED IN NATIONAL SURVEYS** Sana Charania, Melissa

Danielson, Joseph Holbrook, Robert McKeown (National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA, Oak Ridge Institute for Science and Education, Oak Ridge, Tennessee)

National children's health surveys include single-item indicators to describe disorder severity among children with a diagnosed disorder; however, the severity indicator for attention-deficit/hyperactivity disorder (ADHD) has not been validated against report of ADHD symptoms and impairment. This study used data from a nationally drawn survey about children with ADHD to investigate the relationship between a parent-reported, single-item indicator of ADHD severity and a standardized ADHD rating scale. This study considered children with parent-reported current ADHD ($n=2,495$). The respondent parents reported on their child's ADHD severity (mild, moderate, severe) and presence of symptoms ($k=18$) and impairment ($k=8$) using the Vanderbilt ADHD Diagnostic Parent Rating Scale. We considered co-occurring conditions and demographic characteristics as potential confounders. We conducted multinomial logistic regression and ANOVA to quantify the relationship between symptom and impairment item counts and ADHD severity. SUDAAN v11.0.1 was used to account for the complex design and sampling weights. Higher inattentive symptom counts, hyperactive/impulsive symptom counts, and impairment item counts were associated with greater parent-reported ADHD severity. The adjusted mean total ADHD symptom count by severity was 7.0 for mild ADHD, 10.0 for moderate ADHD, and 12.5 for severe ADHD ($p<0.001$) after incorporating confounders. The adjusted mean ADHD impairment item counts were 2.0 for mild ADHD, 2.5 for moderate ADHD, and 3.0 for severe ADHD ($p<0.001$) after incorporating confounders. This study provides evidence for the utility of the parent-report of ADHD severity indicator by showing that children reported as having more severe ADHD had higher symptom and impairment item counts than children reported as having milder ADHD. These findings can be used to interpret results that consider the relationship of ADHD severity to other characteristics or outcomes on national surveys.

NEONATAL POLYUNSATURATED FATTY ACID LEVELS AND AUTISM SPECTRUM DISORDER Kristen Lyall, Kristen Lyall, Gayle Windham, Casey Whitman, Nathaniel Snyder, Rostislav Kuskovsky, Lucy Robinson, Craig Newschaffer (Drexel University)

Polyunsaturated fatty acids (PUFAs) are critical for early neurodevelopment. The purpose of this study was to determine whether neonatal levels of PUFAs differ in children with ASD as compared to those without ASD. We conducted a population-based case-control study including 200 cases, identified from the California Department of Developmental Services (DDS), and 200 controls randomly selected within strata of matching factors (sex, month and year of birth 2011-2013) from birth certificate files after excluding DDS clients. PUFA levels were measured in archived newborn blood spots using liquid chromatography mass spectrometry. The association between PUFA levels (as individual fatty acids and as total PUFAs) and ASD was examined using conditional logistic regression to obtain adjusted odds ratios (ORs) and 95% confidence intervals (CIs), as well as using cubic splines. PUFAs were quantifiable above background levels in newborn bloodspots. Geometric mean levels did not significantly differ between cases and controls. No significant associations were observed between quartiles of PUFAs and ASD. In spline analyses, linoleic acid demonstrated a significant non-linear association with ASD ($p=0.002$), with increasing odds for low levels and decreasing odds for high levels. Non-significant, but suggestive, associations were observed when examining extremes of the distribution relative to the interquartile range (highest 5th percentile $OR=0.25$, 95% CI 0.06, 1.01; lowest 5th percentile $OR=2.20$, 95% CI 0.92, 5.25). Findings from this population-based case control study therefore suggest potential non-linear associations for certain neonatal PUFAs. Further, hypothesized reductions in risk of ASD for those with the very highest levels and increases in risk for those with the very lowest levels of total neonatal PUFAs may be supported, but further examination in larger sample sizes is needed.

DELAYED COGNITIVE AND LANGUAGE DEVELOPMENT IN 4-6-YEAR-OLD HIV-INFECTED CHILDREN COMPARED TO HIV-EXPOSED UNINFECTED AND HIV-UNEXPOSED CHILDREN IN KWAZULU-NATAL, SOUTH AFRICA

Rachel Gruver, Sumaya Mall, Jane Kvalsvig, Justin Knox, Claude Mellins, Chris Desmond, Shuaib Kauchali, Stephen Arpadi, Myra Taylor, Leslie Davidson (Columbia University Mailman School of Public Health)

Background: Perinatal HIV infection is associated with delays in cognitive and language development. However, less is known about these outcomes in children perinatally exposed to HIV but not infected, particularly in low and middle-income countries. We compared cognitive outcomes and language acquisition in HIV-infected (HI) children versus HIV-exposed uninfected (HEU) children and HIV-unexposed uninfected (HUU) children at 4-6 years of age in a population-based sample. **Methods:** The Asenze study enrolled 1581 children 4-6 years old, 77% of those living in 5 areas in KwaZulu-Natal, South Africa. Children completed the South African-validated Grover-Counter Scale of cognitive development (GCS), the Kaufman Assessment Battery for Children II (KABC-II), and the Reynell Developmental Language Scale (RDLS). HIV status of children & primary caregivers was determined by repeated rapid tests (94% and 65% respectively) or caregiver report of prior testing. The final sample with complete HIV data included 922 mother-child pairs. We used ANOVA to compare developmental outcomes by HIV exposure status (multivariable analysis will also be presented). **Results:** HI children scored significantly lower on the GCS (mean[95%CI]: HI=17.9[14.3-21.5], HEU=24.5[22.9-26.2], HUU=24.8[23.7-26.0]), the KABC-II Hand Movement test of nonverbal working memory (HI=3.6[3.1-4.1], HEU=4.6[4.3-4.8], HUU=4.5[4.3-4.7]), and the RDLS (HI=101.6[97.2-106.1], HEU=106.6[105.5-107.7], HUU=106.3[105.5-107.1]). On all measures of cognitive development, children in the HI group (n=38) scored lower compared to HEU (n=257) and HUU (n=627), while the latter two groups had similar scores. **Conclusions:** We found significant developmental and language delays in the HI group compared to the HEU and HUU groups. HEU children had similar outcomes to HUU children. Emerging success of efforts to eliminate vertical transmission of HIV globally may positively impact child development in addition to reducing mortality.

NEWBORN SCREENING THYROID STIMULATING HORMONE CUT-OFFS AND COGNITIVE OUTCOMES: A MATCHED SIBLING ANALYSIS

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Background: Newborn screening (NBS) of infant thyroid hormone (TSH) concentrations in the first few days of life has virtually eliminated intellectual disability caused by congenital hypothyroidism (CH) in developed countries. Our large population-based study showed infants with neonatal TSH levels below NBS cut-offs for CH ($<20\text{mIU/L}$) had increased risk of poor educational outcomes. This observed association may be confounded by genetics or shared family environment. **Aim:** To evaluate the association between neonatal TSH levels and cognitive outcomes amongst a cohort of matched siblings. **Methods:** Population-based record-linkage study of term-born matched sibling pairs without neurological anomalies undergoing NBS from 2001-2007 in New South Wales, Australia, with subsequent school-based assessment of literacy and numeracy. Infants with newborn TSH levels $<5\text{mIU/LWB}$ were classified as having 'normal TSH' and infants with a TSH $8\text{--}<20\text{mIU/LWB}$ classified as 'mildly elevated TSH'. The analysis included 494 sibling pairs of discordant TSH groups. Multivariable logistic regression was used to account for potential perinatal confounders. **Results:** Among the 988 children included, a greater proportion of siblings in the 'mildly elevated TSH' group were males (59% vs 52% of 'normal TSH' group), born via cesarean section (53% vs 46%) and were the older sibling (53% vs 47%). Siblings with 'mildly elevated TSH' were more likely to have poor writing scores (adjusted Odds Ratio (aOR) 2.26 95% CI 1.26-4.04) and poor reading scores (aOR 1.49 95% CI 0.91-2.45), however numeracy scores were not associated with mildly elevated TSH levels (aOR 0.94 95% CI 0.59-1.47). **Conclusions:** Mildly elevated newborn TSH levels below NBS thresholds are significantly associated with poor writing outcomes after adjustment for environmental, genetic and perinatal factors. Lower NBS screening cut-points may be warranted for optimal identification and treatment of children at-risk.

FAMILY PSYCHOSOCIAL ENVIRONMENT, INTERNALIZING BEHAVIOR, AND CHILDHOOD OBESITY: A STRUCTURAL EQUATION MODEL Liying Zhang, Shooshan Danagouliau, Dawn Misra, Samiran Ghosh, Phillip Levy (Wayne State University School of Medicine)

Family psychosocial stressors faced by children have an impact on risk of childhood obesity. The purpose of this study is to assess the pathways between family psychosocial environment and childhood obesity. Secondary data analyses were conducted with the Child Development Supplement of the Panel Study of Income Dynamics. Children aged 6-17 years (N=3,019) were selected as the study sample. BMI was calculated from reported height and weight with overweight/obese categorized by BMI at 85th percentile/higher for age. We used two measures of family stress: family conflict using a subset of questions adapted from the Family Environment Scale (Cronbach's $\alpha=0.71$); parental distress using questions adapted from the Kessler Psychological Distress Scale K10 (Cronbach's $\alpha=0.76$). On the basis of the family conflict and parental distress we built a latent variable of family psychosocial environment. Child internalizing behavior was assessed using 14 questions in the metric of Behavior Problems Index (Cronbach's $\alpha=0.85$). Structural equation modeling was performed using AMOS. Missing data were imputed using multiple imputation. Mean age was 10.9 years (SD=3.34); 50.3% were female; 41.7% were African American. Mean BMI was 20.7 (SD=5.84). About 15% were overweight or obese according to BMI. Internalizing behavior was positively associated with overweight/obesity. A stressful family environment was positively associated with internalizing behavior (path coefficient=0.53, $p<0.001$). Internalizing behavior had a direct effect on overweight/obese (path coefficient=0.067, $p<0.01$). Family psychosocial environment was associated with overweight/obesity only in an indirect path through internalizing behavior (path coefficient=0.036, $p<0.01$). Model-data fit based on the cutoffs of several commonly used indices which suggest that the hypothesized models fit well. Internalizing behavior appears to mediate the connection between family psychosocial environment and childhood obesity.

EFFECT OF EARLY CHILDHOOD CARE ON SCHOOL-AGED CHILDREN'S ADIPOSITY IN QUEBEC, CANADA Tanya Murphy, Jay Kaufman, Seungmi Yang (McGill University)

Objectives: We estimated the effects of early childhood education and care (ECEC) on children's adiposity in the era of a universal childcare program in Quebec, Canada. We also examined whether effects differed for children from more or less advantaged homes, and whether adiposity-by-childcare differences persisted through elementary school. **Methods:** Data from a birth cohort with annual follow-up of 1999 children were analyzed using Bayesian multilevel linear regression. Body mass index z-scores (BMI_z) of children who attended predominantly center-based ECEC (CB) were compared to those who attended unregulated (UH) or regulated home-based care (RH) or did not regularly attend ECEC (P). Childcare effect estimates were adjusted for many pre-ECEC variables that predicted BMI_z, including parents' BMI, and perinatal and socioeconomic variables. Average treatment effects were calculated from the differences between the posterior predictive distribution for four ECEC profiles from the age of 2 to 5 years: 35 hours per week in 1) CB, 2) RH, 3) UH, and 4) <10 hours per week in non-parent care (P). Family disadvantage was measured using a multi-variable score. **Results:** Our model predicted that following CB, children would have a mean BMI_z of 0.18 (95% credible interval [CrI]: 0.03, 0.32) in kindergarten (6 years) and that BMI_z would have been 0.31 SD lower (95% CrI: -0.54, -0.08) for RH, 0.12 SD lower (95% CrI: -0.35, 0.11) for UH, and 0.29 SD lower (95% CrI: -0.52, -0.07) for P. By grade 4 (10 years), mean BMI_z had increased but was similar for all ECEC groups (0.15 to 0.33 SDs). Family disadvantage did not greatly modify the BMI_z-by-childcare effects, but the estimates were imprecise. **Conclusion:** Although center-based ECEC may have caused adiposity to rise earlier, Quebec's ECEC options had no large, enduring effects on adiposity, in general, or for disadvantaged children, in particular.

AN EPIDEMIOLOGIC PROFILE OF MIDDLE CHILDHOOD USING THE 2016-2017 NATIONAL SURVEY OF CHILDREN'S HEALTH

Sarika

Parasuraman, Reem Ghandour (Maternal and Child Health Bureau, Health Resources and Services Administration, US Department of Health and Human Services)

Background: Little research describing the health and determinants associated with middle childhood currently exists. The purpose of this study is to present an epidemiologic profile of middle childhood, and national estimates describing sociodemographic, health status, and behavior characteristics of this population. **Methods:** We analyzed data among children ages 6-11 years using the 2016-2017 National Survey of Children's Health, administered through HRSA's MCHB. Variables covered three categories: sociodemographic, family, and neighborhood characteristics; health status indicators; and behaviors. Weighted descriptive analyses determined the distribution of these characteristics among the middle childhood population, and bivariate analyses examined differences among children by age subgroup for select variables. **Results:** The 2016-2017 NSCH dataset contains information for 21,539 children ages 6-11 years. Regarding health indicators, 21% are children with special health care needs, 21% had allergies, 9% had asthma, and 6.5% had diagnosed anxiety. Regarding behaviors, 33% of these children got less than the recommended 9 or more hours of sleep per night, and 60% report a weekday average of 1-3 hours of screentime. As children aged through middle childhood, there was a significant increase in diagnosed anxiety ($p < 0.001$). Older age was also associated with a decrease in average hours of sleep per day ($p < 0.01$) and an increase in screentime ($p < 0.001$). **Discussion:** This study establishes a baseline to understand the current health state of the middle childhood population, and track trends in health, behaviors, and development through a comprehensive set of indicators. Identifying issues impacting the health and well-being of this population may help us better understand and identify their unique needs, and inform how potential targeted interventions might best serve middle childhood in the continuum of services available between early childhood and adolescents.

BIOMARKERS OF PREGNANCY IRON STATUS AND CHILD

BEHAVIORAL OUTCOMES AT AGE 4-6 Y Jean Kerver, Diana Haggerty, Nicole Talge, Brooke Slawinski, Brooke Ingersoll, Daniel Keating, Karen Racicot, Nigel Paneth (Michigan State University)

We assessed the association of pregnancy iron status with autism spectrum disorder (ASD) symptoms of offspring at age 4-6 y in the Archive for Research in Child Health (ARCH) study, which enrolled women at first prenatal clinic visit in Lansing, MI (2008-2016; n=1,042). Serum was obtained at enrollment, aliquoted, and stored at -80°C. A subset of families participated in the ARCH Child Development study (n=132) where we obtained parent reports of symptoms associated with ASD using the Social Responsiveness Scale (SRS)-2, yielding sex- and age-referenced scores. We used 3 measures of iron status to allow assessment of iron deficiency (ID) in the presence of inflammation: serum ferritin (known to be increased by inflammation), serum soluble transferrin receptor (sTfR), and the sTfR/ferritin ratio or total body iron (TBI). Findings are presented from the 66 mother-infant pairs with complete data on iron status and SRS-2 after excluding twins and infants born before 37 wks. The study sample was 72% White, 13% Black and 15% Latina, with a mean maternal age of 34.4 y. Mean ferritin, sTfR, and TBI levels were 79.5 ng/mL, 1.5 mg/L, and 12.2 mg/kg, respectively. TBI and sTfR showed weak, non-significant correlations with SRS-2, but ferritin was positively correlated with SRS-2 scores (Pearson correlation coefficient: 0.4, p-value: 0.003), and the association remained significant in linear regression models adjusted for maternal age, education, race, parity, household income, offspring sex, the maternal Broad Autism Phenotype Questionnaire score, and the internalizing and externalizing Child Behavior Checklist score. We did not find associations between ID and child behavioral outcomes in our study sample, but did find an association between high serum ferritin—likely indicating inflammation—and SRS-2 scores, supporting our earlier findings showing an association of pregnancy cytomegalovirus sero-positivity and SRS-2 scores (Am J Reprod Immun 79[5]2018:e12840).

**THREE-YEAR GROWTH AND COGNITIVE OUTCOMES AMONG
PRETERM INFANTS WITH NECROTIZING ENTEROCOLITIS**

Krista Wollny, Seham Elmrayed, Tyrone Harrison, Tanis Fenton (University of Calgary)

Necrotizing enterocolitis (NEC), a disease of the gastrointestinal tract, occurs in approximately 1-3 per 1000 births, mainly in preterm infants. Infants who survive NEC face growth challenges due to risk of gastrointestinal complications and malnutrition. This study aims to evaluate the effect of NEC on the growth and IQ of preterm infants. The Preterm Infant Multicentre Growth Study followed preterm infants in level II/III NICUs from three North American cities from 2001-2014 (Calgary, Regina, and San Diego). The growth of preterm infants (23-32 weeks gestation) with and without NEC at 3-years corrected-age was compared using BMI and head-circumference. We also assessed the association between NEC and IQ at 3-years. Results. There were 1417 infants included in the analysis, of which 8.5% had NEC. Of those with NEC (n=121), 78.5% were born before 28-weeks gestation. The mean birthweight of infants with NEC was 845g, compared to 943g in infants without NEC. At 3-years, the difference in sex-specific BMI Z-scores between children with and without NEC was not statistically significant. Whether infants with NEC were fed human milk, formula or both at NICU discharge did not affect sex-specific BMI Z-scores at 3-years. Head-circumference Z-scores at 3-years were significantly associated with NEC ($p=0.002$), even after adjusting for birthweight and small-for-gestational-age (SGA). NEC was significantly associated with lower IQ at 3-years ($p=0.03$), and remained significant when adjusted for infants' head-circumference and SGA. The results suggest that preterm infants with NEC are not at increased risk of suboptimal growth compared to preterm infants without NEC; however, our results suggest that these infants have smaller head circumferences and lower IQs at 3-years. Further investigation should explore the mechanisms by which NEC can compromise head growth and identify potential modifiable factors to support the optimal neurodevelopment of preterm infants with NEC.

ANALGESIC USE AROUND THE TIMES OF OVULATION OR**IMPLANTATION AND FECUNDABILITY** Anne Marie Jukic, Ponnu Padiyara, Michael Bracken, D. Robert McConnaughey, Anne Steiner (NIEHS)

Studies of pain-relieving medications and fecundability have not examined specific windows of exposure during the menstrual cycle. We analyzed data from a prospective time-to-pregnancy cohort of women aged 30-44 with no history of infertility. Participants recorded their medication use in daily diaries. Analgesic medications were classified as acetaminophen, opioids, aspirin, or non-aspirin NSAID and their use during four time periods was quantified: pre-ovulation, peri-ovulation, implantation, and all non-bleeding days of the cycle. Vaginal bleeding and sexual intercourse information from the daily diary were combined with baseline information on contraception use and attempts to conceive to quantify menstrual cycles at risk until conception or study end. Discrete time fecundability models were used to estimate the fecundability ratio (FR) and 95% CI in each of the four time windows of interest and for each pain reliever, compared with women who reported not using any medications in that time window. Models were estimated with minimal adjustment (age, race, and education) and full adjustment (adding BMI, frequency of sexual intercourse, alcohol, caffeine, history of migraines, and history of fibroids) but results did not materially differ. The fully adjusted analyses included approximately 590 women and 1180 cycles (depending on the time window). Non-aspirin NSAIDs and acetaminophen, were not associated with fecundability (all FRs around 1.0). Aspirin use was rare (N=31 exposed cycles), but its use in all time windows was associated with higher fecundability (non-bleeding FR(CI): 1.3 (0.8, 2.1)) and the association was strongest for aspirin use during the implantation window: FR (CI): 2.2 (1.3, 3.8). Results were unchanged in sensitivity analyses for confounding by indication. Aspirin use may improve fecundability; further, the implantation window of the menstrual cycle should be targeted for future investigations of aspirin's potential efficacy.

PRECONCEPTION OPIOID USE AND PREGNANCY OUTCOMES Kerry Flannagan, Jeannie Radoc, Sunni Mumford, Jessica Zolton, Lindsey Sjaarda, Neil Perkins, Keewan Kim, Carrie Nobles, Alexandra Purdue-Smithe, Samrawit Yisahak, Joshua Freeman, Victoria Andriessen, Zeina Alkhalaf, Robert Silver, Enrique Schisterman (National Institute of Child Health and Human Development)

In recent years, opioid use has increased among reproductive-aged women. Opioid use during pregnancy is associated with adverse pregnancy and neonatal outcomes. However, few studies have evaluated the effects of opioid use in the preconception period on pregnancy outcomes and fecundability. Therefore, we examined associations between preconception opioid use and livebirth, pregnancy loss, and time to pregnancy. We followed 1212 women enrolled in the EAGeR Trial who were followed for up to 6 menstrual cycles while trying to conceive and throughout pregnancy for those who became pregnant. We measured urinary concentrations of prescription pain-relieving opioids and heroin at baseline by chemiluminescent immunoassay (Randox Laboratories). We defined opioid use as a positive test for any opioid at baseline, according to manufacturer-defined cut points. We used log binomial regression models to estimate risk ratios (RR) and confidence intervals (CI) for livebirth and pregnancy loss, and discrete Cox proportional hazard models to estimate fecundability odds ratios (FOR). Analyses were adjusted for age, race, BMI, education, smoking, alcohol intake, and any detectable levels of tetrahydrocannabinol (THC). Eighty women (6.6%) tested positive for opioid use, of whom 39 became pregnant and 31 had a livebirth. Opioid use was not significantly associated with livebirth (RR: 0.95; 95% CI: 0.74, 1.21), pregnancy loss (RR: 0.67; 95% CI: 0.34, 1.28), or fecundability (FOR: 0.75; 95% CI: 0.52, 1.09). Objectively-measured preconception opioid use was not associated with livebirth, pregnancy loss, or time to pregnancy. Our results suggest that opioid use before conception may not have adverse reproductive consequences in non-addicted populations, though further studies are warranted to determine whether specific dosages and duration of use could be harmful.

PRECONCEPTION VITAMIN D STATUS AND OFFSPRING SEX RATIO AMONG WOMEN WITH PRIOR PREGNANCY LOSS

Alexandra Purdue-Smithe, Keewan Kim, Carrie Nobles, Enrique Schisterman, Karen Schliep, Neil Perkins, Lindsey Sjaarda, Joshua Freeman, Sonia Robinson, Jeannie Radoc, James Mills, Robert Silver, Sunni Mumford (NICHD)

Experimental data indicate that maternal exposure to factors known to alter inflammatory milieu may be specifically harmful to the conception or survival of male fetuses. Indeed, in a recent clinical trial, preconception administration of low dose aspirin versus placebo restored the skewed sex ratio at birth among women with elevated inflammation, providing direct evidence of this phenomenon in humans. However, it is unknown whether other factors associated with inflammation, such as vitamin D status, are associated with offspring sex ratio at birth. Our objective was thus to evaluate the association of preconception serum 25-hydroxyvitamin D levels [25(OH)D] and male live birth among 1,228 reproductive-age women with a history of 1-2 prior losses who were enrolled in the Effects of Aspirin in Gestation and Reproduction trial between 2007-2011. We estimated RRs and 95% CIs for male live birth according to 25(OH)D sufficiency (≥ 75 vs. 1.95 ng/mL: RR: 1.41; 95% CI: 0.99, 2.00 versus ≤ 1.95 ng/mL RR: 1.11; 95% CI: 0.88, 1.41), a marker of systemic low-grade inflammation. Preconception vitamin D status was associated with male live birth, particularly among women with low-grade inflammation. These data suggest that maternal vitamin D sufficiency may mitigate maternal inflammation that would otherwise be detrimental to male fetal survival.

THE IMPACT OF INTERCOURSE ON MENSTRUAL CYCLE PARAMETERS IN WOMEN WITHOUT KNOWN SUBFERTILITY: A POOLED ANALYSIS OF 3 COHORTS Shahpar Najmabadi, Karen Cecilia Schliep (PhD, MSPH), Sara Ellis Simonsen (PhD, MSPH, CNM), Christina Porucznik (PhD, MSPH), Marlene J Egger (PhD), Joseph Stanford (MD, MSPH) (University of Utah)

In some mammalian species, copulation may induce ovulation, but there are limited data regarding how vaginal-penile intercourse (VPI) may influence ovulation and menstrual cycle characteristics in humans. Study population included 538 women (2647 cycles, including 212 cycles without VPI), aged 18–40, who were heterosexually active, without known subfertility, and not taking exogenous hormones. Women recorded daily vaginal bleeding, mucus discharge and VPI using a standardized protocol for up to 1 year. Linear and generalized linear mixed models were used to evaluate the association between VPI and menstrual cycle parameters. The majority of women (75%) were <30 years of age, non-Hispanic white (88%) and nulliparous (71%). In parity and age-adjusted models, we found that cycles with no VPI, compared to cycles with at least 1 day of VPI, had shorter cycle lengths (29.3 days [95% confidence interval (CI) 28.4, 30.3] versus (vs) 30.2 days [CI 29.6, 30.8]), shorter luteal phases (11.1 days [CI 10.6, 11.5] vs 11.7 days [CI 11.5, 11.9]); and a higher probability of having a luteal phase deficiency (<10 days) (risk ratio (RR) 1.39 [CI 1.07, 1.80]), <2 days of peak-type mucus (RR 1.51 [CI 1.05, 2.17]), and premenstrual spotting in the last 2 days of cycle (RR 2.08 [CI 1.05, 4.11]). We also found that cycles with VPI during menstruation had longer duration of menstrual flow (6.4 days [CI 6.3, 6.5] vs 6.1 days [CI 6.0, 6.2]). In a sensitivity analysis restricted to women who had at least one cycle with and without VPI (n=109), results were similar, with wider CI. Due to lack of information about the occurrence of female orgasm during VPI or the use of barrier methods or withdrawal, we could not evaluate the impact of semen exposure or female orgasm. Our results indicate improved reproductive function in cycles with at least one act of VPI compared to cycles with no VPI.

INTERACTION BETWEEN TOXIC METALS, FOODS, AND REPRODUCTIVE HORMONES AMONG HEALTHY PREMENOPAUSAL WOMEN Keewan Kim, Carrie Nobles, Alexandra Purdue-Smithe, Jean Wactawski-Wende, Anna Pollack, Joshua Freeman, Zeina Alkhalaf, Victoria Andriessen, Jeannie Radoc, Sunni Mumford (NICHD)

Effects of environmental chemicals on reproductive outcomes can be modified by intake of certain foods, such as fish and soy. Our goal was to evaluate joint effects of toxic metals and food intakes on reproductive hormones among premenopausal women. We used data from 249 women in the BioCycle Study who completed a baseline food frequency questionnaire and provided blood samples to measure levels of mercury (Hg), lead (Pb), and cadmium (Cd). Serum reproductive hormones were measured up to 8 times per menstrual cycle for up to 2 cycles. We used linear regression to identify foods associated with metals and weighted linear mixed regression to examine how food intake modified the association between hormones and metals, while adjusting for age, BMI, race, smoking, and intakes of energy, protein, fat, and fiber. Increases in follicle-stimulating hormone with higher Cd were mitigated by any versus no intake of eggs (from 20.6% to 1.8%) and fish (from 17.9% to 9.0%). Similarly, the association of Cd with higher luteinizing hormone was reduced by intakes of eggs, meat, soy foods, and vegetables. While higher Cd was associated with higher testosterone, this was independent of specific food intakes. Increases in estrogen with higher Pb were reduced by intake of 2- \leq 3 vs. \leq 1 servings of vegetables per day (from 20.5% to 5.3%). Associations with Pb and higher testosterone were increased by any versus no intakes of grain, avocados, and coleslaw. We found interdependent associations between Pb and intakes of lunch meats or ground meat with higher progesterone. Associations with Hg and lower estrogen and progesterone were modestly modified by vegetable intake. Intake of fruits reduced the associations with Hg and increases in testosterone, while grain and red pepper increased the effect of Hg. We observed joint effects of metals and intakes of certain foods on reproductive hormone levels among premenopausal women. Further research on hormone-dependent health outcomes may be needed.

THE ASSOCIATION BETWEEN VIGOROUS PHYSICAL ACTIVITY AND TIME TO PREGNANCY

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Introduction Vigorous physical activity (VPA) can modulate hormonal status, including ovulation, and thereby influence time to pregnancy (TTP). However, the association has been inconclusive. Prior studies primarily focused on recreational physical activity, neglecting potentially more common modes of VPA. We aimed to evaluate the association between VPA combining modes and TTP. **Methods** Right from the Start (2000-2012) is a community-based cohort that enrolled women in early pregnancy from southern US. During first-trimester interview, women recalled number of cycles of trying. We used cycles of trying and self-reported cycle length to derive cycles at risk. Women also reported the type, frequency, and duration of up to three activities for each mode of VPA (recreational, outdoor/indoor household, occupational, child/adult care, and other activities). We summed the minutes across activities and modes to obtain the cumulative VPA performed. We used a discrete-time proportional hazards model to estimate fecundability ratios (FRs) and 95% confidence intervals (CIs), adjusting for a priori confounders (maternal age, race, BMI, alcohol/smoking use, education, income, and intercourse frequency). We also assessed for effect modification by BMI using likelihood ratios. **Results** Among 3,357 women, 36% reported some mode of VPA (median [interquartile range] 75 [30-180] minutes/week) and 27% became pregnant during the 1st cycle of trying. We observed no association between hours of VPA performed and TTP (FR [95% CI] 1.01, 0.99-1.02) and no effect modification by BMI ($p=0.19$). Results were also similar when restricted to women enrolled prior to conception. **Conclusion** VPA across modes does not appear to influence TTP in this cohort. Since VPA may vary within individuals across time, future study may benefit from measuring VPA as a time-varying covariate. Additional data about body composition and ovulatory function would also enhance understanding of VPA and fecundability.

EXAMINING ADOPTION AMONG WOMEN WITH HEALTH PROBLEMS RELATED TO CHILDBEARING IN THE UNITED STATES

Chinagozi Ugwu, (National Center for Health Statistics)

Background: The percentage of women in the United States who have ever adopted a child has been decreasing since 2002. Women with fertility problems have been shown in previous studies to adopt at higher percentages compared to women without fertility problems. This study aims to examine adoption among women by fertility-related health issues. **Methods:** Using combined data from three NSFG public-use file releases, 2011-2013, 2013-2015 and 2015-2017, to yield estimates for 2011-2017, women aged 18-44 with previous and current plans to adopt a child are examined. Bivariate associations between women with adoption experience by fertility-related health issues are presented as percentages. Health problems reported at the time of interview included: uterine fibroids, endometriosis, problems with ovulation or menstruation. Other reproductive health problems may be considered, such as cancers that affect fertility. Analysis was conducted using Survey Analysis procedures in SAS software version 9.4. Linear regression modeling was used to determine the significance of linear trends. **Results:** Approximately 0.84% of women aged 18-44 reported having ever adopted a child in 2011-2017. Significantly higher percentage of women with fertility problems (2.09%) had ever adopted compared to women without fertility problems. Women ever diagnosed with uterine fibroids (3.04%) were more likely to have adopted a child than those never diagnosed with uterine fibroids. Higher percentages of women ever diagnosed with endometriosis (3.12%) had ever adopted compared to women never diagnosed with endometriosis (0.69%). Women who ever had ovulation or menstruation problems (1.79%) were more likely to have ever adopted compared with women who never had ovulation and menstruation problems (0.64%). **Conclusions:** Results from this analysis indicate that adoption was higher among women with health problems related to childbearing compared to women without health problems related to childbearing.

MODERATE TO SEVERE ENDOMETRIOSIS IS LINKED WITH SUBSEQUENT RISK OF PRETERM BIRTH

Dabin Yeum, C. Matthew Peterson, Ken Smith, Germaine Buck Louis, Joseph Stanford, Sara Simonsen, Kristina Allen-Brady, Robert Taylor, Kurt Peterson, Karen Schliep (University of Utah)

Background: Emerging evidence indicates that endometriosis may increase risk for preterm birth (PTB); however, there is a lack of population-based samples assessing pregnancies post endometriosis diagnosis. **Methods:** A prospective cohort study (2007–2009) enrolling 506 UT women who were assessed for incident endometriosis diagnosis, then linked to the Utah Population Database statewide birth records in 2018 to determine pregnancies complicated by PTB (<37 weeks gestational age). The operative cohort (n=412/506) included menstruating women ages 18–44 years who were scheduled to undergo a laparoscopy/laparotomy at 1 of 5 participating surgical centers in Salt Lake City, UT. The population cohort (n=94/506) was matched to the operative cohort by age and geographic catchment area. Women in the operative cohort were diagnosed by surgical visualization and rASRM staging criteria; women in the population cohort were diagnosed by magnetic resonance imaging. Women with prior surgically confirmed endometriosis were excluded. Age and BMI adjusted risk ratios (aRR) were calculated to assess risk of PTB by endometriosis diagnosis and staging. **Results:** Among the 506 enrolled women, 11 (12%) women in the population cohort and 173 (42%) women in the operative cohort (71% with stage I/II and 29% with stage III/IV) were diagnosed with endometriosis. Women in the population cohort diagnosed with versus without endometriosis had a 3.6 higher aRR (95% CI: 0.4, 31.8) for subsequent PTB. Women in the operative cohort diagnosed with stage I/II and stage III/IV had a 1.1 higher aRR (95% CI: 0.4, 3.4) and 4.3 higher aRR [95% CI: 1.6, 11.9] of PTB, respectively, compared to women without endometriosis. **Conclusions:** Given that MRI-visualized endometriosis has been shown to be comprised of more advanced disease, risk of PTB among women with moderate to severe endometriosis may be 3–4 fold higher compared to women without endometriosis, in part due to shared inflammatory features.

MATERNAL BMI-INCREASING GENETIC RISK SCORE AND FETAL WEIGHTS AMONG DIVERSE US ETHNIC GROUPS Deepika Shrestha, Mohammad Rahman, Stefanie Hinkle, Tsegaselassie Workalemahu, Fasil Tekola-Ayele (Epidemiology Branch, Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA)

Objective: Maternal genetic risk for obesity contributes to offspring weight at birth, but its contribution to fetal growth remains unknown. We examined associations between maternal genetic risk for obesity and fetal weight across gestation among four race/ethnic groups of the U.S. women. **Methods:** In NICHD Fetal Growth Studies among Singleton cohort (n=2802; 2009-2013) maternal genetic risk score (GRS) of obesity was calculated as the sum of 189 single nucleotide polymorphism variants associated with higher body mass index (BMI) and subsequently categorized to high or low GRS based on the median value. Multivariable linear regression was used to test for associations between GRS and estimated fetal weight at the end of first (13 weeks and 6 days), second (27 weeks and 6 days), and third (40 weeks and 0 days) trimesters within each race/ethnic group. Additional analyses were stratified by prepregnancy BMI, gestational weight gain adequacy, and offspring sex. **Results:** The final analysis was comprised of 603 Whites, 591 Blacks, 535 Hispanics and 216 Asians. High GRS was associated with increased fetal weight at the second (β :22.73; 95% CI:2.35,43.11) and third trimester (β :88.28; 95% CI: 9.01,167.56) among Hispanics. The effect of GRS was stronger among women with normal pre-pregnancy weight (First Trimester β : 3.08, 95% CI:1.05,5.11; Second Trimester β :36.44; 95% CI: 6.71, 66.18) and among Hispanic mothers women with adequate weight gain (β :2.86; 95% CI: 0.38, 5.33) in the first and inadequate weight gain in the second trimester (β :35.28; 95% CI: 4.84, 65.72). Among Asians, high GRS was associated with increased fetal weight among male offspring while decreased fetal weight among female offspring in the first and second trimesters. **Conclusion:** Maternal BMI genetic risk was associated with estimated fetal weight with potential effect modifications by maternal pre-pregnancy BMI, GWG status, and fetal sex.

GESTATIONAL DIABETES AND LONGITUDINAL ULTRASONOGRAPHIC MEASURES OF FETAL GROWTH – A LONGITUDINAL STUDY IN A LARGE MULTI-RACIAL COHORT

Mengying Li, Stefanie Hinkle, Sungduk Kim, Katherine Grantz, Jagteshwar Grewal, William Grobman, Daniel Skupski, Roger Newman, Edward Chien, Anthony Sciscione, Noelia Zork, Deborah Wing, Fasil Tekola-Ayele, Germaine Buck Louis, Paul Albert, Cuilin Zhang (Eunice Kennedy Shriver National Institute of Child Health and Human Development)

Objectives: Gestational diabetes (GDM) is associated with increased risk for large for gestational age birth. Yet, longitudinal fetal growth trajectories in women with GDM and the timing of alterations related to GDM is not well understood, particularly in early pregnancy. This study aims to investigate these critical data gaps. **Study Design:** The NICHD Fetal Growth Studies–Singleton Cohort enrolled women at 8w0d to 13w6d gestation from 12 U.S. clinical centers and randomized them among four ultrasonology schedules for longitudinal fetal measurement. GDM was defined using the Carpenter-Coustan Criteria, impaired glucose tolerance (IGT) was defined as 2-hour plasma glucose in the 75 g or 100 g oral glucose tolerance test (OGTT) 140–199 mg/dL, and normal glucose tolerance (NGT) was defined by no elevated values on either the OGTT or 50 g glucose challenge test. **Results:** One hundred and seven women developed GDM, 118 developed IGT, and 2,020 had NGT. Most fetal growth measures were larger at 10-12 weeks and became smaller at 14-16 weeks in GDM than NGT group. At 28 weeks, abdominal circumference (AC) and estimated fetal weight (EFW) became larger in GDM group, and the differences persisted through 40 weeks (at 40 weeks: AC: 368 vs. 355 mm, $p = 0.03$; EFW: 3866 vs. 3558 g, $p = 0.003$). The associations were modified by the family history of diabetes (p -interaction < 0.001), such that GDM-related early pregnancy growth alterations were only seen in women with a family history of diabetes, whereas GDM-related late pregnancy overgrowth was only seen in those without. IGT group also had larger EFW than the NGT group at 36-40 weeks. **Conclusion:** GDM-related fetal growth alterations appeared to start as early as 10 weeks of gestation. Fetal overgrowth related to GDM was solely driven by AC and started at 28 weeks of gestation, suggesting current GDM diagnosis and treatment timing (often after 24-28 weeks) may be too late to normalize fetal growth.

TREATMENT OF BACTERIAL VAGINOSIS TO PREVENT PRETERM BIRTH- AN IPD META-ANALYSIS WITH IMPUTATION OF MISSING STUDIES

Mark Klebanoff, Ewoud Schuit, Ronald Lamont, Per-Goran Larsson, Hein Odendaal, Austin Ugwumadu, Herbert Kiss, Ljubomir Petricevic, William Andrews, Matthew Hoffman, Andrew Shennan, Paul Seed, Robert Goldenberg, Lynda Emel, Vinay Bhandaru, Steven Weiner, Michael Larsen (The Ohio State University)

OBJECTIVE:To determine, using individual participant data (IPD) and imputing results of trials not providing IPD, whether antibiotic treatment (RX) of bacterial vaginosis (BV) during pregnancy reduced preterm birth (PTB), prolonged pregnancy, is more effective in women with a previous PTB or if given earlier in pregnancy and whether effects of metronidazole (MZ) and clindamycin (CM) differed. **METHODS:**Eligible trials randomized pregnant women with BV who did not already have labor or PROM to antibiotics or control and collected gestational age at delivery. Trials were identified from a Cochrane Systematic Review (2013), and searches of clinicaltrials.gov, Cochrane Central Register of Controlled Trials, WHO ICTRP and Web of Science. References were reviewed for additional trials. Analysis used one-step logistic and Cox random effect models. Subgroup analysis used interaction terms with RX. Trials not providing IPD were incorporated by multiple random hot-deck imputation, with trials providing IPD as donors. Imputation was done separately for MZ and CM trials. **RESULTS:** There were 121 references from 96 studies; 23 trials (11,979 women) were eligible. Thirteen (6915 women) provided IPD. Since the effects of MZ and CM differed, major analyses were stratified by antibiotic. Among IPD trials, MZ did not reduce PTB (odds ratio 1.00, 95% confidence interval 0.84-1.17), but CM reduced PTB by 41% (0.59, 0.42-0.82). Imputing results of non-IPD trials did not change the results for MZ (0.95, 0.81-1.11), but negated the beneficial effect of CM (0.90, 95% CI 0.72-1.12). Hazard ratios mirrored ORs. In IPD studies, CM appeared more beneficial when given at 20-21 wks but not earlier or later. There were no other important or significant interactions observed. **CONCLUSION** Among trials providing IPD, CM but not MZ prevented PTB, but after imputing data from non-IPD trials, the clindamycin IPD results were negated, supporting current clinical recommendations regarding treatment.

ASSOCIATIONS OF MATERNAL BLOOD PRESSURE POLYGENIC RISK SCORE WITH FETAL GROWTH

Tsegaselassie Workalemahu, Marion Ouidir, Jing Wu, Cuilin Zhang, Fasil Tekola-Ayele (The National Institute of Child Health and Human Development)

Background: Maternal pre-pregnancy blood pressure and the trajectory of blood pressure during gestation are associated with variations in fetal weight. However, the association of maternal genetic propensity for elevated blood pressure with fetal weight is unknown. **Objective:** We performed polygenic risk score (PRS) analysis to evaluate the association of maternal genetic propensity for elevated blood pressure with estimated fetal weight (EFW) among four racial/ethnic populations in the U.S. **Methods:** The study was based on singleton pregnancies (n=2065) recruited through the NICHD Fetal Growth Studies. EFWs at approximately 13, 20, 27, and 40 weeks gestation were calculated from five standardized ultrasound measures. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) PRSs for each participant were calculated using the largest genome-wide association study on SBP and DBP. Linear regression models tested the associations between PRS tertile groups and EFWs, adjusting for maternal age, education, parity, genetic structure and fetal sex. **Results:** Hispanics in highest tertile of DBP PRS had 1.9g (95%CI:-3.5, -0.2), 6.8g (95%CI:-13.9, 0.2), 30.1g (95%CI:-55.6, -4.6) and 124.9g (95%CI:-221.7, -28.2) lower EFWs at 13, 20, 27 and 40 weeks gestation compared with those in the lowest tertile groups, respectively (p-trend<0.05 at each gestation week tested). Blacks in the highest tertile of SBP PRSs had 28.7g (95%CI:-51.4, -6.0) and 112.8g (95%CI:-196.3, -29.4) lower EFWs at 27 and 40 weeks gestation, respectively (p-trend<0.05 for SBP PRS at week 40). PRS was not significantly associated with EFW among Asians and Whites. **Conclusion:** Polygenic risk for elevated diastolic and systolic blood pressure was associated with reduced fetal weight in Hispanics and Blacks, respectively. Improved prediction of adverse pregnancy outcomes based on maternal genetic risk for elevated blood pressure may provide opportunities for intervention.

DOES SULFADOXINE-PYRIMETHAMINE ANTIMALARIAL TREATMENT FOR PREGNANT MOTHERS INFLUENCE BIRTHWEIGHT VIA NON-MALARIAL MECHANISMS? Michelle Roh, M. Maria Glymour (University of California, San Francisco, CA, USA)

Background: For pregnant women in sub-Saharan Africa, the World Health Organization recommends intermittent preventive treatment (IPTp) with sulfadoxine-pyrimethamine (SP) to improve birth outcomes, an effect assumed to be mediated by preventing malaria in pregnancy. In East Africa, parasite resistance to SP has led researchers to evaluate dihydroartemisinin-piperaquine (DP) as an alternative to SP. Three trials showed DP is markedly more effective at preventing malaria than SP, but not superior at improving birthweight. We hypothesize SP has non-malarial benefits for birthweight, not mediated by malaria prevention. We conducted a mediation analysis to decompose the non-malarial (direct) and antimalarial (indirect) effects of SP versus DP on birthweight. Methods: For 1645 HIV-uninfected women with singleton pregnancies enrolled in one of three East African IPTp trials, treatment was defined as randomized assignment to SP or DP. The mediator was placental malaria at delivery and the outcome was birthweight. We evaluated treatment-mediator interaction and accounted for mediator-outcome confounders (maternal age, education, household wealth, and gravidity). Meta-regression of linear models was used to obtain pooled estimates of the total, direct, and indirect effect. Results: Random assignment to SP (vs. DP) did not significantly increase birthweight (total effect=23 grams (g); 95% CI: -67, 112). The direct, non-malarial effect of SP increased birthweight by 86g [95% CI: 42, 129] relative to DP. In contrast, DP increased birthweight by 64g [95% CI: -24, 152] relative to SP due to its more potent antimalarial properties. Malaria did not modify the direct effect of SP on birthweight (no treatment-mediator interaction). Conclusion: SP has potent, non-malarial effects on birthweight, independent of its antimalarial activity. Future research should evaluate the combination of SP+DP for IPTp to prevent both malarial and non-malarial causes of poor birth outcomes.

LEISURE-TIME PHYSICAL ACTIVITY BEFORE AND DURING PREGNANCY AND PRETERM BIRTHS IN SOUTH CAROLINA,

2009-2015 Jihong Liu, Andrew Broadway, Nansi Boghossian, Alexander McLain, Sabrina Karim, Chelsea Richard (University of South Carolina)

Objectives: Few studies have examined the association between leisure-time physical activity during pregnancy and preterm birth after controlling for physical activity (PA) levels before pregnancy. **Data and Methods:** Data came from the 2009-2015 South Carolina Pregnancy Risk Assessment Monitoring System, restricting to singleton pregnancies after excluding births <500g, born <22 wks, those with a history of preterm births, being advised for bedrest, and having missing data (n=5107). Being physically active before or during pregnancy was defined as exercising ≥ 3 x/wk for the respective period. For those who were physically active during pregnancy, the months and types of PA were asked. Multiple logistic regression models were used to examine the association after adjusting for maternal age, education, race, gestational weight gain, prepregnancy weight, smoking status, parity, and infant's sex. **Results:** Overall, 8.2% of SC births were born preterm (<37 wks), 46.1% of women were physically active before pregnancy, and 32.5% were active during pregnancy. Compared to the women who were not physically active, women who were active during pregnancy had lower odds of preterm births (OR: 0.44, 95% CI: 0.25-0.78). Activity before pregnancy was not associated with preterm births (OR: 1.13, 95% CI: 0.87-1.45). Walking during pregnancy was associated with preterm births (OR: 0.73, 95% CI: 0.55-0.96), while other non-walking types of PA was not. Women in the top quintile of PA index score (a product of metabolic equivalent of task (MET) score for exercise type and months of being active) had lower odds of preterm births (0.69, 95% CI: 0.50, 0.96). All results were similar when restricting to women without chronic hypertension. **Conclusions:** We found that physical activity during but not before pregnancy was significantly associated with a reduced odds of preterm births in a diverse and representative sample of pregnant women.

LOW CIGARETTE CONSUMPTION BEFORE AND DURING PREGNANCY IN RELATION TO RISK OF PRETERM BIRTH: A LARGE POPULATION-BASED STUDY WITH 22 MILLION MOTHER-INFANT PAIRS Buyun Liu, Guifeng Xu, Yangbo Sun, Yongfu Yu, Linda Snetselaar, Wei Bao (University of Iowa)

Background: Health effects of low-level cigarette consumption during pregnancy are unclear. This study aimed to examine the trimester specific association of maternal cigarette consumption with risk of preterm birth in a large-scale population-based study. Methods: We used the US nationwide birth certificate data from singleton mother-infant pairs in the National Vital Statistics System 2011-2017. Preterm birth was defined as gestational age less than 37 weeks. Participants were divided into 8 groups according to their smoking status (yes or no) before and during pregnancy (1st and 2nd trimester). We used logistic regression to estimate the odds ratio (OR) of preterm birth for smoking vs non-smoking before pregnancy and at each trimester. In addition, the OR of preterm birth with various amounts of cigarette consumption was estimated. Maternal age, race/ethnicity, parity, education, smoking during pregnancy, previous history of preterm birth, marital status, infant sex, and initiation of prenatal care were adjusted. Results: This study included 22,163,580 mother-infant pairs, containing 2,004,139 preterm births. Compared with women who never smoked, women who smoked, even during only one period, had a higher risk of having a preterm birth. The OR (95% confidence interval [CI]) of preterm birth was 1.00 (0.99-1.02), 0.99 (0.98-1.00), 0.96 (0.94-0.97), 1.01 (0.99-1.02), and 1.01 (1.00-1.02) for those who smoked 1-2, 3-5, 6-9, 10-19, and ≥ 20 cigarettes per day before pregnancy, respectively. The corresponding ORs for those who smoked during the first trimester were 1.14 (1.12-1.16), 1.12 (1.10-1.14), 1.13 (1.10-1.15), 1.21 (1.19-1.23), and 1.29 (1.27-1.31), while for those who smoked during the second trimester, the OR was 1.18 (1.15-1.20), 1.17 (1.16-1.19), 1.17 (1.15-1.20), 1.27 (1.25-1.29), and 1.37 (1.35-1.40), respectively. Conclusion: Low-level cigarette consumption during pregnancy, even if only 1-2 cigarette per day, may rise the risk of preterm birth.

INTRAUTERINE GROWTH PATTERN IN RURAL ETHIOPIA: A COMMUNITY-BASED STUDY ON SERIAL ULTRASOUND

MEASUREMENTS Meselech Roro, Wakgari Deressa, Bernt Lindtjørn (Addis Ababa University College of Health Sciences School of Public Health)

Abstract Background: Wellbeing of a child is influenced by foetal growth, and adequate intrauterine growth (IUG) is among basic features of a healthy pregnancy. The aim of our study was to assess IUG pattern in a rural, and drought affected population in the Rift Valley area of Adami Tulu district, Oromia, Ethiopia.

Methods: We conducted a longitudinal community-based study of IUG pattern using serial ultrasound measurements. Data were collected for 17 months, July 2016 to November 2017. We included 675 singleton pregnant foetuses <23 weeks based on ultrasound-derived estimation of gestational age. We obtained head circumference, biparietal diameter, abdominal circumference, femur length, and estimated foetal weight at 26, 30, and 36 weeks. We followed them until delivery. We validated biometric measurements, and estimated foetal weight data of this study against the INTERGROWTH-21st International and the WHO multicentre foetal growth reference standards. Foetal weight was estimated using the Hadlock algorithm, and the 5th, 10th, 25th, 50th, 75th, 90th, and 95th centiles were developed from this model. **Result:** Distribution of biometric measurements, and estimated foetal weights were similar to the WHO and INTERGROWTH 21 references. Most measurements were between -2 and +2 of the reference Z scores. Mean score of estimated foetal weight showed no statistically significant association with baseline maternal nutritional like Mid Upper Arm Circumference (MUAC) 23cm ($P = 0.49$, mean difference = 0.17, 95% CI -0.32, 0.07), and MUAC 21cm ($P = 0.45$, mean difference = -0.03, 95% CI -0.12, 0.05). It also had no statistically significant association with body mass index 18.5 kg/m² ($P = 0.74$, 95% CI -0.09, 0.06).

Conclusion: Our results are similar to the intrauterine growth pattern of INTERGROWTH 21st and WHO multicentre foetal growth reference standards. Our measurements can be used as an Ethiopian reference standard.

WHAT IS THE SAFEST MODE OF BIRTH FOR EXTREMELY PRETERM VERTEX INFANTS? A SYSTEMATIC REVIEW AND META-ANALYSES

Sarah McDonald, Alexander Jarde, Yu Yang Feng, Kristen Viaje, Prakesh Shah
(McMaster University)

Introduction: The safest mode of birth for extremely preterm vertex infants is not clear. In extremely preterm, breech singletons, a recent systematic review suggested that caesarean section was associated with significant decreases in the odds of death and severe intraventricular haemorrhage. **Objective:** To determine the safest mode of birth (caesarean section or vaginal delivery) in extremely preterm (<28 weeks) vertex singletons, who make up over two thirds of all extremely preterm singletons. **Search Strategy:** We searched MEDLINE, EMBASE, CINAHL, Cochrane CENTRAL, Web of Science, and ClinicalTrials.gov from January 1995 to May 14th 2018. **Selection Criteria:** We included studies comparing outcomes by mode of birth in vertex infants born <28 weeks or with birth weight <1500g. **Data Collection and Analysis:** Two reviewers independently extracted data from the included studies using a piloted form. We synthesised the data using random-effects meta-analyses. **Results:** In singleton vertex infants born <28 weeks, caesarean section was associated with reduced adjusted odds of death (adjusted odds ratio [aOR] 0.56, 95% confidence interval [CI], 0.34-0.94). For severe brain injury or a composite of death or severe brain injury, adjusted data were lacking, and raw data did not reach statistical significance (severe brain injury: odds ratio [OR] 0.82, 95% CI 0.64-1.06; composite outcome: OR 0.82, 95% CI 0.67-1.01). In addition, results in the birth weight subgroups corresponding to approximately <28 weeks were consistent with the main results, with reduced adjusted odds of death associated with caesarean section when birth weight was <1250g (500-750g: aOR 0.53, 95% CI 0.49-0.57; 750-1000g: aOR 0.89, 95% CI 0.78-1.01; 1000-1250g: aOR 0.78, 95% CI 0.65-0.93). **Conclusions:** Compared with vaginal birth, caesarean section may be associated with significantly reduced adjusted odds of death in extremely preterm vertex infants, although the quality of evidence was very low.

RACIAL/ETHNIC DIFFERENCES IN THE ASSOCIATION BETWEEN EARLY GESTATION PLASMA COTININE AND NICOTINE CONCENTRATIONS AND NEONATAL ANTHROPOMETRIC MEASURES

Melissa M. Amyx, Rajeshwari Sundaram, Germaine M. Buck Louis, Nicole M. Gerlanc, Alaina M. Bever, Kurunthachalam Kannan, Sunmi Lee, Melissa M. Smarr, Katherine L. Grantz (Eunice Kennedy Shriver National Institute of Child Health and Human Development)

As public health campaigns drastically reduced smoking in pregnancy, understanding health implications at low exposure levels is informative. In a diverse cohort of healthy, self-reported non-smoking pregnant women (NICHD Fetal Growth Studies; n=2101; 562 white, 547 black, 589 Hispanic, 403 Asian), we evaluated associations between smoking exposure biomarkers (log-transformed plasma nicotine, cotinine, and summed nicotine+cotinine [Σ] concentration) measured at 10-13 weeks' gestation and neonatal anthropometrics: birthweight (BW; g); mid-upper arm (ArmC), mid-upper thigh, abdominal circumference [cm]; subscapular, triceps, abdominal flank (AbFS), anterior thigh skinfolds (mm); % fat mass; and fat-free (i.e. skeletal) measures (length; head circumference [cm]) using generalized linear models. Interaction terms evaluated racial/ethnic differences. Biomarker concentrations were low (78% <LOQcotinine[cot]), but differed by race/ethnicity (<LOQcot: 90% white; 50% black; 85% Hispanic; 86% Asian; $p<0.05$), as did neonatal anthropometrics ($p<0.05$). Per 1 log-unit increase in cotinine, BW increased 43g (95%CI -43, 129) in white and 59g (95%CI -66, 184) in Hispanic women, but decreased -141g (95%CI -521, 239) in Asian and -79g (95%CI -131, -26) in black women ($p=.04$). Racial/ethnic differences were found for most non-skeletal measures ($p<0.1$; not ArmC, AbFS) with similar patterns as BW: 1 log-unit increases in cotinine associated with increasing measures among white, lesser increases or decreases in Asian and black, but inconsistent results in Hispanic women. Results were similar for nicotine or their Σ . In a racially diverse cohort with chemical data, novel findings were racial/ethnic differences in associations between smoking biomarkers at low exposure and neonatal non-skeletal measures. Prior findings of reduced neonatal body fat with smoking exposure may be complicated by racial/ethnic differences in smoking, nicotine metabolism, and infant size.

EXPLORING CIRCULATING SHORT-CHAIN FATTY ACIDS IN PRETERM BIRTH: A PILOT CASE-CONTROL STUDY Colette Nickodem, Ramkumar Menon, Thomas McDonald, Brandie Taylor (Temple University)

Short-chain fatty acids (SCFA) are byproducts of microbial metabolism of fibers with anti-inflammatory effects and may protect against diet-induced obesity through modulation of histone acetylation. Further, maternal serum SCFAs are correlated with maternal and fetal metabolic parameters. Given the importance of lipid metabolism for placental function, studies should explore if maternal SCFAs influence pregnancy outcomes. This pilot case-control study measured seven (propionic, methanoic, butanoic, isovaleric, pentanoic, methylpropylbutanoic and methylbutanoic acids) SCFAs in maternal serum of 25 women with preterm delivery <37 weeks gestation and 25 women with a healthy term delivery. All women had singleton pregnancies and provided serum at the time of admission to labor and delivery. SCFAs were measured by Purge and Trap Gas Chromatography/Mass Spectrometry. Logistic regression with penalized likelihood approach examined associations between SCFAs and preterm birth adjusting for age, race, body mass index, and socioeconomic status. We also explored if SCFAs, log-transformed, had a linear association with body mass index. There was a significant negative association between propionic acid and body mass index after adjustments ($\beta=-0.14$, $p=0.0011$). Propionic acid had a negative association with preterm birth [Odds Ratio adj: =0.89, 95% Confidence Interval= 0.75, 0.94). No other significant associations were found. Although absolute conclusions cannot be drawn from this pilot research, larger studies should explore if circulatory SCFAs elicit inflammatory pathways during pregnancy and whether this is related to the development of adverse outcomes.

CO-OCCURRENCE OF DEPRESSION & HYPERTENSION AND RISK FOR PRETERM BIRTH Nichole Nidey, Rebecca Baer, Gretchen Bandoli, Elizabeth Jasper, Brittany Chambers, Elizabeth Rogers, Jennifer Felder, Deborah Karasek, Linda Franck, Sky Feuer, Laura Jelliffe, Kelli Ryckman (University of Iowa)

Maternal depression is a common condition related to pregnancy and childbirth. Although depression during pregnancy has been implicated in the risk of preterm birth (PTB), few studies have examined risk of PTB when depression co-occurs with other pregnancy conditions. The objective of this case-control study is to identify how with the co-occurrence of depression and other pregnancy conditions contribute to the risk of PTB (births prior to 37 weeks of gestation). The study population is drawn from 2,963,888 singleton live births in California from 2007-2012. The birth cohort file includes hospital diagnosis linked to birth certificate data. After exact propensity score matching on smoking and alcohol use during pregnancy, age group, parity, education, insurance type and race/ethnicity among women, the study included 394,446 women (197,223 with PTB and 197,223 with term birth). Conditional logistic regression was used to examine associations between PTB and conditions of pregnancy, along with odds ratios and 95% confidence intervals. For conditions associated with PTB we examined the interactive effects with depression. Conditions during pregnancy found to be positively associated with odds of PTB include depression, diabetes, hypertension in pregnancy, oligohydramnios, polyhydramnios, placenta previa and chorioamnionitis. Interactive effects emerged where women with both HTN and depression had 4.51 (CI: 4.12-4.94) times the odds to give birth preterm than women without either disorder, where women with only HTN had 3.84 (CI 3.76-3.92) times the odds, and women with only depression had 1.62 (CI: 1.56-1.67) times the odds to give birth preterm than women with neither condition. Results from this study suggest depression and HTN together increase the odds of giving birth preterm. Understanding how maternal conditions influence risk of PTB is of clinical and public health importance to target prevention and intervention efforts to women at the highest risk.

**RISK OF PRETERM BIRTH BY TIMING OF LUPUS DIAGNOSIS
AMONG WOMEN IN THE GEORGIA LUPUS REGISTRY** Meghan Anglely,
Penelope P. Howards, Cristina Drenkard, S. Sam Lim (Emory University)

Background: Women with systemic lupus erythematosus (SLE) are at a greater risk of having a preterm birth than the general population. Most studies examine preterm births in women with SLE only after they have been diagnosed with SLE, but it has been established that both symptoms and immune abnormalities can appear years before a clinical diagnosis of SLE is made. **Methods:** The Georgia Lupus Registry (GLR) is a population-based registry of individuals with SLE in 2002-2004 in Atlanta, Georgia. The GLR was matched to Georgia Birth Certificates from 1994-2013. Births were categorized by timing before and after diagnosis (≥ 3 years before, 0-3 years before, 0-3 years after and ≥ 3 years after). Risks of preterm birth (delivery < 37 weeks of gestation) were calculated. Log-risk models with generalized estimating equations accounted for multiple deliveries in the same woman. Only singleton births were analyzed. **Results:** In 189 women, 297 singleton births were identified; 80% were to African American and 18% to white women, and 125 births occurred before and 172 births occurred after diagnosis. For births occurring ≥ 3 years before, 0-3 years before, 0-3 years after and ≥ 3 years after, the risks of preterm birth were 19%, 29%, 34% and 33%, respectively. Compared to women who gave birth ≥ 3 years before, women who gave birth 0-3 years before had slightly elevated risk of preterm birth (risk ratio [RR]: 1.46, 95% confidence interval [CI]: 0.79, 2.68), as did women who gave birth 0-3 years after (RR: 1.64, 95% CI: 0.89, 3.04) and women who gave birth ≥ 3 years after (RR: 1.53, 95% CI: 0.89, 2.62). Analyses controlled for parity, age and race. **Conclusions:** The risk of preterm birth is also increased preceding SLE diagnosis, although lower than that after diagnosis. This suggests late diagnosis of SLE or that immunologic and other factors may impact birth outcomes years before clinical disease.

MATERNAL DIET PATTERNS IN EARLY PREGNANCY AND NEONATAL ANTHROPOMETRY IN THE NICHD FETAL GROWTH STUDY-SINGLETONS Samrawit F. Yisahak, Sunni Mumford, Jagteshwar Grewal, Mengying Li, Stefanie N. Hinkle (NICHD)

Objective: Maternal nutrition is a key determinant of offspring development. Existing studies typically assess nutrition in terms of exposures to single nutrients. However, analysis of comprehensive dietary patterns that capture complex nutrient profiles is more rigorous and better suited for providing recommendations. Using principal components analysis (PCA), we derived maternal diet patterns in early pregnancy, then assessed their association with neonatal anthropometry. **Methods:** We studied 1964 women in a diverse cohort of U.S. pregnant women (2009-2013). Birth weight was abstracted from medical records and neonatal anthropometry (upper-arm, upper-thigh and birth length, head circumference, abdominal circumference, sum of skinfold) was measured post-delivery using a standardized protocol. Women completed a 145-item self-administered Food Frequency Questionnaire at 8-13 weeks gestation reflecting diet over the past 3 months. We conducted PCA of 26 food groups in my pyramid equivalent units. We grouped the derived patterns into quartiles and used the lowest quartile as the referent group in regression models. The models were adjusted for sociodemographic factors, parity, infant sex, pre-pregnancy BMI, pre-pregnancy physical activity, and total energy. **Results:** We identified a “Western” pattern (higher intake of refined grains, solid fats, oils, and meat) and a “Vegetable-based” pattern (higher intake of tomatoes, dark-green, orange, starchy, and other vegetables). These diet patterns together explained 48.47% of the variance. In adjusted models, we found no significant association between the two diet patterns and neonatal anthropometry. **Conclusion:** The two major diet patterns we identified in early pregnancy were not associated with neonatal anthropometry. Dietary assessment in later pregnancy may be more predictive of neonatal outcomes. Further investigation, at different points of gestation, is needed to better understand these diet patterns.

ABSTRACT WITHDRAWN

IMPACT OF PATERNAL ADULTHOOD WEIGHT GAIN ON OFFSPRING'S BIRTH WEIGHT: A PROSPECTIVE BIRTH COHORT STUDY

Minshan Lu, Xueling Wei, Jinhua Lu, Peiyuan Huang, Songying Shen, Mingyang Yuan, Lifang Zhang, Niannian Chen, Huimin Xia, Xiu Qiu (Guangzhou Women and Children's Medical Center)

Background: Compared with the abundant evidence on the influence of maternal pre-pregnancy weight gain on offspring's birth weight, evidence on the effect from the paternal side is still sparse and inconclusive. The aim of this study was to explore the impact of paternal adulthood weight gain on neonatal birth weight. **Methods:** A total of 7933 singleton births and their parents were included from the Born in Guangzhou Cohort Study, a prospective study in China. Paternal weight and height at both age 18 and conception, parental characteristics, and neonatal birth anthropometric data were collected. Paternal adulthood weight gain (PAWG, kg) was represented by weight difference between age 18 and conception. PAWG rate (kg/year) was calculated by dividing PAWG by corresponding years. Offspring's birth weight Z score (BWZ) was calculated on the basis of the INTERGROWTH-21st Century Standard. Multiple linear and logistic regression analyses were performed to assess the associations of PAWG with BWZ, small for gestational age (SGA) birth and large for gestational age (LGA) birth. **Results:** Rates of paternal overweight or obesity (Body mass index ≥ 24.0 kg/m²) at their age 18 and conception (average age of 31) were 8.0% and 42.3%, respectively. On average, the PAWG was 9.87 kg with a rate of 0.81 kg/year. Faster PAWG rate was associated with increased offspring's BWZ [β : 0.07; 95% Confidence Interval (CI): 0.02-0.12]. Comparing the highest (>1.19 kg/year) to the lowest (≤ 0.32 kg/year) quartiles of PAWG rate, adjusted odds ratios (95% CIs) were 0.59 (0.46-0.77) for SGA birth and 1.45 (1.10-1.91) for LGA birth. **Conclusion:** Higher and faster paternal adulthood weight gain was associated with increased offspring's birth weight, lower odds of SGA and higher odds of LGA. The results underscore the importance for expanding the research to the role of paternal weight in birth outcomes and the underlying mechanisms.

EFFECT MEASURE MODIFICATION OF THE ASSOCIATION BETWEEN BIRTHWEIGHT AND EDUCATION BY DIABETES DURING PREGNANCY Lisa Smithers, John Lynch, Ben Mol, Gustaaf Dekker, Murthy Mittinty (University of Adelaide)

BACKGROUND: Among healthy pregnancies, higher birthweight is linked to better cognitive and academic outcomes, likely through better intrauterine conditions. However, diabetes in pregnancy may result in higher birthweights through poor glycaemic control, which may not benefit learning outcomes. We examined whether diabetes in pregnancy modified the association between birthweight and academic achievement. **METHODS:** We used whole-of-population linked administrative data from South Australia ($n > 72,000$). The exposure was birthweight for gestational age z-scores (BWGA) categorized into <20 th, 20-79th and ≥ 80 th percentiles. The outcome was scoring at or below the national minimum standard (\leq NMS) on reading, writing, grammar, spelling and numeracy assessments at 8 years of age. The presence of any diabetes (pre-existing, gestational) was the effect measure modifier. Logistic regression models with inverse probability of treatment weights were used to adjust for a wide range of potential confounders. Effect measure modification was assessed with the Relative Excess Risk due to Interaction (RERI) on the risk-difference scale. **RESULTS:** In the absence of diabetes, BWGA <20 th percentile was associated with higher risks of poor school outcomes and ≥ 80 th with lower risks, compared with the 20-79th percentiles. For example, risks of scoring \leq NMS on spelling was 17% higher for BWGA <20 th (risk ratio (RR) 1.17, 95% CI 1.13, 1.22) and 6% lower for BWGA ≥ 80 th (0.94 (0.90, 0.98)). The pattern of risks for BWGA ≥ 80 th plus diabetes were consistently higher across all school outcomes than BWGA 20-79th, which was reflected in the RERI. For example, scoring \leq NMS on spelling was 38% higher than the 20-79th percentiles (1.38 (1.15, 1.67); RERI 0.49 (95% CI 0.15, 0.83)). **CONCLUSION:** In the whole population, larger babies are at lower risk of poor school outcomes, but babies born to mothers with diabetes who are large, are at higher risk.

VALIDATION OF MATERNAL SELF-REPORTED PREGNANCY COMPLICATIONS USING WEB-BASED QUESTIONNAIRES IN A**PROSPECTIVE COHORT STUDY** Nel Roeleveld, Pim Beekers, Hussein Jamaladin, Joris van Drongelen, Marleen van Gelder (Radboud university medical center, Nijmegen, The Netherlands)

Background: Evidence for the validity of maternal self-reports of common pregnancy complications is conflicting and these reports have not been validated for web-based questionnaires yet. Therefore, we aimed to validate data on gestational diabetes, gestational hypertension, and preeclampsia from web-based questionnaires administered during pregnancy and two months after delivery. Methods: We included 1,809 women who participated in the PRegnancy and Infant DEvelopment (PRIDE) Study and gave birth in 2012–2017, for whom the relevant data were complete. Sensitivity, specificity, and positive and negative predictive values of self-reported diagnosis of gestational diabetes, gestational hypertension, and preeclampsia were determined using obstetric records as reference standard. Furthermore, we determined whether maternal characteristics affected the disagreement between questionnaire and obstetric record. Results: For gestational diabetes and preeclampsia, we observed very few false positive and false negative reports, yielding sensitivities of 93% (95% confidence interval [CI] 86-100) and 88% (95%CI 79-98), respectively, and specificities of 100%. The positive predictive values (PPV) were 91% (95%CI 90-92) and 88% (95%CI 87-90). Depending on the definition of gestational hypertension, sensitivity ranged from 62% to 89% with PVVs of 64% and 88%. The risks of disagreement on gestational hypertension seemed to be lower for women 25-29 years of age (odds ratio [OR] 0.6 (95%CI 0.3-1.0)), with low/intermediate education (OR 0.6, 95%CI 0.3-1.1), and/or having had one or more previous births (OR 0.5, 95%CI 0.3-0.9). Conclusions: We showed that maternal self-reports of preeclampsia and gestational hypertension in web-based questionnaires are valid. Gestational hypertension seemed to be of somewhat lower validity due to relatively high numbers of false positive reports, but it is questionable whether an appropriate reference standard exists to validate these outcomes.

SEXUAL DIMORPHISM IN PRETERM PREECLAMPSIA: BIOLOGICAL OR BIAS? Brandie DePaoli Taylor, Qi Zheng, Enrique Schisterman (Temple University)

Large epidemiologic investigations report associations between male fetal sex and spontaneous abortion, preterm birth and perinatal mortality. Curiously, the male:female sex ratio is reduced in preeclampsia with deliveries < 37 weeks. Similar to the smoking and preeclampsia paradox, Vatten et al. hypothesized that data is biased, where males are more susceptible to implantation and placentation failure and those that survive past 20 weeks are less likely to develop severe subtypes of preeclampsia that require early delivery. Several studies have referred to the Vatten et al. hypothesis, but none have tested the theory. We ran simulations with 5000 individuals and 10,000 replications to determine the association between female fetal sex and preterm preeclampsia considering a male excess in pregnancy loss. The simulation depended on 7 probabilistic parameters of the male:female sex ratio of conception, pregnancy loss, and preterm preeclampsia (observed and theoretically among losses if the fetus survived) with estimates from published studies. The theoretical probability of preterm preeclampsia in losses was based the estimated proportion of losses due to implantation failure, and subsequently, the proportion that would develop preterm preeclampsia. Observed relative risk (RR_{Rob}) was measured using measurable outcomes and actual relative risk (RR_{Rac}) was measured including pregnancy losses. Bias was defined as $RR_{\text{Rob}} - RR_{\text{Rac}}$ and relative error $(RR_{\text{Rob}} - RR_{\text{Rac}}) / RR_{\text{Rac}}$. In scenarios with a male excess of losses (ratio 1.25-2.48), mean RR_{Rac} was 0.33-0.91 vs. mean RR_{Rob} of 0.7-1.1. The risk of preterm preeclampsia among female fetuses was very modest, although similar to a recent meta-analysis (RR 1.1). Bias was greatest when the probability of preterm preeclampsia was higher in fetuses that theoretically survived as opposed to early demise. Results are influenced by assumptions on outcomes that cannot be measured. Additional scenarios based on various populations should be considered.

INTERPREGNANCY INTERVAL AND RISK OF PREECLAMPSIA FOR WOMEN WITH AND WITHOUT PREVIOUS PREECLAMPSIA: A POPULATION-BASED COHORT STUDY IN WESTERN AUSTRALIA, 1980-2015 Amanuel Gebremedhin, Annette Regan, Luke Marinovich, Gavin Pereira (School of Public Health, Curtin University, WA)

Background: Interpregnancy interval (IPI) is a potentially modifiable risk factor for pregnancy outcomes, and short and long IPI may be associated with increased risk of preeclampsia. Our aim was to investigate whether previous preeclampsia modifies effect of IPI on preeclampsia at second pregnancy. **Methods:** A longitudinal retrospective cohort study was conducted using linked records from Western Australian Midwives Notification System and Hospital Morbidity Data Collection to obtain maternal, infant and birth information. We included 251,899 mothers who delivered their first and second singleton births (parity 0,1) between 1980 and 2015. Adjusted odds ratios (ORs) for IPIs and their 95% CI (confidence intervals) were modelled using logistic regression with propensity score stratification for potential confounders using 18-23 months as the reference group. Analysis performed separately based on preeclampsia status in their first pregnancy. **Results:** The incidence of preeclampsia was 9.5%, and 4% in the first pregnancy and second pregnancy respectively. Among mothers with previous preeclampsia risk of recurrence was 19.3%. The interaction between IPI and previous preeclampsia was significant only for women with no previous preeclampsia. For women with no previous preeclampsia, ORs were significantly greater for intervals 0-5 months (1.17, 95% CI 1.02-1.35); 24-59 months (1.16, 95% CI 1.07-1.27); 60-119 months (1.71, 95% CI 1.51-1.92) and ≥ 120 months (2.29, 95% CI 1.89-2.78), compared to 18-23 months. Among women with previous preeclampsia, the adjusted OR for preeclampsia was 0.70 (95% CI 0.36-1.34) for IPI of ≥ 120 months for mothers who changed their partner. **Conclusions:** Short (24 months) IPIs increased the risk of preeclampsia for subsequent pregnancies in mothers with no previous preeclampsia. For mothers with preeclampsia in first pregnancy, partner change is associated with reduced risk of preeclampsia for the second pregnancy.

BLOOD PRESSURE TRAJECTORIES IN RELATION TO PREGNANCY AND BIRTH COMPLICATIONS Kyle Roell, Quaker Harmon, Per Minor Magnus, Kari Klungsøyr, Stephanie Engel (University of North Carolina)

Preeclampsia is part of a family of hypertensive disorders, which carries significant risk of maternal and neonatal morbidity. Diagnosed after 20 weeks' gestation, the phenotype of preeclampsia is heterogeneous in both onset and severity, and can have significant consequences on the health of both mother and baby. There is little research on how blood pressure trajectories across pregnancy affect pregnancy outcomes. Our aim is to assess longitudinal changes in blood pressure over the course of pregnancy, and to examine these trajectories in relation to fetal growth and other parameters of neonatal health. To address this question, we have utilized a nested sub-study of the Norwegian Mother and Child Cohort Study (MoBa), including all cases of preeclampsia ($n = 2,239$) and a sample of non-cases ($n = 2,575$). Antenatal cards were abstracted for gestational week-specific blood pressure and urinalysis measures, and data obtained from the Medical Birth Registry of Norway were linked to provide pregnancy outcome information. We used the k-means clustering algorithm to group women into trajectories, both overall and within case/control subsets. In the overall population, preeclampsia cases were weighted to reflect the prevalence in the source population. Four systolic blood pressure trajectory groups were identified by within-cluster sum of squares. The two clusters with the largest percentage of preeclampsia cases were differentiated by starting blood pressure, and the slope of increase. The cluster with the steepest increase in blood pressure, and a lower starting blood pressure, was more affected by fetal growth restriction, even among non-preeclampsia cases. Additional analyses describing preeclampsia-specific and unaffected pregnancy trajectories will be presented. These data reinforce the importance of blood pressure trajectory on fetal growth, even among pregnancies that do not meet diagnostic criteria for preeclampsia.

IMPLICATIONS OF THE CHOICE OF SAMPLE POPULATION FOR THE DEVELOPMENT OF RISK PREDICTION MODELS FOR LONG-TERM OUTCOMES INCORPORATING PREGNANCY-RELATED PREDICTORS

Sonia Grandi, Kristian B Filion, Robert W Platt (McGill University)

Introduction: To increase the utility of risk prediction models, the sample population used to develop the models should represent the population that are screened in practice. In perinatal epidemiology, the appropriate sample population for models of long-term outcomes incorporating pregnancy-related predictors is unclear since women can contribute more than 1 pregnancy during the follow-up. Although various sampling methods are possible, the impact of sampling one versus all pregnancies on the accuracy of predictions has not been investigated. **Methods:** Four sample cohorts were simulated to examine the long-term risk of cardiovascular disease including obstetrical history. The first cohort includes the first pregnancy per woman and predictors relating to this pregnancy. The second cohort includes a random sample of pregnancies per woman obtained by simple random sampling to recreate the distribution of parity in the original population. Predictors for this cohort include characteristics of the current and prior pregnancies. The last two cohorts include all eligible pregnancies per woman. For the third cohort, the start of follow-up time begins at the first pregnancy and ends at the start of the next pregnancy. The follow-up for all subsequent pregnancies continues until a future pregnancy, an event, or end of the study period, whichever occurs first. In order to account for the correlation between pregnancies an accelerated failure time generalized estimating equation model is used. In the fourth cohort, the follow-up time for each pregnancy is not censored at the start of the subsequent pregnancy and continues until an event or end of the study period. This scenario allows us to assess the impact of censoring and double counting events and follow-up time.

Conclusions: The findings from this work highlight the need for careful consideration when choosing the sample population for development of risk prediction models.

INDIVIDUAL AND NEIGHBORHOOD-LEVEL FACTORS AND PRE-ECLAMPSIA: A CROSS-SECTIONAL STUDY IN VIRGINIA, 2008-2015

DaShaunda Taylor, Hadiza Galadima, Derek Chapman (Virginia Commonwealth University)

Background: Pre-eclampsia is a condition characterized by hypertension and proteinuria that affects approximately 3-8% of pregnancies. Women with pre-eclampsia may experience maternal and fetal morbidity and mortality. Although individual factors have been investigated as potential risk factors, neighborhood-level indicators may play a role in pre-eclampsia outcomes as well. **Purpose:** This cross-sectional study aimed to approximate pre-eclampsia prevalence and to investigate the relationship between individual and neighborhood factors and pre-eclampsia in Virginia. **Methods:** Data from Virginia Health Information, the United States Census Bureau American Community Survey, and the 2010 United States Census Bureau decennial census were utilized. The study population consisted of pregnant women in Virginia hospitals between January 1, 2008 and September 30, 2015. Women who had a hysterectomy, eclampsia, pre-eclampsia or eclampsia superimposed on pre-existing hypertension, unspecified hypertension, or multiple gestation were excluded from analysis. Multilevel modeling was attempted but could not be completed due to data sparsity. Hence, logistic regression was conducted to assess the associations between potential predictors and pre-eclampsia. **Results:** There were 696,078 pregnancy-related discharges from 94 hospitals with a pre-eclampsia prevalence of 3.3% (n=23,167). Several variables were associated with pre-eclampsia, including age ([reference group: 20-29 years] <20 years, adjusted odds ratio [aOR]: 1.31; 95% confidence interval [95% CI]: 1.25-1.37; 30-39 years, aOR: 0.93; 95% CI: 0.90-0.95; ≥ 40 years, aOR: 1.16; 95% CI: 1.08-1.26) and length of stay (aOR: 1.12; 95% CI: 1.12-1.13). **Conclusions:** This study reiterated the importance of individual-level factors regarding pre-eclampsia prevalence. Neighborhood-level indicators should be further explored to establish the extent of associations with pre-eclampsia, keeping in mind the ultimate goal of reducing disparities.

EXAMINATION OF FETAL SEXUAL DIMORPHISM IN IMMUNE MEDIATING BIOMARKERS IN PREECLAMPTIC AND**NORMOTENSIVE WOMEN** Olayinka Abiodun-Ojo, Ramkumar Menon, Brandie DePaoli-Taylor (Emory University)

Fetal sexual dimorphism has been documented in preeclampsia, although the mechanisms by which sexual dimorphism impacts pregnancy outcomes has not been elucidated. Placental based studies have demonstrated sexual dimorphism in immune-related gene expression and cytokine and chemokine expression in mothers with inflammatory conditions such as asthma. This suggest that differences in the fetal response to underlying maternal disease may impact pregnancy outcomes. This pilot study examined fetal-sex specific expression of maternal plasma inflammatory mediators (HMGB1, marker of cellular damage, IL6, marker of inflammation and pentraxin-3, marker of innate immunity measured by ELISA) in women with preeclampsia and normotensive women. Frozen plasma samples were obtained from singleton pregnancies without any chronic health conditions at the time of admission to labor and delivery. A total of 45 preeclamptic cases were matched with 45 normotensive controls by timing of blood draw and parity. Plasma markers were log transformed. All analyses were conducted stratified by fetal sex. Multivariate linear models determined if biomarker levels significantly differed between cases and controls. In both males and females, HMGB1 was significantly lower but Pentraxin-3 significantly higher in preeclampsia compared to controls. IL-6 was elevated in preeclamptic women with female fetuses only. In contrast to placental based studies, we did not observed differences in immune mediators between preeclamptic women and normotensive controls based on fetal sex. In both sexes, preeclamptic women displayed increased innate immune activity but interestingly lower HMGB1. However, preeclamptic women with female fetuses did have elevated IL-6 which may indicate an increased inflammatory response. Larger studies with longitudinal samples from multiple maternal/fetal compartments are needed to understand sexual dimorphism in pregnancy outcomes.

DOES GESTATIONAL WEIGHT GAIN PREDICT GESTATIONAL AGE AT BIRTH IN TWIN PREGNANCIES? Michelle Dimitris, Jennifer Hutcheon, Robert Platt, Michal Abrahamowicz, Marie-Eve Beauchamp, Katherine Himes, Lisa Bodnar, Jay Kaufman (McGill University)

Twin pregnancies in the United States have doubled in recent years. Although both gestational weight gain (GWG) and risk for adverse outcomes (i.e. preterm birth) is increased in this population, the relationship between these characteristics has rarely been studied in twin pregnancies. We aimed to quantify the association between GWG and gestational age (GA) at birth among twins. Non-anomalous dichorionic twin pregnancies delivered at Magee Women's Hospital in Pittsburgh from 1998-2014 were eligible for inclusion. Medical chart information contained in the hospital's perinatal database, supplemented with abstracted serial GWG measurements, were obtained. We interpolated maternal weight gain for each day between clinic visit measurements and converted GWG to GA-specific z-scores using a twin-specific chart. We quantified the relationship between time-varying GWG z-score and time-to-delivery using a flexible extension of the Cox model that accounts for violations of linearity and proportionality of hazards assumptions. Models were adjusted for maternal/pregnancy characteristics. We considered type of labour (spontaneous, induced, none) as competing risks. Both non-linear and time-dependent effects of GWG were observed among all deliveries (n=1927); hazard of delivery was minimized at a GWG z-score of 0.7. At 28 weeks' GA, hazard ratio (HR) of delivery was 2.7 at z=-2 and 1.3 at z=2 relative to z=0. Effect estimates were attenuated at 32 weeks' (HR=1.8 at z=-2, HR=1.2 at z=2), and approached null at 37 weeks' GA. Associations were driven by spontaneous labour, which retained non-linear and time-dependent effects similar to all deliveries; conversely, the shape of the relationship differed markedly for induced and no labour deliveries, while its strength did not appear to change across GA. Among twin pregnancies with spontaneous delivery, gestational weight gain demonstrated both non-linear and time-dependent relationships with gestational age at birth.

HOW IS GESTATIONAL WEIGHT GAIN BETWEEN CLINICAL VISITS BEST ESTIMATED IN TWIN AND SINGLETON PREGNANCIES? Michelle Dimitris, Jay Kaufman, Robert Platt, Katherine Himes, Lisa Bodnar, Jennifer Hutcheon (McGill University)

Studies of maternal weight gain and perinatal outcomes typically use one total cumulative measure of weight gain. While there is growing interest in examining serial weights, analyses (i.e. time-to-event) often require estimation of information collected between measurements. We evaluated the accuracy and precision of models for estimating maternal weight between prenatal visits in both twin and singleton pregnancies. We leveraged serial prenatal weights abstracted for a large cohort of dichorionic twin and case-cohort of singleton pregnancies delivered from 1998-2014 at Magee-Women's Hospital in Pittsburgh, Pennsylvania. We retained pre-pregnancy and delivery weights, as well as those collected at first and glucose screening visits, to mimic a typical data collection schedule. Next, we fit interpolation models, estimated weights among those not retained, and calculated the difference between estimated and observed weights in kilograms. Finally, we compared median, interquartile range (IQR), and mean squared error (MSE) of differences by model. We evaluated 16 models: 4 individual (last value carried forward, linear using proximal weights, linear/quadratic terms) and 12 pooled (mixed effects with random intercept/slope with linear, quadratic, log transformed, fractional polynomial and/or spline terms). Among both twins ($n=2033$, n weights estimated=16127) and singletons ($n=8721$, n weights estimated=70742), pooled models with random effects for pregnancy and gestational age and cubic splines with knots demarcating trimesters performed best (MSE=2.29, median=0.02, IQR=-0.88;0.86 in twins; MSE=2.04, median=0.02, IQR=-0.83;0.80 in singletons). Comparable models included individual linear interpolation using proximal weights (MSE=2.61 and 2.12 in twins and singletons, respectively) and pooled quadratic interpolation with random intercept and slope (MSE=2.86 and MSE=2.42). Generally, approaches benefitted from incorporating both flexibility and individual variation.

PRENATAL PHTHALATE CONCENTRATIONS AND PLACENTAL HORMONES: COMPARING TWO MULTIVARIABLE MODELS Qing Yin, Shyamal Peddada, Xiaoshuang Xun, Shanna Swan, Marianthi-Anna Kioumourtzoglou, Emily Barrett, Sheela Sathyanarayana, Jennifer Adibi (University of Pittsburgh)

Linear models (LM) are often used to model the relationship between prenatal exposures, such as phthalate metabolites and endogenous biomarkers, such as placental hormones. However, there is no evidence to justify the use of LM in all cases. Analyzing data from The Infant Development and Environment Study (TIDES), we discovered that LMs are appropriate in some cases but not in all. Since a priori one does not know the choice of the model, we explored the Generalized Additive Model (GAM), a flexible nonparametric alternative. TIDES data included 1st trimester pregnant women (N=525) enrolled at prenatal clinics in four U.S. cities. We considered the phthalate metabolites, MnBP, MiBP, MBzP, MEHP and MEP, and placental hormones, hCG, PAPP-A, estriol, Inhibin-A and AFP to compare LM and GAM. All analyses were adjusted for specific gravity, stressful life events, study center, gestational age at blood draw, maternal age, race, education, BMI, income and marital status. Residual analysis using LM suggested some nonlinear relationships. In all such instances, GAM had better adjusted R² than LM. Visually and quantitatively, GAM fitted the data better than LM to model the relationship between phthalates and hormones. For example, for MEP and estriol in females, the adjusted R² and p-value from LM were 0.47 and 0.31, respectively. Whereas, the adjusted R² and p-value from GAM were 0.59 and < 0.01, respectively. For MiBP and Inhibin-A in males, the adjusted R² and p-value from LM were 0.07 and 0.77, respectively. Whereas, the adjusted R² and p-value from GAM were 0.25 and 0.047, respectively. In all instances where LM fitted the data well, so did GAM. However, whenever the data exhibited nonlinear patterns, the GAM was a better choice. In summary, we show that GAM is a flexible nonparametric model to describe associations between a prenatal exposure and a placental response, both measured as biomarkers.

DEFINING EARLY-ONSET PREECLAMPSIA IN REGISTER DATA Julia F. Simard, Marios Rossides (Stanford School of Medicine)

Background: Early-onset preeclampsia (EO-PE), traditionally defined as presenting <34 weeks gestation, is associated with placental abruptions, stroke, and fetal death compared to late-onset PE (LO-PE). Women with systemic lupus (SLE) have a higher risk of EO-PE relative to the general population. No one definition is used in research. Consequently, underestimating EO-PE and biasing studies. **Methods:** Women from the Swedish Lupus Linkage, including both SLE patients and general population comparators (GP), with ≥ 1 singleton pregnancy in the Medical Birth Register (MBR) were included (2002-2012). PE was defined via ICD-10: O11, O14-O15. We first used gestational age at delivery (<34 weeks vs ≥ 34 weeks) to define EO-PE v LO-PE. We then applied a second definition to reclassify EO-PE as present if the first PE visit in the National Patient Register (NPR) was <34 estimated gestational weeks (using LMP). We crosstabulated the 2 definitions separately for SLE and GP. Sensitivity and specificity were calculated using the NPR-based definition as the gold standard. Sensitivity analysis included all PE identified in the MBR and assumed that date of delivery was the onset date if no NPR visit was identified. **Results:** 263 pregnancies were diagnosed with PE. The majority (94%, n=247) had PE also coded in the NPR. Of those, 48 were classified as EO-PE based on gestational age at delivery (n SLE=23). Using first visit in the NPR with PE, 7 more cases of EO-PE were identified. 8% of EO-PE in SLE was misclassified as LO-PE compared to ~17% in the GP. Sensitivity and specificity of EO-PE for SLE pregnancies were 92% and 100%, and were comparable in GP (83% and 100%, respectively). **Conclusions:** In the general population, EO-PE was more likely to be misclassified as LO-PE than in the high risk SLE population (17 vs 8%). As a result, research aimed to identify biological and maternal predictors of EO-PE may be dealing with differentially misclassified outcomes or samples.

FUTILITY AND SAFETY MONITORING IN A PEDIATRIC PATIENT CHOICE TRIAL Erinn Hade, Peter Minneci, Yuri Sebastiao (The Ohio State University)

While safety monitoring procedures in randomized clinical trials are well established, similar methods have not been thoroughly investigated for patient choice trials (PCT). PCTs allow consented and eligible participants to choose treatment allocation. PCTs follow similar procedures as would a randomized clinical trial, however due to patient choice, analyses for monitoring and for final inference, need to account for this selection mechanism to facilitate causal inference. Recent work has considered safety monitoring in the observational setting for vaccine trials and surveillance studies and has extended randomized trial group sequential methods to accommodate covariate adjustment. In a multi-site pediatric trial of non-operative management for uncomplicated appendicitis, we investigate the performance of the Lan-Demets error spending approach and the more recent, group sequential estimating equation approach, when adjustment for treatment selection is made through inverse probability weighting (IPW). Assessment of futility to ensure that the success rate of non-operative management achieves a minimum threshold aims to protect children and families from unacceptable therapy. We investigate several model types for estimation of the probability of treatment selection. Simulation results suggest that power after IPW adjusted interim analyses is maintained, particularly when there is strong confounding by site characteristics. At the interim analysis time, when 25% of the non-operative patient target recruitment had achieved one year of follow up, a total of 246 patients had been enrolled (92 in the non-operative management group). Futility was assessed for co-primary endpoints, the success rate and number of disability days. Traditional logistic regression and boosted regression were used to find the treatment selection model that best balanced pre-treatment covariates. In our data, logistic regression provided better balance.

EXPOSURE TO TRAFFIC-RELATED AIR POLLUTION AND THYROID DYSFUNCTION DURING PREGNANCY: A MULTI-COHORT STUDY

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Air pollutants such as polyaromatic hydrocarbons can interfere with the endocrine system, e.g., activation of estrogen receptor gene. Less clear is whether exposure to air pollution might disrupt thyroid function. Thyroid disruption is of particular importance in pregnant women due to the critical role of thyroid hormones for embryonic brain development. We examined the association between exposure to traffic-related air pollution and thyroid function during pregnancy. In 9931 pregnant women from 4 birth cohorts in Europe and 1 cohort in the US, we estimated residential air pollution concentrations (i.e., nitrogen oxide [NO] and particulate matter [PM]), during the 1st trimester of pregnancy using land-use regression or satellite aerosol optical depth models. We measured free thyroxine (T4) and thyroid stimulating hormone (TSH) at around 13 weeks of gestation. We defined hypothyroxinemia as free T4 in the lowest 5th percentile within each cohort with normal TSH and subclinical hypothyroidism as TSH in the highest 5th percentile in the setting of normal free T4. We estimated OR (95%CI) with logistic regression models and combined adjusted cohort-specific effect estimates using random-effects meta-analysis. We applied inverse probability-weighting to correct for missing data. Higher exposures to PM10 and PM2.5 were associated with higher odds of hypothyroxinemia in pregnant women (OR=1.34, 95%CI:1.05-1.71 per $\Delta 10 \mu\text{g}/\text{m}^3$ for PM10 ; OR=1.33, 95%CI:1.11-1.60 per $\Delta 5 \mu\text{g}/\text{m}^3$ for PM2.5). Higher exposures to PM10, PM2.5 and PMcoarse were also positively associated with subclinical hypothyroidism. We found no association between NO exposure and thyroid function. The observed association between PM exposure and low thyroid function in pregnant women has high public health relevance. Traffic-related air pollution exposure is widespread and hypothyroxinemia and subclinical hypothyroidism may adversely influence offspring brain development.

POSTPARTUM DEPRESSIVE SYMPTOMS AND ATTENDANCE AT POSSIBLE SCREENING VENUES, 2012-2015 – 8 PRAMS

JURISDICTIONS Sarah Haight, Sherry Farr, Michael Yogman, Jean Ko (Centers for Disease Control and Prevention (CDC))

Background: Early detection of postpartum depression may result in improved engagement in treatment and outcomes. Screening women for depression only at the 6-week postpartum obstetric visit may miss women who do not attend or whose depressive episode occurs earlier or later postpartum. We evaluated engagement with health services in the postpartum period to identify potential opportunities for postpartum depression screening. **Methods:** We used Pregnancy Risk Assessment Monitoring System (PRAMS) data, 2012-2015, from 8 jurisdictions (n=22,885, representing 1,820,000 women). We calculated percent attending a postpartum check-up, a well-baby visit, and having a postpartum home visit by postpartum depressive symptoms (PDS). PDS was assessed using the 2-item Patient Health Questionnaire. Adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) were calculated to compare visit attendance by PDS status, adjusted for jurisdiction, maternal age, race, marital status, education, insurance status during pregnancy, previous live birth, pre-pregnancy stressors, and infant's NICU status and gestational age. Analyses were conducted in SUDAAN, accounting for complex sampling. **Results:** Among women with and without PDS, respectively, almost all attended a postpartum check-up (85.8% and 91.9%; aPR=0.97, 95% CI= 0.94, 0.99) and well-baby visit (97.6% and 99.0%; aPR=0.99, 95% CI=0.98, 1.00); 13.6% and 11.0% had a home visit (aPR=1.16, 95% CI=1.00, 1.34). Of women with PDS who did not attend a postpartum visit, 91.5% attended a well-baby visit and 13.6% reported home visitation; representing over 27,000 women with PDS who could have been screened for depression, if provided at the other 2 venues. **Conclusion:** Many women with PDS who did not attend their postpartum visits engage in well-baby visits and home visitation services representing a potential opportunity for increasing early identification of PDS and referral for care.

FACTORS ASSOCIATED WITH THE TRAJECTORY OF GESTATIONAL WEIGHT GAIN: A MULTILEVEL ANALYSIS

Kohta Suzuki, Satoshi Shinohara, Shuji Hirata (Aichi Medical University)

Inappropriate birthweight might be a risk factor of inappropriate childhood growth and development based on “Developmental Origins of Health and Disease” concept. It has been suggested that gestational weight gain (GWG) was a major factor which was associated with birthweight. Moreover, GWG is an intermediary of the association between other prenatal factors, such as hypertensive disorders of pregnancy (HDP) and gestational diabetes mellites (GDM) and birthweight. However, there was no study to describe the trajectory of GWG and to explore the factors associated with GWG. This study explored the factors associated with GWG by using multilevel analysis. This study included women who received prenatal checkup and delivered a singleton at the University of Yamanashi Hospital between July 1, 2012 and September 30, 2017. Outcomes were GWG at each prenatal check-up and explanatory variables included maternal age, maternal pregestational weight status (PWS), maternal smoking during pregnancy, HDP, GDM and infertility treatment. Multilevel analyses were conducted by using these outcomes and variables stratified by the sex of children. In total, 37239 prenatal examination results were obtained from 2377 pregnant women. In both sex of children, maternal age, maternal PWS, GDM were significantly associated with trajectory of GWG. Furthermore, interaction terms of maternal age, maternal PWS and GDM with gestational duration were also significantly related with GWG. In boys, HDP and maternal smoking during pregnancy were significantly associated with GWG. On the other hand, in girls, there were significant associations between birth order and interaction terms of birth order and maternal smoking during pregnancy with gestational duration and GWG. In conclusion, it was suggested that GWG might intervene the association between some prenatal factors, such as HDP and GDM, and birthweight.

FOOD INSECURITY AND ANTEPARTUM DEPRESSION IN THE NATIONAL CHILDREN'S STUDY Megan Richards, Ming Li, Molly Rosenberg, Margaret Weigel, Christina Ludema (University of Nevada)

Food insecurity, defined as the limited or uncertain availability of nutritionally adequate food, is a serious problem among pregnant women. Food insecurity is associated with depressive symptoms in adults, supporting the hypothesis that it also increases depression risk among pregnant women. We aimed to assess this relationship in a cohort of pregnant women and to apply this estimate to the US pregnant population by standardizing our cohort results to a nationally representative sample. Among pregnant women who participated in the National Children's Study, Initial Vanguard Study (NCS-IVS) (n=752), food insecurity was collected using the 6-item Household Food Security Survey Module. Depressive symptoms were assessed twice during pregnancy using the Centers for Epidemiologic Study Depression Scale (CES-D). Generalized estimating equations were used to estimate the association between food insecurity and antepartum depressive symptoms, adjusting for demographic factors, mental health history, previous lost pregnancy, and pregnancy intention. Inverse probability of sampling weights were used to standardize the estimates to the US population using the National Health and Nutrition Examination Survey. We accounted for missing data using multiple imputation. In NCS-IVS, 20.5% of women were food insecure and 8.5% of women reported depressive symptoms. Household food insecurity was significantly associated with an increased risk of antepartum depressive symptoms (aRR:2.88; 95% CI: 1.49, 5.56) in the NCS-IVS cohort. Standardization attenuated the results, but still showed a strong association (aRR: 2.56; 95% CI: 0.99, 6.69). Food insecurity is associated with an increased risk of antepartum depressive symptoms in both the NCS-IVS cohort and the US population. Prevention efforts should focus on decreasing food insecurity through food assistance programs as well as increased screening for both food insecurity and mental health conditions at prenatal visits.

METABOLOMIC MARKERS OF ANTEPARTUM DEPRESSION AND SUICIDAL IDEATION Susanna D. Mitro, Gloria T. Larrabure-Torrealva, Sixto E. Sanchez, Samantha A. Molsberry, Michelle A. Williams, Clary Clish, Bizu Gelaye (Graduate School of Arts and Sciences, Harvard University, Boston, MA)

Background: Several recent analyses have described metabolomic markers associated with major depressive disorder (MDD) and suicidal ideation (SI) in non-pregnant adults. We examined the metabolomic profile of MDD and SI during mid-pregnancy, a time of high susceptibility to mood disorders. **Methods:** We collected fasting 2nd trimester blood samples from 100 pregnant Peruvian women. Three hundred and seven metabolites were profiled using liquid chromatography-mass spectrometry. We used the Patient Health Questionnaire 9 (PHQ-9) to define MDD (PHQ-9 score ≥ 10) and SI (having thoughts that you would be better off dead, or of hurting yourself). Multivariate logistic regression was used to calculate odds ratios (ORs), adjusting for age, gestational age, and pre-pregnancy BMI. **Results:** Women with MDD (n=29) and women with SI (n=18) were significantly more likely to have poor sleep, higher anxiety, and greater perceived stress than women without MDD or without SI. In adjusted models, 3 triacylglycerol metabolites were associated with higher odds of MDD and 4 metabolites (betaine (OR=0.56; 95% confidence interval (CI): 0.33-0.95), citrulline (OR=0.58; 95%CI: 0.34-0.98), isovalerylcarnitine (OR=0.59; 95%CI: 0.36-0.99), tiglylcarnitine (OR=0.59; 95%CI: 0.35-0.99)) with lower odds of MDD. Twenty-six metabolites, including thiamine (OR=0.44; 95%CI: 0.22-0.85), choline (OR=0.29; 95%CI: 0.11-0.81), L-phenylalanine (OR=0.41; 95%CI: 0.19-0.91), and betaine (OR=0.52; 95%CI: 0.28-0.99), were associated with lower odds of SI and no metabolites with higher odds of SI. Only betaine was associated with both MDD and SI. No metabolites remained significant after false discovery rate correction. **Conclusions:** Some metabolites associated with MDD or SI in non-pregnant adults, such as betaine, choline, thiamine, and L-phenylalanine, were also associated with antenatal MDD or SI. These metabolites may be predictive markers for depression. Larger studies are needed to corroborate our findings.

DOES PRENATAL EXPOSURE TO AIR POLLUTION IMPACT OBSTETRIC OUTCOMES AMONG WOMEN WITH TYPE 1 DIABETES MELLITUS?

Andrew Williams, Marion Ouidir, Shanshan Li, Seth Sherman, Jenna Kanner, Candace Robledo, Pauline Mendola (Eunice Kennedy Shriver National Institute of Child Health and Human Development)

Background: Women with type 1 diabetes mellitus (T1DM) are at increased risk for poor obstetric outcomes. Prenatal air pollution exposure has also been associated with poor obstetric outcomes. Oxidative stress during pregnancy associated with air pollution exposure may increase risk of adverse outcomes among women with T1DM. **Methods:** Singleton deliveries from the Consortium on Safe Labor (2002-2008) were examined. Women with T1DM (n=507) were compared to 204,384 women without autoimmune disease. Average whole pregnancy criteria air pollutant exposure (ozone (O₃), carbon monoxide (CO), particulate matter >10 microns (PM₁₀), particulate matter >2.5 microns, sulfur dioxide (SO₂), nitrogen oxides) was based on modified Community Multiscale Air Quality models. Poisson regression models with interaction terms for T1DM*pollutant estimated relative risks (RR) and 95% confidence intervals (95% CI) for adverse obstetric outcomes. Models adjusted for maternal characteristics and area of residence. **Results:** Most observations were not statistically significant and some inverse associations were observed. However, O₃ exposure (continuous) was associated with a 10% increase in risk of perinatal mortality (RR: 1.10, 95%CI:1.03,1.18) and a 6% increase in risk for indicated preterm birth (RR:1.06, 95%CI:1.02,1.10). PM₁₀ exposure was associated with a 7% increase in risk of cesarean delivery after induction (RR:1.07, 95%CI:1.00,1.14), and a 12% increase in risk for indicated preterm birth (RR:1.12, 95%CI:1.05,1.18). While babies born to women with T1DM are at increased risk for macrosomia, exposure to criteria air pollutants may increase risk of small for gestational age births by as much as 15% (SO₂ RR:1.15, 95%CI:1.01,1.31). **Conclusion:** Exposure to criteria air pollutants during pregnancy did not consistently increase risk for poor obstetric outcomes among women with T1DM. Further research is warranted in this understudied area since some increased risks were observed.

SEVERE MATERNAL MORBIDITY AMONG STILLBIRTH AND LIVE BIRTH DELIVERIES IN CALIFORNIA

Elizabeth Wall-Wieler, Suzan Carmichael, Anna Girsan, Ron Gibbs, Deirdre Lyell (Stanford University)

Objective: To compare the rate of severe maternal morbidity between women with stillbirth and live birth deliveries, and to describe the rate of severe maternal morbidity by cause of fetal death among women with stillbirth deliveries. **Methods:** Using data from the Office of Statewide Health Planning and Development in California, we performed a cross-sectional study of 6,450,308 deliveries between 1999 and 2011. Severe maternal morbidity was identified using the CDC severe maternal morbidity index. Poisson regression models were used to examine the rate ratios of severe maternal mortality for women with stillbirth and live birth deliveries. **Results:** The rate of severe maternal morbidity was 577.6 per 10,000 stillbirth deliveries and 99.2 per 10,000 births deliveries. After adjusting for maternal characteristics, the rate of severe maternal morbidity was 4.69 (95% CI 4.46, 4.94) times higher among women who had a stillbirth than women who had a live birth. Among women with stillbirths, stillbirths due to hypertensive disorders and placental conditions had the highest rates of severe maternal morbidity (2,355 per 10,000 deliveries and 1,919 per 10,000 deliveries, respectively), and stillbirth due to fetal malformations and/or genetic abnormalities had the lowest rates of severe maternal morbidity (130 per 10,000 deliveries). **Conclusion:** Women who delivery stillbirths have much higher rates of severe maternal morbidity than women who deliver live births. Rates of severe maternal morbidity varied by cause of fetal death, however, all causes of fetal death had higher rates of severe maternal morbidity than live birth deliveries.

ASSOCIATIONS BETWEEN PREGNANCY INTENTION AND MATERNAL AND OFFSPRING HEALTH: A 2012-2015 SOUTH CAROLINA PRAMS ANALYSIS Danielle Stevens, Chelsea Richard, Harley Davis, Kelly Hunt (Medical University of South Carolina)

Background: Unintended pregnancies encompass approximately 45% of the 6.1 million annual pregnancies in the United States. Despite their prevalence, there is uncertainty around the impact unintended childbearing may have on the health and behavior of the mother and infant. **Objective:** To examine the association between pregnancy intention and maternal and infant health and behaviors using the South Carolina (SC) Pregnancy Risk Assessment Monitoring (PRAMS) data from 2012-2015. **Methods:** Unintended pregnancy was defined as responding “I wanted to be pregnant later,” “I didn’t want to be pregnant,” or “I wasn’t sure what I wanted” to the question, “Thinking back to just before you got pregnant with your new baby, how did you feel about becoming pregnant?”. A weighted propensity scores model was run to examine the impact of pregnancy intention (unintended versus intended) on postnatal outcomes related to maternal and infant health (postpartum check-up, depression, diabetes, birth control use, Cesarean delivery, neonatal intensive care unit admission, premature birth, low birth weight birth, small-for-gestational-age birth, large-for-gestational-age birth, and breastfeeding) among 3,029 participants in SC PRAMS from 2012-2015. **Results:** After propensity scores adjustment for maternal sociodemographics, behaviors, health and previous births, we found significantly reduced odds of a mother receiving a postpartum check-up (Odds Ratio [OR]: 0.10, 95% Confidence Interval [CI]: 0.04, 0.30), initiating breastfeeding (OR: 0.42, 95% CI: 0.23, 0.78), and delivering via a Cesarean section (OR: 0.40, 95% CI: 0.22, 0.74) among women with unintended versus intended pregnancies. **Conclusions:** Unintended childbearing results in reductions in key maternal healthy behaviors in the postnatal period, but does not appear to significantly impact perinatal health. Additional research is needed on the long-term infant health outcomes of unintended pregnancies.

THE ASSOCIATION BETWEEN WOMEN'S INTER-BIRTH INTERVALS AND CARDIOVASCULAR MORTALITY Yiska Loewenberg Weisband, Ronit Calderon-Margalit, Ora B Palitel, Yechiel Friedlander, Hagit Hochner, Orly Manor (Braun School of Public Health, Hebrew University-Hadassah, Jerusalem, Israel)

Background:Conflicting results were shown for the association between women's inter-birth interval (IBI) and future cardiovascular disease (CVD) risk; both a J-shaped and no association have been reported. We aimed to assess whether IBI was associated with all-cause and CVD-related mortality. **Methods:**The Jerusalem Perinatal Study cohort includes all births to residents of Jerusalem in 1964-1976. Follow-up data on all-cause and cause-specific mortality through 2016 was obtained via record linkage. This study included women with at least two singleton births (N=18,546, total person-years=880,399). We calculated intervals between women's first and second birth in the cohort, and minimum intervals between births, as both continuous and categorical variables. We used Cox's proportional hazards models to estimate the associations between IBI and all-cause and CVD mortality, adjusting for age, parity, education, origin, and socioeconomic status. **Results:**In this highly parous population (mean parity=3.5), women with IBIs <15 months had higher all-cause mortality rates (Hazard Ratio(HR) 1.15; 95% Confidence Interval(CI): 1.03–1.29) compared to women with 20-30 month IBIs. No difference was found for women with 30-45 month IBIs (HR 0.97; 95% CI: 0.88–1.08). The linear trend was significant (HR 0.96; 95% CI: 0.93–0.98). Rates of CVD mortality were not statistically significantly different for women with IBIs<15 months (HR 1.13; 95% CI: 0.81–1.57), compared to those with 20-30 month IBIs, but women with 30-45 month IBIs had substantially lower rates (HR 0.69; 95% CI: 0.50–0.95). The linear trend for CVD mortality was also significant (HR 0.90; 95% CI: 0.83-0.97). We found similar trends using minimum IBIs. **Discussion:**In this large population-based study IBI was inversely associated with mortality, suggesting that women with longer IBIs may have sufficient time to recover from the physiological stress of previous pregnancies, leading to reduced CVD mortality.

THE ASSOCIATION BETWEEN WOMEN'S INTER-BIRTH INTERVALS AND CANCER INCIDENCE

Yiska Loewenberg Weisband, Ronit Calderon-Margalit, Ora B Palitel, Yechiel Friedlander, Hagit Hochner, Orly Manor (Braun School of Public Health, Hebrew University-Hadassah, Jerusalem, Israel)

Background: Reproductive characteristics are important risk factors for cancer in women. Little is known about whether inter-birth intervals (IBI) are independently associated with cancer incidence. We aimed to assess the association between IBIs and incidence of any-cancer, as well as breast, colorectal, cervical, and ovarian cancer. **Methods:** Data from the population-based Jerusalem Perinatal Study cohort, that included all residents of Jerusalem who gave birth between 1964-1976, was linked with Israel's National Cancer Registry (total person-years=880,399). For women with at least two live singleton births (N=18,501), we calculated the interval between women's first and second birth in the cohort, and minimum intervals between births. Intervals were grouped into 5 categories (<15 months, 15- <20, 20- <30, 30-45 months had higher risk of breast cancer incidence (Hazard Ratio (HR) 1.17; 95% Confidence Interval (CI): 1.01–1.36) compared to women with 20-30 month IBIs. Women with <15 month IBIs had increased risk of colorectal cancer incidence (HR 1.38; 95% CI: 1.00–1.90) compared to women with 20-30 month IBIs. We did not find evidence of an association between IBI and cervical and ovarian cancer incidence. Results were similar when assessing minimum IBIs and when limiting the analysis to primiparas, to assess the interval between women's first and second birth. **Discussion** To the best of our knowledge, this is one of the first studies to estimate the association of IBI with cancer incidence. Our findings are in line with known breast cancer risk factors such as age at first birth and parity, and highlight IBI as an additional important risk factor for breast cancer incidence.

GESTATIONAL AGE, KINDERGARTEN READINESS, AND EFFECT MODERATION BY MATERNAL SOCIODEMOGRAPHIC FACTORS

David Mallinson, Eric Grodsky, Lawrence Berger, Deborah Ehrenthal (University of Wisconsin-Madison)

Background: Gestational age at birth is associated with children's academic performance, but whether sociodemographic factors modify this relation is uncertain. We examined the association of gestational age with kindergarten readiness and its moderation by maternal sociodemographic characteristics. **Methods:** Data came from a cohort of all Wisconsin birth records linked to Medicaid claims and public education data. Our analytic sample included 151,592 singletons (born 2007-2010; 71% of all eligible births) that matched to Phonological Awareness Literacy Screening–Kindergarten (PALS-K) scores (2012-2016 school years). The exposure was gestational age in weeks. The two outcomes were the PALS-K standardized score (mean 0, standard deviation 1) and meeting the PALS-K school readiness benchmark (≥ 28 points; range 0-102 points). Adjusted linear regressions tested gestational age's association with PALS-K performance and interactions by five maternal sociodemographic variables at delivery: Medicaid coverage for delivery, education, age, race/ethnicity, and marital status. **Results:** Each completed gestational week was associated with a 0.5 percentage point increase in the probability of meeting the readiness benchmark (95% confidence interval [CI] 0.4-0.6 percentage points). Insurance status was the strongest observed modifier. For each completed gestational week, the probability of meeting the PALS-K benchmark was stronger for children of Medicaid-insured mothers by 0.5 percentage points (95% CI 0.3-0.7 percentage points) relative to children whose mothers were not Medicaid covered. This moderation persisted after excluding very preterm births (< 32 weeks gestation). We observed a similar relation with the PALS-K standardized score, although moderation by Medicaid coverage was not significant without very preterm births. **Conclusions:** The costs of preterm birth on school readiness at entry to Kindergarten may be greatest for children whose birth was Medicaid-covered.

RISK FACTORS FOR DUAL BURDEN OF PRETERM BIRTH AND SEVERE MATERNAL MORBIDITY IN CALIFORNIA: VARIATION IN EFFECT BY INSURANCE PAYOR Alison El Ayadi, Rebecca Baer, Caryl Gay, Henry Lee, Laura Jelliffe-Pawlowski, Audrey Lyndon (University of California, San Francisco)

Preterm birth and severe maternal morbidity are independent causes of poor maternal and child health, each with significant long-term consequences. Preterm birth and severe maternal morbidity are also correlated; in California, about 1900 families suffer the dual burden of prematurity and severe maternal morbidity annually. Quality care is critical for mitigating morbidity severity, and varies by insurance coverage. We sought to understand the predictors of dual burden stratified by payor in a retrospective analysis of California livebirths (n=3,059,156) from 2007-2012. We estimated relative risks of dual burden (severe maternal morbidity and preterm birth) by maternal sociodemographic and pregnancy-related characteristics obtained from birth certificates and hospital discharge records using Poisson regression, accounting for hospital clustering, and stratified by delivery payor. Dual burden ranged from 0.36% of privately-insured births to 0.41% of self-paid births. Obstetric comorbidities, multiple gestation, parity, and mode of birth conferred the largest risks across all payors, but effect magnitude varied. For example, the adjusted relative risk of dual burden from preexisting hypertension with preeclampsia ranged from 9.1 (95% CI 7.6-10.9) for privately insured to 15.9 (95% CI 9.1-27.6) among self-payors. Similarly, the adjusted relative risk from cesarean birth ranged from 3.1 (95% CI 2.7-3.5) for women with Medi-Cal to 5.4 (95% CI 3.5-8.2) for women with other insurance among primiparas, and 7.0 (95% CI 6.0-8.3) for privately-insured to 19.4 (95% CI 10.3-36.3) for self-payors among multiparas. Risks of dual burden vary by payor, with disparate risks observed among women without insurance and with non-private insurance. These findings are consistent with literature confirming quality of care variability by insurance for other conditions, and suggest that explicit attention to peripartum care access and processes by payor is needed to reduce disparities.

BEVERAGE INTAKE ACROSS PREGNANCY AND GESTATIONAL DIABETES RISK

Stefanie Hinkle, Mengying Li, Jagteshwar Grewal, Samrawit Yisahak, Katherine Grantz, Aparna Ajjarapu, Cuilin Zhang (Eunice Kennedy Shriver National Institute of Child Health and Human Development)

There is limited data on use of sugar and artificially sweetened beverages (SSB/ASB), coffee, and tea in pregnancy and gestational diabetes (GDM) risk or cardiometabolic profiles. We aimed to examine longitudinal associations between SSB, ASB, coffee, and tea intake in pregnancy with GDM risk. In two separate sub-samples, we also examined 1) associations between these beverages and cardiometabolic biomarkers and 2) caffeine metabolites and GDM risk. We used data from U.S. pregnant women (2009-2013; N=2802) in the NICHD Fetal Growth Studies. Women completed a food frequency questionnaire at enrollment at 8-13 gestational weeks (GW) regarding 1st trimester diet, and an Automated Self-Administered 24-Hour dietary recall was completed at 16-22, 24-29, 30-33, and 34-37 GW (N=1993). Plasma caffeine and paraxanthine were measured at 8-13 GW in a sub-sample of women without obesity (N=2106). GDM (N=85; 4.3%) was ascertained from medical records. Cardiometabolic biomarkers were measured in a sub-sample at 8-13 and 16-22 GW (N=221). All models were adjusted for relevant confounders including diet quality. No significant associations between 1st trimester SSBs (≥ 1 serving/d vs. none, adjusted relative risk [RR]=1.16 [95% CI 0.59, 2.28]), ASBs (RR=0.53 [0.16, 1.80]), coffee (RR=1.04 [0.53, 2.07]), or tea (RR=1.23 [0.57, 2.63]) and GDM risk were observed. Results were similar for intake at 16-22 and 24-29 GW. No consistent associations were observed with cardiometabolic markers. There was no association between plasma caffeine (Quartile 4 vs Quartile 1, RR=0.94 [0.47, 1.88]), paraxanthine (RR=0.81 [0.41, 1.60]) or their sum (RR=0.86 [0.45, 1.66]) at 8-13 GW and GDM risk. In conclusion, in this cohort of low-risk U.S. pregnant women with relatively low consumption of SSBs, ASBs, coffee, and tea, no significant associations were observed with GDM risk or cardiometabolic profile. In addition, plasma caffeine metabolites were not significantly associated with GDM risk.

WEIGHT GAIN DURING PREGNANCY AND SEVERE MATERNAL MORBIDITY: THE ROLES OF MATERNAL COMORBIDITIES AND CESAREAN BIRTH Stephanie Leonard, Suzan Carmichael, Elliott Main, Deirdre Lyell, Barbara Abrams (Stanford University)

Low and high prepregnancy body mass index (BMI) been associated with an increased risk of severe maternal morbidity (SMM). Weight gain during pregnancy may be more modifiable than prepregnancy BMI and its relationship with SMM is uncertain. We conducted a population-based cohort study in California to evaluate the association between pregnancy weight gain and SMM, and potential mediation by gestational comorbidities and/or cesarean birth. We used gestational weight gain z-score charts to standardize for gestational duration and project full-term weight gain. We then categorized gestational weight gain following the Institute of Medicine (IOM) recommendations. Multivariable logistic regression was used to model total associations and an inverse probability weighting approach for multiple mediators was used to estimate absolute and relative natural direct effects. Women with normal weight (18.5-24.5 kg/m²) and adequate weight gain had the lowest SMM prevalence (1.2%) and women with obesity class 3 (≥ 40 kg/m²) and excessive weight gain had the highest SMM prevalence (2.1%). Excessive weight gain increased SMM risk, except in women with prepregnancy underweight; inadequate weight gain also increased SMM risk, except in women with prepregnancy obesity. After accounting for mediation by comorbidities and cesarean birth, the risk of SMM associated with weight gain outside the recommended range was attenuated. In women with obesity class 3, the confounder-adjusted risk ratio for the association between excessive weight gain and SMM decreased from 1.22 (95% CI: 1.06, 1.40) to 1.10 (95% CI: 0.98, 1.22) after accounting for mediation. These data suggest that promotion of weight gain within IOM recommendations could support efforts to reduce the risk of SMM. Weight gain outside of recommendations may confer risk through increased risk of gestational comorbidities, cesarean birth, and other pathways that remain to be explored.

ACUTE AMBIENT AIR POLLUTION EXPOSURE AND UTERINE ARTERY DOPPLER NOTCHING IN THE NICHD FETAL GROWTH STUDIES – SINGLETON COHORT

Marion Ouidir, Fasil Tekola-Ayele, Katherine Grantz, Rena Jones, Rajeshwari Sundaram, Andrew Williams, Pauline Mendola (NICHD/NIH)

Purpose: Increased placental vascular resistance is a proposed mechanism by which ambient air pollution exposure lowers birth weight. We examined the impact of acute maternal air pollution exposure on uterine artery doppler notching, an indicator of placental vascular resistance. **Methods:** After a first ultrasound to confirm gestational age, 2,334 pregnant women with low-risk antenatal profiles were recruited and underwent up to 5 standardized ultrasounds with doppler measurements. Particulate matter < 2.5 microns (PM_{2.5}) and 8-hour maximum average ozone (O₃) at the clinic sites were estimated at the census tract level by the U.S. Environmental Protection Agency's Downscaler model, which uses both monitoring station data and Community Multiscale Air Quality models. Exposures on the day of the ultrasound and the day before were assessed. We used mixed logistic regression to study the longitudinal relative risk (RR) of any, uni- or bi-lateral systolic and diastolic notching compared to no notching by each inter-quartile range increase (IQR; 6 µg/m³ for PM_{2.5}; 18.2 ppb for O₃) adjusted for maternal pre-pregnancy weight, height, education, race/ethnicity, parity, marital status, fetal sex, gestational age at ultrasound, season of conception and daily temperature. **Results:** Each IQR increase in PM_{2.5} on the day of ultrasound was significantly associated with a higher risk of bilateral diastolic notch (RR: 1.10, 95% CI: 1.00-1.20), but we observed decreased risks of any systolic notch (RR: 0.57, 95% CI: 0.45-0.73 the day of) and bilateral systolic notch (RR: 0.41, 95% CI: 0.26-0.64 the day of, RR: 0.45, 95% CI: 0.28-0.71 the day before). Each IQR increase in O₃ on the day before was associated with a decreased risk of unilateral diastolic notch (RR: 0.86, 95% CI: 0.77-0.97). **Conclusion:** Our results suggest average daily acute O₃ and PM_{2.5} exposure do not increase risk of uterine artery doppler notching. No biological plausibility can explain the potential decreased risk.

PREDICTION OF EXCESS PREGNANCY WEIGHT GAIN USING PSYCHOLOGICAL, PHYSICAL AND SOCIAL PREDICTORS: A VALIDATED MODEL IN A PROSPECTIVE COHORT STUDY

Sarah McDonald, Michael Yu, Sherry Van Blyderveen, Louis Schmidt, Wendy Sword, Meredith Vanstone, Anne Biringer, Azadeh Moaveni, Joseph Beyene (McMaster University)

Introduction: World-wide excess pregnancy weight gain (PWG) impacts a large proportion of women, increasing maternal and infant risks. Interventions to date have been largely unsuccessful, with calls for a broader understanding of predictors of PWG, including psychological ones. **Objective:** To develop and validate a prediction model for excess PWG. **Design:** Prospective cohort study.

Setting/Participants/Exposures: We recruited English-speaking women with a singleton pregnancy between 8+0 to 20+6 weeks from 12 obstetrical, family medicine and midwifery centers in Ontario, Canada. We collected data on psychological, physical and social factors. We used stepwise logistic regression analysis to develop a multivariable model to predict excess pregnancy weight gain, with random selection of 2/3 of women for training data and 1/3 for testing data.

Main Outcomes and Measures: Total excess pregnancy weight gain. **Results:** Of 1296 women approached, 81% were recruited. In the final model, based on 970 women (92%), at a mean of 14.8 weeks, nine variables predicted excess PWG.

Variables that positively predicted excess PWG included nulliparity, being overweight, planning to gain in excess of recommendations, eating in front of a screen, low self-efficacy regarding PWG, thinking that family or friends agree or strongly agree that pregnant women should eat two times as much as before pregnancy, identifying as being agreeable and having difficulties with emotion control. The training and testing models yielded areas under the receiver operating characteristic curve of 0.76 (95% confidence interval [CI], 0.72 to 0.80,) and 0.62 (95% CI 0.56 to 0.68), respectively. **Conclusions:** In this first validated prediction model in early pregnancy, we found that excess PWG was moderately predicted by nine factors, including relatively easily modifiable ones such as appropriate plans for PWG and mindfulness during eating, and more challenging domains such as self-efficacy.

GESTATIONAL WEIGHT GAIN AND PREGNANCY OUTCOMES IN WOMEN WITH CHRONIC HYPERTENSION Sylvia Badon, Sascha Dublin, Nerissa Nance, Romain Neugebauer, Thomas Easterling, Craig Cheetham, Lu Chen, Victoria Holt, Lyndsay Avalos (Kaiser Permanente Northern California Division of Research)

Background: Gestational weight gain (GWG) is a potentially modifiable risk factor for pregnancy complications and fetal growth. The Institute of Medicine (IOM) has published GWG guidelines but relationships may be different in women with chronic hypertension, a group at high risk for pregnancy complications. We assessed associations of GWG with adverse pregnancy outcomes in women with chronic hypertension. **Methods:** This retrospective cohort study used routine clinical data for women with chronic hypertension in three integrated health care delivery systems from 2005-2014. We categorized total GWG for outcomes occurring at delivery and rate of GWG for preeclampsia according to the IOM GWG recommendations. We identified outcomes using electronic health records (preeclampsia, cesarean delivery, birthweight, and neonatal intensive care unit (NICU) admission) and birthweight-for-gestational age curves (small-for-gestational age (SGA)). We used log-binomial models to calculate RRs and 95% CIs, adjusted for sociodemographic and medical characteristics. **Results:** In our cohort of 10,813 women with chronic hypertension, 29% of women gained less than, 24% gained within, and 48% gained more than the IOM recommendations. Rates of preeclampsia were 18%, 17%, and 25% and rates of SGA were 16%, 12%, and 8% in each GWG category, respectively. GWG below the IOM recommendations was associated with 42% greater risk of SGA (RR=1.42; 95% CI: 1.24, 1.62). GWG above the IOM recommendations was associated with 52% greater risk of preeclampsia (RR=1.52; 95% CI: 1.34, 1.71) and 23% lower risk of SGA (RR=0.77; 95% CI: 0.67, 0.89). GWG was not associated with risk of Cesarean delivery or NICU admission. **Conclusion:** In women with chronic hypertension, lower GWG was associated with greater risk of SGA, while higher GWG was associated with preeclampsia. Our findings support counseling women with chronic hypertension to gain weight according to the IOM recommendations.

RECURRENCE RISK OF PREGNANCY COMPLICATIONS IN TWIN AND SINGLETON DELIVERIES Maria Sevoyan, Nansi Boghossian (University of South Carolina)

Aim: To estimate and compare the recurrence risk of preterm birth (PTB), gestational diabetes (GDM), gestational hypertension (GH), and preeclampsia (PE) in three groups of women with: (1) singleton following singleton (N=49,868); (2) singleton following twin (N=448); and (3) twin following singleton pregnancy (N=723). **Methods:** We studied women from NICHD Consecutive Pregnancy Study (2002-2010) with ≥ 2 singleton or twin deliveries. Adjusted relative risks (RR) and 95% confidence intervals (CI) of subsequent PTB, GDM, GH and PE were estimated using separate Poisson regression models with robust variance estimators. Women without each respective pregnancy complication in the prior pregnancy formed the reference group. **Results:** For women with two singleton pregnancies, the recurrence risks were increased for subsequent PTB (RR PTB vs no PTB=5.1, 95%CI: 4.8, 5.5), subsequent GDM (RR GDM vs no GDM=22.7, 95%CI: 20.8, 24.8), subsequent GH (RR GH vs no GH=5.8, 95%CI: 5.1, 6.6) and subsequent PE (RR PE vs no PE=8.1, 95%CI: 7.0, 9.3). Similarly, for women where a singleton followed a twin pregnancy, the recurrence risks were increased for PTB (RR PTB vs no PTB =2.5, 95%CI: 1.1, 5.9); GDM (RR GDM vs no GDM=5.2, 95%CI: 2.3, 11.8); GH (RR GH vs no GH =7.6, 95%CI: 2.8, 20.5); and PE (RR PE vs no PE=9.2, 95%CI: 2.9, 28.6). For women where a twin followed a singleton pregnancy, the recurrence risks were increased for subsequent PTB (RR PTB vs no PTB=1.4, 95%CI: 1.3, 1.6); GDM (RR GDM vs no GDM=20.8, 95%CI: 11.6, 37.2); GH (RR GH vs no GH=2.8, 95%CI: 1.0, 7.7); and PE (RR PE vs no PE=3.2, 95%CI: 1.2, 8.2). **Conclusion:** Women who had history of PTB, GDM, GH and PE compared to those without had increased risk of recurrence. Increased risks persisted in all three groups of women. However, recurrence risk magnitude particularly for GDM, varied whether a singleton pregnancy followed a singleton or a twin pregnancy. This information can be used for managing subsequent pregnancies.

ASSOCIATIONS BETWEEN MATERNAL, FETAL AND PLACENTAL FACTORS AND MEDICALLY-INDICATED PRETERM AND EARLY TERM DELIVERIES Maria Sevoyan, Nansi Boghossian (University of South Carolina)

Aim: To examine the association between maternal, fetal and placental factors and medically-indicated preterm birth (PTB) and medically indicated early-term birth (ETB) compared to full-term deliveries. **Methods:** We studied women who delivered the first liveborn, singleton pregnancy in National Institute of Child Health and Human Development Consecutive Pregnancy Study in Utah (2002-2010). Adjusted odds ratios (aOR) and their 95% confidence intervals (CI) of PTB and ETB were estimated for maternal, fetal and placental factors using multinomial logistic regression. Full-term deliveries were used as a reference group. The outcome was the occurrence of medically-indicated PTB (<37 weeks of gestation, n=510), early-term (37-38 weeks, n=2,099) or full-term (≥ 39 weeks, n=32,626) deliveries. Maternal factors include pre-existing and gestational diabetes, pre-existing and gestational hypertension, chorioamnionitis, preeclampsia, and other chronic conditions. Fetal factors include oligohydramnios, polyhydramnios, fetal congenital anomalies, and small for gestational infants. Placental factors include placental abruption and placenta previa. Maternal age, race, prepregnancy body mass index, health insurance, marital status and smoking during pregnancy were controlled in the models. **Results:** Maternal, fetal and placental factors were associated with increased odds of both PTB and ETB compared to full-term deliveries. The magnitude of estimates was higher for PTB compared to ETB, particularly for preeclampsia, fetal congenital abnormalities, placental abruption, and placenta previa. Among maternal chronic health conditions, gestational diabetes was associated with increased odds of ETB (aOR=5.8, 95%CI: 4.9, 6.8) to a larger extent as compared to PTB (aOR=3.3, 95%CI: 2.3-4.7). **Conclusion:** Risk factors associated with medically-indicated PTB and ETB are heterogeneous. This information may help to identify deferential high-risk groups among infants born preterm or early-term.

CONSISTENCY OF MATERNAL RECALL OF FEEDING AT THE BREAST AND EXPRESSED MILK FEEDING ACROSS 6 YEARS Rui Li, Taniqua Ingol, Katie Smith, Reena Oza-Frank, Sarah Keim (Nationwide Children's Hospital)

Background The validity of breastfeeding recall has been established, but most infants today are fed expressed (pumped) milk at least sometimes, not always at the breast. The accuracy of long term recall of this practice has not been assessed. **Objective** To examine the consistency of maternal recall of feeding at the breast and expressed milk feeding between 12 months and 6 years post-delivery. **Methods** At 12 months postpartum, 499 women completed the Brief Breastfeeding and Milk Expression Recall Survey (BaByMERS) to capture ever/never and duration of feeding at the breast, ever/never and duration of feeding expressed milk, and demographics. They were followed up at age 6 to complete the BaByMERS again. Kappa, intraclass correlation coefficient, and Bland-Altman plots examined agreement (consistency) between timepoints. ICC's were stratified by demographics to identify sub-groups with poor consistency. **Results** 299 dyads completed both timepoints. 35% had a post graduate education, 27% had income <\$35,000, 82% identified as White/Caucasian. There was substantial consistency between time points for "ever breastfed or fed breastmilk" ($k=0.71$, 95% CI: 0.44-0.98) and "ever breastfed directly at the breast" ($k=0.76$, CI: 0.62-0.89), but moderate agreement for "ever drink pumped or expressed breastmilk" (ICC=0.48). Recalled duration of feeding at the breast at the 2 timepoints was highly correlated (ICC=0.94). Reporting duration of feeding expressed milk (ICC=0.84) was somewhat less consistent, especially for Black/African-American or unmarried women or women with \leq high school/GED education (ICC=0.59-0.72). **Conclusions** The consistency of maternal recall of feeding at the breast and feeding expressed milk was quite consistent between 1 and 6 years after delivery. BaByMERS can be used to provide a good quality recall up to 6 years post-delivery. However, some sub-groups of women appeared to have difficulty reporting feeding expressed milk.

MATERNAL DIETARY PATTERNS AND DEPRESSIVE SYMPTOMS

DURING PREGNANCY Peiyuan Huang, Xueling Wei, Minshan Lu, Dongmei Wei, Jinhua Lu, Songying Shen, Mingyang Yuan, Niannian Chen, Huimin Xia, Xiu Qiu (Guangzhou Women and Children's Medical Center, Guangzhou Medical University)

Objective: To explore associations between maternal dietary patterns and depressive symptoms in early and late pregnancy in Chinese population. **Methods:** 17439 pregnant women from the prospective Born in Guangzhou Cohort Study, were included. Maternal diet information was collected by a validated self-administered food frequency questionnaire at 24-27w of gestation. Dietary patterns were identified by cluster analysis. Depressive symptoms were measured by Self-rating Depression Scale in both early(<20w) and late(35-38w) pregnancy, with scores ≥ 53 defined as the presence of symptoms. Depressive symptoms during pregnancy were categorized as 'absent'(-/-), 'early pregnancy only'(+/-), 'late pregnancy only'(-/+), and 'persistent'(+/+). Multinomial logistic regression was used to explore associations between dietary patterns and depressive symptoms. **Results:** 6 dietary patterns were identified: 'Fruits and nuts'(N=2242,12.9%), 'Meats'(N=2956,17.0%), 'Varied'(N=3868,22.2%), 'Traditional'(N=2728,15.6%), 'Dairy and eggs'(N=2376,13.6%), and 'Vegetables'(N=3269,18.8%). There were 12755(73.1%), 1945(11.2%), 1319(7.6%), and 1420(8.1%) women in 'absent', 'early pregnancy only', 'late pregnancy only', and 'persistent' groups of depressive symptoms, respectively. When other groups were compared with 'absent' group, women with 'Varied' pattern (richer in non-leafy and non-cruciferous vegetables, fish, seafood, sweets, and desserts) had higher risk of persistent depressive symptoms than those with 'Fruits and nuts' pattern (adjusted odds ratio 1.24, 95% confidence interval 1.02-1.51). **Conclusion:** Maternal dietary patterns were associated with depressive symptoms during pregnancy. Diets richer in fruits and nuts might contribute to lower risk of persistent depressive symptoms in Chinese pregnant women. Further research is needed to explore potential interactions between nutrition and mental health during pregnancy.

GESTATIONAL WEIGHT GAIN AMONG CIGARETTE SMOKERS AND QUITTERS: SWITCHING FROM INADEQUATE TO EXCESSIVE

Xiaozhong Wen, Josua Sorrentino, Fedora Jeanty-Fils, Eve Reid (State University of New York at Buffalo)

Objectives: Appropriate gestational weight gain (GWG) is crucial for maternal and child health. GWG can be influenced by smoking and smoking cessation, given effects of nicotine on suppressing appetite and enhancing resting metabolic rate. But current guidelines on GWG do not consider smoking or smoking cessation status.

We aimed to examine GWG among persistent cigarette smokers and quitters.

Methods: Within the UB Pregnancy and Smoking Cessation Study (2015-2018), we analyzed weight data of 23 daily smoking pregnant women in Buffalo, NY. Smoking abstinence was confirmed by breath carbon monoxide and urine cotinine tests.

Women reported their pre-pregnancy weight at enrollment and we measured their weight repeatedly at pre-test, initial intervention, post-test, end of pregnancy, pre-delivery, and then monthly visits from delivery to 12 months postpartum. We calculated total GWG by subtracting pre-pregnancy weight from the last weight measure before delivery (≥ 35 weeks of pregnancy). According to the Institute of Medicine (IOM) guidelines, we classified total GWG into 3 categories (inadequate, appropriate, and excessive) by pre-pregnancy body mass index. We compared mean GWG using t-test and GWG categories using Fisher's Exact Test. **Results:** Seventeen of 23 participants (73.9%) quit smoking successfully by our smoking cessation intervention. Quitters had much higher total GWG (mean [SD], 41.4 [21.8] pounds), compared to non-quitters (9.9 [23.7] pounds; $p=0.012$). Only 11.8% of quitters and 16.7% of non-quitters had appropriate GWG. Patterns of inappropriate GWG were strikingly distinct ($p=0.001$) between quitters and non-quitters: 76.5% of quitters (13/17) had excessive GWG, whereas 83.3% of non-quitters (5/6) had inadequate GWG. **Conclusion:** Smoking is associated with inadequate GWG, while smoking cessation is associated with excessive GWG. Weight management intervention is needed for both pregnant smokers and ex-smokers to achieve healthy weight gain.

MATERNAL AND NEONATAL OUTCOMES OF FETAL MACROSOMIA IN THE COMMUNITY BIRTH SETTING Sabrina Pillai, Marit Bovbjerg, Melissa Cheyney (Oregon State University)

Introduction. Fetal macrosomia is associated with negative outcomes for both pregnant women and neonates, though little work has been done comparing different severities of macrosomia. Planned community births in the United States have higher rates of gestational age-adjusted macrosomia than do planned hospital births, providing increased statistical power through all high birthweights (BW). **Methods.** Maternal and neonatal outcomes associated with low (4000-4499 g), medium (4500-4999 g), and high (≥ 5000 g) macrosomia were compared to normal BW neonates (2500-3999 g), using medical records-based data from a registry of planned community births, 2012-2017 (N=63,437). Maternal outcomes included cesarean delivery, perineal trauma, and postpartum hemorrhage. Neonatal outcomes included birth injury, shoulder dystocia, respiratory distress, neonatal intensive care unit admission, and fetal/neonatal death. Logistic regressions controlled for primiparity, pre-gravid body mass index, gestational diabetes, and preeclampsia. **Results.** One-fifth (n=12,363) of the sample were macrosomic (81% of these were low, 16.7% medium, and 2% high). Low, medium, and high macrosomia were associated in a dose-response fashion with higher odds of all outcomes, compared to normal BW. For example, the adjusted odds ratios and 95% confidence intervals for maternal hemorrhage for low, medium, and high macrosomia vs. normal BW were 1.7 (1.5-2.0), 2.3 (1.8-2.8), and 5.4 (3.6-8.1), respectively. For shoulder dystocia, low: 4.9 (4.3-5.5), medium: 12.6 (10.8-14.8), high: 29.5 (21.7-40.1). Other outcomes had similar patterns. **Discussion.** Unnuanced macrosomia definitions of >4000 g mask heterogenous risks that increase substantially as fetal weight increases.

GENETIC RISK SCORE OF TYPE 2 DIABETES AND PROGRESSION RISK FROM GESTATIONAL DIABETES TO TYPE 2 DIABETES: RESULTS FROM TWO INDEPENDENT POPULATIONS Mengying Li, Mohammad Rahman, Jing Wu, Ming Ding, Jorge Chavarro, Yuan Lin, Sylvia Ley, Wei Bao, Louise Grunnet, Stefanie Hinkle, Anne Cathrine Thuesen, Edwina Yeung, Robert Gore-Langton, Seth Sherman, Line Hjort, Freja Bach Kampmann, Peter Damm, Fasil Tekola-Ayele, Aiyi Liu, James Mills, Allan Vaag, Sjurdur Olsen, Frank Hu, Cuilin Zhang (Eunice Kennedy Shriver National Institute of Child Health and Human Development)

Background: Women with prior gestational diabetes (GDM) are at exceptionally high risk for type 2 diabetes (T2D). Yet, little is known about genetic determinants for the progression to T2D from GDM. Further, inference from existing data is hindered by small sample size. In a large study based on two independent populations, we examined a genetic risk score (GRS) for T2D in relation to the progression risk. **Methods:** This study included white women in the Diabetes & Women's Health Study, which followed women with GDM from the Nurses' Health Study II (NHSII, N = 1998) and the Danish National Birth Cohort (DNBC, N = 550). A GRS of T2D was calculated using 59 T2D SNPs (GRS59) from genome-wide association studies in European populations. GRS scores for beta-cell function (GRSBC) and insulin resistance (GRSIR) were derived based on subsets of these SNPs. The RRs of progression to T2D were estimated using log-binomial regression. RRs from the two cohorts were meta-analyzed using fixed effects models. **Results:** During the study follow-ups of more than 10 years after the index pregnancy, 416 (20.8%) in NHSII and 155 (28.2%) women in DNBC developed T2D. GRS59 was positively related to the risk of progression to T2D. RRs (95% CI) for increasing quartiles of GRS59 were 1.00, 0.99 (0.79, 1.23), 1.26 (1.03, 1.55), and 1.25 (1.01, 1.53), respectively (p-trend = 0.008). The associations were significantly stronger among lean (pre-pregnant BMI < 25 kg/m²) than overweight or obese women (p-interaction < 0.001). Further, GRSIR, but not GRSBC, was related to the risk of T2D. RRs (95% CI) for increasing quartiles of GRSIR were 1.00, 1.25 (1.02, 1.55), 1.32 (1.07, 1.64), and 1.29 (1.05, 1.58), respectively (p-trend = 0.02). The results were generally consistent across the two cohorts. **Conclusion:** In this large prospective study of women with prior GDM, greater GRS of T2D, especially GRS of insulin resistance, was associated with a greater risk of progression to T2D.

ATOVAQUONE-PROGUANIL EXPOSURE IN PREGNANCY AND RISK FOR ADVERSE FETAL AND INFANT OUTCOMES

Clinton Hall, Julie Gutman, Kathrine Tan, Zeina Khodr, Anna Bukowinski, Gia Gumbs, Ava Marie Conlin, Natalie Wells (Naval Health Research Center)

Malaria infection in pregnancy can lead to maternal and fetal complications. Only chloroquine (CQ) and mefloquine (MQ) are recommended for chemoprophylaxis in pregnancy, but parasite resistance and contraindications may leave some women with no recommended options. Limited data suggest atovaquone-proguanil (AP), a highly effective antimalarial, might be suitable for malaria prevention in pregnancy, but more evidence is needed. Data for pregnancies and live births among active duty women, 2003-2014, from the Department of Defense Birth and Infant Health Research program were linked with pharmacy data to determine antimalarial exposure, defined as a drug dispensation date in pregnancy. Multivariable Cox and logistic regression models were used to assess the relationship between antimalarial exposure and fetal and infant outcomes, respectively. Among 199,017 pregnancies, 51 were exposed to AP, 159 to MQ, and 133 to CQ. Overall, 15.1% of unexposed pregnancies and 27.5%, 13.8%, and 4.5% of pregnancies exposed to AP, MQ, and CQ, respectively, ended in miscarriage (adjusted hazard ratios [aHR]=1.72, 95% confidence interval [CI]=1.02-2.90; aHR=1.03, 95% CI=0.68-1.57; and aHR=0.38, 95% CI=0.17-0.85, respectively). Among 160,944 live births, 36 were exposed to AP, 130 to MQ, and 122 to CQ. Compared with unexposed infants, there was a statistically insignificant increased risk for a composite poor live birth outcome (preterm birth, low birthweight, or small for gestational age) among AP exposed infants (adjusted odds ratio=2.02, 95% CI=0.88-4.60), but not MQ or CQ exposed infants. Birth defects were seen in 3.0% of unexposed and 5.6%, 0.8%, and 0.8% of infants exposed to AP, MQ, and CQ, respectively. The small number of AP exposed pregnancies highlights the difficulty in assessing safety. While definitive conclusions are not possible, these data suggest further research of AP exposure in pregnancy and fetal loss is warranted.

ASSOCIATION OF REPRODUCTIVE FACTORS WITH ANTI-MÜLLERIAN HORMONE LEVELS

Nydjie Grimes, Brian Whitcomb, Alexandra Purdue-Smithe, Katherine Reeves, Susan Hankinson, Bernard Rosen, JoAnn Manson, Elizabeth Bertone-Johnson (University of Massachusetts Amherst)

Anti-Müllerian hormone (AMH) has been established as a marker of ovarian aging and time to menopause. It is unclear how pregnancy and breastfeeding affect ovarian function, rate of ovarian aging and AMH. The relation of parity and breastfeeding with AMH levels has been evaluated only in a few cross-sectional studies and findings have been inconsistent. We assessed the association of each reproductive factor with AMH levels prospectively among participants in the Nurses' Health Study 2. Participants (n=1619) were women 32-49 years of age when providing premenopausal blood sample in 1996-99; AMH was measured using an ultra-sensitive ELISA assay (picoAMH). Parity and breastfeeding duration up until the time of blood collection were measured via biennial questionnaires. AMH values were natural log transformed for analysis, then exponentiated for interpretability. In multivariable linear regression models adjusting for age, smoking, history of infertility, assay characteristics, and other factors, higher parity was associated with higher AMH levels. Geometric mean AMH levels (95% confidence interval) for women with 0, 1, 2, and ≥ 3 pregnancies were 962 (821 – 1128), 1276 (1076 – 1513), 1313 (1172– 1471) and 1380 (1212– 1572) pg/ml, respectively (P for trend = 0.005). However, results were largely attenuated when adjusted for breastfeeding (P for trend = 0.644). In contrast, breastfeeding was related to higher AMH in multivariable models adjusting for parity. Geometric mean AMH levels for women reporting 1, $\geq 1 - 12$, $>12 - 24$, and >24 cumulative months of breastfeeding were 1228 (966 – 1562), 1220 (1064 – 1398), 1356 (1181 – 1556) and 1616 (1391 – 1878) pg/ml, respectively (P for trend = 0.036). Findings suggest that breastfeeding duration is positively associated with AMH levels even after accounting for parity and may potentially slow the rate of ovarian decline.

**RISK OF NEONATAL ABSTINENCE SYNDROME FOLLOWING
PRENATAL EXPOSURE TO METHADONE OR BUPRENORPHINE** Mollie
Wood, Milada Mahic, Marte Handal, Svetlana Skurtveit, Ingunn Olea Lund, Sonia
Hernandez-Diaz (Harvard TH Chan School of Public Health)

Rising rates of opioid addiction mean that pregnant women are more often on opioid maintenance therapy (OMT), necessitating a clinical choice between methadone and buprenorphine. Randomized trials and observational studies have shown that maternal Methadone (M) exposure is associated with higher risk of neonatal abstinence syndrome (NAS) in infants, compared to buprenorphine (B), with effects estimated at about a 20% increased risk. However, residual confounding may explain this, as women on B have worse adherence and more often relapse in pregnancy. We linked Norwegian National Registries data collected from 2009-2015 with data from specialized addiction services. We used log-binomial regression to assess the relative risk of NAS in M vs B exposed pregnancies after adjusting for confounders using inverse probability of treatment weights in the main sample and using the addiction services internal validation sample to further adjust for additional addiction severity confounders. In the main registry data, 77% of the 41 infants exposed to M at the beginning of pregnancy had a diagnosis of NAS compared to 68% of the 72 exposed to B, with similar rates in the xx women with data from the specialized addiction services. Women on M vs those on B more often reported use of heroin in the past 6 months (52 vs 44%), including during pregnancy (18 vs 9%); depression or anxiety (93 vs 80%); and switching OMT within the last 5 years (41 vs 12%). The relative risk of NAS for M vs B 1st trimester-exposed infants was unchanged from a crude of 1.13 to 1.14 (95% CI 0.91, 1.43) after full confounder adjustment; estimates for exposure in the 30 days before delivery were 0.96 and 1.04 (95% CI 0.86 to 1.24), respectively. We found a slightly higher NAS risk for M than for B treatment in early pregnancy but not near delivery, suggesting residual confounding. However, the association was not explained by measured confounding by severity of addiction.

IN UTERO AND NEONATAL EXPOSURES AND LATER RISK OF YOUNG-ONSET BREAST CANCER

Mary Diaz Santana, Katie O'Brien, Aimee D'Aloisio, Gloria Regalado, Dale Sandler, Clarice Weinberg (National Institute of Environmental Health Science)

In utero and neonatal factors have been demonstrated to be associated with certain adult health outcomes, but such influences have not been well studied for young-onset breast cancer. We used a sister-matched case-control study to address this. Cases were women in the Two Sister Study who had been diagnosed with invasive or ductal carcinoma in situ breast cancer before the age of 50, and who had a sister control who had not had breast cancer herself and had also been under age 50 at the time of the diagnosis. In utero and neonatal factors considered were self-reported, and included: mother's preeclampsia, gestational hypertension, diethylstilbestrol use, and gestational diabetes, as well as low birth weight (less than 5.5 pounds), high birthweight (greater than 8.8 pounds), and short gestational age (less than 38 completed weeks). Perinatal factors included being breast-fed or being fed soy formula. In conditional logistic regression analyses, only birthweight was strongly associated with risk. The odds ratio (OR) for low birth weight was 1.52 (95% confidence interval [CI]: 0.97, 2.4) and for high birth weight was 1.91 (95% CI: 1.15, 3.17). We also carried out case-only analyses to assess etiologic heterogeneity for ER-positive versus ER-negative cancer. With age adjustment, being breast fed was associated with reduced odds of ER-negative young-onset cancer, with an OR of 0.66 (95% CI: 0.47, 0.94). Women who had gestated in a preeclamptic pregnancy and later developed young-onset breast cancer were at increased odds for ER-negative cancer 2.17 (95% CI: 1.01, 4.66). The results from this study suggest that certain pre- and perinatal exposures may contribute to subsequent breast cancer risk and tumor type among young women.

PROFILES OF ANTIDEPRESSANTS USED DURING PREGNANCY

OVER 19 YEARS IN DENMARK Yuelian Sun, Julie Werenberg Dreier, Merete Lund Mægbæk, Trine Munk-Olsen, Jakob Christensen (Aarhus University Hospital; National Center for Register-based Research)

Both depression and use of antidepressants (ADs) during pregnancy are of concern when considering the health in mothers and unborn children. Exploring profiles of ADs used during pregnancy is important for deeper research. We studied the use of ADs by using national data over 19 years in Denmark. We identified 1,197,130 live born children between 01 January 1997 and 31 December 2015 in Denmark in the study population. To identify AD use in early pregnancy from available ADs prescribed before pregnancy, we defined the pregnancy period from one month before pregnancy to birth. Information on ADs was obtained from the Danish National Prescription Register. Information on indication of medication was available from 1 April 2004. In total, 28,201 (2.4%) children were born of mothers with at least one AD prescription during pregnancy. Maternal AD prescription during pregnancy constantly increased from 0.4% in 1997 to 4.6% in 2011, but decreased in recent years to 3.0% in 2015. Children whose mothers filled 1, 2, or 3 prescriptions made up 67.7% of the population (31.0%, 19.3%, and 17.4%, respectively). Most children (83.2%) were exposed to one type of AD while 14.9% and 1.9% children were exposed to two or three more types of ADs during pregnancy respectively. Most children (82.2%) were exposed to selective serotonin reuptake inhibitors (SSRIs). Citalopram, Sertraline, Fluoxetine were the drugs most frequently used SSRIs during pregnancy. Among those with information on indication, on average 82.9% SSRIs were prescribed for depression while 18.3% were prescribed for anxiety. However, for Paroxetine 57.4% and 42.7% were prescribed for depression and anxiety, respectively. In conclusion, maternal use of ADs during pregnancy constantly increased from 1997 and reached peak in 2011 but then decreased in the recent years. It is important to monitor use of ADs in pregnancy to ensure health of the pregnant women and the unborn children.

DIFFERENCES IN PRE-PREGNANCY DIET QUALITY BY

OCCUPATION AMONG EMPLOYED WOMEN Ibrahim Zaganjor, Suzan Carmichael, A.J. Agopian, Andrew Olshan, Tania Desrosiers (University of North Carolina at Chapel Hill)

Objective: Maternal diet quality is known to be important for optimal pregnancy health. Thus, understanding the factors associated with diet quality and identifying target populations for future interventions are essential. We examined whether pre-pregnancy diet quality varies by occupation in a population-based sample of employed women. **Methods:** We analyzed interview data from mothers of infants born between 1997 and 2011 who participated in a national case-control study of pregnancy outcomes. In the present analysis, we included 7,341 mothers who reported having a job in the 3 months before conception. Jobs were coded using Standard Occupational Classification (SOC) codes for major occupational groups. Pre-pregnancy diet quality was evaluated using food frequency questionnaire responses to categorize each woman's periconceptional diet according to the Diet Quality Index for Pregnancy (DQI-P); low diet quality was defined as the lowest quartile of the distribution of DQI-P composite and component scores. Logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CI) for the association between 23 occupations and low diet quality. **Results:** None of the occupational groups were strongly associated with low diet quality. Moderate associations (ORs 0.5 to 1.4), most of which included the null, were observed for women employed in management (OR: 1.3; 95% CI: 1.1, 1.7); arts, design, entertainment, sports, and media (OR: 1.4; 95% CI: 0.9, 2.1); protective service (OR 1.3; 95% CI: 0.7, 2.5); and farming fishing, and forestry occupations (OR: 0.5; 95% CI: 0.2, 1.1). **Conclusions:** Our analyses suggest that women in certain occupations may have lower diet quality in the months before pregnancy. Further research is needed to ultimately determine whether certain occupations could benefit from interventions to improve diet quality in the workplace, particularly for women of reproductive age.

MATERNAL EXPOSURE TO INVOLUNTARY CHILD REMOVAL AND POOR SELF-RATED HEALTH: EVIDENCE FROM A PROSPECTIVE COHORT OF MARGINALIZED AND CRIMINALIZED MOTHERS IN A CANADIAN SETTING. Kathleen Kenny, Flo Ranville, Sherri Green, Putu Duff, Melissa Braschel, Ronald Abrahams, Kate Shannon (University of North Carolina at Chapel Hill and University of Manitoba)

Background: Maternal loss of children via the child protection system disproportionately affects racially and socially marginalized mothers, yet health effects on them are not well characterized. This study prospectively examined the relationship of child removal on marginalized sex workers' self-rated health. Given high levels of intergenerational familial separation in this population, we also estimated joint effects of child removal spanning two generations. Methods: Analyses drew on 2010-2015 data from AESHA (An Evaluation of Sex Workers' Health Access), an open prospective cohort of sex workers (n=950) in Vancouver, Canada. Using logistic regression with generalized estimating equations, we modeled the association of past child removal with current self-rated health in a sample of 466 sex workers who ever had a live birth. Joint effects of child removal and childhood history of removal from own parents were also investigated. All models were adjusted for a priori selected confounders: age, education, Indigenous identity, childhood trauma, residential stability, social support, place of solicitation, and violence. Results: Of 466 sex workers, 180 (38.6%) reported child removal at baseline and 147 (31.6%) had a history of removal from own parents. Child removal was associated with increased adjusted odds of poorer self-rated health (odds ratio [OR] =1.50, 95% confidence interval [CI] =1.04, 2.16). Joint effects showed higher odds of poorer self-rated health (OR=2.04, 95% CI=1.27, 3.27) among women with intergenerational familial separation. Conclusion: Child removal was negatively associated with sex workers' self-rated health that was worsened when separation spanned two generations. Findings underscore need to implement sex worker-led family support and preservation services.

PREGNANCY INTENTION AND PHTHALATE LEVELS AMONG PREGNANT WOMEN IN THE INFANT DEVELOPMENT AND ENVIRONMENT STUDY (TIDES) COHORT

Grace Lyden, Emily Barrett, Sheela Sathyanarayana, Nicole Bush, Shanna Swan, Ruby Nguyen (University of Minnesota)

Background: Preconception care plays a pivotal role in positively impacting the health of a pregnancy, and this includes the reduction of exposure to endocrine-disrupting chemicals such as phthalates. We have previously found that women planning a pregnancy with assisted reproductive technology have lower phthalate levels than their non-ART-using counterparts. Therefore, we now hypothesize that, in general, women who intended to become pregnant had lower first trimester phthalate levels than those who had an unintended pregnancy. **Methods:** 804 women enrolled in The Infant Development and Environment Study (TIDES), a prospective pregnancy cohort; 537 (66.8%) women said their pregnancy was planned. Urine samples from first trimester visits were analyzed for 10 phthalate metabolites, which were adjusted for specific gravity and natural-log-transformed to normalize distributions. Unequal-variance t-tests and multiple linear regression, controlling for race, age, income, education, marital status, and parity, were employed to determine whether phthalate levels differed by pregnancy intention. **Results:** In univariate analyses, all first trimester phthalate geometric means were higher in women with unplanned pregnancies, and significantly higher for MBP, MBzP, MECPP, MEHHP, MEHP, MiBP, and Σ DEHP. However, when we controlled for confounders, only MiBP remained significantly associated with unplanned pregnancy (β (95% CI)=-0.22 (-0.38,-0.05)), and the association changed direction so that unintended pregnancies had significantly lower MiBP levels. In a sensitivity analysis with non-whites only and adjusted for confounders, MEP levels were also significantly higher in planned pregnancies. **Conclusions:** In this sample of women, sociodemographic variables modify the potential effects of unintended pregnancy on phthalate levels in the first trimester. Further analyses of the mediating or modifying role of such variables on phthalate levels in pregnancy should be explored.

METABOLIC TRAJECTORIES ACROSS EARLY ADOLESCENCE: DIFFERENCES BY SEX, WEIGHT, PUBERTAL STATUS, AND RACE/ETHNICITY

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Objective: Characterize change in metabolic biomarkers across early adolescence in a multi-ethnic cohort. **Methods:** Among 891 participants in Project Viva we estimated changes in fasting insulin resistance (HOMA-IR), lipids, adipokines, and systolic blood pressure (SBP) between age 6-10 y and 11-16 y. We used multivariable linear regression to examine relations of sex, baseline overweight/obesity (OWOB), baseline pubertal status, and race/ethnicity with changes in the biomarkers during follow-up. **Results:** Participants were median age 7.9 y at baseline and 13.1 y at follow-up. Half (50.2%) of the sample was male, and 65% was White. Mean \pm SD change in biomarkers was: -3.5 ± 20.7 mg/dL glucose, 8.8 ± 18.6 uU/mL insulin, 1.7 ± 4.4 units HOMA-IR, 6.0 ± 12.0 ng/mL leptin, -9.2 ± 7.7 ng/mL adiponectin, -5.1 ± 26.3 mg/dL total cholesterol, -0.9 ± 12.1 mg/dL high density lipoprotein (HDL), -6.1 ± 20.4 mg/dL low density lipoprotein (LDL), 9.9 ± 29.6 mg/dL triglycerides, and 12.5 \pm 9.9 mmHg SBP. Boys exhibited a larger decrease in adiponectin (-0.7 [95% CI: $-1.1, -0.2$] ng/mL) and a greater increase in SBP (3.2 [2.1, 4.3] mmHg) than girls. Participants who were OWOB at baseline experienced larger increases in HOMA-IR (1.3 [0.1, 2.4]), leptin (8.4 [5.7, 11.1] ng/mL), and triglycerides (6.5 [0.2, 12.7] mg/dL); and a steeper decrease in HDL (-3.8 [$-6.2, -1.4$] mg/dL). Pubertal youth had larger decreases in total (-8.0 [$-13.9, -2.1$] mg/dL) and LDL (-7.2 [$-11.9, -2.4$] mg/dL) cholesterol than pre-pubertal youth. In comparison to White youth, Black participants had a larger increase in HOMA-IR (2.0 [0.6, 3.3]), and Hispanics exhibited larger decreases in adiponectin (-1.8 [$-2.8, -0.8$] ng/mL) and HDL (-5.0 [$-9.3, -0.6$] mg/dL). **Conclusions:** We identified differences in metabolic profile trajectories among teens based on sex, race, weight and pubertal status. Whether these differences reflect normal physiological changes of puberty or presage discrepancies in future disease risk is unclear.

THE EFFECT OF PHOTOTHERAPY ON BREASTFEEDING Jean Digitale, Pearl Chang, Michael Kuzniewicz, Thomas Newman (UCSF)

Phototherapy (PT) is a common treatment for jaundice in newborns and may negatively affect breastfeeding (BF). Previous studies of its effect on BF have not controlled for bilirubin levels, which may be higher if BF is not going well. This study evaluated whether PT affected any BF or exclusive BF at two months of age. We obtained electronic medical records on 42,426 infants born in 2010-2014 at ≥ 35 weeks' gestation in 16 Kaiser Permanente Northern California Hospitals with a qualifying bilirubin level (bilirubin within -3 to +4.9 mg/dL of PT threshold for age). Exposures of interest were PT during the birth hospitalization, home PT, and readmission for PT. Outcomes were exclusive BF and any BF reported by caregivers at 2-month well-child visits. We estimated logistic regression models, adjusting for qualifying bilirubin level and other confounding variables. Coefficients from these models were used to estimate marginal risk differences (RD). Of the eligible sample, 28,886 (68%) had 2-month BF data available, of whom 28,746 (99.5%) had complete covariate data. Of these, 25% received PT during the birth hospitalization, 16% received home PT, and 11% were readmitted for PT; 6% had more than one exposure to PT. At two months, 39% were breastfed exclusively and 76% were breastfed at all. While PT during birth hospitalization was associated with lower reported exclusive BF (OR: 0.80, 95% CI: 0.76, 0.85), the association was nearly fully attenuated after adjusting for confounders (adjusted OR: 0.94, adjusted RD: -1.53%, 95% CI: -3.06%, 0.00%). PT during birth hospitalization did not affect any BF at two months after adjusting for confounders (crude OR: 0.92, 95% CI: 0.87, 0.98; adjusted OR: 1.04, adjusted RD: 0.66%, 95% CI: -0.65%, 1.98%). Similarly, neither home PT nor readmission for PT affected any BF outcomes after adjusting for confounding variables. In a large sample of infants from a hospital system that supports BF, PT does not appear to affect BF at 2 months.

RACIAL DISPARITIES IN BREASTFEEDING DURATION AMONG U.S. INFANTS AND THE IMPACT OF DISPARITIES IN BREASTFEEDING INITIATION

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Background: Routine U.S. surveillance of breastfeeding duration, calculated among all infants regardless of whether they ever breastfed, consistently shows disparities between non-Hispanic black (black) and non-Hispanic white (white) infants. We assessed whether the black-white disparity in breastfeeding at 3 months persisted when calculated only among infants who initiated breastfeeding. **Methods:** Breastfeeding data on U.S. infants born in 2011-2015 were obtained from the National Immunization Survey-Child. We calculated breastfeeding initiation rates ($\% \pm \text{half } 95\% \text{ CI}$) by race/ethnicity for each birth cohort. We also calculated rates of any breastfeeding at 3 months by race/ethnicity for each birth cohort, using two sets of denominators: (1) all infants regardless of breastfeeding initiation and (2) only infants who initiated breastfeeding. **Results:** From 2011 to 2015, breastfeeding initiation rates increased from $62.4 \pm 3.3\%$ to $69.4 \pm 3.5\%$ among black infants and from $80.7 \pm 1.2\%$ to $85.9 \pm 1.2\%$ among white infants; the black-white disparity in initiation ranged from 16.2-18.3 percentage points across birth cohorts. Among all black infants, rates of any breastfeeding at 3 months increased from $48.8 \pm 3.4\%$ to $58.0 \pm 3.8\%$. Among black infants who initiated breastfeeding, rates of any breastfeeding at 3 months increased from $78.1 \pm 3.5\%$ to $83.5 \pm 3.2\%$. Calculated among all infants, rates of any breastfeeding at 3 months ranged from 13.7-17.5 percentage points lower among black infants compared with white infants. The disparity was reduced to -0.6-3.8 percentage points when these rates were calculated only among infants who initiated breastfeeding. **Conclusion:** The black-white disparity in breastfeeding at 3 months could be impacted by disparities in breastfeeding initiation. Interventions to support breastfeeding initiation among black mothers (e.g., improving maternity care practices, increasing prenatal intentions to breastfeed) may help reduce breastfeeding disparities.

EFFECT OF DAILY PRENATAL ASPIRIN THERAPY ON CORD BLOOD INFLAMMATORY BIOMARKERS

Lindsey Sjaarda, Edwina Yeung, Sunni Mumford, Keewan Kim, Elizabeth DeVilbiss, Carrie Nobles, Kerry Flannagan, Alexandra Purdue-Smithe, Jessica Zolton, Neil Perkins, Robert Silver, Enrique Schisterman (NICHD)

Objective: Aspirin is used increasingly in pregnancy to reduce adverse pregnancy outcomes such as preeclampsia and preterm birth, among others. The Effects of Aspirin in Gestation and Reproduction (EAGeR) trial noted that preconception-initiated low-dose aspirin (LDA) therapy lowered excessive high sensitivity C-reactive protein (hsCRP) concentrations across pregnancy among women with higher preconception hsCRP. However, it is unknown whether daily maternal aspirin use modifies the neonatal inflammatory profile. Thus, we studied the effect of maternal LDA on an array of inflammatory biomarkers in cord blood in the EAGeR trial. **Methods:** Women trying to become pregnant were randomized to 81 mg aspirin (LDA) or placebo daily, initiated prior to conception. Study drugs were taken while attempting pregnancy and, for those who conceived, through 36 weeks' gestation. Inflammatory biomarkers (i.e., interferon-gamma, interleukin (IL)-1a, IL-2, IL-4, IL-5, IL-10, IL-15, IL-23, TNFa, and hsCRP) were measured in cord blood plasma from 377 live births using a multiplex ELISA immunoassay. An intent-to-treat approach evaluated the effect of LDA versus placebo on cord blood inflammatory biomarker concentrations using Wilcoxon rank sum tests, both overall and stratified by tertile of maternal hsCRP at enrollment. **Results:** Cord blood inflammatory biomarkers were similar between treatment groups (p-values ranged 0.14 to 0.88). When comparisons were stratified by maternal baseline hsCRP tertiles, results remained null within all maternal inflammation levels, with the exception of IL-15 being higher in the LDA group compared to placebo among women in the middle hsCRP tertile. **Conclusions:** Daily LDA use in women trying to become pregnant and during pregnancy does not impact cord blood inflammatory biomarkers. Thus, maternal LDA through 36 weeks' gestation does not appear to have effects on peripheral markers of neonatal immune function.

UNDERDIAGNOSIS OF OBESITY IN PEDIATRIC CLINICAL CARE SETTINGS AMONG CHILDREN BORN PRETERM: A RETROSPECTIVE COHORT STUDY Taniqua Ingol, Rachel Ronau, Rina Li, Mark Klebanoff, Reena Oza-Frank, Joseph Rausch, Kelly Boone, Sarah Keim (Nationwide Children's Hospital)

Background: Rapid catch-up growth in preterm infants has been associated with an increased risk of childhood obesity. Because children born preterm tend to have more demanding health care needs, obesity may be likely to go undiagnosed by providers. **Objective:** To examine undiagnosed obesity among children born preterm in clinical care compared to children born at term. **Methods:** Data for children born in 2010-15, who had ≥ 1 weight measurement and either attended a Nationwide Children's Hospital (NCH) Primary Care clinic or were born at <37 completed weeks' gestation and attended any NCH clinic were assembled and linked to Ohio birth certificates. Children were considered to have measured obesity if they had ≥ 2 weight-for-age values ≥ 95 th percentile before 24 months of age or BMI values ≥ 95 th pctl at or after 24 months of age. Children were considered to have diagnosed obesity if the medical record had an obesity-related phrase or billing code recorded. Bivariate tests and log-binomial regression were used to compare risk of obesity undiagnosis and factors related to undiagnosis among obese children born preterm and at term. **Results:** 4783 children had measured obesity, 3120 (65%) of which were undiagnosed. Children born preterm were 20% more likely to be undiagnosed compared to children born at term (Relative Risk=1.20, 95% CI: 1.15, 1.26) after adjustment for confounders. The risk was slightly lower for children of minority race, born to unmarried mothers, and with public/no health insurance. Primary care and subspecialties were common settings for undiagnosed obesity. For instance, 36% of preterm children were undiagnosed in primary care and 30% were undiagnosed in subspecialty clinics (56% and 14% of term children, respectively). **Conclusions:** Preterm birth status was found to be associated with increased risk of undiagnosed obesity in early childhood. Our findings highlight the need to enhance obesity screening, particularly in the preterm population.

MODIFIABLE ROOT CAUSES FOR SOCIOECONOMIC DISPARITIES IN RISK OF CHILDHOOD OBESITY AMONG US CHILDREN Xiaozhong Wen, (State University of New York at Buffalo)

Background: There are alarming widening socioeconomic disparities in childhood obesity in the US. It remains unclear which early life determinants cause these disparities. **Methods:** We analyzed 6,300 mother-child dyads at the 5-year follow-up in the U.S. Early Childhood Longitudinal Study - Birth (ECLS-B, 2001-2007). Child weight and height at age 5 years were measured by trained research staff. Using the CDC 2000 sex-specific Growth Charts, we defined obesity as body mass index (BMI) at or above 95th percentile. Maternal education attainment was classified into a binary variable: high school or less vs. college. Mediators of interest included parental preconception BMI, maternal smoking, diabetes, gestational weight gain, food security, method of delivery, large-for-gestational-age, breastfeeding duration, timing of introduction of solid foods, infant sleep duration and quality, and parenting. Based on the causal step method, we conducted mediation analysis to identify significant mediators. **Results:** The risk of childhood obesity at 5 y was significantly higher (14.9% vs. 9.1%, $p < 0.001$) among children of mothers with high school or lower education than among children of college-educated mothers. The crude odds ratio (OR) of childhood obesity for low maternal education was 1.74 (95% confidence interval or CI, 1.50 to 2.03). This association was substantially mediated by prepregnancy BMI, smoking, and breastfeeding. Specifically, after including prepregnancy BMI into the multivariable logistic regression model, the OR for low maternal education was attenuated to 1.64 (95% CI, 1.40 to 1.92). Further inclusion of smoking during pregnancy into the model attenuated the OR to 1.57 (95% CI, 1.33 to 1.84). Further inclusion of breastfeeding duration attenuated the OR to 1.47 (95% CI, 1.24 to 1.74). **Conclusion:** High prepregnancy BMI, smoking during pregnancy, and insufficient breastfeeding could partially mediate socioeconomic disparities in early childhood obesity.

PREVALENCE AND PREDICTORS OF HIGH BLOOD PRESSURE AMONG GUATEMALAN SCHOOL-AGE CHILDREN IN 2017

Cassandra Pickens, Rafael Flores-Ayala, O. Yaw Addo, Ralph Whitehead, Mireya Palmieri, Manuel Ramirez-Zea, Yuling Hong, Maria Jefferds (Centers for Disease Control and Prevention)

Background: Children with high blood pressure (HBP) are at increased risk of cardiovascular disease. However, data on the prevalence and predictors of HBP in school-age children (SAC) are sparse. **Methods:** We analyzed the prevalence and predictors of HBP in 1,049 Guatemalan SAC 6-14 years participating in a cross-sectional, nationally representative household survey in 2017. Blood pressure (BP) was measured in a seated position using a digital monitor; the second and third BP measurements were averaged. HBP was defined as systolic or diastolic BP ≥ 95 th percentile for age, sex, and height (referent: normal weight children, Pediatric Task Force database), systolic BP ≥ 130 mmHg, or diastolic BP ≥ 80 mmHg. We used multivariable logistic regression to identify predictors of HBP ($P+1$ to $+2$ SD) and obesity ($BMIZ > +2$) were 11.7% (9.2%–14.2%) and 6.3% (4.4%–8.1%). In multivariable models, significant predictors of HBP were obesity (adjusted odds ratio [AOR] 5.9 [3.5–10.0], $Z > +2$ vs. $+1$ to $+2$ vs. $< +1$). In children 10-14 years, predictors of HBP were obesity (AOR 9.1 [4.1–20.2]), overweight (AOR 4.4 [2.0–9.9]), and indigenous status (AOR 2.2 [1.3–3.8]); PA was not associated with HBP. **Conclusions:** The prevalence of HBP was high in Guatemalan SAC. Overweight and obesity were strong risk factors for HBP. Obesity prevention and control programs might help reduce HBP prevalence in Guatemalan children.

PERINATAL HEALTH OF REFUGEE AND ASYLUM-SEEKING WOMEN IN SWEDEN 2014-17: A REGISTER-BASED COHORT STUDY Can Liu, Mia Ahlberg, Anders Hjern, Olof Stephansson (Karolinska Institutet)

Background: An increasing number of migrants have fled armed conflict, persecution and deteriorating living conditions during the current decade and many have risked their lives to reach European countries. Despite this, little is known about the perinatal health of certain categories of particularly vulnerable migrant women, like refugees, asylum-seekers, and undocumented migrants, and their access to perinatal care in their new host countries. **Methods:** Using the Swedish Pregnancy Register, we analysed indicators of perinatal health and health care usage in 31,897 migrant women, from the top five refugee countries of origin in 2014-17. We also compared them to native-born Swedish women. **Results:** Migrant women from Syria, Iraq, Somali, Eritrea and Afghanistan had higher risks of poor self-rated health and gestational diabetes than Swedish-born women. They also had higher risks of stillbirth and infants with low birthweight. Within the migrant population, asylum-seekers and undocumented migrants had a higher risk of poor maternal self-rated health before pregnancy than refugee women, with an adjusted risk ratio (RR) of 1.84 and 95% confidence interval (95% CI) of 1.72-1.97. They also had a higher risk of preterm birth (RR 1.47, 95% CI 1.21-1.79) and missed postpartum care visits (RR 1.15, 95% CI 1.10-1.22). **Conclusion:** Refugee, asylum-seeking, and undocumented migrant women were vulnerable during pregnancy and childbirth. Living without residence permit negatively affected pregnancy and birth of asylum-seekers and undocumented migrants. Migrant women's special needs should be addressed by those involved in the asylum process and by health care providers.

IMPROVING PRENATAL AND POSTPARTUM CARE UTILIZATION FOR MEDICAID-INSURED WOMEN: A QUASI-EXPERIMENTAL EVALUATION OF AN INTEGRATED SYSTEM OF CARE APPROACH

Kelly Strutz, Lee Anne Roman, Jennifer Raffo, Zhehui Luo, Melinda Johnson, Susan Henning, Cristian Meghea (Michigan State University)

Given persistent racial/ethnic and socioeconomic disparities in maternal and infant health, population-based systems of care that integrate clinical and community care are needed to reach high-risk women with complex medical and social problems. Many Medicaid beneficiaries are eligible for enhanced prenatal/postpartum care (EPC; e.g. care coordination, home visits), but <1/3 of eligible women take up services. The objective of this study was to evaluate the population impacts of system-level changes over a 7-year period in a Michigan county on timely health service utilization (early EPC, prenatal emergency department (ED) use, and postpartum care) for Medicaid-insured women who gave singleton birth from 2009-15 (n=30,533) compared to a matched statewide population, with subgroup analyses for African-American (AA) women (n=6671) and for women in two EPC-integrated prenatal clinics (n=6010). A quasi-experimental pre-post design was used, with propensity score-weighted difference-in-difference (DID) analyses. While EPC enrollment remained similar for all women and AA women, there was a significant improvement in EPC participation in the clinics (in absolute percentage points (APP), DID estimate=15.2). For all women in the county, in clinics, and in the AA subgroup, significant improvement in first trimester EPC participation was noted (DID estimate=13.7, 28.3, 8.8 APP respectively). ED use during pregnancy decreased in the clinics by 2.4 APP but increased by 10.4 in the state comparison women. Postpartum care within 60 days improved more in the demonstration county and in the AA subgroup than the rest of the state (DID estimate=7.1 and 10.4 APP respectively). Our findings lend further support to maternity home prenatal and postpartum care innovations, although the demonstration highlighted the difficulty of moving population utilization indicators within resource constraints.

IDENTIFYING FACTORS ASSOCIATED WITH RAPID REPEAT PREGNANCY: A PROSPECTIVE ANALYSIS OF A HEALTHY START PROGRAM IN KENT COUNTY, MICHIGAN Sarah Schmidt, Kelly Strutz, Jeffrey Wing, Kathryn Barnhart, Ran Meng, Peggy Vander Meule, Jennifer Raffo, Lee Anne Roman (Grand Valley State University)

Strong Beginnings (SB) is a federal Healthy Start Program aiming to improve the health and well-being of African American and Latina families by promoting racial/ethnic equity and eliminating disparities in birth outcomes, including in rapid repeat pregnancy (RRP; secondary pregnancy within 18 months of index birth). To better prevent the occurrence of RRP, this study prospectively explores potential individual, social, and environmental determinants of RRP, many of which have not been investigated in previous literature. Linked data for this study included information from SB, the Maternal Infant Health Program, Medicaid claims, and birth certificates. The sample includes women enrolled in SB Interconception Care with an index birth between 2013 and 2015 (n=601). Chi-square tests of independence were used to assess the association between the predictor variables and prospective RRP, and logistic regressions were run to obtain adjusted odds ratios for factors associated with RRP, controlling for potential confounders. Preliminary results indicate that those aged 18 to 24 have greater odds of RRP compared to those ages 25 to 34 (Odds Ratio=2.46 95% Confidence Interval=1.45, 4.66). No individual or social factors were found to be significant in the preliminary analysis. Further analysis will include the exploration of environmental factors and their association with RRP. Contradictory to previous literature that indicates women under 20 and over 30 have increased rates of RRP, this study found that being aged 18 to 24 is associated with RRP. Using these results, SB staff can target their intervention methods toward this age group.

OVERALL AND RACIAL/ETHNIC TRENDS IN BREASTFEEDING

INITIATION BY PRENATAL WIC PARTICIPATION Marie Thoma, Dane DeSilva, Young Jo, Jinhee Kim, Michel Boudreaux (University of Maryland, School of Public Health)

Background: As of 2009, all states had implemented the most comprehensive revision of the Special Supplemental Nutrition Program for Women, Infants and Children (WIC) services since 1980, including updating rules to increase breastfeeding promotion. We sought to examine overall and select racial/ethnic trends in breastfeeding initiation by prenatal WIC participation from 2009 to 2017. Methods: We used revised national birth certificate data. Analyses assessed term births paid for by among states adopting the revised birth certificate by 2009. Predicted margins from logistic regression were used to estimate adjusted breastfeeding initiation prevalence, risk ratios (RR) and 95% confidence intervals (CI). Models adjusted for maternal sociodemographic characteristics, parity and prenatal care initiation. Results: Prenatal WIC participation declined from 79% (2009) to 68% (2017). WIC participants were more likely to be younger, Hispanic, unmarried, have lower education, initiate prenatal care early, and have no prior births compared to non-participants. Breastfeeding initiation increased comparably over time by WIC participation (WIC, non-participants) (2009: 68%, 71%; 2017: 78%, 81%), but were consistently lower in WIC participants (RR: 0.953, 95% CI:0.952,0.954). Among non-Hispanic white women, WIC participants were less likely to initiate breastfeeding (RR: 0.912, 95% CI:0.911,0.913), which persisted over time (2009: 63%, 69%; 2017:74%, 79%). However, differences among non-Hispanic black women (2009: 58%, 57%; 2017: 73%, 73%) and Hispanic women (2009: 80%, 79%; 2017: 87%, 87%) were comparable over time. Conclusion: Breastfeeding initiation increased in WIC participants and non-participants comparably over time. Non-Hispanic white WIC participants had persistently lower breastfeeding initiation compared with non-participants. These differences were not observed for Hispanic and non-Hispanic black women. Future studies should explore factors that influence these trends.

THE ROLE OF MATERNAL AGE AND PREGNANCY HISTORY IN RISK OF MISCARRIAGE Maria Magnus, Allen Wilcox, Nils-Halvdan Morken, Clare Weinberg, Siri Eldevik Håberg (Norwegian Institute of Public Health)

Objectives: To estimate the burden of miscarriage in the Norwegian population and to evaluate associations with maternal age and pregnancy history. **Design:**

Prospective cohort study. **Setting:** All registered pregnancies in Norway.

Participants: All Norwegian women who were pregnant between 2009 and 2013, as identified through the Medical Birth Registry of Norway, the Norwegian Patient Registry and the abortion registry. **Main outcome measures:** Risk of miscarriage according to the woman's age and pregnancy history using logistic regression.

Results: There were 421,201 pregnancies during the study period. Miscarriage risk was lowest among women age 25-29 years (10%), and rose rapidly after age thirty, reaching 53% among women 45 years and older. There was a strong recurrence risk of miscarriage, with age-adjusted odds ratios (aORs) of 1.5 (95% CI: 1.5 to 1.6) after one miscarriage, 2.2 (95% CI: 2.0 to 2.4) after two, and 4.0 (95% CI: 3.3 to 4.8) after three consecutive miscarriages. Risk was modestly increased if the previous birth ended in a preterm delivery (1.22; 95% CI: 1.12 to 1.29), stillbirth (1.30; 1.11 to 1.54), caesarean section (1.16 95% CI: 1.12 to 1.21), or if woman had gestational diabetes in the previous pregnancy (1.19; 95% CI: 1.05 to 1.36). Risk of miscarriage was slightly higher among women who themselves had been small-for-gestational age (1.08; 95% CI: 1.04 to 1.13). **Conclusions:** The risk of miscarriage varies greatly by maternal age, shows a strong pattern of recurrence, and is increased after some adverse pregnancy outcomes.

TERM PREECLAMPSIA AND NEURODEVELOPMENTAL DISORDERS IN OFFSPRING Allen Wilcox, Bob Sun, Dag Moster, Quaker Harmon (NIEHS / NIH)

Background: Preeclampsia during term pregnancy increases the risk of cerebral palsy in offspring. Little is known about a possible role of term preeclampsia in other neurodevelopmental disorders. **Methods:** We investigated the relationship between preeclampsia and a range of neurodevelopmental outcomes among singleton live term births in Norway between 1991 and 2015 who were alive at age five or at last follow-up. Data were obtained from the Medical Birth Registry of Norway and linked to other demographic, social, and health information by Statistics Norway. We used multivariable logistic regression to model associations between preeclampsia and neurodevelopmental outcomes, adjusting for sex, year of birth, mother's age, parity, marital status, maternal and paternal education, and parental immigrant status. **Results:** Study sample comprised 1,303,061 children born at 37+ weeks, of whom 33,861 (2.6%) were exposed to preeclampsia. Exposure to preeclampsia was associated with increased odds of a range of adverse neurodevelopmental outcomes including cerebral palsy (OR, 1.39; 95% CI, 1.02-1.90), epilepsy (1.52; 1.18-1.96), intellectual disability (1.49; 1.13-1.96), disorders of psychological development, behavior, and emotion, including attention deficit hyperactivity disorder (1.27; 1.16-1.40), and autism spectrum disorder (1.33; 1.12-1.58). **Conclusion:** While term preeclampsia is a threat to the mother, it is usually regarded as less important for the long-term health of the offspring. Our findings suggest that preeclampsia at term may have lasting effects on the neurodevelopment of the child. Biological pathways may include fetal exposure to oxidative stress and inflammation.

PRENATAL CARE AMONG MOTHERS INVOLVED WITH CHILD PROTECTION SERVICES IN MANITOBA: A RETROSPECTIVE COHORT STUDY USING LINKED ADMINISTRATIVE DATA

Elizabeth Wall-Wieler, Kathleen Kenny, Janelle Lee, Kellie Thiessen, Margaret Morris, Leslie L. Roos (Stanford University)

Background: Prenatal care is one of the most widely used preventive health services; however, prenatal care use varies substantially. Our objective was to examine levels of prenatal care among women with a history of having children placed in out-of-home, and whether these levels differed from those seen among women who did not. Methods: Linkable administrative data were used to create a population-based cohort of women whose first two children were born in Manitoba, Canada between April 1, 1998 and March 1, 2015 (n = 52,438). Level of prenatal care was measured using the Revised-Graduated Prenatal Care Utilization Index, which categorizes care into five groups: intensive, adequate, intermediate, inadequate, and no care. Results: Mothers whose first child was placed in care had much higher rates of inadequate prenatal care during the pregnancy of their second child than mothers whose first child was not placed in care (33.0% versus 13.4%). The odds of having inadequate rather than adequate prenatal care are more than four times higher for women who had their first child placed in care than for women who did not have their first child placed in care (OR = 4.29; 95% CI 3.68, 5.01). Interpretation: Mothers with a history of involvement in the child welfare system are at high risk of having inadequate or no prenatal care in subsequent pregnancies. To ensure better access to prenatal care among this group of women, non-judgmental, low-barrier approaches to relationship-building with pregnant women should be employed.