

SOCIETY FOR PEDIATRIC AND PERINATAL EPIDEMIOLOGIC RESEARCH reproduction | pregnancy | fetal development | child | adolescent health



28<sup>th</sup> Annual Meeting Denver, Colorado June 15-16, 2015

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### 2015 AWARD WINNERS

The Society wishes to extend our congratulations and best wishes to this year's award winners!

### **Student Prize Paper: Winner**

"Prenatal triptan exposure increases externalizing behavior at three years: Results from the Norwegian Mother and Child Cohort Study"

Mollie Wood, MPH

Department of Quantitative Health Sciences, Department of Psychiatry, University of Massachusetts Medical School, Worcester, MA

### **Student Prize Paper: Honorable mention**

"Development of a risk predictive model for Cesarean delivery after labor induction"

Valery A. Danilack, MPH, PhD

Brown University School of Public Health, Department of Epidemiology; Women & Infants Hospital, Division of Research, Providence, RI

### **Heinz Berendes International Travel Award**

"Changes in objectively measured smoking by time and legislative changes" Tuija I Männistö, MD, PhD, Oulu University Hospital, Finland

### **Mentoring Award**

Allen Wilcox, MD, PhD, MPH Epidemiology Branch, National Institute of Environmental Health Sciences Research Triangle Park, NC

### **Rising Star Award**

Edwina Yeung, PhD, ScM

Epidemiology Branch, Division of Intramural Population Health Research Eunice Kennedy Shriver National Institute of Child Health and Human Development Bethesda, MD

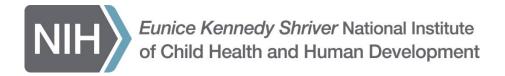
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Pauline Mendola, PhD

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### ACKNOWLEDGMENTS

The Society wishes to acknowledge
the generous financial support for this annual meeting provided by *The Eunice Kennedy Shriver*National Institute of Child Health and Human Development.



We also wish to acknowledge our Society's journal:



Paediatric and Perinatal Epidemiology, published by Wiley-Blackwell, is an international, peer reviewed journal that crosses the boundaries between epidemiologists, paediatricians, developmental psychologists, environmental specialists, obstetricians, child health specialists and genetic epidemiologists. Its main focus is to ensure that the most important paediatric, reproductive, obstetric and perinatal studies reach those researchers and clinicians for whom the results are especially relevant. It publishes original research articles commentaries, book reviews, study designs, detailed methodologies and review articles.

### Society for Pediatric and Perinatal Epidemiologic Research

### 28<sup>th</sup> Annual Meeting

June 15-16<sup>th</sup>, 2015 - Denver, Colorado

### **Program**

Program	
Monday, June 15th, 2015	
• /	·
1:00 – 4:00 pm 2:00 – 4:30 pm	Executive Committee Meeting Mt. Oxford
	<b>Advanced Methods Workshop</b> (separate registration required) <i>Mt. Sopris</i>
	<b>Applied spatial analysis in perinatal and pediatric epidemiology</b> Michael Kramer
	Methods to account for multiple exposures Franco Momoli & Jillian Ashley-Martin
4:30 – 7:30 pm	Registration
5:00 – 6:30 pm	Panel Discussion: Valid Use of Big Data for Pediatric and Perinatal Epidemiology  Mt. Sopris
	Moderator: Allen Wilcox
	Helle Kieler (Karolinska Institutet, Sweden) Katherine Laughon Grantz (Epidemiology Branch, NICHD) Sascha Dublin (MEPREP, Group Health Research Institute)
6:30 – 8:30 pm	<b>Welcome Reception and Poster Session A</b> <i>Grand Ballroom</i>
	Poster tours will be available at 7:00  Birth defects

 Obstetrics
 A83-A103

 Pediatrics
 A104-A115

Heinz Berendes International Travel Award A85 Student Prize Paper Honorable Mention A100

### Tuesday, June 16<sup>th</sup>, 2015

6:30 – 8:10 am Continental breakfast

Grand Ballroom and Foyer

7:00 –10:00 am **Registration** 

2<sup>nd</sup> floor elevator bank

7:00 – 8:00 am Round Table Discussions: by ticket only (sign up at registration)

**Round Table 1**. Biomarkers for hormonal cycles and fecundability: Joseph Stanford

Maroon Peak

Round Table 2. Features and diagnosis of autism spectrum disorders: Irva Hertz-

Picciotto - Mt. Princeton

Round Table 3. Preterm delivery: Katherine Laughon Grantz - Mt. Oxford

8:10 – 8:15 am Welcome Remarks: Sonia Hernandez-Diaz, President

Imperial Ballroom

8:15 – 9:30 am Plenary Session I – Determinants of fertility

Imperial Ballroom

Moderator: Laura Schieve

Racial disparities in visiting a doctor for help getting pregnant: A report from the

FUCHSIA Women's Study

Helen B. Chin

The impact of preconception maternal self-reported stress on fecundability

Kira C. Taylor

Serum caffeine and paraxanthine and menstrual cycle function

Karen C. Schliep

Estrogen use is associated with increased 25-hydroxy vitamin D

Quaker E. Harmon

The effects of preconception low dose aspirin treatment on clinical pregnancy and

live birth: the impact of inflammatory status

Lindsey Sjaarda

### 9:30 – 10:00 am Morning Break

Grand Ballroom and Foyer

### 10:00 – 11:15 am Plenary Session II – Advanced Methods in Perinatal Epidemiology

Imperial Ballroom

**Moderator:** Cande Ananth

The NICHD Fetal Growth Studies: Twin Trajectories

Katherine Laughon Grantz

The reporting of stabilized and risk-adjusted rates of stillbirth and neonatal death in the United Kingdom: MBRRACE-UK

**Brad Manktelow** 

Geographic variation in infant mortality disparities in the U.S.

Lauren Rossen

High maternal BMI in early pregnancy and risk of infant mortality – a

population-based sibling study in Sweden

Anna Lindam

Accounting for the relative severity of adverse events in composite

perinatal outcomes

Jennifer Hutcheon

### 11:15 – 11:45am Student Prize Paper – presented by: Suzan Carmichael, President-Elect

Prenatal triptan exposure increases externalizing behavior at three years:

Results from the Norwegian Mother and Child Cohort Study

Mollie Wood

### 11:45 – 12:00 pm Award Presentations

Mentoring Award – presented by: Suzan Carmichael, President-Elect

Awardee: Allen Wilcox

**Rising Star Award** – presented by: Suzan Carmichael, President-Elect

Awardee: Edwina Yeung

### **Heinz Berendes Travel Award --**

presented by: Martha Werler, Past President

Awardee: Tuija I Männistö

**President's Award** – presented by: Sonia Hernandez-Diaz, President

Awardee: Pauline Mendola

### 11:45 – 1:30 pm Lunch and Poster Session B

Grand Ballroom and Foyer

### Poster tours will be available at 12:45

B1-B9
B10-B23
B24-B37
B38-B55
B56-B66
B67-B69
B70-B92
B93-B112
B116-B118

### 1:30 – 2:30 pm Keynote Address: Are we asking the right questions?

Dr. Wanda D. Barfield

Director, CDC's Division of Reproductive Health

Imperial Ballroom

### 2:30 – 3:45 pm Plenary Session III – Translational Obstetric Epidemiology

Imperial Ballroom

**Moderator:** David Savitz

Blood Pressure During Pregnancy and Risk of Hypertension Later in Life: a Longitudinal Study of POUCHMoms
Galit Dunietz

Cumulative exposure to blood pressure elevations and coronary artery calcification among women with preterm birth
Janet Catov

Maternal dietary patterns and cardiometabolic markers during pregnancy Chantel Martin

Can declining pregnancy hypertension rates be explained by increasing planned deliveries?

Christine Roberts

What was the impact of Oregon's hard-stop policy to limit elective early-term deliveries?

**Brian Quigley** 

### **3:45 – 4:15 pm Afternoon Break**

Imperial Ballroom 1

### 4:15 – 5:30 pm Plenary Session IV – Origins of Pediatric Diseases

Imperial Ballroom

**Moderator:** Nigel Paneth

Autism, Pesticides and Gene Expression Irva Hertz-Picciotto

Measuring estrogen response in vaginal and urethral epithelial cells of infants: a study of soy-based infant formula feeding
Margaret Adgent

Determinants of mental health disorders in children of parents with parental multiple sclerosis Neda Razaz

Associations of pre- and postnatal weight gain with body composition and cardiometabolic risk during mid-childhood in Project Viva Wei Perng

Cesarean delivery and childhood asthma incidence in a birth cohort Audrey Flak

### 5:30 – 5:35 pm Closing Remarks – Sonia Hernandez-Diaz, President

### 5:35 – 6:40 pm Society business meeting

Imperial Ballroom 1

**Poster Session A** 

Monday, June 15<sup>th</sup> 6:30 – 8:30 pm



**FLUCONAZOLE USE AND BIRTH DEFECTS AMONG MOTHERS IN THE NATIONAL BIRTH DEFECTS PREVENTION STUDY**. Howley MM\*, Carter TC, Browne ML, Romitti PA, Cunniff CM, Druschel CM for the National Birth Defects Prevention Study (New York State Department of Health)

Low-dose fluconazole is commonly used to treat vulvovaginal candidiasis, a condition occurring frequently during pregnancy. Conflicting information exists on the association between low-dose fluconazole use among pregnant women and risk of major birth defects. Initial case reports suggested links between fluconazole use and craniofacial, skeletal, and heart defects, although recent epidemiologic studies have not identified increased risks for these defects. We evaluated associations between low-dose fluconazole use and several major birth defects using data from the National Birth Defects Prevention Study (NBDPS). In the NBDPS, early pregnancy fluconazole use was collected by maternal self-report. Logistic regression analysis was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for birth defects with 5 or more exposed cases, controlling for maternal age, state of residence at delivery, race/ethnicity, smoking, and gestational diabetes. Of the 38,009 mothers interviewed, 5 control and 42 case mothers reported using fluconazole. Six exposed infants had a cleft lip with cleft palate (CLP; OR=6.55; CI=1.88-22.81). While no other defect had five or more exposed cases, the following defects had three exposed cases: hypospadias, d-transposition of the great arteries, pulmonary valve stenosis, and atrial septal defect. In this preliminary analysis, an association was found between maternal fluconazole use in early pregnancy and CLP. This finding differs from recent epidemiologic studies, but is consistent with earlier published case reports. Despite the larger sample size in the NBDPS, fluconazole use was rare and differential recall bias may have influenced the findings. Results should be interpreted cautiously.

# A2 POPULATION ATTRIBUTABLE FRACTIONS FOR ESTABLISHED AND SUSPECTED RISK FACTORS FOR HYPOPLASTIC LEFT HEART SYNDROME. RM Simeone\*, SC Tinker, SM Gilboa, A.J. Agopian, ME Oster, L Botto, MA Honein, and The National Birth Defects Prevention Study (Centers for Disease Control and Prevention)

Risk factors for hypoplastic left heart syndrome (HLHS), a congenital heart defect (CHD), have been identified, but their contribution in the presence of other risk factors is unclear. We calculated average population attributable fractions (PAFs) to estimate the proportion of HLHS due to known or suspected risk factors, adjusted for other risk factors. We analyzed National Birth Defects Prevention Study data from 514 HLHS cases and 10,200 liveborn controls born during 1997-2009. We selected risk factors based on a literature review. Potentially modifiable maternal risk factors were pre-pregnancy diabetes, obesity, and fever, as well as use of opioids, trimethoprim/sulfamethoxazole or nitrofurantoin, and oral contraceptives. Non-modifiable risk factors included infant male sex, family history of CHDs, and non-Hispanic white race. Average PAFs were estimated by removing risk factors from adjusted logistic regression models and averaging PAFs for all combinations of risk factors. Preliminary analyses indicate that, among modifiable risk factors, obesity had the greatest average PAF (3.3%), followed by opioid use (1.6%), and fever (1.2%). In this study population, approximately 8.3% and 42.9% of HLHS cases can be attributed to potentially modifiable and non-modifiable risk factors, respectively; thus, 48.8% of cases cannot be attributed to the main effects of established and suspected risk factors. These results underscore the need to identify additional risk factors that constitute the remaining burden of HLHS, understand whether non-modifiable risk factors are markers for modifiable exposures, and explore why HLHS is associated with these risk factors.

# A3 ASSESSMENT OF YOUTUBE VIDEOS AS A SOURCE OF INFORMATION ON MEDICATION USE IN PREGNANCY. C Hansen, JD Interrante, EC Ailes, MT Frey, CS Broussard, VJ Godoshian, C Lewis, KN Polen, AP Garcia, SM Gilboa\* (Centers for Disease Control and Prevention, Atlanta, GA)

Background: Many women consult the Internet when making decisions around medication use in pregnancy. Our aim was to assess the content of videos discussing medication use in pregnancy that are accessible on YouTube. Methods: Using a combination of 289 medication terms and seven pregnancy-related terms, 2,023 distinct paired search terms related to medications and pregnancy were used to extract metadata from the YouTube Application Programming Interface in June 2014. After excluding videos that did not have at least one medication and one pregnancy-related term in the title, we viewed and recorded additional information about each video, including any medications and associated adverse outcomes mentioned. For selected medications, we compared the Teratogen Information System (TERIS) ratings to the assessments of safety reported in the videos. Results: Of 651 videos with at least one medication and one pregnancy-related search term in the title, 314 had relevant information about medication use in pregnancy and were included in the analyses. Selective serotonin reuptake inhibitors (SSRIs) were the most common medication type mentioned (225/314 videos; 72%). In 88% of those videos (198/225), the SSRI was noted as unsafe; in contrast, the TERIS risk ratings for SSRIs range from "unlikely" to pose a teratogenic risk to "minimal" risk. Conclusions: For selected medications, such as SSRIs, the current content does not adequately reflect what is known about the safety of their use in pregnancy. Given the high utilization of the Internet for health information, YouTube could serve as a valuable platform for communicating evidence-based medication safety information.

# A4 PERICONCEPTIONAL BENZODIAZEPINE USE AND THE RISK FOR BIRTH DEFECTS: DATA FROM THE NATIONAL BIRTH DEFECTS PREVENTION STUDY. \*S. Tinker, J. Reefhuis, C. Broussard, S. Gilboa, R. Bitsko, M. Werler, A. Mitchell (Centers for Disease Control and Prevention, Atlanta, GA)

Benzodiazepine medications can be used to treat anxiety, which affects 15% of women of childbearing age in the United States. We assessed whether periconceptional use of benzodiazepines was associated with an increased risk for selected birth defects using data from the population-based, multisite National Birth Defects Prevention Study. Logistic regression was used to estimate odds ratios for defect categories for which there were at least three exposed cases. Benzodiazepine use during the periconceptional period (month before to three months after conception) was reported by 0.7% (71/10,136) of mothers of control infants (liveborn without major birth defects). Alprazolam accounted for half of benzodiazepine exposures. Benzodiazepine use decreased dramatically between the first and third month of pregnancy, corresponding to pregnancy recognition. Associations were observed for periconceptional use of: alprazolam with esophageal atresia (crude odds ratio [cOR]: 3.6; 95% Confidence Interval [CI]: 1.7, 7.7) and hypospadias (cOR: 0.3; 95% CI: 0.1, 0.9); clonazepam with anotia/microtia (cOR: 3.9; 95% CI: 1.1, 13.8) and tetralogy of Fallot (cOR: 2.7; 95% CI: 1.1, 6.6); and lorazepam with pulmonary valve stenosis (cOR: 4.1; 95% CI: 1.2, 14.2), coarctation of the aorta (cOR: 4.4; 95% CI: 1.1, 16.9), and gastroschisis (cOR: 4.9; 95% CI: 1.4, 16.6). Individual adjustment for maternal age, race/ethnicity, education, and smoking did not affect OR estimates, except for gastroschisis, for which age adjustment tended to strengthen associations. Many associations were tested and these results warrant additional study. Future analyses using empirical Bayesian methods will address confounding and data instability due to small sample size.

TIME TRENDS OF SELECTED MATERNAL EXPOSURES IN THE NATIONAL BIRTH **DEFECTS PREVENTION STUDY**. April L. Dawson\*, Hilda Razzaghi, Annelise Arth, Mark A. Canfield, Samantha E. Parker, Jennita Reefhuis (CDC, Atlanta, GA) Our objective was to describe time trends in selected pregnancy exposures in the National Birth Defects Prevention Study (NBDPS). We analyzed data from the NBDPS for mothers of live-born infants without birth defects (controls), with an expected date of delivery (EDD) from 1998 -2011. Mothers from the 10 participating centers across the United States were interviewed by phone between six weeks and two years after the EDD. We focused on maternal race-ethnicity and five maternal risk factors; obesity, use of folic acid-containing multivitamins, opioid analgesics, selective serotonin reuptake inhibitors (SSRIs), and the antihistamine, loratadine, because of their prevalence of use and some reports of associations with major birth defects. Prevalence time trends were examined using the Kendall's τβ test statistic. The exposure trend analysis included 11,484 control mothers. We observed a significant increase in obesity prevalence among control mothers (from 15% to 23%), as well as use of SSRIs (from 2.4% to 5.9%) and loratadine (from 3.6% to 6.4%). We also observed an increase in the periconceptional use of folic acid-containing multivitamins (from 48% to 60%). No remarkable change in the overall use of opioid analgesics was observed. The racial/ethnic distribution of mothers changed slightly during the study period. Different trends over time were observed for individual SSRIs. Long-term, population-based case-control studies continue to be an effective way to assess exposure-birth defects associations and provide guidance to health care providers. However, investigators examining rare outcomes covering many years of data

### **A6**

AKYLOGLOSSIA: WHERE CONGENITAL ANOMALY SURVEILLANCE MEETS THE BABY FRIENDLY INITIATIVE. Joseph KS\*, Kinniburgh B, Metcalfe A, Razaz N, Sabr Y, Lisonkova S (University of British Columbia)

collection need to be cognizant of time trends in exposures.

Background: Routine surveillance of congenital anomalies has shown an increase in ankyloglossia (tonque-tie) rates. We studied ankyloglossia and its treatment (frenotomy) since several pediatric societies, including the Canadian Paediatric Society, have stated that frenotomy cannot be recommended based on current evidence. Methods: We studied all live births in British Columbia, Canada, from 2004 to 2013 using data from the British Columbia Perinatal Data Registry. Temporal trends in ankyloglossia and frenotomy, and associations with maternal and infant characteristics, were quantified using logistic regression. Results: There were 459,445 live births and 3,022 cases of ankyloglossia between 2004 and 2013. The prevalence of ankyloglossia was 6.6 per 1,000 live births (95% CI 6.3-6.8); rates increased from 5.0 in 2004 to 8.4 per 1.000 live births in 2013 (P<0.0001). Nulliparity (adjusted rate ratio [aRR] 1.47, 95% CI 1.36-1.59), multiple birth (aRR 0.68, 95% CI 0.63-0.74), male infant sex (aRR 1.74, 95% CI 1.61-1.89), birth weight (aRR ≥4500 vs 3000-3499 g 1.39, 95% CI 1.11-1.76) and year (aRR 2013 vs 2004 1.70, 95% CI 1.43-2.02) were associated with ankyloglossia. Ankyloglossia rates were correlated with the proportion of babies receiving breast milk (correlation coefficient=0.93, P<0.0001); the latter rates increased from 93% in 2004 to 95% in 2013. Frenotomy rates increased from 2.8 in 2004 to 5.3 per 1000 live births in 2013 (89%) increase, 95% CI 52-134%). Conclusion: Ankyloglossia and frenotomy rates increased significantly from 2004 to 2013, highlighting the potential for a diagnostic suspicion bias and increasing use of a potentially unnecessary surgery for infants.

**FACTORS ASSOCIATED WITH BIRTH DEFECTS IN THE REGION OF CORPUS CHRISTI, TEXAS.** Lobdell DT\*, K Messier, PH Langlois, TJ Wade (U.S. Environmental Protection Agency, Chapel Hill, NC)

A high prevalence of certain birth defects in the Corpus Christi, TX region has previously been documented. We examined associations between drinking water sources and proximity to hazardous waste sites with birth defects in this region. Records from the Birth Defects Epidemiology & Surveillance Branch of the Texas Department of State Health Services (DSHS) of birth defects and live births, 1997-2008, were obtained for 5 counties near Corpus Christi. Using geocoded records, cases were all birth defects, excluding minor defects (n=5158) and controls were live births without a birth defect (n=83034). Residences were mapped to water utility service areas using information provided by the State of Texas Department of Environmental Quality. Water system violations and locations of hazardous waste sites and toxic releases inventory sites (TRI) were obtained from the US EPA. Birth defects associations were estimated using logistic regression controlling for age, race/ethnicity, birth year and county of residence (Odds Ratio [95% confidence interval]). No associations were observed between water source type (surface vs. ground; private vs. public), or drinking water violations for most rules. However, residence in a water system that had more than three Total Coliform violations during the year before delivery was associated with an increased risk of a birth defects (1.64[ 1.17,2.31]). Birth defects were also associated with the density of Superfund sites, TRI sites, and Brownfields within 5 km of residence at the time of birth (e.g., 2 or more Superfund sites within 5 km (1.33[1.06,1.67]). This abstract does not represent EPA policy.

**A8** 

Α9

CONGENITAL HEART DISEASE AND INDICES OF FETO-PLACENTAL GROWTH IN A NATIONWIDE COHORT OF 973,141 LIVEBORN INFANTS. Matthiesen NB\*, Henriksen TB, Gaynor JW, Agergaard P, Bach CC, Hjortdal V, Ostergaard JR (Department of Pediatrics, Aarhus University Hospital, Aarhus University, Denmark)

Background: Placental anomalies have recently been associated with fetal congenital heart disease (CHD), growth in fetuses with CHD, and neurodevelopmental disorders in children with CHD. We investigated the association between subtypes of CHD and placental weight (PW) and placental weight to birth weight ratio (PWR) in a large cohort. Methods: All Danish livebirths 1997-2012 were included. CHD, PW, PWR and potential confounders were identified in national registries. In 30% of infants with CHD diagnostic validity and genetic anomalies were assessed in detail. The association between CHD and placental measures was analyzed by multiple linear regression adjusted for potential confounders with/without adjustment for gestational age. The study further includes a sibling analysis and a comparison cohort of other major birth defects. Results: 973,141 livebirths were included (8,220 with CHD). Overall, CHD was associated with lower PW and larger PWR, adjusted -22g (95%CI-28;-16), +0.010 (0.008;0.012). Most subtypes of CHD were associated with reduced PW and increased PWR. Atrial septal defects were associated with the largest PWR. Major ventricular septal defects and tetralogy of Fallot were associated with the lowest PW. Sensitivity analyses revealed that the associations were not explained by conditioning on livebirth or gestational age. Conclusion: Overall CHD was strongly associated with PW and PWR in several subgroups. We confirm the association between placental anomalies and fetal CHD. It remains uncertain whether placental anomalies in early gestation may be implicated in the causation of CHD, whether they share a common cause or whether CHD in some instances may cause placental anomalies.

CONGENITAL HEART DISEASE AND INDICES OF FETAL GROWTH IN A NATIONWIDE COHORT OF CHILDREN WITH DOWN SYNDROME. Matthiesen NB\*, Agergaard P, Henriksen TB, Gaynor JW, Bach CC, Hjortdal V, Ostergaard JR (Department of Pediatrics, Aarhus University Hospital, Aarhus University, Denmark)

Background: Neurodevelopmental disorders are common in children with congenital heart disease (CHD). These disorders are highly correlated to fetal cerebral growth i.e. small head circumference at birth. It remains unknown whether this is due to cerebral hypoxia caused by CHD, environmental or genetic causes. Down syndrome is a known cause of CHD, neurodevelopmental disorders and impaired cerebral growth. We aimed to assess the association between CHD and proxy measures of fetal growth in a large cohort of children with Down syndrome, possibly eliminating unknown genetic confounding. Methods: All Danish Down syndrome livebirths 1997-2012 were included. Karvotypes (trisomy, translocation, mosaicism). CHD, pregnancy outcomes and potential confounders were identified in national registries. The association between CHD and proxy measures of fetal growth was analyzed by multiple linear regression adjusted for potential confounders (including karyotype) with/without adjustment for gestational age. Results: 710 livebirths were included (362 with CHD). We found no association between CHD and head circumference or birth weight in children with Down syndrome, adjusted differences: 0.0cm (95%CI-0.2;0.3), 33g (-42;108). We found no differences by severity of CHD. According to sensitivity analyses the results were not explained by conditioning on live birth or gestational age. Conclusions: We found no association between impaired fetal growth and CHD in a large cohort of infants with Down syndrome. We suggest that the most common types of CHD in Down syndrome do not impair fetal cerebral growth. Previously demonstrated associations in populations with unknown causes of CHD may have been confounded by unknown genetic causes.

### A11

CLASSIFYING BIRTH DEFECTS BY CAUSE AND CLINICAL PRESENTATION: A POPULATION-BASED STUDY. ML Feldkamp\*, LD Botto, JLB Byrne, S Krikov, JC Carev (Division of Medical Genetics, Department of Pediatrics, University of Utah) Understanding the causes of common birth defects is both a research and a public healthy priority. Epidemiologic studies report many associations with genetic or environmental factors; however, few studies explored directly the applicability of these findings in clinically well-defined population-based cohorts. To this end, we developed a multidimensional classification system that considers etiology (known, unknown), morphology (isolated, multiple major, minors only), and pathogenesis (sequence, development field, pattern). We used it to assess a cohort with major birth defects among all pregnancy outcomes (livebirths, stillbirths, pregnancy terminations) from Utah's population-based birth defect surveillance system. Excluding selected mild conditions (e.g., muscular septal defect) we generated a final cohort of 5.629 cases (birth prevalence, 2.1%). Using strict and systematic criteria for causal assignment, 22.1% were assigned a known etiology (n=1,279), mostly chromosomal or genetic conditions (21.9%), but rarely teratogens (47 or 0.83%) such as uncontrolled pregestational diabetes or abnormalities of twinning (twin-twin, conjoined or acardiac; 25 or 0.31%). Overall, 76.5% of cases (n=4,325) could not be assigned a clear etiology; most were isolated birth defects (3,805 or 88%). In summary, for many risk factors, evidence was too weak for definitive assignment of exposures to individual cases. These findings underscore the current gaps in causal knowledge that hinder the translation of epidemiologic associations to specific cases of birth defects, even for risk factors deemed to be well known (e.g., smoking or diabetes). These minimum estimates of cases directly attributable to specific factors underscore the need to dramatically improve the causal knowledge of birth defects.

THE ASSOCIATION BETWEEN PATCHING ADHERENCE AND VISUAL ACUITY AT AGE 4½ IN THE INFANT APHAKIA TREATMENT STUDY. Drews-Botsch CD\*, Celano M, Hartmann EE, Lambert SR. (Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA)

We examine the relationship between patching and visual acuity in the Infant Aphakia Treatment Study. Cataract extraction was performed between 28 and 209 days of age on 114 infants with a unilateral congenital cataract. 57 were randomized to receive an IOL; the remaining 57 were left aphakic. Recognition acuity was assessed at age 41/2. Patching was prescribed until age 5. Adherence to prescribed patching was assessed using quarterly telephone interviews and annual patching diaries. Occlusion was the average number of hours of patching reported on at least 3 adherence assessments within 5 age bands: 0-<12 months of age, 12-<24 months, 24-<36 months, 26-<48 months, 48-<60 months. Average hours of patching in each age band, was correlated with patching at all other time points. Patching was strongly correlated with acuity. Correlation coefficients ranged from -0.32 for patching in the 5th year of life to -0.42 for patching in the 2nd year, were similar for pseudophakic and aphakic children, and were not confounded by adverse events, age at surgery, gender, race or type of insurance. Few (n=5) caregivers reported averaging more than 3 hours of patching per day in years 3-5 if they had not done so in the first 2 years. We affirm the importance of patching to visual acuity in children after unilateral cataract extraction in infancy. Patching in the first years after surgery may be particularly important as caregivers who are able to adhere to patching in infancy are more likely to adhere to prescribed patching later.

### A13

GESTATIONAL WEIGHT GAIN, PREPREGNANCY BODY MASS INDEX, AND OFFSPRING ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS AND BEHAVIOR AT AGE 10.

Pugh SJ\*, Hutcheon JA, Richardson GA, Brooks MM, Himes KP, Bodnar LM (The University of Pittsburgh, Pittsburgh, PA)

Our objective was to estimate the association between gestational weight gain (GWG) and prepregnancy BMI on offspring attention-deficit hyperactivity disorder (ADHD) symptoms and behavior at age 10. Mother-infant dyads (n=763) enrolled in a birth cohort study were followed through pregnancy to 10 years. Child ADHD symptoms were assessed with the Conners' Continuous Performance Test. Child behavior was assessed by maternal and teacher ratings on the Child Behavior Checklist and Teacher Report Form, respectively. Self-reported total GWG was converted to gestational-age-standardized z-scores. Multivariable linear or negative binomial regression were used to estimate effects of GWG and BMI on outcomes while adjusting for maternal race, child sex, parity, income, employment, maternal intelligence, home stimulation, and prenatal substance use. The mean(SD) total GWG(kg) was 14.5(5.9) and 28% of women had a pregravid BMI≥25. On the Child Behavior Checklist, prepregnancy obesity was associated with increased offspring problem behaviors including withdrawn or somatic complaints (adj β:5.1, 95% CI:2.6, 7.6), delinquent or aggressive behaviors (adj β:4.6, 95% CI:2.2, 6.9), and attention problems (adj β:3.5, 95% CI:1.7, 5.3), compared with children of normal weight mothers. Increased offspring impulsivity was associated with low GWG among lean mothers (adj IRR:1.2 95% CI:0.9, 1.5) and high GWG among overweight mothers (adj IRR:1.7, 95% CI:0.9, 2.8), but additional behavior and ADHD symptoms did not differ by GWG z-score. We found little evidence that GWG is important for child ADHD symptoms or behavior at age 10. Interventions to reduce maternal obesity may have a large impact on child ADHD and behavioral development.

## A14 MATERNAL MEDICAL CONDITIONS DURING PREGNANCY AND CHILDREN'S GROSS MOTOR DEVELOPMENT UP TO AGE 24 MONTHS IN THE UPSTATE KIDS STUDY. A

Ghassabian \*, R Sundaram, A Wylie, E Bell, SC Bello, E Yeung (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) Maternal health before or during pregnancy is related to children's neurodevelopment. Less clear is whether children born to mothers with a medical condition in pregnancy experience mild delays in motor milestones. In this study, we obtained information on medical conditions before/during pregnancy using self-reports, birth certificates, and hospital records in 4909 mothers participating in Upstate KIDS, a population-based birth cohort. Mothers reported on their children's motor milestone achievement at 4, 8, 12, 18, and 24 months of age. Failure time modeling under a Weibull distribution was used to examine the prospective relation of maternal medical conditions with time to achieve milestones in children. Hazard ratios (HR) <1 correspond to a longer time to achievement. After adjustment for confounders such as prepregnancy body mass index, children of mothers with gestational diabetes had a longer time to achieve sitting without support (HR:0.85, 95%CI: 0.76-0.95), walking with assistance (HR:0.88, 95%CI: 0.77-0.99) and walking alone (HR:0.88, 95%CI: 0.77-0.99) compared to children of women with no diabetes. Associations slightly attenuated after adjustment for perinatal factors. Similar findings emerged for maternal diabetes diagnosed prior to pregnancy (HR:0.82, 95%CI: 0.66-0.98 for walking with assistance; HR:0.79, 95%CI: 0.62-0.96 for walking alone). Maternal hypertensive disorders of pregnancy were related to a longer time to achieve motor milestones, but the associations were not significant after adjustment for gestational age. Our data support the notion that children exposed to maternal diabetes, gestational or pregestational, may take longer to achieve motor milestones than children not exposed to diabetes, independent of maternal obesity.

## A15 ASSOCIATIONS BETWEEN EARLY LIFE SOCIOECONOMIC POSITION, CANDIDATE GENE METHYLATION, AND ADULT CARDIOMETABOLIC PHENOTYPES IN YOUNG ADULT WOMEN IN THE JERUSALEM PERINATAL FAMILY FOLLOW-UP STUDY. Jonathan

Y Huang\*, Amelia R Gavin, Thomas S. Richardson, Ali Rowhani-Rahbar, David S. Siscovick, Hagit Hochner, Yechiel Friedlander, Daniel A. Enquobahrie (Institute for Health and Social Policy, McGill University, Montreal, QC; Department of Epidemiology, University of Washington, Seattle, WA) Background: Early life socioeconomic position (SEP) has been related to adult cardiometabolic health. Empirical evidence for epigenetic mechanisms remains limited. Methods: Among 613 adult women (mean age = 32 years) of the Jerusalem Perinatal Study Family Follow-Up, we investigated early life SEP - adult DNA methylation associations at five cardiometabolic and stress genes: ABCA1, INSIGF, LEP, HSD11B2, and NR3C1. Early life SEP was defined using father's occupational class (6 levels) and parental education years at offspring birth. Sequenom MassARRAY was used to quantify gene-specific, percent DNA methylation in adult peripheral blood. We used multivariable linear regression and marginal structural models (MSM) to estimate early life SEP – adult methylation associations under two proposed causal structures. We also examined whether methylation mediated SEP-adult cardiometabolic phenotype relationships using MSM and product-of-coefficients, adjusting for adolescent overweight, education, religiosity, marital status, parity, and cigarette or alcohol use. All models were adjusted for age at blood draw and sampling criteria. Results: Average methylation ranged from 5.7% (HSD11B2) to 77.3% (INS-IGF). Increasing maternal and paternal education from ≤ 8 years to 9-12 years were associated with 0.5 %-point (95% Confidence Interval: 0.1, 0.8) higher HSD11B2 and 3.6 %-point (95% CI: 0.8, 6.5) higher NR3C1 Exon 1F methylation, respectively. HSD11B2 methylation was associated with weight, total cholesterol, and LDL-cholesterol levels while and NR3C1 was associated with height and blood pressure. We did not find evidence for mediation. Conclusions: We found some evidence of associations between HSD11B2 and NR3C1 and both early life SEP and adult cardiometabolic phenotypes.

### UMBILICAL CORD BLOOD ANDROGEN LEVELS AND ASD-RELATED PHENOTYPES AT

**12 MONTHS**. Park BY\*, Lee B, Burstyn I, Tabb LP, Keelan JA, Whitehouse AJ, Croen L, Fallen D, Hertz-Picciotto I, Montgomery O, Newschaffer CJ (\*Drexel University School of Public Health, Philadelphia, PA)

Background: Autism spectrum disorder (ASD) affects more than 1% of children in the United States with male-to-female prevalence ratio of roughly 4:1. This gender disparity is a wellrecognized but poorly-understood phenomenon. An explicit focus on potential etiologic pathways consistent with this gender difference should be a priority in attempts to elucidate ASD causal mechanisms. Methods: Umbilical cord bloods from 175 births in the EARLI (Early Autism Risk Longitudinal Investigation) pregnancy cohort, that follows mothers of a child with ASD at the start of a subsequent pregnancy, were used to measure testosterone (T), androstenedione (A4) and dehyroepiandrosterone (DHEA) levels. These androgens were measured using a highly specific liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay. Linear regression models were used to determine association between androgen levels at birth and AOSI (Autism Observational Scales in Infants) scores at 12 months. Results: Levels of T were on average higher in males (mean; SD) (0.7; 0.46) verses females (0.34; 0.17) (P<0.0001). Levels of A4 were also higher in males but did not reach statistical significance, while DHEA levels were on average higher in females (10.5; 8.68) compared to males (8.9; 11.1) (P 0.002). In an unadjusted model, increase in T from the first quartile median to the fourth quartile median was associated with an average 1 point increase in AOSI score (P 0.06). Conclusion: Our preliminary findings suggest that umbilical cord blood T have weak positive association with ASD related phenotype at 12 month, among high risk infant siblings.

### A17

SELF-REPORTED REPRODUCTIVE TRACT INFECTIONS AND ULTRASOUND DIAGNOSED UTERINE FIBROIDS IN AFRICAN-AMERICAN WOMEN. Moore KR\*, Cole SR Dittmer DP Schoenbach VJ Smith JS Baird DD (National Institutes of Health, Research Triangle Park, NC)

Background: For decades it has been hypothesized that reproductive tract infections (RTIs) are risk factors for uterine fibroids. However, only 2 recent studies have been conducted. This study aimed to investigate the relationship between RTIs and fibroids in a large study using ultrasound screening for fibroids. Methods: We used cross-sectional enrollment data from African-American women ages 23-34 with no previous fibroid diagnosis. RTI history was measured by self-report and fibroid status by standardized ultrasound. Secondary fibroid outcomes were size, number, and total volume. Age- and multivariable-adjusted logistic regression were used to estimate odds ratios (ORs). Results: In total, 1,656 women were included; 22% had fibroids. Bacterial vaginosis (BV) was associated with a 21% increased odds of fibroids [a(adjusted)OR: 1.21 95% confidence interval (CI) (0.93-1.58)]. Chlamydia infection and pelvic inflammatory disease were associated with a 38% [aOR: 0.62 95%CI (0.40-0.97)] and a 46% [aOR: 0.54 95%CI (0.25-1.17)] reduced odds of having 2 or more fibroids, respectively. Those with a previous BV diagnosis had a 47% increased odds of having 2 or more fibroids [aOR: 1.47 95%CI (0.98-2.21)] and a 41% increased odds of having a larger total fibroid volume [aOR: 1.41 95%CI (0.98-2.04)]. Conclusions: Our study was the first to explore the relationship between RTIs and fibroid size, number and total volume. There appeared to be no strong association between selfreported RTIs and fibroids. Studies using serology, a biochemical measure of past infection, are needed to better investigate associations between RTIs and fibroids.

GROWTH FROM BIRTH TO 18 MONTHS AMONG INFANTS CONCEIVED BY INFERTILITY TREATMENT IN UPSTATE KIDS. EH Yeung\*, R Sundaram, E Bell, C Druschel, C Kus, Xie Y, G Louis (NICHD, Bethesda, MD)

Background Although studies have found that babies conceived with infertility treatment are born lighter and earlier than infants conceived spontaneously, limited research has assessed growth by treatment type. Methods Upstate KIDS is a matched exposure cohort investigating the growth and development of children in relation to mode of conception. Infants born (2008-2010) to Upstate New York mothers with infertility treatment indicated on birth certificates were recruited and frequency matched (ratio 1:3) on region of birth to infants without treatment. Mothers reported height and weight from infant well visits. Self-reported infertility treatment was verified by linkage with the national SART database. Mixed linear models with a random slope and cubic splines for age and age-gender interactions were used to estimate mean differences in growth from birth to 18 months adjusting for maternal age, race, education, marital status, insurance and pregnancy smoking. Analyses were weighted for the sampling framework. Results Compared with spontaneously conceived singletons (n=2427), singletons conceived by infertility treatment (442 by assisted reproductive technologies (ART) and 523 by ovulation induction or other treatments) did not differ in weight or length. Compared with spontaneous twin conceptions (n=536), twins conceived with ART (n=224) or other treatments (n=180) weighed less (ART: -70 grams; 95%CI: -129,-10; non-ART: -140g 95%CI:-207,-73) but did not differ in length. Conclusion Singletons conceived by infertility treatment did not differ in infant growth but lower average weights were observed for twins in comparison to spontaneously conceived children. Still, the observed differences were small representing <2% difference in body weight.

### A19

**EARLY LIFE FACTORS AND UTERINE FIBROIDS IN A COHORT OF YOUNG AFRICAN AMERICAN WOMEN.** Upson K\*, Baird DD (National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA)

Uterine fibroids are common in reproductive-age women and may confer substantial morbidity. Laboratory animal studies demonstrate that select intrauterine and infant exposures increase the risk of fibroid development in adulthood. However, two prior studies evaluating early life factors and fibroids yielded inconsistent results. We examined this relationship using data from the Study of Environment, Lifestyle & Fibroids (SELF), a study of 1,696 African American women ages 23-34 years who were screened by ultrasound for fibroids at enrollment. Early life factors were ascertained by questionnaire, with most participants receiving assistance from their mothers. We estimated the relative risk (RR) and 95% confidence interval (CI) using logbinomial regression, adjusting for confounding factors. The factor most strongly associated with fibroids was mother's birth decade. Participants whose mothers were born in the 1950s had a 40% increased risk of fibroids compared to those with mothers born in the 1960s (RR 1.4, CI: 1.1-1.8); the association was modest for those with mothers born in the 1940s (RR 1.3, CI: 0.9-1.9). The associations appeared stronger if the participant was the mother's firstborn child (1940s/firstborn, RR 1.7, CI: 0.9-3.4; 1940s/later-born RR 1.5, CI:0.9-2.4; 1950s/firstborn RR 1.8, CI:1.2-2.7; 1950s/later-born, RR 1.6, CI:1.1-2.4; 1960s/firstborn, RR 1.4, CI:0.9-2.1; vs. 1960s/later-born). Our results may be consistent with the broad application of persistent pesticides during these decades, particularly the 1950s. Body burden decreases with parity and breastfeeding, possibly explaining the association with participants' birth order. Our results suggest that early life may be a critical exposure window for fibroid development in adulthood.

SOY-BASED INFANT FORMULA FEEDING AND MENSTRUAL PAIN IN A COHORT OF YOUNG AFRICAN AMERICAN WOMEN. Upson K\*, Baird DD (National Institute of

Environmental Health Sciences, Research Triangle Park, NC, USA)

Phytoestrogen exposure from soy formula feeding may disrupt reproductive system development, resulting in menstrual problems after menarche. A greater risk of menstrual discomfort with soy formula feeding was reported in a prior study conducted among young adults who participated as infants in a clinical trial and were assigned to soy or cow-based formula feeding. We investigated this relationship using data from the Study of Environment, Lifestyle & Fibroids (SELF), a study of 1,696 African American women ages 23-34 years in Detriot, MI. Data on infant soy formula feeding, 89% retrospectively reported by the participants' mothers, and several indicators of menstrual pain were available for 1,553 participants. We estimated the relative risk (RR) and 95% confidence interval (CI) using log-binomial regression. or log multinomial regression, adjusting for participant age and maternal education. Soy formula feeding was associated with 40% increased risk of ever use of a contraceptive method for menstrual pain (RR 1.4, CI: 1.1-1.9). Women fed soy formula were more likely than unexposed women to report moderate/severe menstrual discomfort/pain with "most periods", but not "every period", during early adulthood (ages 18-22 when not using hormonal contraception) (RR 1.5, CI: 1.1-1.9). Our data suggested only a modest association between exposure and women reporting a big/medium problem with menstrual cramps/discomfort in the prior 12 months. Consistent with dysmenorrhea decreasing with age, associations were generally stronger among women ages ≤30 years. Our observations suggest that infancy may be a critical exposure window for biological changes influencing menstrual pain in early adulthood.

## A21 SINGLE INSTITUTION STUDY OF MEDICAL RADIATION EXPOSURE IN A COHORT OF CHILDREN DIAGNOSED WITH SOLID TUMORS, 1985-2005. Robin Rohrer

Background: Pre-natal or early childhood exposure to medical radiation used in diagnosis or treatment is an identified risk for childhood cancers but can be difficult to document. The author developed a family questionnaire/interview form to identify possible exposures. Aims: This retrospective study examines pre-natal and early childhood medical radiation exposure in a cohort of children diagnosed with a solid tumor including brain tumors from 1985-2005 at the Children's Hospital of Pittsburgh (CHP). The hospital is a tri-state regional referral center which treats about 150-180 new cases of cancer in children per year. About 70% are diagnosed with a solid tumor. Methods: Each consented family so far (approximately 50% of the cohort) has been interviewed in person or by phone call. Medical staff and psycho-social staff referred patient families for interview with the author. Results: Among the families interviewed to date at least one medical radiation exposure has been identified (pre-conception, pre-natal or early childhood) in over 70% of diagnosed children. These exposures have included pre-conception sinus or chest CT or x-ray in either parent, sinus CT or x-ray in mother or diagnostic radiation of chest or abdomen in children. Conclusions: Exposures to medical radiation for a child later diagnosed with cancer may occur at several critical junctures. These exposures may well contribute to a "perfect storm" in the still elusive causes of childhood cancer. The author plans to expand the study from 1980 to present to hopefully further document these junctures.

NO ASSOCIATION FOUND BETWEEN PRENATAL EXPOSURE TO PCBS AND TOTAL SERUM TESTOSTERONE IN ADULT MALE OFFSPRING OF THE CHILD HEALTH AND DEVELOPMENT STUDIES. Linda G. Kahn\*, Piera Cirillo, Barbara Cohn, June-Soo Park, Myrto Petreas, Pam Factor-Litvak (Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY)

Introduction The coincident rise in widespread use of industrial and agricultural chemicals and reported decline in semen quality and increase in testicular cancer in developed countries has led researchers to hypothesize that persistent organic pollutants such as polychlorinated biphenyls (PCBs) might interfere with the production and/or regulation of male reproductive hormones. In contrast with cross-sectional studies of PCBs and testosterone, which suggest an inverse relationship between the two, investigations into the effect of prenatal PCB exposure on total testosterone have found no association at endpoints ranging from birth through adolescence. In this study, we explore whether this apparent lack of association between prenatal PCB and testosterone persists into adulthood. Methods Using data from a follow-up study of 196 men who were part of the Child Health and Development Studies birth cohort, we evaluated the associations between prenatal exposure to total PCBs as well as to 15 PCB congeners, both individually and grouped according to chlorination patterns and proposed biological mechanism, and testosterone measured at mean age 43. PCBs were measured in stored maternal blood samples taken immediately postpartum; testosterone and follicle stimulating hormone (FSH) were measured in blood samples collected from the adult male offspring. Results In multivariable linear regression analyses we found no association between total prenatal PCBs, individual PCB congeners, and PCB groupings and serum testosterone in the adult male offspring controlling for maternal weight, race, coffee intake, and income, and men's age, smoking status, perceived stress, and total serum lipids. We additionally found no association between prenatal PCBs and either FSH or the ratio of FSH to testosterone. Conclusion Prenatal exposure to PCBs is not associated with total serum testosterone in our data, confirming findings in other birth cohorts that included younger participants.

### **A23**

## **UPPER RESPIRATORY INFECTION DURING PREGNANCY AND NEURODEVELOPMENTAL OUTCOMES AMONG OFFSPRING**. Lijewski, Virginia A.\* (Boston University), Parker, Samantha E., Werler, Martha M.

Upper respiratory infections (URI) are one of the most common infections during pregnancy and are thought to influence fetal brain development through maternal immune activation. The aim of this study was to investigate the association between maternal URI and childhood neurodevelopment and to determine differences based on timing, duration, and treatment of infection. Eligible participants were mother-child pairs, who served as controls in a case-control study of prenatal exposures and a craniofacial malformation. Data on illnesses during pregnancy were collected through a maternal interview conducted on average 12 months after delivery. Neurodevelopmental assessments were conducted at ages 5-12 years to measure psychosocial behavior according to mother and teacher report using the Child Behavior Checklist (CBCL) and the Teacher Report Form (TRF), respectively and neurocognitive outcomes using the Peabody Picture Vocabulary Test (PPVT-III) and the Beery-Buktenica Test of Visual Motor Integration (VMI-5). Adjusted linear regression models were used to calculate mean differences (MD) in scores between children of mothers with and without URI. Of the 523 mothers included in the study, 38% reported a URI during pregnancy. URI was associated with more behavior problems according to both mother and teacher report (MD: 3.51; CI:1.67,5.34(CBCL) and MD:2.89;CI:1.07,4.71(TRF)). There were no associations between URI and neurocognitive outcomes. Associations between URI and behavior problems were most notable for infections occurring after the first trimester and infections lasting >10 days. Treatment with antibiotics was associated with poorer childhood psychosocial outcomes than was treatment with acetaminophen or decongestants. Exposure to maternal URI was associated with psychosocial, but not neurocognitive development in childhood.

MATERNAL ACETAMINOPHEN USE AND CHILDHOOD NEURODEVELOPMENT. SE Parker\*, MM Werler (Boston University School of Public Health, Boston, MA) Acetaminophen use during pregnancy has been hypothesized to influence fetal brain development through interference with hormones and cytokines necessary for development. The aim of this study was to investigate the association between maternal acetaminophen use and several measures of childhood neurodevelopment. Participants were mother-child dyads (n=560) that served as controls in a previously conducted case-control study of prenatal exposures and a malformation. Information on maternal demographics, illnesses during pregnancy, and medication use was collected through an interview conducted on average one year after delivery. Measures of childhood neurodevelopment at ages 5-12 years included verbal (Peabody Picture Vocabulary Test(PPVT)) and non-verbal (Visual Motor Integration(VMI)) functioning and behavioral adaptation according to mother-report (Child Behavior Checklist(CBCL)) and teacher-report (Teacher Report Form(TRF)). Linear regression models adjusting for maternal age, race, education, and indication were used to calculate mean differences (MD) in scores between children of acetaminophen users and non-users. Trimester and duration of acetaminophen use were also explored. Acetaminophen use during pregnancy was reported by more than half of all mothers (59%). It was most commonly indicated for the treatment of headaches, migraines, upper respiratory symptoms, and sinus infections. Compared to children unexposed to acetaminophen during pregnancy, children of mothers reporting acetaminophen use during pregnancy had slightly poorer verbal functioning measured by the PPVT (MD:-2.2; CI:-5.0, 0.5). Differences in PPVT scores were more pronounced when the mother reported extended use (≥200 days) of acetaminophen (MD:-3.3; CI: -6.3,-0.3).

### **A25**

TRANSGENERATIONAL BODY MASS INDEX (BMI) AS A PREDICTOR OF BIRTHWEIGHT: THE BOGALUSA HEART STUDY. EW Harville\*, M Jacobs (Tulane University School of Public Health and Tropical Medicine, New Orleans, LA)

Differences in non-verbal functioning and behavioral adaptation were not observed between

children of acetaminophen users and non-users.

Background: Since the development of the Barker hypothesis, interest has focused on how in utero metabolism may alter epigenetics or other systems in ways that program long-term health. Such changes could affect not only the fetus, but also future generations. Methods: Data from the Bogalusa Heart Study were linked to Louisiana vital statistics data, leading to an analysis file including 202 grandmother-mother-infant triads, with cardiovascular risk factor information available on the grandmother and mother and birthweight information available on the mother and infant. As an initial analysis of how metabolism in pregnancy might affect later generations. we examined the grandmother's pre-pregnancy BMI as a predictor of grandchild's birthweight using linear regression, adjusted for mother's birthweight, age, and smoking during pregnancy. Results: In bivariate analysis, grandmother's BMI was correlated with mother's BMI (r=0.39, p<0.01), but not infant's birthweight (r=0.01, p=0.85). Mother's pre-pregnancy BMI (r=0.24, p<0.01) and own birthweight (r=0.21, p<0.01) were correlated with infant's birthweight. In multivariable analysis, mother's BMI was positively associated with infant birthweight (adjusted beta=30 g, p=0.01), while grandmother's birthweight was negatively associated (-35 g, p<0.01). Conclusions: Studies of in utero exposures should explore mechanisms by which intergenerational exposures might produce metabolic risk.

PRECONCEPTION AND PRENATAL VERSUS POSTPARTUM RECALL OF MATERNAL EXPOSURE TO CHILDHOOD ABUSE AND NEGLECT: DIFFERING ASSOCIATIONS WITH PERINATAL OUTCOMES? Cammack AL\*, Hogue CJ, Drews-Botsch CD, Kramer MR, Pearce BD, Knight BT, Stowe ZN, Newport DJ (Emory University)

Background: Childhood trauma is a common exposure that has been associated with several perinatal epidemiology outcomes. However, measurement is often collected through retrospective self-report, which is prone to information bias. We sought to examine the potential role of recall bias with respect to selected perinatal outcomes. Methods: Participants consisted of 244 women with history of psychiatric illness at the Emory Women's Mental Health Program. Childhood abuse (physical, emotional, and sexual) and neglect (emotional and physical) was measured with the Childhood Trauma Questionnaire Short-Form during two time periods for each participant; 1) the preconception or prenatal period (pre-delivery) and 2) postpartum or post-delivery. Odds ratios comparing pre-delivery versus post-delivery measured trauma associations with selected chart abstracted outcomes (preterm birth, low birth weight, NICU admission, maternal medical complications) were computed. A difference of 20% between predelivery and post-delivery point estimates was considered meaningful. Results: For most adverse outcomes, post-delivery estimates of physical neglect were larger than pre-delivery estimates (e.g., for low birth weight, pre-delivery OR=.40 (95% CI:0.05-3.11) versus postdelivery OR=3.02 (95% CI:1.00-9.16); for maternal medical complications pre-delivery OR=.69 (95% CI:0.23-2.04) versus post-delivery OR=2.29 (95% CI:0.90-5.82)). For some outcomes, post-delivery estimates for sexual abuse were larger than pre-delivery estimates (e.g., for NICU admission, pre-delivery OR=1.62 (95% CI: 0.60-4.33) versus post-delivery OR=2.33 (95% CI:0.97-5.58)). Conclusion: These findings suggest retrospective reporting of childhood trauma may be prone to recall bias with respect to perinatal outcomes. Further studies, such as those employing use of a gold standard trauma measure, may be useful.

### **A27**

MATERNAL AEROBIC AND STRENGTH TRAINING PHYSICAL ACTIVITY AND BIRTHWEIGHT: THE OMEGA STUDY. Sylvia E Badon\*: Chunfang Qiu: Michelle A Williams: Daniel A Enquobahrie (University of Washington School of Public Health, Seattle WA) Background: Despite differing cardiometabolic benefits of aerobic physical activity and strength training, and increasing participation in strength training among women, few studies have assessed associations of maternal aerobic activity and strength training with offspring birthweight (BW). Methods: Study participants (N= 2907) were identified from the Omega study, a prospective pregnancy cohort. During a structured interview at 15 weeks gestation, participants reported leisure time physical activities performed in the year before pregnancy (ppLTPA) and in the week before the interview (epLTPA). BW was abstracted from medical records. Regression models were used to determine mean difference in BW across activity categories: inactive, strength training and aerobic LTPA, or aerobic LTPA only. Stratified analyses were used to assess if associations differ by infant sex or pre-pregnancy overweight/obese status (BMI≥25kg/m2). Results: During pre-pregnancy and early pregnancy, 65% and 64% of participants, respectively, performed aerobic LTPA only, while 26% and 11% of participants, respectively, performed aerobic and strength training LTPA. Participants who performed strength training only were excluded from analyses (ppLTPA: 0.5%; epLTPA: 0.4%). No difference in BW was observed between women who participated in strength training and aerobic ppLTPA compared to women who only participated in aerobic ppLTPA (β= -10q: 95% CI: -46, 26). Similarly, no difference was observed by type of epLTPA (β= -34g; 95% CI: -84, 17). Neither infant sex nor pre-pregnancy overweight/obese status modified the associations. Conclusion: Maternal LTPA type was not associated with birthweight. Future studies in other populations are needed to inform LTPA recommendations prior to and during pregnancy.

**USING THE BEHAVIORAL RISK FACTOR SURVEILLANCE SYSTEM TO EXPLORE FEMALE INFERTILITY**. Kuwabara SA\*, Smith R, Crawford S, Grigorescu V (The Centers for Disease Control and Prevention, ORISE Fellow, Atlanta, GA)

Introduction: Population-level data on infertility are sparse. As patient-generated-data gain more attention, we explored the use of Centers for Disease Control and Prevention (CDC)'s Behavioral Risk Factor Surveillance System (BRFSS) to assess the prevalence of infertility in the context of behaviors and other chronic conditions, as well as factors associated with access to services and treatment utilization. BRFSS is a coordinated collection of population health surveys conducted by state's public health departments. Methods: 2013 BRFSS data from 5 states (CT, KY, MA, OH, UT) that administered questions related to infertility to women age 18-50 were used. Prevalence estimates of female infertility were measured. Multinomial logistic regression was used to 1) identify factors associated with female infertility (categorized as infertility, difficulty staying pregnant and no infertility), and 2) explore the impact of health care coverage on type of treatment received among women with infertility. Results: Lifetime prevalence of female infertility averaged 11.7%, ranging from 10.6% in CT to 13.2% in UT. Controlling for age and marital status, history of depressive disorder was associated with having ever experienced female infertility (OR=1.89, 95% CI: 1.28, 2.79). The most common treatment received was medication alone to improve or stimulate ovulation (23%). Having health care coverage was associated with receiving either medication (OR=3.79, 95%CI: 1.60, 8.97) or IUI and/or ART (OR=8.89, 95% CI: 2.13, 37.0) compared to no treatment. Conclusions: Use of existing and ongoing epidemiologic data collection systems such as BRFSS provides an opportunity to obtain population-based measures of the burden of infertility and serves as effective method for gathering state-specific data on health and access to care. Expanding the use of such systems would enable tracking of trends, allow for comparability of measures across states and is adaptable for local use.

### **A29**

GENETIC VARIATION IN TOLL-LIKE RECEPTOR 6 IS ASSOCIATED WITH LEPTOTRICHIA AMNIONII INFECTION IN WOMEN WITH PELVIC INFLAMMATORY DISEASE. BD Taylor\*, PA Totten, SG Astete, MJ Ferris, J Norori, RE Ferrell, RB Ness, DH Martin, CL Haggerty (Texas A&M University, College Station, TX)

Objective: Variation in the host innate immune response has been linked to alterations in the vaginal flora and subsequent reproductive complications. We have previously found that Toll-like (TLR) receptor gene variation may be associated with bacterial vaginosis (BV). As not all BV-associated organisms lead to pathology, we examined associations between TLR genetic variants and novel fastidious BV-associated microbes among women with pelvic inflammatory disease (PID). Methods: We obtained data on 9 variants in four TLR genes (TLR 1,2,4, and 6) from 205 African American women enrolled in the PID Evaluation and Clinical Health (PEACH) study. Select fastidious microorganisms [Leptotrichia sanguinegens, Leptotrichia amnionii, Atopobium vaginae, bacterial vaginosis-associated bacterium 1 (BVAB1), and *Ureaplasma* species] in the cervix and/or endometrium were measured by targeted PCR. Logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (CI) adjusting for age. The false discovery rate was used to correct for multiple comparisons. Results: The TT genotype for TLR6 rs1039559 significantly increased the odds of Leptotrichia sanguinegens (OR 2.4, 95% CI 1.2-4.9), Leptotrichia amnionii (OR 2.7, 95% CI 1.3-5.5), and Atopobium vaginae (OR 2.8, 95% CI 1.1-7.3). After multiple comparison correction, the association between rs1039559 and Leptotrichia amnionii remained significant (q=0.02). No other significant associations were found following adjustment for multiple comparisons. Conclusions: Among African American women with PID, the rs1039559 TT genotype was associated with Leptotrichia amnionii. Further studies are needed to replicate results and provide additional insight into immunogenetic pathways that may alter the vaginal flora and increase reproductive morbidity.

**SERUM PERFLUOROALKYL ACIDS AND TIME TO PREGNANCY IN NULLIPAROUS DANISH WOMEN.** Bach CC\*, Bech BH, Nøhr EA, Matthiesen NB, Olsen J, Bonefeld-Jørgensen EC, Henriksen TB. (Perinatal Epidemiology Research Unit, Aarhus University Hospital, Aarhus, Denmark)

Background Studies on exposure to perfluoroalkyl acids (PFAAs) and female fecundability or infertility provided conflicting results. We aimed to investigate the association between several PFAAs and time to pregnancy. We restricted the study to nulliparous women to eliminate reverse causality among parous women. Methods From 2008 - 2013, we included 1385 women from the Aarhus Birth Cohort who gave a blood sample before 14 gestational weeks and had data on time to pregnancy. We measured levels of 16 PFAAs in maternal serum and report data for seven compounds with at least 75 % of all samples above the limit of quantification. We used discrete-time survival analysis to estimate fecundability ratios according to quartiles of PFAAs, adjusted for potential confounders chosen with guidance from a directed acyclic graph. We estimated the association between PFAAs and infertility (time to pregnancy>12 months or infertility treatment prior to the studied pregnancy) by multivariate logistic regression. Results Median levels of perfluorooctane sulfonate and perfluorooctanoate were 8.3 and 2.0 ng/mL. respectively. Overall, no obvious associations were apparent between any PFAAs and fecundability ratios or infertility odds ratios (e.g. the adjusted fecundability ratio for perfluorooctane sulfonate was 1.06 (95 % confidence interval 0.89 - 1.26, highest versus lowest quartile). Conclusion We found no association between serum levels of PFAAs and time to pregnancy or infertility in a recent sample of women with lower average exposure levels compared to most studies. This study adds to the sparse knowledge on other PFAAs than perfluorooctane sulfonate and perfluorooctanoate.

### A31

MENSTRUAL CYCLE CHARACTERISTICS AND FECUNDABILITY IN A NORTH AMERICAN PRECONCEPTION COHORT. AK Wesselink\*, S Mahalingaiah, EE Hatch, KJ Rothman, EM Mikkelsen, CJ McKinnon, LA Wise (Boston University School of Public Health, Boston, MA) Abnormal menstrual cycle patterns may be an important indicator of reduced fertility. We examined the association between menstrual cycle characteristics and fecundability in the Pregnancy Study Online (PRESTO), a preconception cohort study. Female pregnancy planners completed a baseline questionnaire in which they reported cycle length, duration and heaviness of menstrual flow, age at menarche, and time from menarche until cycle regularity. Outcome data were updated every 8 weeks until clinically-recognized pregnancy, fertility treatment, loss to follow-up, or end of observation (12 months). Adjusted fecundability ratios (FR) and 95% CIs were estimated using a proportional probabilities model. Among 1291 women, FRs for cycle lengths of <25, 25-26, 30-31, 32-33, and ≥34 days were 0.60 (CI: 0.36-1.00), 0.86 (CI: 0.67-1.16), 0.86 (Cl; 0.72-1.03), 1.06 (Cl; 0.81-1.37), and 1.04 (Cl; 0.81-1.33), respectively. compared to average cycle lengths (27-29 days). FRs for early (<12 years) and late (≥15 years) menarche were 0.93 (CI: 0.78-1.10) and 0.86 (CI: 0.67-1.09), respectively, compared to ages at menarche of 12-13 years. Relative to women whose menstrual cycles became regular <2 years after menarche, FRs for women whose cycles took 2-3 years to become regular, at least 4 years to become regular and whose cycles never became regular were 0.95 (CI: 0.73-1.23), 0.81 (CI: 0.57-1.17) and 0.74 (CI: 0.62-0.89), respectively. Duration and heaviness of flow were not appreciably associated with fecundability. Our findings are consistent with results from previous studies and suggest that short cycle length and cycle irregularity may be important indicators of reduced fertility potential.

PHYSICAL ACTIVITY AND REPRODUCTIVE OUTCOMES AMONG WOMEN UNDERGOING ASSISTED REPRODUCTION. AJ Gaskins\*, PL Williams, TL Toth, R Hauser, JE Chavarro (Harvard T.H. Chan School of Public Health, Boston, MA)

Background: Physical activity could beneficially impact reproductive function through its ability to regulate energy balance and improve insulin sensitivity, but its association with assisted reproductive technology (ART) treatments remains unclear. Methods: This analysis included 273 women in a prospective cohort study at the Massachusetts General Hospital Fertility Center. Time spent in physical and sedentary activities over the past year was self-reported using a validated questionnaire prior to treatment initiation. Outcomes of ART were abstracted from medical records. Generalized linear mixed models with random intercepts were used to evaluate the association of physical and sedentary activities with ART outcomes adjusting for age. BMI, race, infertility diagnosis, and education level. Results: Time spent in physical activities was not significantly associated with implantation, clinical pregnancy, or live birth rates. However there was a significant heterogeneity in the effect of physical activity on live birth rates by BMI (p-interaction=0.05). While vigorous activity was not associated with live birth rates in overweight or obese women (p-value=0.36), vigorous activity was positively associated with live birth rates in women of normal BMI (18.5-24.9 k/m2) (p-value=0.04). Greater time spent in in aerobics or on aerobic exercise equipment appeared to be driving this association as live birth rates were 24% (95% CI 5, 41%) higher among normal BMI women reporting >1.5 hours/week of aerobics compared to those reporting none. Time spent in sedentary activities was not associated with outcomes of ART. Conclusions: In women of normal BMI, higher vigorous activity was associated with increased success of ART treatment.

### **A33**

VAGINAL LUBRICANT USE AND TIME TO PREGNANCY: A PROSPECTIVE COHORT STUDY. KA Hahn\*, EE Hatch, AZ Steiner, EM Mikkelsen, TM Snerum, KJ Rothman, LA Wise (Boston University School of Public Health, Boston, MA)

Several in vitro studies have found that exposure to common vaginal lubricants (such as KY Jelly, Astroglide), but not water-based, pH balanced, "fertility-friendly" lubricants (such as Pre-Seed), diminishes sperm motility. However, in vivo studies of the impact of vaginal lubricants on fertility are limited. We conducted a combined analysis of data from two preconception cohorts in North America (Pregnancy Study Online, 2013-2014) and Denmark (Snart Foraeldre, 2011-2014). Analyses were restricted to women attempting pregnancy for 6 or fewer cycles at study entry. Participants reported data on current lubricant use at baseline and were contacted every 8 weeks for 12 months or until clinically-recognized pregnancy, whichever came first. Lubricant brands were separated into the following mutually exclusive categories: water-based, "fertilityfriendly", and other lubricants (silicone, oil, petroleum-based, mixed and unknown types). Proportional probabilities regression models were used to estimate fecundability ratios (FR) and 95% Cls, with control for age, BMI, parity, intercourse frequency, oral contraceptive use. smoking and cohort. Overall, 508 of 3,144 women (12.5%) reported current lubricant use. A higher proportion of women (19.3%) from North America reported lubricant use than women from Denmark (7.1%). Multivariable FRs were 1.13 for water-based lubricants (CI: 0.96, 1.34), 1.08 for "fertility-friendly" lubricants (CI: 0.84, 1.38)), and 1.05 for other lubricants (CI: 0.90, 1.22), compared with non-users. Results changed little when stratified on attempt time at entry (<3 vs. ≥3 cycles) and age (<30 vs. ≥30 years). No decrease in fecundability was seen among women who used vaginal lubricants while attempting to get pregnant.

**DIETARY IRON INTAKE AND TIME-TO-PREGNANCY**. KA Hahn\*, LA Wise, KL Tucker, VK Knudsen, EM Mikkelsen, AH Riis, KJ Rothman, A Wesselink, EE Hatch (Boston University School of Public Health, Boston, MA)

Iron supplements and dietary non-heme iron have been suggested to increase pregnancy rates among women with fertility problems and decrease the risk of ovulatory infertility. We conducted parallel analyses of participants from two internet-based preconception cohort studies from North America (N=1100) and Denmark (N=905) (Pregnancy Study Online (PRESTO) and Snart Foraeldre). Analyses were restricted to women trying for 6 or fewer cycles at entry. We used validated population-specific food frequency questionnaires to estimate daily intake of heme. non-heme, and total iron (mg/day) at baseline. Participants completed follow-up questionnaires to update pregnancy status every 8 weeks for 12 cycles or until clinically-recognized pregnancy, whichever came first. We used proportional probabilities models to determine the cycle-specific probability of conception, expressed as a fecundability ratio (FR). Multivariable models included female age, education, BMI, physical activity, smoking, alcohol intake, last method of contraception, iron and vitamin C supplement use, dietary vitamin C and total energy. In PRESTO, we also adjusted for race/ethnicity. In PRESTO, compared with <8 mg/day of nonheme iron, the FRs for 8-10 and ≥11 mg/day were 1.08 (95% CI: 0.76, 1.52) and 1.15 (95% CI: 0.81, 1.62), respectively. In Snart Foraeldre the observed FRs for non-heme iron were 1.30 (95% CI: 0.96, 1.76) and 1.27 (95% CI: 0.87, 1.84) for 8-10 and ≥11 mg/day compared with <8 mg/day. Dietary intake of total iron and heme iron were not materially associated with fecundability. Our results suggest that higher levels of dietary non-heme iron may be associated with a small increase in fecundability.

#### A35

PREDICTORS OF POOR FERTILIZATION FOLLOWING IN VITRO FERTILIZATION (IVF) WITH OR WITHOUT INTRACYTOPLASMIC SPERM INJECTION (ICSI) AMONG NORMAL RESPONDERS. LE Dodge\*; JS Sisti; BA Malizia; AS Penzias; MR Hacker (Beth Israel Deaconess Medical Center, Boston, MA; Harvard Medical School, Boston, MA) BACKGROUND: Poor fertilization is a disappointing outcome for couples undergoing in vitro fertilization (IVF). This study aimed to identify predictors of poor fertilization among women undergoing IVF and IVF with intracytoplasmic sperm injection (ICSI) among normal responders. METHODS: Data were collected from women undergoing their first fresh non-donor IVF cycle at an academically-affiliated infertility treatment center from January 1995 through April 2012. Only normal responders were included in the analysis; these were women from whom ≥8 mature oocytes were retrieved. Poor fertilization was defined as having ≤2 mature oocytes normally fertilized, which was defined as having two pronuclei. Multivariable logistic regression was used to examine the relationship between each predictor and poor fertilization. RESULTS: A total of 6,797 cycles were performed among normal responders; 2,232 were ICSI cycles. The median number of mature oocytes retrieved in both the ICSI and non-ICSI groups was 11.5. Poor fertilization was found in 6% and 5% of ICSI and non-ICSI cycles, respectively. Fewer mature oocytes retrieved and male factor infertility were associated with poor fertilization among both ICSI and non-ICSI cycles (all P<0.001). Being underweight was associated with poor fertilization among ICSI cycles (P=0.006), while earlier year of cycle start (P<0.001) and older female age (P=0.02) were associated with poor fertilization among non-ICSI cycles. CONCLUSION: Having male factor infertility and fewer mature oocytes were significantly associated with poor fertilization regardless of ICSI utilization. While older female age was associated with poor fertilization in non-ICSI cycles, it had no effect among ICSI cycles.

THE FREQUENCY OF MYCOPLASMA GENITALIUM IN A POPULATION OF MEXICAN WOMEN. Abiodun-Ojo OA\*, Taylor BD, Villagrana-Zesati R, López-Hurtado M, de Haro-Cruz M, Guerra-Infante FM (Texas A&M Health Science Center, College Station, TX) Objective: Mycoplasma genitalium is an emerging sexually transmitted pathogen that has been linked to pelvic inflammatory disease and infertility. Prevalence in low risk populations is reported to be 1-3% but reaches 20% in high risk individuals. There are gaps in our understanding of M. genitalium in many populations such as in Mexico where no studies have determined the prevalence of M. genitalium. The objective of this pilot study was to determine the frequency of M. genitalium in a population of Mexican women. Methods: We obtained frozen endocervical swabs from 89 women aged 18-40 who participated in a study comparing treatment regimens for vaginal infections. We calculated the frequency of M. genitalium, Trichomonas vaginalis. Mycoplasma hominis. Chlamydia trachomatis. Neisseria gonorrhoeae and Ureaplasma urealyticum/parvum measured using a multiplex polymerase chain reaction method. Results: All women in this study had symptoms of vaginal infection. A total of 7(7.9%) women tested positive for M. genitalium, 4(4.5%) for T. vaginalis, 1(1.1%) for M. hominis, 28(31.5%) for C. trachomatis, 31(34.8%) for N. gonorrhoeae, and 39(43.8%) for U. urealyticum/parvum. Five women with M. genitalium (71.4%) had co-infection with at least one pathogen. Conclusions: This pilot study is one of the first studies to report that M. genitalium is prevalent in Mexican women with symptoms of vaginal infection. Our future work will focus on the epidemiology of M. genitalium in this population, as well as its association with infertility. A better understanding of M. genitalium will lead to improved strategies for prevention and control of this emerging pathogen.

#### **A37**

A COMPARISON OF THREE APPROACHES TO COLLECTING DATA ON PREGNANCY ATTEMPT DURATION AMONG WOMEN WITH A HISTORY OF PRIMARY INFERTILITY.. J

Sanders\* S Simonsen, C Porucznik, A Hammoud, K Smith, J Stanford (University of Utah) Background: The duration of regular unprotected intercourse without achieving conception, is an important concept as it is central to how infertility is defined and diagnosed. The aim of this study is to examine how women with a history of primary infertility recall their TARP when asked about attempt duration with different questioning techniques. Methods: The Fertility Experiences Study (FES) is a retrospective cohort study conducted at the University of Utah between April 2010 and September 2012. Questions about pregnancy attempt duration were repeated over the course of the FES and were asked at different times using the different approaches: a single question approach, a date-approach, and an active date-approach. Results: We found that misestimation of longest single attempt duration occurred frequently when information was solicited using the common single question approach. Only a third (34%) of women accurately reported their longest attempt duration based on this single question when compared to information obtained using the date-based approach (+/- 3 months), while 37% of women overestimated and 29% of women underestimated their TARP using the single question approach. The sensitivity and specificity of the single question for capturing a person who had been trying for 24 months was good with over 90% being correctly identified as infertile. Conclusions: Physicians, in primary care and specialty settings, should avoid the use of a single question when assessing how long a couple has been having regular unprotected intercourse. Detailed attempt histories should be used to capture a more accurate and complete picture of "time trying to conceive."

**ASSOCIATION BETWEEN DIETARY MAGNESIUM AND SYMPTOMS OF PREMENSTRUAL SYNDROME**. Kalwerisky RA\*; Ye A; Sjaarda LA; Perkins NJ; Schliep KC; Plowden T; Zarek SM; Radin RG; Wactawski-Wende J; Mumford SL (Eunice Kennedy Shriver National Institute of Child Health and Human Development)

Nearly all regularly menstruating women of reproductive age are affected by Premenstrual Syndrome (PMS) symptoms in the weeks prior to menses, and thus there is a need to explore potential modifiable factors that might relieve symptoms. Evidence suggests that micronutrient—specifically, magnesium—intake could play a role in alleviating symptoms. We aimed to further explore the association between dietary magnesium intake and PMS symptoms among a cohort of 259 healthy premenopausal women ages 18-44 who were followed for up to 2 menstrual cycles in the BioCycle study. Dietary intake was evaluated 4 times per cycle using 24-hour recalls and averaged per cycle, while 27 PMS symptoms (including anxiety, depression, craving, hydration, or other), and their respective severities were assessed up to 4 times per cycle via standardized questionnaires. Linear mixed models adjusted for energy intake, age, and race were used to evaluate associations. We observed that dietary magnesium intake above versus below the recommended levels (≥310 mg/day [n=28, 10.8%] versus <310 mg/day [n=231, 89.2%]) was not associated with reported PMS-related physical pains and sicknesses. like flu, cold, or other non-specific pain symptoms (beta: -0.24, 95% CI: -0.93, 0.45). Magnesium was also not associated with psychological symptoms—such as depression or anxiety (beta: 0.43, 95% CI:-0.74,1.6)—or food cravings (beta: 0.39, 95% CI: -0.65,1.43). These data do not support the hypothesis that dietary magnesium intake may provide natural relief for symptoms of PMS. Future research is needed to determine other potential dietary and lifestyle factors that may relieve symptoms.

### A39

PHYTOESTROGENS AND ENDOMETRIOSIS: THE ENDOMETRIOSIS, NATURAL HISTORY, DIAGNOSIS AND OUTCOMES (ENDO) STUDY. SL Mumford\*, R Sundaram, K Kannan, G Buck Louis, J Weck (Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Rockville, MD) Phytoestrogens have been associated with subtle hormonal changes, though effects on endometriosis are largely unknown. These associations are of great interest as dietary factors may influence the physiological and pathological processes of the disease. Our objective was to assess the association between urinary concentrations of phytoestrogens and incident endometriosis. This study was a matched cohort comprised of 495 premenopausal women undergoing laparoscopies/laparotomies at 14 clinical sites between 2007-2009 (operative cohort) and 131 women sampled from the same geographic area who were matched on age and menstruation status (population cohort). Endometriosis in the population cohort was assessed using pelvic magnetic resonance imaging, while disease in the surgical cohort was assessed by surgical visualization (clinical gold standard). Levels of daidzein, enterodiol, enterolactone, equal, genistein, and O-desmethylangolensin were quantified in urine (nmol/L) at baseline. Logistic regression analysis was used to estimate the odds of an endometriosis diagnosis for each cohort after adjusting for age and body mass index. Separate models were run for each phytoestrogen. Geometric mean concentrations of phytoestrogens were not significantly different by endometriosis status in either cohort. Adjusted ORs for endometriosis ranged from 0.98 to 1.03 for the 6 phytoestrogens measured, with all confidence intervals including one. Phytoestrogens were not associated with severity of endometriosis when restricting the analysis to women with rASRM moderate/severe staged disease. Further, no associations were observed between self-reported high soy intake and endometriosis. Despite endometriosis being an estrogen-dependent disease, we found no evidence that urinary phytoestrogens were associated with higher odds of an endometriosis diagnosis.

CANCER TREATMENT-INDUCED HYPOTHYROIDISM AND THE ABILITY TO MEET REPRODUCTIVE GOALS AMONG A COHORT OF YOUNG ADULT FEMALE CANCER SURVIVORS. Jacobson MH\*, Chin HB, Interrante JD, Mertens AC, Spencer JB, Howards PP. (Emory University, Atlanta, GA)

Some cancer treatments have deleterious side effects including impaired fertility, as well as other health conditions such as hypothyroidism. Additionally, evidence suggests that hypothyroidism can lead to reduced fertility, anovulation, and miscarriage. Most studies have focused on direct effects of cancer treatment or hypothyroidism on fertility, but it is unclear if those who experience treatment-induced hypothyroidism are at an increased risk of infertility compared with those who only receive cancer treatment and do not develop hypothyroidism. The FUCHSIA Women's Study recruited reproductive-age female cancer survivors (22-45 years), diagnosed between the ages of 20-35, who were at least 2 years post-diagnosis. All invasive cancers and in situ breast cancers were eligible except non-melanoma skin cancer. There were 904 women not diagnosed with hypothyroidism before cancer or thyroid cancer. Women with hypothyroidism after cancer treatment were almost twice as likely to have fewer children than desired compared with those who never developed hypothyroidism (adjusted odds ratio (aOR)=1.95; 95% confidence interval (CI): 1.12, 3.38). Results remained consistent when other fertility outcomes were examined; women diagnosed with hypothyroidism were more likely to: have fewer children than desired due to fertility-related reasons (aOR=1.33: 95% CI 0.73. 2.43), be childless at the time of interview (aOR=2.34; 95% CI 1.38, 3.98), and report a period of infertility after cancer treatment (aOR=1.56; 95% CI 0.80, 3.07). These results highlight the importance of considering other medical conditions that occur after cancer treatment when estimating effects of cancer and cancer treatment on future fertility.

### Δ41

CAFFEINE CONSUMPTION DURING PREGNANCY AND MISCARRIAGE: A META-ANALYSIS. LE Dodge\*; E Mostofsky; AY Liu; MR Hacker (Beth Israel Deaconess Medical Center, Boston, MA; Harvard Medical School, Boston, MA)

BACKGROUND: The association between caffeine consumption and pregnancy loss has long been debated, and the American Congress of Obstetricians and Gynecologists states that there is no conclusion regarding the association between miscarriage and consumption of more than 200 mg of caffeine per day. The aim of this meta-analysis was to elucidate the dose-response relationship between caffeine intake and miscarriage. METHODS: We performed a literature search of the MEDLINE, Embase, and CINAHL databases from January 1, 1953 to July 9, 2012 using the terms [("caffeine" OR "coffee" OR "tea" OR "cola") AND ("abortion" OR "pregnancy loss" OR "miscarriage")] without restrictions. Abstracts were independently reviewed by two investigators for inclusion criteria, and discrepancies were adjudicated. Included studies were then abstracted for relevant study details and results. Analyses will be stratified by type of caffeine (i.e., coffee, total intake), timing of consumption (i.e., before pregnancy, first trimester, during pregnancy), and whether studies controlled for nausea, which is an important confounder of the relationship between caffeine intake and miscarriage. RESULTS: We identified 530 references; 154 duplicates were excluded, yielding 376 potential references. Of these, 59 were included following initial review of the abstract. Following review of the full-text papers, an additional 19 were excluded, yielding a total of 40 references for inclusion. CONCLUSIONS: The relationship between caffeine intake and miscarriage has long been debated in the field of obstetrics. A meta-analysis of all previous studies considering the dose-response relationship and proper confounders will help to elucidate the true nature of the relationship.

ASSESSED MATERNAL OCCUPATIONAL EXPOSURE TO CHLORINATED. AROMATIC AND STODDARD SOLVENTS DURING PREGNANCY AND RISK OF FETAL GROWTH RESTRICTION IN OFFSPRING. Desrosiers TA\*, Lawson CC, Meyer RE, Stewart PA, Waters MA, Correa A, Olshan AF, and the National Birth Defects Prevention Study (Department of Epidemiology, Gillings School of Global Public Health, UNC Chapel Hill, NC) Objective: We evaluated the association between expert-assessed occupational solvent exposure and risk of small for gestational age (SGA) in a population-based sample of women from 8 US states in the National Birth Defects Prevention Study. Methods: We analyzed data from 2.886 mothers and their infants born 1997-2002 without a major congenital anomaly. Job histories were self-reported via interview. Probability of occupational exposure to 6 chlorinated, 3 aromatic, and 1 petroleum solvent was assessed by industrial hygienists. SGA was defined as birthweight <10th percentile of birthweight-by-gestational age in a national reference. Logistic regression was used to estimate ORs and 95% CIs to assess the association between SGA and exposure to any solvent or specific solvent classes, adjusting for maternal age and education. Results: Approximately 8% of infants were classified as SGA. Exposure prevalence to any solvent was 10% and 8% among mothers of SGA and non-SGA infants, respectively. Any solvent exposure was not associated with an increased odds of SGA (OR=1.16; 95% CI=0.73, 1.83). Among women with ≥50% exposure probability, we observed elevated but imprecise associations between SGA and exposure to any solvent (1.71; 0.86, 3.40), chlorinated solvents (1.70; 0.69, 4.01), and aromatic solvents (1.87; 0.78, 4.50). Conclusions: This is the first population-based study in the US to investigate the potential association between SGA and assessed maternal occupational exposure during pregnancy to distinct classes of organic solvents. The potential associations observed between SGA and exposure to chlorinated and aromatic solvents are based on small numbers and merit further investigation.

### A43

POSTPARTUM CONTRACEPTIVE METHOD USE AMONG WOMEN WITH A RECENT PRETERM BIRTH. CL Robbins\*, SL Farr, LB Zapata, DV D'Angelo, WM Callaghan (Centers for Disease Control and Prevention, Atlanta, GA)

Short inter-pregnancy intervals are associated with preterm birth. We used Pregnancy Risk Assessment Monitoring System data from nine states to estimate the prevalence of postpartum contraceptive use by any method, highly effective methods (shot, pills, patch, ring, implants, intrauterine device, and sterilization), and highly effective user-independent methods (implants, intrauterine device, and sterilization) among women with live births (2009-2011). We assessed differences in contraceptive use by gestational age (chi-square tests, p<.05) and modeled the associations between preterm birth (≤27, 28-33, or 34-36 weeks versus term) and use of highly effective contraception using multivariable logistic regression with weighted data. A higher percentage of women with recent extreme preterm birth (≤27 weeks gestation) reported using no method (31%) compared with all other women (15-16%, p<.0001). Women delivering extreme preterm infants had decreased odds of using any highly effective method (adjusted odds ratio [aOR]=0.5, 95% confidence interval [CI]: 0.4 – 0.6) or user-independent methods (aOR=0.5, 95% CI: 0.4 – 0.7) compared with women having term births (>37 weeks). Wanting to get pregnant was more frequently reported as a reason for contraceptive nonuse by women with an extreme preterm birth overall (45%) than all other women (15-17%, p<.0001). Over half (54%) of women with extreme preterm birth whose babies died (n=71) reported this reason for contraceptive non-use. Infant death occurred in 41% of extreme preterm births. Women with recent extreme preterm birth, particularly those who lost their babies, may not use contraception because they want to get pregnant. Providers should consider this possibility during contraceptive counseling.

INTERGENERATIONAL TRANSMISSION OF THE HEALTHY IMMIGRANT EFFECT (HIE) THROUGH BIRTH WEIGHT: A SYSTEMATIC REVIEW AND META-ANALYSIS. Chantel Ramraj\*, Ariel Pulver, Arjumand Siddiqi (Dalla Lana School of Public Health, University of Toronto)

Objectives: To assess the effects of generational status on the birth weight of infants born to first-generation and second-generation immigrant mothers and how this varies by country of origin and receiving country. Methods: We searched MEDLINE, EMBASE, Web of Science, PubMed, and ProQuest from inception to October 2014 for articles that recorded the birth weight of an immigrant's infant and at least one subsequent generation of infants' birth weight (mean birth weight (in grams) or odds of low birth weight (LBW)). Studies were meta-analyzed using RevMan 5.3 software. Results: We identified 10 studies including approximately 158,843 first generation and second-generation immigrant women. Six studies were meta-analyzed for mean birth weight and 7 for LBW. Although not statistically significant, a decrease in mean birth weight in the second-generation infants was consistently seen across all studies and subgroups. Second-generation infants were also at higher odds of LBW across all of the studies (7 studies, [147,854 births]; OR=1.21 [95% CI, 1.15, 1.27]) and subgroups, especially among infants of Mexican decent (3 studies, [46,099 births]; OR=1.47 [95% CI, 1.28, 1.69]). In the United States, second-generation infants were at 34% higher odds of LBW (4 studies, [52,941 births]; OR=1.34 [95% CI, 1.13, 1.58]) when compared to the first generation. Conclusion: With more time spent in the receiving country, the deterioration of birth weight is apparent among infants of secondgeneration immigrant mothers. The magnitude and direction of birth weight differences varies depending on the country of origin of the mother, and the receiving country.

### A45

UNTANGLING TIME AMONG PRETERM PREDICTORS: A SURVIVAL APPROACH TO **PRETERM DELIVERY.** Mitchell EM\*, Hinkle SN, and Schisterman EF (NICHD, Bethesda, MD) There is substantial interest in understanding the impact of gestational weight gain (GWG) on preterm birth (delivery < 37 weeks). The major difficulty in analyzing the association between GWG and preterm birth lies in their mutual dependence on gestational age, as GWG naturally increases with increasing pregnancy duration. In this study, we untangle this inherent association by reframing preterm birth as time to delivery and assessing the relationship through a survival framework, which is particularly amenable to dealing with time-dependent covariates such as GWG. We derive the appropriate analytical model for assessing the relationship between GWG and time to delivery when measurements of GWG at multiple time points are available. Since epidemiological data may be limited to GWG measurements taken at only a few time points or at delivery only, we conduct simulation studies to illustrate how several strategically timed measurements can yield unbiased risk estimates. Analysis of the NICHD Study of Successive Small-for-Gestational-Age Births demonstrates that a naive analysis that does not account for the confounding effect of time on GWG suggests a highly significant association between higher GWG and later delivery (HR 0.89, 95% CI: 0.84 to 0.93). Properly accounting for the confounding effect of time using a survival model, however, mitigates this bias (HR 0.98, 95% CI: 0.97, 1.00). These results emphasize the importance of considering the effect of gestational age on time-varying covariates during pregnancy, and the proposed methods offer a convenient mechanism to appropriately analyze such data.

PROXIMITY OF MATERNAL RESIDENCE TO PULP MILLS AND THE RISK OF PRETERM BIRTH. ND Pace\*, TJ Luben, RE Meyer (The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina)

Increased ambient levels of several air pollutants are associated with an increased risk of preterm birth (PTB). Air emissions from pulp mills are known to emit many harmful pollutants. We examined the association between PTB and geographic proximity of maternal residence at time of delivery to pulp mills, a proxy for pulp mill air pollutants or other regional factors. We conducted a retrospective cohort study of 306,866 births registered in North Carolina from 2006-2008 of which 27,663 (9%) were preterm. Location point data for pulp mills (n=23) in North Carolina and bordering states were obtained from the USDA Forest Service. Log-binomial regression was used to calculate risk ratios and 95% confidence intervals. Proximity was categorized into three buffer zones: ≤2 miles, 2-10 miles, and >10 miles representing 0.3, 1.9. and 97.9% of maternal addresses respectively. Mothers who lived within 2 miles of a pulp mill during pregnancy had 1.25 times (95% CI: 1.03, 1.51) the risk of having a PTB compared to mothers who lived more than 10 miles from a mill, after adjusting for maternal race, education, age, and smoking. Mothers who lived 2-10 miles away had 1.06 (0.98, 1.15) times the risk of having a PTB compared to the same reference group (>10 miles). Results remained consistent when buffer zones were modified in sensitivity analyses. Living near a pulp mill is associated with an increased risk of PTB with less risk at greater distances. An investigation using measured air or other regional variants from pulp mills is needed.

### **A47**

**PERFLUOROALKYL ACIDS IN MATERNAL SERUM AND BIRTH WEIGHT IN THE AARHUS BIRTH COHORT**. Bach CC\*, Bech BH, Nøhr EA, Matthiesen NB, Olsen J, Bonefeld-Jørgensen EC, Bossi R, Henriksen TB. (Perinatal Epidemiology Research Unit, Aarhus University Hospital, Aarhus, Denmark)

Background Previous studies indicated an association between intrauterine exposure to perfluorooctane sulfonate or perfluorooctanoate and birth weight. However, these two perfluoroalkyl acids (PFAAs) have to some extent been substituted by other compounds on which little is known. We aimed to investigate the association between levels of specific PFAAs and birth weight. Methods We studied 1488 first time mothers and their children from the Aarhus Birth Cohort (2008-2013). We measured 16 PFAAs in maternal serum (before 14 gestational weeks) and report results for those with more than 75 % of samples above the limit of quantification (seven compounds). The associations between PFAA quartiles and birth weight were determined by linear regression adjusted for potential confounders identified by directed acyclic graphs. Results For most PFAAs, no obvious association was apparent with birth weight. For perfluorooctanoate, the adjusted regression coefficient (95 % confidence interval) was 27 (-45: 100) a for the highest versus lowest quartile. Three compounds with a sulfonate group indicated possible associations (perfluorohexane sulfonate, perfluoroheptane sulfonate, and perfluoroctane sulfonate). These associations were stronger in term births and after additional adjustment for gestational age or modeling of z-scores. For perfluorooctane sulfonate the corresponding estimate was -52 (-125; 21) g in all births and [-64 (-129; 0) g] in term births. Conclusions Overall, we found no strong associations between PFAA exposures and birth weight. A few compounds showed tendencies towards an association. Two of these, perfluorohexane sulfonate and perfluoroheptane sulfonate, have only been studied sparsely.

A CONTEMPORARY EVALUATION OF NURSE-FAMILY PARTNERSHIP BIRTH OUTCOMES. Currie DW\*, Thorland W (Nurse-Family Partnership National Service Office, Denver, CO).

Background. The Nurse-Family Partnership (NFP) is a national, evidence-based home visiting program currently serving over 30,000 first-time, low-income moms. Three randomized controlled trials have demonstrated program effectiveness in achieving beneficial birth, child development, and maternal life-course outcomes. This study describes birth outcomes of contemporary NFP clients compared to a reference cohort, and examines predictors of outcomes within the NFP cohort. Methods. A cohort of NFP clients beginning the program 7/1/2007-6/30/2010 was compared to a reference cohort of first-time moms from publicly available birth data (US Natality Data). NFP clients (n=27,194) were matched to three controls on maternal age group, race, smoking status, education, and marital status. We compared low birth weight (<2500 grams) and preterm birth (<37 weeks of gestation) outcomes between clients and matched controls using McNemar's Tests, and used logistic regression to identify predictors of outcomes. Results. We found no significant difference in low birth weight (NFP: 9.4%, matched controls: 9.6%, p=0.20). However, NFP clients were significantly less likely than matched controls to give birth to a premature baby (8.7% vs. 12.3%, respectively; p<0.0001). Among NFP clients, weight gain below Institute of Medicine (IOM) standards was a strong predictor of both preterm birth (OR: 2.06, 95% CI: 1.78, 2.39) and low birth weight (OR: 2.00, 95% CI: 1.74, 2.29). Discussion. Preterm birth in NFP clients compares favorably to a demographically similar general population reference group. Gestational weight gain represents a modifiable risk factor that can be targeted in future home visits that may reduce undesirable birth outcomes.

### **A49**

EXAMINING THE JOINT EFFECTS OF EVERYDAY DISCRIMINATION AND LOW HOUSEHOLD AUTONOMY ON SMOKING DURING PREGNANCY AND LOW BIRTH WEIGHT AMONG ROMANI WOMEN. Teresa Janevic\*, Kristefer Stojanovski, Daniel Gundersen, Janko Jankovic, Zeljka Nikolic, Blasko Kasapinov (Rutgers School of Public Health)

Romani women in the Balkans experience poor pregnancy outcomes in the context of social exclusion and patriarchal gender norms. Our objective was to assess the independent and joint associations between everyday discrimination and low household autonomy with smoking during pregnancy and low birthweight. In 2012-2013 we surveyed 410 Romani women in settlements in Serbia and Macedonia using purposeful sampling. We assessed exposures using a version of the Everyday Discrimination Scale validated among Romani women and a question regarding autonomy of health decisions. Outcomes were assessed by self-report, and low birthweight categorized as <2500g. Relative risks were estimated using log-Poisson regression with a robust variance estimator to account for clustering within settlements. In main effect models adjusted for education, household wealth, parity, and age, women who experienced high everyday discrimination compared to low were 1.7 times more likely to smoke during pregnancy (95%confidence interval(CI)=1.3, 2.2) and 2.3 times more likely to have a low birth weight infant (95%CI=1.2, 4.3). Low household autonomy was not associated with either outcome. In joint effect models, when compared with women with neither exposure, women with both exposures had an adjusted relative risk (aRR) of 1.9 (95%Cl=1.1, 3.2), women experiencing only high everyday discrimination had an aRR of 2.0 (95%CI=1.2, 3.2), and women experiencing only low household autonomy had an aRR of 1.2 (95%CI=0.7, 2.2). In our study of Romani women, everyday discrimination was associated with both smoking during pregnancy and low birthweight but did not act synergistically with low household autonomy to influence these outcomes.

ASSOCIATION BETWEEN EXCLUSIVE BREASTFEEDING HISTORY AND DIETARY VARIETY AMONG PRETERM CHILDREN AGED 1-3 YEARS. JS Husk\*, SA Keim (Research Institute at Nationwide Children's Hospital, Columbus, Ohio)

Among full-term infants, breastfeeding history is associated with increased dietary variety and vegetable consumption. Pre-term birth limits early feeding options while increasing risk for negative health outcomes that could be mitigated by diet. We analyzed data from two clinical trials investigating the effect of fatty acid supplementation on cognitive development for 10-39 month old children born before 35 weeks gestation (n=189). Mothers reported breastfeeding history and completed a 161-item food frequency questionnaire (modified Willett) for their child's diet at trial baseline. Dietary variety was assessed via: (1) proportion food items consumed at least once. (2) servings of given food item consumed relative to total food servings. (3) daily probability of consuming a given food item. Overall, 47% of children were ever exclusively breastfed (mean duration=38 days, range=0-240). On average, children consumed 44% (SD=12%) of all foods, 66% (SD =15%) of grains, 52% (SD =15%) of fruits, 49% (SD =19%) of meats/fishes, and 48% (SD =18%) of vegetables at least once per month. Dietary variety for vegetables and meats/fishes increased with exclusive breastfeeding duration for all 3 variety measures (e.g. proportion of vegetables consumed increased by 1.47% (95% CI=0.15-2.82), and meats/fishes by 1.68% (95% CI=0.36-3.00) for each extra month of exclusive feeding, after adjustment for age, race, sex, weeks gestation, maternal age, parental education, family income, and WIC participation). These results are consistent with those in full term children, and could support exclusive breastfeeding as a means of improving diet and health in preterm children if the association is causal.

### A51

MATERNAL APOLIPOPROTEIN E PHENOTYPE AS A POTENTIAL RISK FACTOR FOR POOR BIRTH OUTCOMES IN A BIRACIAL POPULATION: THE BOGALUSA HEART STUDY. MB Jacobs\*, EW Harville, TN Kelly, LA Bazzano, W Chen (Tulane University, New Orleans, LA)

Apolipoprotein E (apoE) genotype, which encodes isoforms of a protein integral to cholesterol metabolism, has been investigated as a risk factor for preeclampsia and pregnancy loss. However, no existing studies have assessed the association between apoE and preterm birth (PTB) or low birth weight (LBW), two of the most common pregnancy complications. The aim of the present study was to assess the association of maternal apoE phenotype with LBW, PTB, and small-for-gestational age (SGA) in a biracial cohort. Women who underwent apoE phenotyping (n=688) were linked to 1,065 singleton births occurring in Louisiana from 1990-2009. LBW, PTB, and SGA were categorized dichotomously in the first birth and any subsequent birth identified. ApoE allele frequencies were compared among outcome groups, and risk of each outcome was estimated among women having at least one e2 or e4 allele compared to those with the most common phenotype (e3/e3) using logistic regression. The e2 allele was more common among women who had a LBW or SGA birth (p < 0.01) but not a PTB. Compared to the e3/e3 phenotype, women with an e2 allele were more likely to have a LBW or SGA birth, controlling for mother's age, education, race, and tobacco use during pregnancy (OR = 2.44, 95% CI = 1.06 - 5.60, and OR = 2.17, 95% CI = 1.08 - 4.37, respectively). Results suggest that apoE genotype may be a marker for risk of poor birth outcomes. More studies are needed to fully examine the influence of maternal apoE genotype on fetal growth.

THE VIRULENT MALE: PRETERM BIRTH AND GROWTH RESTRICTION FOLLOWING A FIRST-BORN SON. Bruckner TA\*, Mayo JA, Gould JB, Stevenson DK, Shaw GM, Carmichael SM (Public Health, University of California, Irvine)

In Scandinavia, delivery of a first-born son elevates the risk of preterm delivery and intrauterine growth restriction of the next-born infant. Explanations for this finding invoke maternal immunological responses that are shared across populations. However, the external validity of Scandinavian results remains unclear. We test the virulent male hypothesis for preterm delivery and growth restriction using the linked California birth cohort file. Given the different baseline risks of adverse outcomes across race/ethnicity, we examined these groups separately. We retrieved data on 2,852,976 births to 1,426,488 mothers with at least two live births. Our withinmother tests applied Cox proportional hazards (preterm delivery) and linear regression models (birthweight for gestational age). For non-Hispanic whites, Hispanics, Asians, and American Indian / Alaska Natives, analyses indicate heightened risk of preterm delivery and growth restriction following a first-born male. The race-specific hazard ratios for preterm delivery range from 1.07 to 1.18. Coefficients for birthweight-for-gestational-age percentile range from -0.73 to -1.49. The 95% CIs for the preterm and growth restriction estimates do not contain the null. By contrast, we could not reject the null for non-Hispanic black mothers. Propensity score analyses, which control for selection into a second live birth, yielded essentially the same results. Findings also remain robust to unmeasured confounding from shared factors across pregnancies. Whereas findings in California generally support those from Scandinavia, the null results among non-Hispanic black mothers suggest that the virulence of a first-born male does not appear fixed across all racial/ethnic groups.

# **A53**

# EARLY PREGNANCY SEAFOOD INTAKE AND FETAL GROWTH: THE OMEGA STUDY.

April F Mohanty\*, David S Siscovick, Mary Lou Thompson, Thomas M Burbacher; Michelle A Williams; Daniel A Enquobahrie (Univ of Washington Seattle, Seattle, WA) Background: Previous reports of associations of maternal seafood intake with fetal growth were inconsistent. Further, little is known whether associations differ across seafood subtypes or fetal growth indices. Methods: Among 3,141 participants of the Omega study, a pregnancy cohort study, we investigated associations of periconceptional shell-, lean-, and fatty-fish intake with fetal growth indices. We categorized food frequency questionnaire reported seafood intake into frequencies of: <0.2 servings/month, 0.2 servings/month-<0.5 servings/week, 0.5-1 servings/week, and >1 servings/week. We abstracted birthweight, birth length, and head circumference from medical records. Using generalized linear models with a log link, the Poisson family, and robust standard errors, we estimated relative risks and 95% confidence intervals (CIs) for low birthweight (LBW, <2500 g) and linear regression models to estimate mean differences for continuous fetal growth indices across seafood intake categories. Results: Medians (interguartile ranges) of shell-, lean-, and fatty-fish intake were 0.3 (0-0.9), 0.5 (0-1.0), and 0.5 (0.1-1.0) servings/week, respectively. Lean fish intake of >1 servings/week (versus <0.2 servings/month) was associated with a 2.2-fold higher risk of LBW [95% CI: 1.2, 4.1]. Shellfish intake of >1 servings/week (versus <0.2 servings/month) was associated with a 0.6 kg/m3 higher mean ponderal index [95% CI: 0.0, 1.2 kg/m3]. There was no evidence for associations of total seafood or seafood subtype intake with other fetal growth indices. Conclusions: Higher intakes of lean- and shell-fish were associated with a higher risk of LBW and higher mean ponderal index, respectively. Findings highlight the importance of considerations of seafood subtype in similar investigations.

**BENZODIAZEPINE EXPOSURE DURING PREGNANCY AND ADVERSE OUTCOMES AMONG INFANTS**. Kathryn A. McInerney\*, Lee S. Cohen, Abigail C. Davies, Marlene P. Freeman (Boston University School of Public Health)

Benzodiazepines are used during pregnancy to alleviate severe psychiatric symptoms, specifically anxiety, though little is known about their reproductive safety. Prior studies indicate possible association between benzodiazepine use during pregnancy and adverse neonatal and obstetric outcomes including preterm birth, low birth weight, NICU admissions, and neonatal withdrawal. We examined the relationship between benzodiazepine use anytime during pregnancy and a variety of neonatal (prematurity, low/high birth weight, small head circumference, low APGAR score, NICU admissions, breathing difficulties, feeding difficulties, muscular symptoms of withdrawal) and obstetric (cesarean section, preeclampsia) outcomes. Data from the National Pregnancy Registry for Atypical Antipsychotics were used. Participants complete telephone interviews at enrollment, 7 months pregnant, and 3 months postpartum. Medication information is obtained at each timepoint. Outcome information is predominately obtained through medical record review. 304 women were included in this analysis, including 82 who used a benzodiazepine any time during pregnancy and 222 psychiatrically ill women who remained unexposed to this class of medications. Crude and exposure propensity score adjusted logistic regression models were used to examine the exposure-outcome relationships of interest. Benzodiazepine use was associated with increased odds of newborn breathing difficulty (OR: 2.26, CI: 1.04, 4.94), and NICU admissions (OR: 2.87, CI: 1.43, 5.77). Effect modification by use of selective serotonin reuptake inhibitors (SSRI) was assessed with null findings. Overall, use of a benzodiazepine during pregnancy was associated with an increased risk for some adverse neonatal outcomes.

### **A55**

# CHARACTERIZING THE SHAPE OF THE RELATIONSHIP BETWEEN GESTATIONAL AGE AT BIRTH AND COGNITIVE DEVELOPMENT IN A NATIONALLY REPRESENTATIVE U.S.

**BIRTH COHORT.** Jennifer L. Richards\*, Michael R. Kramer (Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA)

Preterm-born children have higher risk of cognitive and academic deficits. Those born the earliest experience the most severe outcomes; however, deficits persist through late preterm and early term births. Recent evidence of variation in cognitive ability by gestational week even among term-born children suggests the need to evaluate how cognitive and academic outcomes vary by gestational week across the entire gestational age distribution (i.e., 20-47 weeks). Therefore, we characterized the shape of the relationships between continuous gestational age at birth and cognitive ability at age 2 (Bayley Short Form Mental Scale) and academic achievement score in kindergarten (reading and mathematics assessments). The data source is approximately 5,200 singleton children enrolled in the Early Childhood Longitudinal Study-Birth Cohort, a nationally representative cohort study of children born in 2001 who completed cognitive assessments at 2 years and kindergarten. We used both parametric (linear regression) and non-parametric (loess curves) approaches to estimate gestational age-specific curves, defining gestational age continuously as LMP-based completed weeks and allowing for spline knots where appropriate. Results suggest non-linearities in the relationships between gestational week and cognitive/academic scores, such that scores are optimal at full term (39-41 weeks), and decrease both as children are born earlier (<39 weeks) or later (>41 weeks). Per-week gains (pre-39 weeks) and losses (post-41 weeks) appear to be roughly linear. From the perspectives of clinicians as well as children's parents and teachers, this analysis provides an important continuous picture of the cognitive and academic impacts of gestational age at delivery.

PRE-PREGNANCY ANTIOXIDANT LEVELS AND SUBSEQUENT PERINATAL OUTCOMES IN BLACK AND WHITE WOMEN: THE CARDIA STUDY. EW Harville\*, CE Lewis, A Solivan, JM Catov, D Jacobs, Myron Gross, EP Gunderson (Tulane University School of Public Health and Tropical Medicine, New Orleans, LA)

Background: Observational studies have reported protective associations between antioxidant intake during pregnancy and outcomes, but randomized trials have been almost uniformly ineffective. We hypothesized that supplementation during pregnancy may be too late, and that pre-pregnancy nutrient status would be more influential on pregnancy outcomes. Methods: We used longitudinal data from the multicenter CARDIA Study. Pre-pregnancy fasting serum concentrations of antioxidants (carotenoids alpha- and beta-carotene, lycopene, zeaxanthin/lutein, and betacryptoxanthin) were measured at study baseline, and an interviewer-administered food frequency questionnaire assessed diet and supplement use. Pregnancy outcomes were reported at subsequent exams every 2 to 5 years. The analysis included 1215 women with one or more singleton live births delivered post-baseline. Multiple linear and logistic regression models evaluated pre-pregnancy antioxidants levels (as standardized continuous predictors and quartiles) with infant birthweight and length of gestation. Results: In adjusted models, serum lycopene was associated with an increased risk of low birthweight (<2500 g; aOR 1.37 per 1-SD unit, 95% CI 1.11-1.69; aOR for highest quartile 2.15, 95% 1.16-3.98) and shorter gestational age (adjusted beta -0.21 weeks per SD, p=0.02; -0.51 weeks, p=0.04 for highest quartile). Dietary intake of tocopherols was associated with lower birthweight, while supplement use of vitamin C was associated with increased gestational age. Significant interactions were found with age: among women <30 years, higher beta-carotene, alpha-carotene, the sum of the carotenoids, and lycopene were associated with increased risk of low birthweight, which was not seen in older women. Discussion: Our results do not support the hypothesis that higher preconception antioxidant levels improve birth outcomes.

# **A57**

DO MATERNAL AND FETAL CHARACTERISTICS EXPLAIN TEMPORAL TRENDS IN PRETERM DELIVERIES IN PUERTO RICO FROM 1995 - 2012? Gibbs Pickens CM,\* Hogue CJR (Rollins School of Public Health, Emory University, Atlanta, GA)

Background: Preterm births (live births at <37 weeks' gestation) recently rose steeply in Puerto Rico, from 12.3% in 1995 to 19.9% in 2006, decreasing to 16.9% in 2012. Using U.S. Vital Statistics Records, we extend our previous analysis of trends in very preterm delivery (VPTD, liveborn and stillborn deliveries of <32 weeks' gestation) and moderately preterm delivery (MPTD, all deliveries at 32-36 weeks' gestation) from 1995-2006 to include the years 2007-2012. Hypothesis: Birth year will have a significant effect on the odds of VPTD and MPTD after accounting for other known fetal and maternal predictors of preterm delivery. Methods: We excluded 4.614 observations with missing information or <20 weeks' gestation (0.49% of 949,776 deliveries). We used multivariable polytomous logistic regression with year of delivery modeled as a linear spline with one node at year 2006. Independent variables with sufficient information for all years included maternal age, marital status, infant sex, plurality, parity/history of stillbirth, maternal comorbidities, delivery method, and birth year. Results: MPTD peaked in 2006 (17.6% of all deliveries). After accounting for maternal and infant characteristics, increasing birth year remained a significant predictor of VPTD and MPTD (p<.0001 for all linear spline terms). Adjusted odds ratios for VPTD and MPTD were highest in 2006 (odds ratio for MPTD, year 2006 vs. 1995=1.88 [95% Confidence Interval 1.84, 1.92]) and decreased thereafter. Conclusion: Time trends in VPTD and MPTD remained after accounting for known risk factors. Future research should focus on how societal-level factors like healthcare access contributed to these trends.

IS LOW GESTATIONAL WEIGHT GAIN OR WEIGHT LOSS ASSOCIATED WITH ADVERSE BIRTH OUTCOMES AMONG SEVERELY OBESE WOMEN?. LM Bodnar\*, SJ Pugh, JA Hutcheon, KP Himes, SM Parisi, B Abrams (University of Pittsburgh, Pittsburgh PA) There is a contentious debate surrounding optimal gestational weight gain for obese women. Our objective was to estimate the association between gestational weight gain and preterm birth, small- and large-for-gestational age birth (SGA, LGA), and cesarean delivery in severely obese women. All singleton infants born in Pennsylvania (2003-2011) to obese class 1 (BMI 30-34.9 n=148,232), class 2 (BMI 35-39.9, n=72,064), or class 3 mothers (BMI ≥40, n=47,537) were included. Weight gain was converted to z-scores using gestational age- and BMI-specific charts and specified as restricted cubic splines. Multivariable Poisson regression models stratified by obesity class were used to estimate the association between z-score and each outcome after confounder adjustment. We calculated risk differences between weight gain zscores of -2 and -1SD (0 and 5kg, -4 and 2kg, -8 and -2kg in obesity classes 1-3, respectively) and the reference z-score of 0SD. Weight gain z-scores of -2 and -1SD were associated with 3.0 (95% CI: 2.5, 3.4) and 2.2 (2.9, 2.5) excess cases of SGA per 100 births and 0.4 (0.3, 0.5) and 0.2 (0.1, 0.3) excess cases of preterm birth per 100 births among obese class 1 mothers. Risk differences were attenuated for obese class 2 and 3 mothers. Absolute risks of SGA and preterm birth were never >10% in any group. Low weight gain was associated with reduced risk of LGA and cesarean delivery in all women. These results suggest that weight gain may be restricted in obese women without adversely affecting fetal growth or gestational age at delivery.

# A59

VARIATIONS IN VERY PRETERM BIRTHS RATES IN EUROPE: CAN VALID COMPARISONS BE MADE USING ROUTINE DATA? . Delnord M\*, Mohangoo A, Zeitlin J and the Euro-Peristat Group (Inserm UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team (Epopé), Center for Epidemiology and Statistics Sorbonne Paris Cité, Paris Descartes University)

Objective: Preterm birth rates vary greatly in Europe, but less is known about variations in very preterm birth (<32 weeks gestational age (GA)). We investigated very preterm birth (VPTB) rates in Europe and assessed the impact of periviable births and stillbirths on country rates and rankings. Methods: Using routine aggregate data from 2010 collected by the Euro-Peristat project from 32 European countries/regions covering 4,450,135 births, we computed extremely and VPTB rates. We studied the impact of stillbirths and births at 22-23 weeks GA on these rates. Results: VPTB rates ranged between 8.8-19.8 per 1000 total births with a median of 12.9 (IQR 11.5-14.3) and between 6.5-14.1 per 1000 live births with a median of 10.3 (IQR 8.2-13.0). Removing births at 22-23 weeks GA reduced the median to 11.7 per 1000 total births and to 10.0 per 1000 live births, with reductions of 20% in some countries. Stillbirths represented between 2% and 62% of births 24-27 weeks GA (median: 21%) and between 3% and 26% of births 28-31 weeks GA (median: 8%). For births at 28-31 weeks GA, rankings were almost identical with and without stillbirths (rho=0.94, p=0.00); this association was also strong at 24-27 weeks GA (rho=0.80, p=0.00) and weaker for births at 22-27 weeks GA (rho=0.56, p=0.00). Conclusion: VPTB rates vary greatly in Europe, but these variations may reflect differences in registration practices for births at 22-23 weeks GA and for stillbirths. Sensitivity analyses removing stillbirths and periviable births can flag countries where registration practices require further investigation.

CONGENITAL HEART DISEASE AND INDICES OF FETAL GROWTH IN A NATIONWIDE COHORT OF 973,141 LIVEBORN INFANTS. Matthiesen NB\*, Henriksen TB, Gaynor JW, Agergaard P, Bach CC, Hjortdal V, Ostergaard JR (Department of Pediatrics, Aarhus University Hospital, Aarhus University, Denmark)

Background: In children with congenital heart disease (CHD) neurodevelopmental disorders are prevalent. Fetal cerebral growth i.e. small head circumference at birth is highly correlated with these disorders. It remains unsettled which types of CHD are associated with smaller head circumference, and whether head size is small compared to overall size of the infant. We investigated the association between subtypes of CHD and size at birth in a large cohort. Methods: All Danish livebirths 1997-2012 were included. CHD, pregnancy outcomes and potential confounders were identified in national registries. The association between CHD and infant size was analyzed by multiple linear regression adjusted for potential confounders with/without adjustment for gestational age. The study further includes a sibling analysis and a comparison cohort of other major birth defects. Results: 973,141 livebirths were included (8,220 with CHD). Overall, CHD was associated with smaller head circumference and lower birth weight, adjusted -0.5cm (95%CI-0.6;-0.4), -208g (95%CI-237;-179). Most subtypes of CHD (e.g. univentricular hearts, septal defects) were associated with reduced measures of both. Only hypoplastic left hearts and transposed great arteries were associated with smaller heads and birth weights close to normal. Sensitivity analyses revealed that these associations were not explained by conditioning on live birth or gestational age. Conclusion: Overall CHD was strongly associated with head circumference and birth weight in most subgroups. This was also the case in less severe defects not likely to cause growth restriction per se. Only 2 subtypes had smaller heads compared to overall size, consistent with theories of preferential cerebral hypoxia.

# **A61**

PREGNANCY LOSS HISTORY AT FIRST PARITY AND RISK OF ADVERSE PERINATAL OUTCOMES, NSFG 2006-2013. Ahrens KA\*, Rossen LM, Branum A (Infant, Child, and Women's Health Statistics Branch, Office of Analysis and Epidemiology, National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, MD) Repeated pregnancy loss is a common occurrence but its etiology and association with other perinatal outcomes is poorly understood. We investigated the association between history of pregnancy loss (<20 weeks) and perinatal outcomes among 9883 parous women surveyed in the National Survey of Family Growth 2006–2013. Complete pregnancy history was obtained during a computer-assisted personal interview. Pregnancy loss history at first pregnancy longer than 20 weeks ("first parity") was categorized by number of losses (1,2,3+), maximum gestational age of loss (<6 weeks, 6-10 weeks, >10 weeks), and a combined measure of these two factors (single loss < 6 weeks, single loss 6-10 weeks, 2+ losses). We evaluated the associations between measures of pregnancy loss history and preterm birth, stillbirth and low birthweight at first parity, as well as those in any subsequent future pregnancy reported, using logistic regression adjusted for maternal age. Number of pregnancy losses (3+ vs. no loss) was associated with increased risk of stillbirth at first parity (OR=5.9, 95% CI: 1.4-24.6). Maximum gestational age of loss (>10 weeks vs. no loss) was associated with increased risk of low birthweight in any subsequent pregnancy (OR=1.9, 1.1-3.6). The combined measure of loss number and maximal gestational age (single loss <6 weeks vs. no loss) was associated with decreased risk of stillbirth at first parity (OR=0.18, 0.04-0.77). No other associations were statistically significant. In a nationally representative sample of U.S. reproductive aged women, we found pregnancy loss history to not be consistently associated with an increased risk of adverse perinatal outcomes.

THE INFLUENCE OF MATERNAL CHARACTERISTICS AND DIAGNOSES AND ACCESS TO HOSPITAL CARE ON BIRTH OUTCOMES IN INDONESIA. Trisari Anggondowati A, Kiely M\*, El-Mohandes AAE (City University of New York School of Public Health) Stillbirth and early neonatal death are important indicators of obstetric and neonatal care. Indonesia has had a decline in infant, but not equaled in neonatal mortality. Socioeconomic and care barriers, as well as obstetric complications affect perinatal outcomes. This study investigated the impact of maternal characteristics, perinatal complications and access to care on birth outcomes among Indonesian-born singletons. We prospectively collected data on all singleton hospital births at 2 hospitals in East Java between 10/1/2009 and 3/15/2010. Reduced multivariate models were constructed to elucidate the relationship between maternal characteristics and birth outcomes. Referral from another facility significantly reduced the risk of low and very low birth weight (VLBW)(AOR=0.28, 95% CI=0.11-0.69, AOR=0.18, 95% CI=0.04-0.75, respectively), and neonatal death (AOR=0.2, 95% CI=0.05-0.81). Mothers being <20 years increased the risk of VLBW (AOR=6.39, 95% CI=1.82-22.35) and neonatal death (AOR=4.10, 95% CI=1.29-13.02). Malpresentation increased the risk of asphyxia (AOR=4.65, 95% CI=2.23-9.70) and perinatal death (AOR=3.89 95% CI=1.42-10.64). Postpartum hemorrhage increased the risk of neonatal (AOR=4.11 95% CI=1.03-16.39) and perinatal death (AOR=3.96 95% CI=1.41-11.15). Near-miss on admission increased the risk of neonatal (AOR=11.67, 95% CI=2.08-65.65) and perinatal death (AOR=13.08 95% CI=3.77-45.37). The importance of severity of maternal illness as a predictor for neonatal death and the protective effect that a referral from a health facility has over self-referral highlights the importance in engaging the mothers with the health care delivery system and upgrading the education of primary health care providers to protect mothers from arriving at the hospital with irreversible medical complications.

# A63

HAS NEONATAL RESUSCITATION PROGRAM MADE A DIFFERENCE ON THE APGAR SCORE AT 5 MINUTES IN THE LAST 30 YEARS?. Jagjit S Teji\* (Department of Pediatrics, University of Chicago, Chicago, Illinois)

Background: The neonatal resuscitation program, NRP, was instituted in 1987. It is widely accepted that appar score at 5 minutes, Apq5, has been inversely associated with neonatal morbidity and mortality, NMM, and infant mortality, IMR. Objective: How has the Apg5 changed in the last 30 years in the USA? Design/Methods: The data from the birth certificates data from the NCHS from 1983 thru 2012. Yearly variables used for analysis consisted of Apg5, year of birth, gestational age, birth weight, plurality, race, ethnicity, maternal age and education, maternal risk factors and mortality. STATA 13.0 and Excel 2010 were used in the analysis. Results: Out of 120 million newborns Apg5 of 10 and 0 that declined from 24.96% to 3.32% and 0.07% to 0.03%, respectively, Logistical regression on infant mortality demonstrated OR 150.93 (CI 148-152), p>0.0005 for Apg5 from 0-3; and 25.23 (CI 24.8-25.2) P>0.000 for Apg5 from 4-6; with OR =1 for Apg5 7-10. Significantly lower Apg5 were noted for male, preterm, non-Hispanic black, low birth weight, multiple births, unmarried, non-college educated, and those with maternal risk factors compared to controls. Conclusions: 1. To date this is the largest population study of Apg5 for newborns. 2. NRP impact may be implied in the rising Apg5 of 9 and sharp decline in Apg5 of 10 and 0 by proper assignment of apgars and resuscitation efficiency of sick newborns in addition to technological advancement have improved. 3. Apg5 over the study period of 30 years shows gradual decline in mortality for Apg5<7.

IS THERE AN ASSOCIATION BETWEEN THYROID STIMULATING HORMONE (TSH) AND PREGNANCY LOSS? Plowden, TC\*, Sjaarda L, Ye A, Perkins NJ, Zarek SM, Schliep K, Kalwerisky R, Schisterman EF, Wactawski-Wende J, Townsend J, Lynch A, Silver R, Lesher L, Galai N, Faraggi D, Radin R, Mitchell E, DeCherney AH, Mumford SL (Epidemiology Branch, Division of Intramural Population Health Research, Eunice Kennedy Shriver NICHD; Program in Reproductive and Adult Endocrinology, NICHD, Bethesda, MD) Introduction: Overt hypothyroidism adversely impacts the female reproductive system. However, less is known about subclinical hypothyroidism, typically defined as TSH >4mIU/L with normal

Introduction: Overt hypothyroidism adversely impacts the female reproductive system. However, less is known about subclinical hypothyroidism, typically defined as TSH >4mIU/L with normal free thyroxine (fT4), and its effect on reproduction. Recent studies suggest that TSH levels 2.5-4 may also negatively affect reproduction. Our objective was to examine the association between pre-pregnancy TSH levels and pregnancy loss. Methods: This study is a secondary analysis of a large, randomized controlled trial evaluating healthy, fertile women who have had 1 or 2 prior pregnancy losses (n=1228). TSH and fT4 levels were measured from serum samples obtained at baseline. Participants were categorized as TSH <2.5 or ≥2.5 mIU/L. RR and 95% CIs for pregnancy loss were estimated using generalized linear models adjusted for age and body mass index and the probability of confirmed pregnancy using stabilized inverse-probability-weights. Results: Among women with an HCG detected pregnancy, 566 women had TSH<2.5 and 202 had TSH of ≥2.5. There was no statistically significant difference in pregnancy loss between the two groups (24% versus 26%, RR 0.92, 95% CI 0.70, 1.20). Conclusion: Women with a TSH level of ≥2.5 did not have a statistically significant difference in risk of pregnancy loss when compared to women with TSH level <2.5. Subclinical hypothyroidism may not influence early pregnancy loss in a healthy fertile population.

# A65

IS THERE AN ASSOCIATION BETWEEN PRESENCE OF THYROID ANTIBODIES AND PREGNANCY LOSS? Plowden, TC\*, Sjaarda L, Ye A, Perkins NJ, Zarek SM, Schliep K, Kalwerisky R, Schisterman EF, Wactawski-Wende J, Townsend J, Lynch A, Silver R, Lesher L, Galai N, Faraggi D, Radin R, Mitchell E, DeCherney AH, Mumford SL (Epidemiology Branch, Division of Intramural Population Health Research, Program in Reproductive and Adult Endocrinology, Eunice Kennedy Shriver NICHD, Bethesda, MD) Introduction: Overt thyroid dysfunction been associated with infertility, early pregnancy loss and other adverse obstetrical and fetal outcomes. However, results of studies assessing the relationship between thyroid antibodies and pregnancy loss have varied. Thus, our objective was to examine the association between pre-pregnancy presence or absence of anti-thyroid antibodies and pregnancy loss. Methods: This study is a secondary analysis of a large, randomized controlled trial evaluating healthy fertile women (n=1228). Women with 1 or 2 prior pregnancy losses were enrolled and followed for up to 6 menstrual cycles of attempting pregnancy. Prior to conception, TSH, fT4, anti-thyrodlubulin antibody (anti-TG) and anti-thyroid peroxidase antibody (anti-TPO) levels were measured. RR and 95% CIs for pregnancy loss were estimated using generalized linear models adjusting for age and body mass index. Results: 119 women had anti-TG antibodies and 103 women had anti-TPO antibodies. Neither women with anti-TG antibodies nor those with anti-TPO antibodies were shown to have a higher likelihood of any pregnancy loss (RR 1.01, 95% CI: 0.67, 1.52 and RR 0.92, 95% CI 0.58, 1.45 respectively). A subgroup analysis of women with a clinical pregnancy loss did not find any correlation with presence of thyroid antibodies. In the subset of women who became pregnant during the study, there also was no association between these antibodies and pregnancy loss. Conclusion: Among healthy fertile women with a history of 1 or 2 losses, the presence of antithyroid antibodies (anti-TG or anti-TPO) was not associated with pregnancy loss.

# TRENDS IN SUDDEN UNEXPECTED INFANT DEATHS, UNITED STATES, 2000-2012.

Shapiro-Mendoza CK\*, Lambert AE, Parks SE (Centers for Disease Control and Prevention, Atlanta, GA)

Background: Declining sudden unexpected infant death (SUID) rates during the 1990s can be traced to safe sleep interventions. Less is known about more recent trends and hence the ongoing success of these interventions. Methods: To investigate SUID trends from 2000-2012. we analyzed US infant mortality files and identified SUID using codes for sudden infant death syndrome (SIDS), accidental suffocation and strangulation in bed (ASSB), and unknown cause. We examined annual infant mortality rates (deaths per 100,000 live births using 3-year rolling averages) due to SUID for the United States and individual states. Average annual percentage changes (AAPC) were also calculated. Results: SUID rates declined from 94.5 per 100,000 live births in 2000-2002 to 88.0 in 2010-2012. This absolute decline of 6.5 points translates to a nonsignificant AAPC decline (-0.2%, P =0.54). From 2002-2012, the AAPC declined 1.2% for SIDS (P<0.01), 1.3% for cause unknown (P<0.01), and increased 6.5% for ASSB (P<0.01). Although ASSB had the steepest rate increase, the SIDS rate in 2010-2012 was nearly double that for unknown cause and triple that for ASSB. SUID-specific mortality rates varied by state; in 2010-2012, New Hampshire had the lowest overall SUID rate and Mississippi the highest (31.1 per 100,000 live births versus 188.4). Conclusions: Declines in SUID rates from 2000-2012 are less dramatic than the 1990s and deaths due to ASSB have increased, while other causes have declined. Adapting safe sleep interventions and practices that contributed to state-specific declines in SUID rates may be beneficial for those states not experiencing declines.

### **A67**

**HEAT EXPOSURE INCREASES THE RISK OF FETAL DEATHS IN CALIFORNIA**. \*Basu R<sup>1</sup>, Sarovar V<sup>2</sup>, Malig B<sup>1</sup> (<sup>1</sup>California Office of Environmental Health Hazard Assessment, Oakland, CA; <sup>2</sup>UC Berkeley School of Public Health, Berkeley, CA)

Recent studies have linked heat to adverse birth outcomes, such as preterm birth, but other outcomes have not been well studied. In this study, we examined 16,295 fetal deaths in California to examine the association between mean daily apparent temperature, a combination of temperature and humidity, and risk of fetal death (20+ gestational weeks). To focus on heatrelated deaths, we limited our study to the warm season of May through September 1999-2009. Data were provided by the California Department of Public Health (fetal death records) and the US Environmental Protection Agency, National Climatic Data Center, and California Irrigation Management Information System (apparent temperature data). Only mothers whose residential zip codes were within 10 kilometers of a meteorologic monitor were included. A time-stratified case-crossover design was used to examine multiple temperature exposure periods (lag 2, 3, 4, 5, 6 and cumulative averages 2-3, 2-4, 2-5, 2-6). For every 10 degree Fahrenheit increase in apparent temperature (cumulative lag 2-6), we found a 6.9% (95% confidence interval: 1.0. 13.2%) increase in the excess risk of fetal death overall. These effects were independent of the air pollutants evaluated (fine particles, ozone, carbon monoxide, and nitrogen dioxide). Risk varied by race/ethnicity, and was observed to be greater for younger women, those who had completed less than a high school education, and male infants. Null associations were found for full-term losses. This study adds to the growing body of literature that identifies pregnant women and their fetuses as vulnerable subgroups facing greater risk from heat exposure.

**DIFFERENCES IN MORTALITY RATES FOR VERY PRETERM BIRTHS ACROSS EUROPE: THE EPICE STUDY**. BN Manktelow\*, ES Draper, M Bonet, J Zeitlin, on behalf of the EPICE Group (University of Leicester, UK)

Background: Wide variation in the mortality rates for very preterm births (VPTBs) across Europe has been reported. Here we investigate the contribution of potential explanatory factors to this variation using the standardised population-based cohort of VPTBs from 19 regions in 11 European countries participating in the EPICE (Effective Perinatal Intensive Care in Europe) study. Methods: All births between 22+0 and 31+6 weeks gestational age in each EPICE region were included in the cohort. Standardised data collection was undertaken in each region and ascertainment validated against birth registers. All VPTBs were followed to death or discharge home. Mortality rates were calculated for the total cohort (n=10,328), live born infants and those admitted for neonatal care as appropriate. Potential maternal and infant explanatory factors for the variations in mortality rates were investigated. Results: Over half of the observed variation was due to variations in terminations of pregnancy (TOP) and major congenital anomalies. Excluding TOPs and major congenital anomaly, crude in-hospital mortality rates for the regions for all VPTBs ranged from 19.7% to 35.8%, 7.9%-20.1% for live births and 6.0%-14.9% for admissions to neonatal care. Following adjustment for maternal and infant characteristics, the range in these rates reduced to 18.6%-30.8%, 7.7%-18.7% and 4.9%-13.9% respectively. Variation persisted by gestational age and by time of death. Conclusions: Only a small proportion of the variation in mortality rates was explained by maternal and infant factors. Variations in perinatal and neonatal care provision require investigation to identify factors that may account for the remaining variation in mortality.

# A69

CIRCULATING INFLUENZA VIRUS AND ADVERSE PREGNANCY OUTCOMES: AN ECOLOGIC TIME-SERIES STUDY. Fell DB\* (Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal QC), Buckeridge DL, Platt RW, Kaufman JS, Basso O, Wilson K

Introduction: Although pregnant women are considered a high-risk group for severe influenza illness, risks to the fetus are unclear. Since influenza activity affects the entire population and is routinely measured through a system of sentinel laboratories, we used an ecologic time-series approach to determine whether fluctuation in influenza virus circulation was associated with short-term variation in rates of preterm birth, stillbirth and perinatal death. Methods: Using a database of linked maternal-newborn records, we included all live births and stillbirths delivered in Ontario hospitals between 2003 and 2012, a time period encompassing nine influenza epidemics and two waves of a contemporary influenza pandemic. The relationship between the weekly level of circulating influenza virus (measured using provincial influenza surveillance data) and aggregated weekly counts of study outcomes was assessed using Poisson regression. models offset by the number of ongoing gestations-at-risk, and adjusted for seasonal and longterm temporal patterns and respiratory syncytial virus co-circulation. Results: The rate of preterm birth was not associated with the level of circulating influenza during the week before birth (adjusted rate ratio: 1.01, 95% CI: 0.99-1.02), nor in other exposure windows (last month or first month of gestation). These findings were robust to alternate specification of the exposure measure in sensitivity analyses. The rates of stillbirth and perinatal death were also not associated with influenza activity in late pregnancy exposure windows. Conclusion: In this ecologic time-series study, we found no association between population-level influenza activity and short-term variation in rates of preterm birth, stillbirth or perinatal death.

MATERNAL OBESITY AND THE BLACK-WHITE GAP IN INFANT MORTALITY. Siminerio LL\* (University of Pittsburgh, Pittsburgh, PA), Naimi Al, Abrams B, Kaufman JS, Bodnar LM Compared with White women, Black women in the U.S. experience 2 times the risk of infant mortality, and are also more likely to be obese. Prepregnancy obesity is consistently associated with infant mortality. We sought to determine the extent to which maternal obesity explains the Black-White gap in infant and neonatal mortality. We studied 1,062,258 singleton infants born to non-Hispanic Black and non-Hispanic White women in Pennsylvania from 2003-2011. We used inverse probability weighted marginal structural models to estimate counterfactual disparity measures for the relation between race, prepregnancy obesity, and infant mortality. Weights accounted for confounding by maternal education, age, parity, marital status, smoking, WIC use, height, insurance, urban residence, the hospital's level of NICU care, and year of birth. Approximately 30% of Black and 21% of White women were obese (pregravid BMI>30kg/m2). Risks of infant and neonatal death per 1,000 live born infants were higher in Black (10.9 and 7.3, respectively) than White (4.5 and 3.0 respectively) mothers. The total risk difference (95% CI) for the association between race and infant mortality was 6.8 (6.2, 7.4) per 1,000 births. The corresponding risk difference (95% CI) that would be observed if prepregnancy obesity were eliminated was 6.0 (5.3, 6.7), which represents an estimated 12.4% (bootstrapped 95% CI 7.3%, 21.1%) of the racial inequality in infant mortality in this sample. Findings were similar for neonatal mortality. Our results suggest prepregnancy obesity may partially mediate the Black-White gap in infant/neonatal mortality.

# A71

RACIAL/ETHNIC TRENDS IN SUDDEN UNEXPECTED INFANT DEATHS-UNITED STATES 2000-2012. Parks SE, Shapiro-Mendoza CK, Lambert AE, (Centers for Disease Control and Prevention, Atlanta, GA)

Background: Since 2000, sudden unexpected infant death (SUID) rates [including sudden infant death syndrome (SIDS), accidental suffocation and strangulation in bed (ASSB), and unknown causes] have remained relatively stable (93.4 per 100,000 live births). However the rate for SIDS has declined while rates for unknown causes and ASSB have increased. Recent racial/ethnic trends in SUID have not been fully studied. Methods: We used 2000-2012 U.S. period linked birth-infant death data to evaluate rates per 100.000 live births for SUID and SIDS. unknown causes, and ASSB by racial/ethnic groups non-Hispanic White (NHW), non-Hispanic Black (NHB) and American Indian/Alaskan Native (Al/AN). Unadjusted linear regression was used to evaluate trends (p <0.05) in rates. To examine racial/ethnic disparities, we calculated rate ratios with NHW as the referent group. Results: Changes in racial/ethnic-specific rates were observed from 2000-2012. ASSB rates increased significantly for NHW, NHB, and Al/AN, [average annual percent change (AAPC): +6.9, 5.9, 7.6, respectively], SIDS rates decreased significantly among NHB and Al/AN (AAPCs: -2.1). Rates of unknown cause deaths decreased among NHB (AAPC: -4.9). Overall SUID rates were stable for NHW, NHB and AI/AN. The disparity between NHW and NHB for SUID decreased significantly from 2000 to 2012 (NHB rate ratios: 2.2 to 2.1). Conclusions: Disparities were greatest when comparing NHB and AI/AN to NHW. Though the disparity in SUID rates between NHB and NHW narrowed from 2000-2012. racial/ethnic disparities in SUID persist. Evidence-based risk reduction strategies which target the highest risk racial/ethnic minority communities and individuals are needed.

QUANTIFYING THE EFFECT OF LABOR INDUCTION AND CESAREAN DELIVERY ON STILLBIRTH RATES. S Lisonkova\* University of British Columbia, BC, Canada, G Muraca-Muir, KS Joseph

Background: latrogenic delivery (through labor induction and/or cesarean) is indicated for maternal or fetal compromise but quantifying beneficial effects through non-experimental studies is challenging. Objective: To determine whether the probability of iatrogenic delivery corresponds with the stillbirth rate. Methods: All singleton births in Washington state between 2003 and 2008 delivered at >=34 weeks gestation were included (n=424,985). We used the fetuses-at-risk approach and logistic regression models to estimate the probability of iatrogenic delivery at 34-36 weeks and at >=37 weeks. Maternal age, education, marital status, previous caesarean delivery, infertility treatment, fetal presentation, maternal morbidity, antepartum hemorrhage, etc. were included in the model. Area under the curve (AUC) and calibration indices were used to assess prognostic model performance. Results: Overall, 2.8% of late preterm and 43.8% of term deliveries were iatrogenic. The AUC for late preterm and term models for iatrogenic delivery was 0.78 and 0.70, respectively, with good calibration for both. There was no association between the probability of late preterm iatrogenic delivery and stillbirth. However, stillbirth rates increased significantly with increasing predicted probability of iatrogenic delivery: 1.65 per 1000 fetuses-at-risk among women with high probability, 0.82 among women with a moderate probability and 0.00 per 1000 among women with a low probability of iatrogenic delivery (p<0.001). Conclusion: The risk of iatrogenic delivery was concordant with the risk of stillbirth at term gestation suggesting that iatrogenic delivery contributes to a significant reduction in stillbirths at term.

# A73

MATERNAL HYPERTENSION, ANTIHYPERTENSIVE MEDICATION USE, AND SMALL FOR GESTATIONAL AGE (SGA) BIRTHS IN THE NATIONAL BIRTH DEFECTS PREVENTION STUDY (NBDPS), 1997-2009. Fisher SC\*, Van Zutphen AR, Romitti PA, Browne ML for the National Birth Defects Prevention Study (Congenital Malformations Registry, New York State Department of Health, Albany, NY)

Maternal hypertension is associated with several adverse pregnancy outcomes, but risks associated with maternal antihypertensive medication use are less understood. We analyzed the risk of SGA birth associated with maternal hypertension and antihypertensive medication use among non-malformed singleton controls in the NBDPS (n=9,902). We defined SGA as birthweight<10th percentile for a given gestational age, sex, race/ethnicity, and parity. After excluding subjects who reported pre-existing diabetes or antihypertensive medications for other indications (n=117), or were missing SGA or hypertension information (n=139), we used logistic regression analysis to estimate odds ratios (ORs) and 95% confidence intervals for associations between SGA and maternal hypertension and antihypertensive medication use, adjusting for maternal race/ethnicity, body mass index, folic acid use, smoking, and study site. After exclusions, 911 (9.4%) of 9,646 births were SGA, 872 women (9.0%) reported maternal hypertension, and 151 (1.6%) reported antihypertensive medication use, specifically centrallyacting antiadrenergics (0.7%), beta blockers (0.5%), calcium channel blockers (0.2%), diuretics (0.2%), direct vasodilators (<0.1%), ACE inhibitors (<0.1%), and angiotensin receptor blockers (<0.1%). Compared to normotensive controls, maternal use of any antihypertensive medication during pregnancy (adjusted OR 1.8 [1.1, 3.1]) and untreated maternal hypertension (adjusted OR 1.4 [1.1, 1.8]) were associated with SGA. We observed positive, but not significant, estimates for many specific medication classes and third trimester use. Consistent with the literature, our preliminary findings suggest a slightly increased risk of SGA associated with maternal antihypertensive medication use. However, given the underlying association between untreated maternal hypertension and SGA, we cannot rule out confounding by indication.

ASSOCIATION OF BLOOD PRESSURE WITH PREMENSTRUAL SYNDROME IN YOUNG ADULT WOMEN. Bertone-Johnson ER\*, Houghton SA, Ronnenberg AG, Whitcomb BW (School of Public Health and Health Sciences, University of Massachusetts, Amherst, MA) Clinically significant premenstrual syndrome (PMS) is experienced by 8-15% of premenopausal women. Several mechanisms potentially contributing to PMS are also involved in hypertension, including renin-angiotensin-aldosterone system dysfunction and vitamin D deficiency, but it is unknown how PMS is associated with systolic and diastolic blood pressure. We evaluated this association in a population-based study of 409 women aged 18-30. Participants reported the occurrence, severity and personal impact of premenstrual symptoms and other factors by validated questionnaire. Blood pressure was measured during each participant's mid-luteal phase. We identified 78 women meeting established criteria for clinically significant PMS, and 88 comparison women experiencing few if any premenstrual symptoms. Geometric mean diastolic blood pressure was significantly higher in PMS cases than controls. After adjustment for age, smoking, body mass index and other factors, mean diastolic blood pressure in PMS cases was 72.3 vs. 69.1 mmHg in controls (P = 0.02). Mean diastolic blood pressure was also significantly higher in women reporting moderate to severe premenstrual nausea, acne, depression and abdominal cramping, but not other symptoms. For example, mean diastolic blood pressure in women reporting premenstrual nausea was 77.9 vs. 71.2 mmHg in women without nausea (P = 0.006). Systolic blood pressure was not higher in PMS cases vs. controls (114.2 vs. 113.2 mmHg; P = 0.52). This is among the first studies to suggest that diastolic blood pressure is elevated in young women with PMS. Prospective studies are needed to determine whether women experiencing PMS are more likely to develop hypertension than symptom-free women.

# A75

# RETINOL-BINDING PROTEIN 4 AND LIPIDS MEASURED DURING EARLY TO MID-PREGNANCY IN RELATION TO SUBSEQUENT PREECLAMPSIA AND PRETERM BIRTH.

Mendola P\*, Ghassabian A, Mills JL, Zhang C, Liu A, Tsai MY, and Yeung E (Eunice Kennedy Shriver National Institute of Child Health and Human Development, Rockville, MD) Whether maternal lipid levels and retinol-binding protein 4 (RBP4) can be used as early pregnancy biomarkers of preterm birth and preeclampsia has been debated in the literature. Healthy lipid metabolism is important during pregnancy and early perturbations may be predictive of poor outcome. We analyzed serum samples collected at entry to the Calcium for Preeclampsia Prevention trial (1992-1995) for cholesterol measures, trialycerides, lipoprotein A and RBP4 (mean gestational age 16 weeks, range 6-22 weeks). The odds ratio (OR) and 95% Confidence Interval (CI) for preterm birth and preeclampsia were estimated using logistic regression with adjustment for age, race, body mass index, insurance, current smoking, marital status and center. All biomarkers were log-transformed. RBP4 was associated with preeclampsia diagnosed before 37 weeks (n=71; OR=4.93, CI=1.29-18.95) but not for preeclampsia diagnosed at term (n=107; OR=0.77, CI=0.23-2.56). The odds were elevated for RBP4 and total preterm birth (with and without preeclampsia), but did not reach statistical significance (n=167; OR=2.52, CI=0.90-7.09) and the results were further attenuated after restriction to preterm births without preeclampsia (n=107; OR=1.69, CI=0.49-5.35). Although cholesterol measures were inversely associated with preterm preeclampsia and preterm delivery, no significant associations were observed for any cholesterol measurements (high-density lipoprotein (HDL), low-density lipoprotein, total cholesterol, non-HDL cholesterol). No associations were observed for triglycerides or lipoprotein A. Additional adjustment for gestational age at baseline did not substantively change the results. Whether RBP4 can help predict preterm birth independent of preeclampsia is unclear, but RBP4 appears to be useful as a biomarker for early-onset preeclampsia.

# THE RELATIONSHIP BETWEEN MEAN LEUKOCYTE TELOMERE LENGTH AND MEASURES OF ALLOSTATIC LOAD AMONG REPRODUCTIVE AGED WOMEN IN THE US,

**NHANES 1999–2002**. Ahrens KA\*, Rossen LM, Simon AE (Infant, Child, and Women's Health Statistics Branch, Office of Analysis and Epidemiology, National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, MD)

Disparities in reproductive health may be partly explained by the cumulative effects of chronic stress experienced by socially disadvantaged groups. Telomere length and allostatic load score have each been used as biological markers of such stress in epidemiologic analysis, though the relationship between these two measures is unknown. We investigated the association between leukocyte telomere length and allostatic load score in 1503 non-pregnant women (20-44 years) participating in the National Health and Nutrition Examination Survey (NHANES), 1999–2002. Based on previously published studies using NHANES data, we constructed 5 different 10-point allostatic load scores using either quartile- or clinical-based cut-points for 13 biomarkers. We estimated associations between telomere length and both allostatic load scores and individual biomarkers using linear regression with interaction terms for race/ethnicity. After adjustment for age, longer telomere length was associated with higher HDL cholesterol (p<0.01) but not with 12 other allostatic load biomarkers. Shorter telomere length was associated with higher allostatic load scores for the 2 scores based on clinical cut-points (p<0.05); it was not associated with the 3 scores based on quartile cut-points (p>0.05). Differences by race/ethnicity were observed for associations between telomere length and HbA1c and triglycerides, but not for other allostatic load biomarkers or scores. Although telomere length and allostatic load score are both considered to measure cumulative, chronic stress, most individual component biomarkers and scores using quartile-based cut-points were not associated with telomere length. Epidemiologic analyses concerning mechanisms of reproductive health disparities should carefully consider how cumulative, chronic stress is operationalized.

# **A77**

**SPATIOTEMPORAL VARIATION IN TEEN BIRTH RATES IN THE U.S., 2003 TO 2012**. Khan D, Rossen LM\*, Dienes E, He Y, Hamilton B, Wei R\* (Infant, Child, and Women's Health Statistics Branch, Office of Analysis and Epidemiology, National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, MD)

In 2013, there were 26.5 births for every 1,000 adolescent females (15-19 years), a decline of 57% from teen birth rates in 1991. Teen birth rates vary by state, with nearly a four-fold range between the states with the lowest teen birth rates (e.g., Northeast) to states with the highest teen birth rates (e.g., South and Southwestern regions). Moreover, the declines in teen birth rates over the past decades have varied by state, with steeper declines in the Southeast, Mountain, Pacific and Northeast regions. However, county-level variation in teen birth rates and corresponding trends over time have not been explored, largely due to potential instability in estimating teen birth rates at the county level. The objective of this analysis was to explore spatiotemporal variation in teen birth rates across counties in the U.S., from 2003 to 2012. Hierarchical Bayesian models with space-time interaction terms were implemented in R2WinBUGS to predict annual county-level teen birth rates, accounting for the spatially and temporally correlated structure of the data. Results suggest that teen birth rates declined for 80% of counties from 2003-2012, rising for only 20% of counties. In 2012, 36% of counties had teen birth rates significantly below the Healthy People 2020 target of 36 births per 1,000 adolescents (p<0.05). Findings highlight U.S. counties where teen birth rates are significantly high or low and how trends over time vary geographically. These findings may inform efforts to further reduce birth rates to adolescents in the U.S.

ASSESSING NONIGNORABLE LOSS TO FOLLOW-UP IN A LONGITUDINAL BIRTH COHORT STUDY OF BODY FAT IN CHILDHOOD. Buckley JP\*, Engel SM, Herring AH (University of North Carolina, Chapel Hill, USA)

Nonignorable loss to follow-up might occur in studies of childhood obesity if visit attendance depends on body size concerns. In a study of prenatal phthalate exposures and childhood fat mass, we used selection models to assess: 1) whether observation depended on fat mass at the time of follow-up, and 2) the degree of resulting bias in effect estimates. Of 380 members of a birth cohort enrolled in New York City during 1998-2002 with measured phthalate exposures, percent fat mass was ascertained for 181 children at multiple visits between ages 4 and 9 years (N=367 visits). We first estimated associations between phthalates and percent fat mass in the complete data using a linear mixed model. We then used a selection model approach to model this association among all 380 finalchildren under a potentially nonignorable missing data mechanism. For this analysis, we jointly fit the outcome model with a logistic mixed model for a binary indictor of outcome missingness, conditional on (possibly unobserved) percent fat mass and covariates. Children with more fat mass were less likely to be lost to follow-up: for each 1 percent increase in fat mass, the OR for loss to follow-up was 0.81 (95% CI: 0.69, 0.94). However, associations between phthalates and percent fat mass were similar to the complete data analysis. Although we did not observe evidence of biased associations in this sensitivity analysis, our findings suggest that missing obesity outcomes may be nonignorable in studies of other prenatal exposures that are more strongly related to follow-up.

# A79

**CUMULATIVE RISK AND ADVERSE BIRTH OUTCOMES: THE GROWH STUDY**. EW Harville\*, M Jacobs, A Shankar, J Wickliffe (Tulane University School of Public Health and Tropical Medicine, New Orleans, LA)

Background: Although components of the physical environment (such as lead, mercury, and air pollution) and the social environment (poverty, trauma, discrimination) have been associated with worse pregnancy outcomes, it is common for people to be exposed to a combination of risk factors in both domains. Cumulative risk assessment, the characterization of combined risks to health from multiple types of stressors, aims to overcome this limitation. Methods: As part of the GROWH study, 261 women were interviewed about trauma, disaster, and poverty, and had metals measured in blood samples. Women gave a complete reproductive history. A cumulative risk scale was created by calculating the number of markers for which the woman was in the top quartile. Logistic regression was used to model the outcome of any history of low birthweight (<2500 g) or preterm birth (<37 weeks), adjusting for age and pregnancy status. Results: Median blood lead was 0.54 ug/dL, IQR 0.38-0.74, mercury was 1.59 ug/L, IQR 1.21-1.80, and cadmium was 0.60 ug/dL, IQR 0.35-0.68. 16% of the women were high (at least 1 SD above the mean) for the sum of the metals z-scores, while 18% were high for the total social adversity scale. 21% had had at least one low birthweight baby, while 23% had at least one preterm birth. A cumulative risk score based on metals and social adversities (trauma, disaster, economic hardship) was associated with low birthweight (aOR 3.96, 95% CI 1.48-10.61), but not preterm birth (aOR 1.04, 0.10-10.67). A cumulative risk score based on multiple metals and multiple trauma exposures only was associated with low birthweight (aOR 11.76, 2.29-60.47) and preterm birth (aOR 4.05, 95% CI 1.03-15.89). Conclusion: Cumulative risk scores are worth further study as possible predictors of adverse birth outcomes.

AGREEMENT OF PERINATAL DATA FROM MATERNAL INTERVIEW AND MEDICAL RECORDS IN A CASE-CONTROL STUDY. Cordero C\*, Croen L, Fallin M, Schieve L, Thompson W, Windham G, Daniels J (The University of North Carolina at Chapel Hill, Chapel Hill, NC)

Various data collection methods are used to characterize the perinatal events that are of interest in studies of birth and childhood outcomes. We used data from the Study to Explore Early Development (SEED) to evaluate concordance of common complications of the pregnancy and neonatal periods. We compared prenatal and neonatal medical records with maternal interview, 3-5 years after the pregnancy, for 1,525 participants with both data sources. From each, we documented indication of maternal diabetes (medical record: 8.5%; interview: 7.8%), maternal hypertension (medical record: 15.5%; interview: 12.4%), and neonatal jaundice (medical record: 19.9%; interview: 39.8%). We calculated Cohen's kappa (K) with 95% confidence intervals (CI). We compared agreement level for three study groups: children with confirmed autism spectrum disorder (ASD: n=419), non-ASD developmental delays (DD: n=518), and non-ASD control children randomly sampled from the population (n=588). Overall, agreement among data sources was substantial for maternal diabetes (κ= 0.80, CI 0.74-0.86) and hypertension (κ=0.62, CI 0.57-0.68), but fair for neonatal jaundice ( $\kappa$ =0.30, CI 0.25-0.34). Concordance was only slightly higher among ASD than controls for maternal diabetes ( $\kappa$ =0.78, CI 0.67-0.90 vs.  $\kappa$ =0.71, CI 0.58-0.84), maternal hypertension ( $\kappa$ =0.64, CI 0.54-0.74 vs.  $\kappa$ =0.58, CI 0.47-0.70) and neonatal jaundice (κ=0.32 Cl 0.24-0.40 vs. κ=0.24 Cl 0.16-0.31). Agreement was similar among ASD and DD. Fair agreement for neonatal jaundice may reflect maternal awareness of less severe or brief periods of jaundice that resolve without medical care; further research is needed. Substantial agreement for pregnancy complications supports use of post-partum maternal interview data in epidemiologic studies.

# **A81**

CORTISOL VALIDATION STUDY: ONE AWAKENING SALIVARY CORTISOL SAMPLE IS RELIABLE IN PREGNANT WOMEN. . R. Vlenterie, N. Roeleveld\*, M van Gelder (Department for Health Evidence / Department of Pediatrics, Radboud Institute for Health Sciences, Radboud university medical centre, Nijmegen, The Netherlands)

Background: Maternal depression, anxiety, and stress during pregnancy have been associated with adverse effects on maternal and fetal health and adverse pregnancy outcomes. Elevated cortisol levels measured in saliva are associated with these mood and stress disorders. Several studies among pregnant women used multiple saliva samples collected on consecutive days, which may lead to participation burden and high costs. Objective: The aim of this validation study was to examine whether one awakening salivary cortisol measurement suffices to classify pregnant women as having normal or elevated cortisol levels. Methods: Saliva samples were collected in a sub-cohort of the PRegnancy and Infant DEvelopment (PRIDE) Study, Women were asked to collect three saliva samples on consecutive working days within 10 minutes after waking up. We calculated the intraclass correlation coefficient (ICC) and Cohen's kappa coefficient between salivary cortisol levels measured on day one and the averages of cortisol levels measured on three consecutive days. Sub-analyses stratified by time of sampling, employment, and other maternal characteristics were performed to further examine the reliability of the cortisol measurements. Results: The study population consisted of 199 women. The overall ICC between day one and the average of awakening cortisol levels on three consecutive days was 0.79 (95% CI 0.73-0.84). The kappa coefficient for agreement between the two measurements was 0.74 (95% CI 0.63-0.85). Conclusion: Although these values may be slightly overestimated, one awakening salivary cortisol sample seems to provide a reliable measurement to classify pregnant women as having normal or elevated cortisol levels in epidemiologic studies.

ESTIMATING GESTATIONAL AGE IN VIETNAM: COMPARING ESTIMATES FROM LAST MENSTRUAL PERIOD AND FARR NEONATAL EXAMINATION ESTIMATES WITH ESTIMATES FROM ULTRASOUND. Deputy NP\*, Nguyen P, Pham H, Nguyen S, Neufeld L, Martorell R, Ramakrishnan U (Nutrition and Health Sciences Program, Laney Graduate School, Emory University. Atlanta, GA)

Accurate gestational age (GA) estimation has important clinical and public health implications. Fetal ultrasound estimates of GA are considered most accurate but are frequently unavailable in developing settings. We compared GA estimates from last menstrual period (LMP) recalled in the first trimester or from the Farr neonatal examination of maturity (Farr) with estimates from second trimester ultrasound measurements, considered the gold standard. Data are from 614 women who participated in a pre-conceptual micronutrient supplementation trial in Vietnam. We computed mean differences, intraclass correlation coefficients (ICC) and concordance correlation coefficients (CCC) comparing LMP or Farr with ultrasound estimates. We used linear regression to assess variance in ultrasound estimates explained by LMP or Farr estimates and Kappa coefficients to estimate agreement in preterm, term and post-term classification by the different estimation methods. Mean GA estimated from LMP (274.4 ± 1.0 days) did not differ from ultrasound estimate (p=0.64) while Farr overestimated GA by 11.6 days (p<0.01). Ultrasound estimates of GA were moderately correlated with LMP (ICC=0.43) but weakly correlated with Farr estimates (ICC=0.12). The CCC for LMP and Farr estimates was 0.52 and 0.05, respectively. LMP and ultrasound estimates were within ± 14 days for 83% of the sample. GA estimated by LMP explained 30% of the variance in ultrasound estimate whereas Farr estimates explained 3%. Compared to ultrasound, LMP estimates had fair (κ =0.31) and Farr estimates had poor agreement (κ =0.05) in term classification. Overall, LMP estimates of GA performed better than Farr compared with ultrasound estimates of GA.

# A83 POSTPARTUM WEIGHT RETENTION AND SUBSEQUENT PREGNANCY OUTCOMES.

Luke, Sabrina,\* Kirby, Russell, Wright, Lauri (University of South Florida, Tampa, FL) Objective: The effects of postpartum weight retention on gestational weight gain in successive pregnancies require elucidation. We sought to examine the association between postpartum weight retention and subsequent adherence to IOM gestational weight gain guidelines, and to determine if the association varies by body-mass-index (BMI) status and affects birth outcomes. Study Design: Florida vital records for 2005-2010 were analyzed using Chi-square tests and multivariable Poisson regression, adjusted for inter-pregnancy interval, tobacco use, maternal age, and race/ethnicity, Results: Obese women who gained inadequate weight were more likely to retain weight between pregnancies compared to obese women who met or exceeded the recommended weight gain. Risks for preterm birth increased among women with inadequate weight gain and decreased for women who gained in excess. Gaining excessive weight was protective for small-for-gestational age infants in all BMI categories but increased the risks for large-for-gestational age infants. Underweight and normal weight women who gained in excess were 40% more likely to develop hypertension compared to normal weight women who gained within the recommended amount. Conclusion: Women who retain or gain weight postpartum are at increased risk for inadequate weight gain in a successive pregnancy. Achieving optimal gestational weight gain is essential for preventing adverse maternal and infant outcomes.

UTERINE FIBROID SEVERITY, PAIN, AND BLEEDING IN THE FIRST TRIMESTER. Kara A. Michels\*; Katherine E. Hartmann; Kristin R. Archer; Fei Ye; Digna R. Velez Edwards (Vanderbilt Epidemiology Center, Institute for Medicine and Public Health, Vanderbilt University, Nashville, TN; Epidemiology Branch, Division of Intramural Population Health Research, Eunice Kennedy Shriver Institute of Child Health and Human Development, National Institutes of Health, Rockville, MD)

Background: Few studies comment on fibroid-associated symptoms among pregnant womenmost are retrospective and few assess the influence of disease severity (volume or number of tumors) on risk of symptoms. Methods: Right from the Start, was a prospective pregnancy cohort that enrolled pregnant women from the southeastern United States between 2000-2012. In the first trimester, all participants had standardized ultrasounds to determine the presence or absence of fibroids and then described symptoms as part of a telephone survey. We used logistic and polytomous logistic regression to model risk of bleeding, pain, or both symptoms in relation to increasing total fibroid volume and number. Results: Among 4,392 participants, the prevalence of fibroids was 11%. Eight percent of women reported only bleeding, 43% reported only pain, and 18% reported both symptoms. After assessing effect modification by maternal race and adjusting for confounders, white women with the smallest fibroid volumes were more likely to report both symptoms than those without fibroids (odds ratio (OR) 1.84, 95% confidence interval [1.16, 2.92]). Volume was not associated with symptoms among black women. Increasing number of fibroids was associated with pain (OR 1.19 [1.03, 1.37]) and both symptoms (OR 1.20 [1.02, 1.41]); no modification by race was detected. Conclusions: The relationship between first trimester symptoms and total fibroid volume differs by maternal race. Increasing number of tumors corresponded to linear increases in symptom risks. Symptoms attributed to fibroids may be common, but their use in forming a differential diagnosis makes understanding their relationship with fibroid severity important.

# **A85**

CHANGES IN OBJECTIVELY MEASURED SMOKING IN PREGNANCY BY TIME AND LEGISLATIVE CHANGES. Männistö TI\*, Bloigu A, Gissler M, Surcel HM (National Institute for Health and Welfare, Oulu and Helsinki, Finland)

Background: The prevalence of cigarette smoking among non-pregnant and pregnant women remains high. There is little data evaluating the changes in characteristics and outcomes of pregnant smokers over time. Methods: Our data consists of 10,196 randomly selected pregnancies from the Finnish Maternity Cohort (1987-2012), with demographic characteristics and pregnancy and perinatal data obtained from the Medical Birth Registry and early pregnancy serum samples analyzed for cotinine levels. Women were categorized based on their selfreported smoking status and measured cotinine levels (≥4.73 ng/mL deemed high). Data was stratified to three time periods based on legislative changes in the Tobacco Act. Results: 7.7% of women undisclosed smoking, whereas 16.7% were inactive smokers (self-report smoking with low cotinine levels), 4.9% were active smokers and 70.7% of were nonsmokers. We observed no changes in the prevalence of nonsmokers, inactive or active smokers or women who undisclosed smoking by time or legislative changes. Women who undisclosed smoking had similar characteristics and perinatal outcomes as inactive and active smokers. Compared to nonsmokers, women who undisclosed smoking were more likely to be <35 years (OR 1.40, 95%CI 1.16-1.70), not married (OR 2.40, 95%CI 2.05-2.80), have a socioeconomic status lower than upper or middle class (1.71, 95%CI 1.40-2.15) and have a preterm birth (1.53, 95%CI 1.18-1.99). There were no major differences in these outcomes by time. Conclusions: Women who undisclosed smoking were very similar to pregnant cigarette smokers. Time and legislative changes in the Tobacco Act have not affected the characteristics or even the prevalence of pregnant smokers.

MATERNAL PERFLUORINATED COMPOUND EXPOSURE AND GESTATIONAL WEIGHT GAIN. J Ashley-Martin,\* L Dodds, TE Arbuckle, AS Ettinger, GD Shapiro, M Fisher, S Taback, MF Bouchard, P Monnier, R Dallaire, AS Morisset, WD Fraser (Dalhousie University) A majority of North American women exceed the recommended amount of gestational weight gain and face an increased risk of adverse maternal and fetal seguelae. Though exposure to environmental chemicals, such as perfluorinated compounds, has been hypothesized to alter weight gain patterns, the epidemiologic evidence is limited. Perfluorinated compounds are persistent, ubiquitous and widely used in the production of non-stick cookware, furniture, and clothing. The objective was to examine the association between maternal perfluorinated compound exposure and gestational weight gain (GWG). This study utilized data collected in the Maternal-Infant Research on Environmental Chemicals (MIREC) Study, a Canadian birth cohort study of 2001 women. Three perfluorinated compounds were measured in first trimester maternal plasma. GWG was examined as a continuous variable and according to the US Institute of Medicine (IOM) gestational weight gain guidelines (inadequate, adequate, excess). Multivariate logistic regression models were used to estimate the association between perfluorinated compound exposure and excess GWG. The relationships between perfluorinated compounds and continuous GWG were evaluated using restricted cubic splines. Elevated plasma concentrations (4th vs 1st quartile) of perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS), and perfluorohexane sulfonate (PFHxS) were associated with an increased risk of excess GWG (PFOA: OR=1.4 95% CI: 1.0-2.0; PFOS OR=1.4 95% CI:1.0-1.9, PFHxS OR= 1.2 95% CI:0.9-1.6). In the spline analyses, PFOA, but not PFOS or PFHxS, was positively associated with GWG (p-value association = 0.03). Given the ubiquity of both PFOA exposure and excess weight gain during pregnancy, further investigation into the mechanisms underlying these relationships is warranted.

# **A87**

**VALIDATION OF THE ASTHMA CONTROL TEST DURING PREGNANCY**. Palmsten K\*, Schatz M, Chan PH, Johnson DL, Chambers CD (University of California, San Diego, La Jolla, CA)

Suboptimal asthma control during pregnancy may impact both maternal health and perinatal outcomes. US guidelines recommend using questionnaires to assess asthma control including the Asthma Control Test (ACT). The study objective is to validate telephone administration of the ACT during pregnancy. MothertoBaby Pregnancy Studies (2011-2013) enrolled 159 pregnant asthmatic women before gestational week 20. Participants were interviewed by telephone at up to four time points: enrollment, approximately week 20, approximately week 32, and postpartum. The ACT score ranges from 5-25; higher score indicates better control. Women answered ACT and guideline-based impairment questions and reported asthma course changes and exacerbations. The median gestational weeks at enrollment was 12.3 and 86.2% completed the final interview. Cronbach's alpha for internal consistency was similar across time points. 0.84-0.90. ACT score varied by impairment; e.g., at enrollment, the mean score was 23.2 for well controlled versus 17.9 for not well to poorly controlled asthma, p<0.01. ACT score change between interviews differed by asthma course change; e.g., women reporting that their asthma was much better at week 20 than enrollment had a mean score increase of 4.7, whereas women reporting that their asthma was a little worse had mean decrease of 1.3, p<0.01. ACT score was associated with prior exacerbations but was not a strong predictor of future exacerbations. The ACT demonstrated good to excellent internal consistency, varied by impairment level, and was responsive to changes in asthma course. These data suggest that telephone administration of the ACT is useful for assessing asthma control during pregnancy.

# **WOMEN WHO PUMP WITHOUT FEEDING AT THE BREAST: WHO ARE THEY?** S Keim, K McNamara, R Oza-Frank, S Geraghty

Pumping (breast milk expression) has become increasingly common. Some women pump and never feed at the breast, but their characteristics are unknown. Women who delivered a singleton, liveborn infant at >24 weeks' gestation were invited to complete a postal questionnaire at 12 months postpartum (Moms2Moms Study). Women who intended to exclusively formula feed were excluded. Women reported socio-demographics and the timing of start/stop of pumping and feeding at the breast. Obstetric records were abstracted. Of 499 respondents (62% response), 96% ever provided milk for their infant (at the breast or pumped). Of these women, 7% pumped but never fed at the breast. Women who pumped but never fed at the breast pumped for a median 52 days (IQR=103, range 1-359 days) and fell into 3 categories: "hospital pumpers" - pumped milk during infant NICU stay and stopped at discharge, "short-term pumpers" – had healthy infant but pumped for <1 month, and "dedicated pumpers" – pumped for 2-12 months. After adjusting for length of infant hospitalization, women who pumped but never fed at the breast were more likely to have household income <\$35,000/vr (OR=3.25, 95% CI: 1.41, 7.77), some college/associate's degree or less education (OR=4.30, 95% CI: 1.82, 10.80), and delivered preterm (OR=6.69, 95% CI: 2.54, 17.40), compared to all other lactating women, per exact logistic regression. Further investigation into the motivations of and difficulties encountered by women who pump but do not feed at the breast is needed so lactation support can address their specific needs.

# **A89**

# INFLAMMATORY BOWEL DISEASE IN PREGNANCY: A POPULATION-BASED STUDY.

Shand AW, Chen JS, Selby W, Solomon M, Roberts CL\* (Clinical and Population Perinatal Health Research, Kolling Institute, University of Sydney, Sydney, Australia) Background: The chronic inflammatory bowel diseases (IBD), Ulcerative Colitis (UC) and Crohn's Disease (CD), most commonly occur in the childbearing years. Improved care for IBDs and delayed childbearing mean that there are increasing numbers of pregnant women with IBDs. The aim of this study was to determine the prevalence of the IBDs in pregnant women and determine pregnancy outcomes. Methods: Information on IBDs and pregnancy outcomes was obtained from linked birth and hospital records for 993,567 deliveries among 630,742 women in Australia, 2001-2011. Multivariate models were used to determine the associations between IBD and study outcomes adjusted for covariates. Outcomes included: cesarean delivery, severe maternal morbidity, preterm birth <37 weeks (spontaneous and planned), small for gestational age (birthweight <10th centile), and perinatal mortality. Results: 1960 women (0.31%) with IBD had 2781 deliveries (1183 UC, 1287 CD, and 311 indeterminate IBD). Women with IBD were more likely than women without IBD to have a cesarean delivery (41.5% vs. 28.2%, adjusted risk ratio (aRR) 1.38, 95% confidence interval (CI) 1.31-1.45), severe maternal morbidity (2.6% vs.1.6%, aRR1.54, 95%CI 1.17-2.03), preterm birth (9.7% vs. 6.6%, aRR 1.47, 95%CI 1.30-1.66), planned preterm birth (5.3% vs. 2.9%, aRR 1.74, 95%CI 1.47-2.07), and their infants to be small for gestational age (9.7% vs.9.5%, aRR 1.19, 95%CI 1.04-1.36). There was no difference in perinatal mortality. Conclusion: IBD is more common in pregnancy than previously reported. Pregnancies among women with IBDs have significantly higher rates of adverse pregnancy outcomes than women without IBD.

PREMATURE RUPTURE OF MEMBRANES FOLLOWING ACUTE EXPOSURE TO OZONE. Wallace, ME,\* Mendola, P, Liu, D, Zhu, Y, Kim, S, Grantz KL (Epidemiology Branch, Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Rockville, MD) Premature rupture of membranes (PROM) is rupture that occurs before the onset of labor. One

third of preterm deliveries <37 weeks is preceded by preterm PROM. Previous work has suggested associations between air pollution and preterm birth, but evidence of a relationship to PROM is sparse. Exposure to air pollution results in acutely increased systemic inflammation and oxidative stress initiation which may lead to rupture of membranes already weakened by physiologic or pathologic processes. Modified Community Multiscale Air Quality models estimated average daily and hourly exposures to ozone (O3) among women in the Consortium on Safe Labor, a medical record-based cohort of 223.502 singleton deliveries (2002-2008), Cox proportional hazards models estimated the hazard ratio (HR) for PROM at any gestational age compared to deliveries without PROM per interguartile range (IQR) increase in O3 for the day of admission and the 5 hours prior to hospital admission for delivery. Models controlled for maternal age, race, parity, pre-pregnancy body mass index, insurance, smoking and alcohol use, and site. Exposure to O3 was associated with PROM on the day of admission (HR: 1.04, 95% CI: 1.02, 1.07). Risk for PROM was consistently increased in hours prior to admission from 1.06 (95% CI: 1.04, 1.09) in hour 5 up to 1.11 (1.08, 1.13) 2 hours prior to admission. Restricting the analysis to spontaneous preterm births <37 weeks gestation resulted in similar findings. Acute exposure to O3 may contribute to rupture of membranes prior to the onset of labor at both term and preterm.

# A91

MEDICAL COMPLICATIONS OF PREGNANCY IN WOMEN WITH INTELLECTUAL AND DEVELOPMENTAL DISABILITIES. HK Brown\*, V Cobigo, Y Lunsky, S Vigod (Women's College Hospital and University of Toronto, Toronto, ON)

Women with intellectual and developmental disabilities (IDD) have high rates of metabolic and cardiovascular disease. However, the state of their health during pregnancy is relatively unknown. Our objective was to determine whether women with IDD are at increased risk, compared to women without IDD, for medical complications of pregnancy. In this populationbased retrospective cohort study using linked Ontario (Canada) health and social services administrative data, we identified singleton obstetrical deliveries to women with (N=3,932) and without (N=382,774) IDD (2002-2011 fiscal years). Primary outcomes included complications for which women with IDD were hypothesized to be at increased risk due to their metabolic and cardiovascular vulnerability: gestational diabetes, gestational hypertension, preeclampsia/eclampsia, and venous thromboembolism. We also examined several secondary outcomes. Multivariable modified Poisson regression was used to assess risk, adjusted for measured confounders (maternal age, parity, baseline social and health characteristics); we used target-adjustment sensitivity analyses to explore the impact of unmeasured confounders (maternal smoking, BMI). Compared to women without IDD, women with IDD were not at increased risk for gestational diabetes or gestational hypertension. After adjusting for confounders, they were at increased risk for preeclampsia/eclampsia (1.7% vs. 1.1%; aRR=1.47, 95% CI 1.14-1.89) and venous thromboembolism (1.1% vs. 0.7%; aRR=1.64, 95% CI 1.21-2.23). They were also at increased risk for peripartum hemorrhage, severe obstetric morbidity (e.g., uterine rupture), and systemic maternal complications (e.g., cardiac failure). Results were robust to the impact of residual confounding. These findings suggest the need to mobilize accessible supports to improve perinatal outcomes for this vulnerable group.

USE OF INTRACYTOPLASMIC SPERM INJECTION IN WOMEN CONCEIVED BY IN VITRO FERTILIZATION IN THE US: FREQUENCY, MATERNAL CHARACTERISTICS AND BIRTH OUTCOMES. \*Xu Xiong, MD, PhD, Richard P. Dickey, MD, PhD, Pierre Buekens, MD, PhD, and Gabriella Pridjian, MD (Tulane University School of Public Health and Tropical Medicine, New Orleans, LA 70122)

Objective: The use of intracytoplasmic sperm injection (ICSI) has been reported to be associated with an increased risk of adverse birth outcomes. The objective of this study was to study frequency, maternal characteristics and birth outcomes of women who conceived by using ICSI in the US. Methods: A retrospective cohort study was conducted in 141030 pregnancies resulting from fresh non-donor in vitro fertilization (IVF) cycles using 2006-2010 data from the Society for Assisted Reproductive Technology (SART) Clinic Online Reporting System. Results: The frequency of ICSI use was 71.5%, increasing from 68.9% in 2006 to 73.1% in 73.1% in 2010. Among women with male factor infertility, 92.8 % of them were conceived by ICSI. However, 57% women without male factor infertility were also conceived by ICSI. There were no major differences in maternal characteristics (e.g., maternal age, gravidity, BMI, race/ethnicity, and smoking) between women who conceived by ICSI and conventional IVF. Compared to the conventional IVF, ICSI use was not clinically significantly associated with lower rates of multiple pregnancies (30.6% vs. 31.2%; RR, 0.98; 95% CI: 0.96-1.00), preterm birth (28.6% vs. 29.5%; RR, 0.97; 95% CI: 0.95-0.99), stillbirth (0.7% vs. 0.8%; RR, 0.94; 95% CI: 0.86-1.03) Conclusion: There are no clinically significant differences in maternal characteristics and birth outcomes between ICSI and the conventional IVF. Acknowledgement: SART wishes to thank all of its members for providing clinical information to the SART CORS database for use by patients and researchers. Without the efforts of our members, this research would not have been possible.

# A93

# CONSTRUCT VALIDITY AND FACTOR STRUCTURE OF THE PITTSBURGH SLEEP QUALITY INDEX AMONG PREGNANT WOMEN IN A PACIFIC-NORTHWEST COHORT. C

Qiu\*, B Gelaye, Q Zhong, DA Enquobahrie, IO Frederick, MA Williams (Center for Perinatal Studies, Swedish Medical Center, Seattle, WA)

Objectives: Despite its routine use as sleep quality assessment scale among men and nonpregnant women the psychometric properties of the Pittsburgh Sleep Quality (PSQI) have not been assessed among pregnant women in the US. We sought to evaluate the construct validity and factor structure of the PSQI among 1,488 pregnant women. Methods: A structured interview was used to collect information about demographics and sleep characteristics in early pregnancy. The Patient Health Questionnaire-9 (PHQ-9) and Depression, Anxiety, and Stress Scale-21 (DASS-21) were used to assess symptoms of depression, anxiety and stress. Consistency indices, exploratory and confirmatory factor analyses (EFA and CFA), correlations, and logistic regression were used. Results: The Cronbach's alpha for the PSQI items was 0.74. The results of the EFA showed the PSQI contained two factors with eigenvalues >1.0 accounting for 52.9% of the variance. The PSQI was significantly positively correlated with the PHQ-9 (r=0.47) and DASS-21 (r=0.42) total scores. Poor sleepers (PSQI global score >5) had significantly increased odds of experiencing depression (OR=6.47; 95%CI:4.96-9.18), anxiety (OR=3.59;95%CI:2.45-5.26) and stress (OR=4.37; 95%CI:2.88-6.65) demonstrating evidence of good construct validity. The CFA results corroborated the EFA suggesting two factors with comparative fit index of 0.975 and root mean square error of approximation of 0.035, indicators of goodness of fit. Conclusions: The PSQI instrument has good construct validity and reliability for assessing sleep quality among pregnant women. Further assessment and validation studies are needed to determine whether the two factor-specific scoring of the PSQI is favored over the PSQI-global score in pregnancy.

ARE 'OLDER' RED BLOOD CELL TRANSFUSIONS ASSOCIATED WITH ADVERSE OUTCOMES IN AN OBSTETRIC POPULATION? Patterson JA, Irving DO, Morris JM, Roberts CL, Ford JB\*

Background: Rates of red blood cell transfusion in pregnancy are increasing. Although blood can be stored for up to 42 days before transfusion, there is debate around whether use of older blood increases rates of adverse outcomes. Observational studies in other disciplines have found conflicting results. Randomised trials have failed to find an effect. Methods: Routinely collected statewide hospital and birth data were linked with blood pack information from hospital blood banks and the Red Cross Blood Service and used to identify women receiving 1-4 units of red blood cells in Australia, between 2006-2010. Generalised propensity score methods were used to determine the effect of increased age of blood transfused and adverse outcome rates (severe maternal morbidity and readmission), accounting for the different propensity of receiving older blood depending on location, blood type and timing of the transfusion. Results: Data were available for 2990 transfusions across 54 hospitals, with the median age of blood transfused being 20 days (interguartile range 14,27 days). The median age of blood transfused was similar between women with and without severe morbidity (22 (16,30) vs 22 (15,30) days), and in women readmitted or not (22 (14,28) vs 22 (16,30) days). No relationship was found between the age of the blood transfused and rates of either severe morbidity or readmission. Conclusion: Among women receiving 1-4 units of red blood cells, there was no evidence of an increased risk of severe morbidity or readmission when transfused with older compared with fresher blood.

### A95

ASSOCIATION OF INTIMATE PARTNER VIOLENCE WITH SLEEP DISTURBANCES

**DURING PREGNANCY**. Qiu-Yue Zhong\*; Bizu Gelaye; Suhayla Islam; Sixto Sanchez; Michelle A Williams (Harvard T.H. Chan School of Public Health, Boston, MA) Intimate partner violence (IPV) is an important health risk to mothers and fetuses. We examined the associations of IPV with stress induced sleep disturbance measured by the Ford Insomnia Response to Stress Test (FIRST) and sleep quality measured by the Pittsburgh Sleep Quality Index (PSQI) during pregnancy. This cross-sectional study included 634 pregnant Peruvian women. In-person interviews were conducted in early pregnancy to collect information regarding demographics, IPV, and sleep disturbances. Adjusted odds ratios (aOR) and 95% confidence intervals (95% CIs) were calculated using logistic regression procedures. Lifetime IPV was associated with a 1.54-fold increased odds of stress induced sleep disturbance (95% CI: 1.08-2.17) and a 1.93-fold increased odds of poor sleep quality. Compared with women experiencing no IPV during lifetime, the aOR (95% CI) for stress induced sleep disturbance associated with each type of IPV were: physical abuse only 1.24 (0.84-1.83), sexual abuse only 3.44 (1.07-11.05), and physical and sexual abuse 2.51 (1.27-4.96). The corresponding aORs (95% CI) for poor sleep quality were 1.72 (1.13-2.61), 2.82 (0.99-8.03), and 2.50 (1.30-4.81), respectively. Women reporting any IPV in the year prior to pregnancy were at increased odds of stress induced sleep disturbance (aOR = 2.07; 95% CI: 1.17-3.67) and poor sleep quality (aOR = 2.27; 95% CI: 1.30-3.97) during pregnancy. IPV during lifetime and the year prior to pregnancy is associated with stress induced sleep disturbance and poor sleep quality during pregnancy. Sleep disturbances may be important mechanisms that underlie the lasting adverse effects of IPV on maternal and perinatal health.

RACE DISPARITIES IN PLACENTAL VASCULAR LESIONS. Janet M. Catov, W. Tony Parks (University of Pittsburgh School of Medicine, Dept. of Ob/Gyn/RS)

There are profound and persistent race disparities in adverse pregnancy outcomes, with African American women having rates of preeclamspsia, preterm birth (PTB) and small for gestational age (SGA) deliveries that are up to two times higher than White women. Placental evidence of malperfusion is linked to these outcomes, and we considered this common underlying etiology may reveal clues about race disparities. We evaluated placental pathology records among 18,717 deliveries at Magee-Womens Hospital (Pittsburgh, PA) from 2008 to 2012 (45% of all births; n=14,228 White; n=4,489 African American). Placental lesions were abstracted and categorized as malperfusion, ascending intrauterine infection (AIUI), chronic villitis, fetal thrombosis, and chorangiosis using established criteria. African American women with placental records had higher rates of preeclampsia (14.1 vs 12.0%, p<0.0001) and spontaneous PTB (15.2 vs 13.3%, p=0.004) compared to White women. African American vs. White women had higher risk of vasculopathy, the underlying cause of infarcts and abruption identified via failed vessel remodeling and atherosclerosis-like features. This excess risk was present following term, spontaneous PTB or indicated PTB and persisted after adjustment for age, smoking, gestational age and pre-pregnancy BMI (OR 1.32, 95% CI 1.08, 1.61). African American vs. White women with spontaneous PTB were more likely to have AIUI (47.2 vs. 33.1, p<0.0001), independent of confounders (OR 1.52 [1.03, 2.24]). This race-specific risk for spontaneous PTB was particularly high when placentas were affected by both malperfusion and AIUI (OR 1.77 [1.19, 2.62]). Our results indicated African American women had excess risk of the most prominent malperfusion lesion, and risk of spontaneous PTB was high in African American women affected by both vascular and infectious lesions. Race disparities in adverse pregnancy outcomes may be linked to co-occurrence of vascular and infectious pathways.

# A97

**SELECT PRECONCEPTION CARE BEHAVIORS AMONG HISPANIC WOMEN IN THE UNITED STATES**. Interrante JD\*, Flores AL (U.S. Centers for Disease Control and Prevention, Atlanta, GA)

Background: Folic acid consumption and medication use counseling are elements of preconception care for improving pregnancy outcomes; however, Hispanic women are less likely to consume folic acid and receive preconception risk counseling than women of other race/ethnic groups. Methods: We analyzed responses to questions about multivitamin use and healthcare provider medication counseling from Porter Novelli's 2013 Estilos survey of 2,609 U.S. Hispanic adults in the Offerwise QueOpinas Panel via descriptive statistics and chi-square tests. Results of 1,000 completed surveys were weighted to the 2012 U.S. Census Hispanic proportions for sex, age, income, household size, education, region, country of origin, and acculturation level (based on years in the United States, language spoken at home, cultural selfidentification, and use of Spanish language media). Results: Of the fifty percent female survey respondents, 37% reported daily multivitamin consumption. Women with medium and high acculturation reported significantly higher daily use (47% and 37%, respectively) than women with low acculturation (25%, p<0.01). Forty percent of women had children under age 18 years and were asked about medication counseling concerning their last pregnancy. Of those, 47% reported preconception counseling. Women with medium and high acculturation received significantly less preconception counseling (44% and 26%, respectively) than women with low acculturation (57%, p<0.01). Conclusions: Literature indicates that preconception care disparities exist between race/ethnic groups. These data suggest that differences in preconception care, specifically daily multivitamin use and preconception medication counseling, also exist among Hispanic sub-segments based on level of acculturation.

PREDICTORS OF HEALTH RISK BEHAVIORS IN A DIVERSE POPULATION OF PREGNANT WOMEN. C Nobles,\* B Marcus, B Whitcomb, B Braun, E Stanek, G Markenson, L Chasan-Taber (University of Massachusetts Amherst, Amherst, MA) Cigarette smoking, limited moderate-intensity exercise, and sedentary behavior during pregnancy are modifiable risk factors for adverse pregnancy outcomes, but studies among Hispanic women are sparse. We assessed demographic and family-level factors related to pregnancy health-risk behaviors using baseline data from the Behaviors Affecting Baby and You (B.A.B.Y.) Study, a randomized controlled trial of exercise on risk of gestational diabetes. Smoking was assessed using a modified version of the PRAMS questionnaire and sedentary behavior and exercise were assessed via the Pregnancy Physical Activity Questionnaire. Participants (n=488) enrolled at a mean of 12.4 (SD 3.6) weeks gestation and were predominantly Hispanic (54.3%). A total of 16% reported smoking, 25.1% reported < 28 METhrs/wk moderate exercise, and 26.3% reported ≥4 hrs/day sedentary behavior. A health risk index calculated the number of these health risk behaviors (possible range 0-3). The mean health-risk index was 1.1 (SD 0.7) with 44.1% engaging in 1, 10.9% engaging in 2, and 1.2% engaging in 3 health-risk behaviors. In multivariable models, low income (OR 2.3, 95% CI 1.2-4.5), lack of a partner (OR 2.4, 95% CI 1.2-4.5) and not having children in the household (OR 2.5, 95% CI 1.4-4.4) were associated with engaging in at least one health-risk behavior. While Hispanic ethnicity was not associated with the health-risk index, it was inversely associated with smoking (OR 0.5, 95% CI 0.3-0.9). Obesity, education, and parity were not associated with the health-risk index. Findings help to better characterize high-risk groups and inform interventions targeting health-risk behaviors.

# A99

MATERNAL NATIVITY AND PRENATAL CARE UTILIZATION AMONG WOMEN WITH CHRONIC CONDITIONS. Samantha Goldfarb, Whitney Smith\*; Anne Epstein; Martha Wingate (Florida State University, Tallahassee, FL)

The study aim was to determine if nativity influenced prenatal care utilization (PNCU) among women with chronic conditions. We hypothesize that despite similar—and in some cases higher—prevalence of chronic conditions and other risk factors, foreign-born women have lower odds compared to U.S.-born women of adequate PNCU. Utilizing 2011-2012 NCHS-requested detailed natality files from 36 states and D.C., we included singleton live births to U.S. resident mothers (n=6,644,577). The dependent variable was PNCU, based on the R-GINDEX. Maternal nativity was based on maternal place of birth and chronic conditions were defined as diabetes or hypertensive disorder. We calculated descriptive statistics and odds ratios with 95% CIs for each PNCU group and chronic condition, adjusting for race, ethnicity, marital status, education, and parity. The proportion of diabetes was significantly higher overall in foreign-born (7.5%) compared to U.S.-born mothers (5.1%); for hypertensive disorder, proportion was higher in U.S.-born women (6.3% vs. 3.7%). Foreign-born women with diabetes had significantly higher odds of inadequate PNCU (aOR=1.32, 95% CI=1.27-1.37) compared to U.S.-born mothers. A similar pattern was observed for women with hypertensive disorders (aOR=1.20, 95% CI=1.15-1.24). Despite higher rates of select adverse sociodemographic factors, foreign-born mothers with chronic conditions had lower levels of adequate PNCU compared to U.S.-born women with similar risk factors and conditions. This study showed that PNCU patterns among foreign-born women are dissimilar to U.S.-born women despite outcomes, suggesting that positive outcomes among foreign-born women, even among those of higher risk, may be associated with factors beyond access to prenatal care.

DEVELOPMENT OF A RISK PREDICTION MODEL FOR CESAREAN DELIVERY AFTER LABOR INDUCTION. Danilack VA\*, Hutcheon JA, Triche EW, Dore D, Muri JH, Phipps M, Savitz DA (Brown University School of Public Health, Providence, RI) Labor induction may increase the risk of cesarean delivery in certain women, but prediction models to date have had limited ability to help guide clinical practice. Unlike prior studies that focused on characteristics at the onset of induction, we used demographic factors, maternal conditions, and pregnancy complications to develop a prediction model for cesarean delivery after labor induction. Starting with k=50 candidate predictors, we used logistic regression with forward stepwise selection and determined the best model based on incremental improvement in the area under the receiver operating characteristic curve (AUC). We assessed model calibration and discrimination and used bootstrapping to evaluate internal validation. We examined predictive ability of the model by hospital size, teaching status of hospital, and whether the induction was medically indicated. The final model contained 10 variables gestational age, maternal race, parity, maternal age, obesity, fibroids, excessive fetal growth, chorioamnionitis, placental abruption, and high station - and was well-calibrated with good risk stratification at the extremes of predicted probability. The model had an AUC of 0.81 (95% confidence interval: 0.81-0.82), with average bias of 0.001 with internal validation. A predicted probability ≥ 17% to define a positive test had 84% sensitivity and 63% specificity. There was minimal difference in AUC by hospital size or teaching status, but non-medically indicated inductions had a higher AUC than medically indicated inductions. While external validation is needed, such a prediction model could be used by clinicians to estimate an individual's risk of cesarean delivery when considering whether to induce labor.

# A101

# PREGNANCY SPACING AND PERINATAL OUTCOMES IN DAR ES SALAAM, TANZANIA.

Boundy EO\*, Lieberman ES, Spiegelman D, Missmer SA, Fawzi WW (Harvard School of Public Health, Boston, MA)

Background: Short and long pregnancy intervals have been associated with adverse pregnancy outcomes. Research on the effects of pregnancy spacing has been limited in sub-Saharan Africa. Methods: We examined the effect of pregnancy spacing on perinatal outcomes in a cohort of 4515 women between 2001 and 2004 in Dar es Salaam, Tanzania. Pregnancy interval was defined as time from the end of the previous pregnancy until the last menstrual period of the current pregnancy. Outcomes included preterm birth, small for gestational age, low birth weight, stillbirth, neonatal death, and maternal anemia. We used log binomial regression to obtain risk ratios and 95% confidence intervals. Results were stratified by last pregnancy outcome type as live birth, still birth, or abortion. Results: The median pregnancy interval was 41 months. Among women whose last pregnancy was a live birth (n=3732), pregnancy intervals less than 6 months increased the risk of a low-birth weight baby more than 2-fold (RR 2.38; 95% CI 1.10, 5.14). Among women whose last pregnancy was a stillbirth (n=241), intervals less than 18 months increased the risk of stillbirth and neonatal death in the first week of life. After an abortion, pregnancy intervals less than 18 months were associated with a non-significant increase in risk of maternal anemia. Conclusion: Pregnancy intervals less than 6 months following a live birth and less than 18 months following a stillbirth increased the risk of some perinatal outcomes. Family planning counseling should include this information.

TRIAL OF LABOR AFTER CESAREAN (TOLAC): PERSPECTIVES ON RISK. Bovbjerg ML\*, Chevney MJ, Cox K, Leeman L (Oregon State University, Corvallis, OR) Background: Hospital policies often restrict access to TOLAC, particularly in non-teaching facilities. Methods: We studied medical records for 20,819 women who were under the care of a midwife at labor onset. We used logistic regression to compare maternal and neonatal outcomes across a variety of "moderate-risk" subgroups, controlling for Medicaid, education, and race/ethnicity. Low-risk multiparas comprised the control group. Results: Unsurprisingly, women in the TOLAC group (n=1157) fared worse than low-risk multiparas across all outcomes (transfer to an obstetrician, cesarean, low 5-minute Appar, hemorrhage, perineal trauma, neonatal intensive care unit (NICU) admission, maternal or neonatal hospitalization in the first 6 weeks). However, TOLACs had comparable outcomes to other moderate-risk subgroups: primiparas, twins, breech fetus, obese women, women over age 35, and women with gestational diabetes. For instance, the adjusted odds ratio (95% CI) of NICU admission, for TOLACs compared to low-risk multiparas, was 1.85 (1.15 – 2.95). Across all other moderaterisk subgroups, the AORs for NICU admission ranged from 1.25 (0.80 – 1.94) for obese women, to 2.76 (1.00 – 7.62) for women carrying a breech fetus. Conclusions: Women undergoing TOLAC—regardless of whether the eventual delivery was vaginal—had outcomes no worse than other moderate-risk subgroups. Most notably, TOLAC births in our sample were no riskier than primiparous births. Furthermore, these 20,819 labors all started either at home or in a birth center. calling into question the common "requirement" that TOLAC occur only in high-level hospitals with 24/7 anesthesiology on-site. Such policies universally restricting access to TOLAC seem unsubstantiated by the evidence.

### A103

# FACTORS AFFECTING ONSET OF LACTOGENESIS II WITHIN A PROSPECTIVE COHORT.

Porucznik CA, Cox KJ, Szczotka KM, Stanford JB\* (University of Utah, Salt Lake City, UT) Background: Delayed or failed achievement of lactogenesis II (DLII)—the onset of copious milk volume—contributes to early cessation of any and/or exclusive breastfeeding. Methods: 68 women from an ongoing, prospective cohort in Utah gave birth during 2012-2014 and completed a survey three weeks following delivery. Multivariate logistic regression models were used to estimate associations of DLII with pregnancy, delivery, and postnatal characteristics. Results: 15 (22%) women reported DLII, defined as >3 days following delivery. Women with normal onset of lactogenesis delivered at mean 39.1±1.7 gestational weeks compared to women with DLII delivering at 38.8±2.1 gestational weeks (p=0.63). After controlling for maternal age, prepregnancy BMI, gestational age, infant birth weight, parity, and BFHI practices, the odds of DLII increased by 1.57 (95% CI 0.37, 6.78) for inductions and spontaneous labor with augmentation compared to spontaneous labor without augmentation, among vaginal deliveries (n=46). A protective effect was observed for maternal age (AOR 0.85, 95% CI 0.69, 1.05) and infant birth weight (AOR 0.68, 95% CI 0.34, 1.36), Conclusion: Preliminary findings from this ongoing, prospective cohort are consistent with previous research. DLII is more likely among women with induced labor and caesarean delivery. Maternal age and infant birth weight are protective. Future work will evaluate the association between environmental exposures to endocrine disruptors and DLII. Policies and interventions should aim to support initiation and exclusive breastfeeding by mitigating these risk factors.

NEONATAL OUTCOMES ASSOCIATED WITH PLACENTAL ABRUPTION. KL Downes\* (University of Maryland, College Park, MD; Eunice Kennedy Shriver National Institute of Child Health and Human Development, Rockville, MD) ED Shenassa KL Grantz Placental abruption, early separation of the placenta, complicates 1% of all pregnancies. Abruption has been associated with increased risk of preterm birth, low birth weight (BW), and perinatal mortality, but association with other neonatal morbidities and utilization of medical intervention has remained under-studied. We examined the association between placental abruption and newborn resuscitation, neonatal intensive care unit (NICU) length of stay (LOS), apnea, respiratory distress syndrome (RDS), asphyxia, and perinatal mortality. A retrospective, multi-site study of electronic medical records (2002-2008) in the U.S., restricted to singleton births (n=223,252) was utilized for analysis. Relative risks (RR) and 99% confidence intervals (CI) were estimated using modified Poisson and negative binomial regression, adjusting for maternal age, race, parity, insurance, marital status, pre-pregnancy body-mass-index and study site. Gestational age (GA), birth weight and mode of delivery were evaluated by conditioning on the intermediate with sensitivity analysis. Incidence of placental abruption was 1.6% (n=3,613). Abruption was associated with an elevated risk of newborn resuscitation (RR=1.55, 99% CI: 1.48-1.62), apnea (RR=6.61, 99% CI: 5.84-7.38), asphyxia (RR=8.96, 99% CI: 6.06-11.86), RDS (RR=7.40, 99% CI: 6.77-8.04), perinatal mortality (RR=7.31, 99% CI: 5.89-8.73) and increased NICU LOS (RR=1.98, 99% CI: 1.48-1.62). All associations persisted in the sensitivity analyses for GA, BW and delivery mode. In this study, we found increased morbidity among surviving neonates. These findings add to the burgeoning literature highlighting the importance of placental functioning on health during infancy.

# A105

MATERNAL SERUM CAFFEINE METABOLITES DURING PREGNANCY AND CHILD COGNITION AND BEHAVIOR. Mark A. Klebanoff\* and Sarah A. Keim (Nationwide Children's Hospital and The Ohio State University, Columbus, OH)

Animal data indicate negative cognitive and behavioral effects of in utero caffeine on offspring, but few studies have evaluated associations in humans. We studied 2318 mother-child pairs from the Collaborative Perinatal Project (1959-66), The Stanford-Binet (48 mos) and WISC (84 mos) scales measured IQ, and psychologists observed child behavior. Maternal serum at <20 and ≥26 weeks was assayed for paraxanthine (caffeine's primary metabolite) by HPLC. Outcomes were IQ; and internalizing behavior at 48 & 84 months; oppositional at 48; hyperactive at 48; and externalizing at 84 (Donatelli, 2010). Covariates included maternal age, race, education, smoking, pre-pregnant weight and gestation at blood draw; secondary analyses included maternal IQ. Restricted cubic splines assessed non-linearity. After adjustment, serum paraxanthine <20 weeks was not significantly associated with any outcome. Maximum odds ratios for abnormal behavior over the range of paraxanthine were 1.4; mean IQ deficits for the 90th percentile of paraxanthine were <1 point. Paraxanthine ≥26 weeks manifested an inverted-U association with 84 month IQ, which increased to +1 point at ~750 ng/ml (66th percentile). returning to null at ~1685 ng/ml (92nd percentile, nonlinear p=.04; overall p=0.051). Results were of smaller magnitude for 48 month IQ. Paraxanthine ≥26 weeks had a positive, linear association with internalizing behavior at 48 mos (OR per 1000 ng/ml increase=1.6, 95% CI 1.1-2.4). No other associations approached significance. Adjustment for maternal IQ did not change results in the reduced sample. In general these results do not support an adverse effect of maternal caffeine use on child cognition or behavior.

MATERNAL NEUROTICISM AND BIRTH WEIGHT: A MEDIATION ANALYSIS. Mengxiong Wang\*, Xinguang Chen, Jing Jin, Yaqiong Zhu (Department of Epidemiology, College of Public Health and Health Professions, University of Florida, FL)

Background: Evidence from diverse sources indicate that psychological stress is a significant predictor for many negative reproductive outcomes, including preterm birth and low birth weight. Moreover, certain maternal personality traits are correlated with unhealthy behaviors, such as smoking and alcohol consumption, mediating the effect of stress on reproductive outcomes. Aim: The purpose of this study is to investigate the association between maternal neuroticism and birth weight, and the effect of cigarette smoking and alcohol consumption in medicating the effect of maternal neuroticism on birth weight. Method: Data used for this study were derived from Wave I and Wave IV of National Longitudinal Study of Adolescent Health. Young women aged 24-32 in the sample were included for analysis. Linear regression approach was used to assess the direct effect from maternal neuroticism on birth weight and the indirect effect mediated through tobacco/alcohol use during pregnancy. Results: A total of 5799 participants were included with an average age of 29 years (SD=1.75). Modeling results indicated that maternal neuroticism score (p=0.0184) and tobacco use during pregnancy (p<0.0001) significantly predicted babies' birth weight, and the association between alcohol use during pregnancy and child birth weight was not statistically significant (p=0.1020). Tobacco use during pregnancy significantly mediated the relationship between maternal neuroticism and birth weight. Conclusion: In addition to a direct effect, neuroticism increases the risk of low birth weight of children by increasing the risk of tobacco use during pregnancy. Maternal care should pay attention to tobacco control particularly among those mothers who are neurotic.

# A107

PREDICTORS OF A PROLONGED LENGTH OF STAY IN CHILDREN WITH PERFORATED APPENDICITIS. IS Pathak\*, IA Sayed, L Wise, M Sippel, LL Hernadez, ZD Mulla (Department of Pediatrics, Texas Tech University Health Sciences Center at El Paso, El Paso, TX) Background: Appendicitis is a common surgical emergency in children. We conducted a retrospective cohort study to identify clinical and demographic factors associated with a prolonged length of stay (PLOS) in children with perforated appendicitis (rupture and spillage of intestinal contents into the abdominal cavity). Methods: The records of 197 children 0 through 17 years of age with perforated appendicitis who were hospitalized at one of two teaching hospitals located in El Paso, TX, and discharged January 2008-January 2014 were included in our sample. PLOS was defined as a length of stay greater than the 75th percentile value in our patient cohort which was 7 days. An initial log-binomial regression model failed to converge and hence logistic regression was used to calculate adjusted incidence odds ratios (OR) and 95% confidence intervals (CI). Results: The overall risk of PLOS was 23.4% (46/197). Approximately 76% of the children who experienced PLOS and 94% of those who did not were Hispanic. After adjusting for private insurance status, presence of an abscess, asthma, consulting interventional radiology, and various antibiotics, Hispanics were less likely than non-Hispanics to experience PLOS: adjusted OR=0.19, 95% CI: 0.06-0.59. Children whose providers consulted the interventional radiologist had an increased odds of PLOS: adjusted OR=3.43, 95% CI: 1.22-9.67. The adjusted OR for PLOS for having private insurance (vs. another payor) was 0.52 (95% CI: 0.16-1.72). Conclusions: Hispanic ethnicity was associated with a lower odds of PLOS while children who required the services of an interventional radiologist were more likely to experience PLOS.

PERFLUOROALKYL ACID EXPOSURE AND INFANTILE COLIC: A STUDY IN THE DANISH NATIONAL BIRTH COHORT. Bach CC\*, Milidou I, Bech BH, Nohr EA, Søndergaard C, Olsen J, Henriksen TB. (Perinatal Epidemiology Research Unit, Aarhus University Hospital, Aarhus, Denmark)

Background Perfluoroalkyl acids (PFAAs) are environmentally persistent chemicals measurable in blood samples from populations worldwide and known to cross the placenta. Infantile colic is a common condition of unknown etiology characterized by excessive crying during the first months of life. Our objective was to investigate the association between maternal levels of the two most common PFAAs, perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS). and infantile colic in the offspring. Methods We studied 1728 live-born singletons from two cohort samples from the Danish National Birth Cohort (1996-2002). Women gave blood samples in early pregnancy and participated in computer assisted telephone interviews assessing infant crying symptoms at 6 months postpartum. Infantile colic was defined according to the modified Wessel's criteria (crying or fussing for > 3 hours per day, >3 days per week), starting before the age of 3 months. We investigated the association between quartiles of PFOA or PFOS and infantile colic (binary) by multivariate logistic regression. Covariates chosen with quidance from a directed acyclic graph included cohort sample, socio-economic status, maternal pre-pregnancy body mass index, age, and parity. Results There was no obvious association between PFAA exposure and infantile colic [adjusted odds ratios (95 % confidence intervals) for the highest PFOA and PFOS quartiles compared to the lowest were 1.04 (0.59 – 1.82) and 0.70 (0.40 – 1.22), respectively]. Conclusions In the first study to investigate the association between PFAA exposure and infantile colic we found no association. Larger studies, preferably with higher exposure contrasts, are needed.

# A109

TRENDS IN ACADEMIC PERFORMANCE IN ELEMENTARY AND MIDDLE SCHOOL CHILDREN WITH A NONSYNDROMIC OROFACIAL CLEFT. Stephanie Watkins PhD, MSPH, MSPT\* (University of North Carolina at Chapel Hill), Robert Meyer PhD, MPH, Arthur S. Aylsworth, MD, Ronald Strauss, DMD, PhD

Background and Purpose: Children with orofacial clefts (OFC) may experience impairments in speech and language development leading to poor reading proficiency, learning disabilities, and academic underachievement. Methods: We examined the association between nonsyndromic (NS) OFC and reading and math end of grade performance (EOG) across elementary and middle school. We identified 712 children with an OFC from the NC Birth Defects Monitoring Program, and a random sample of 6,822 children without a structural birth defect identified from birth certificates born between 1997 and 2003. Using ICD9/BPA codes and clinical review, we classified 559 children with testing records with a NS OFC. Using longitudinal methods; we estimated the odds of scoring below grade level standards and the average growth in developmental scale scores adjusting for maternal education, public pre-kindergarten enrollment, and race. Results: Children with a NS OFC were 1.22 (95% CI: 1.00, 1.50) times as likely to underperform in reading in third grade compared to children without a structural birth defect. The odds of underachievement in reading increased linearly through fifth grade. Reading scores improved on average by 4.5 (SE: 0.08) points between third and eighth grade, and the average rate of growth was not statistically different (p=0.78) by cleft status. The effect for math performance was similar to reading. Conclusions: Children with a NS OFC may experience a small increase in the odds of underachievement in reading and math through elementary school. Their rate of growth through middle school is similar to that of children without a birth defect.

THE EFFECT OF PARENTAL SMOKING ON CHILDHOOD LEUKEMIA INCIDENCE: A SYSTEMATIC REVIEW AND META-ANALYSIS.. Zhang D\*, Zhang L, Poole C, Zhou J, Zhang Y, Kaushiva A (University of North Carolina at Chapel Hill, Chapel Hill, NC) Objective. To assess the association between parental smoking and childhood leukemia incidence. Methods. We searched MEDLINE, EMBASE, WEB of SCIENCE, SCOPUS and abstracts from annual meetings of American Society for Hematology between 2011 and 2013. We selected eligible articles reporting original observational studies investigating how parental smoking affected childhood leukemia incidence. Data extraction and risk of bias assessment were done for all included studies and pooled estimates were calculated through random-effect model in meta-analysis. Statistical heterogeneity was assessed by value of tau-squared, Isquared and Chi-square test of Cochrane Q statistic. Publication bias was assessed through funnel plot and results of Egger's test, Results, 50 studies were included for review, Among them, 40 reported childhood acute lymphoblastic leukemia (ALL), 31 reported childhood acute myeloid leukemia (AML) and 6 reported childhood leukemia without specifying the type. 40 studies were included for meta-analysis, and results showed that the odds ratios (ORs) for maternal smoking were never statistically significant regardless of leukemia type or exposure time-window. However paternal smoking showed modest statistically significant associations between ALL in all exposure time-window (before conception [OR=1.20, 95%CI: 1.05-1.38], during pregnancy [OR=1.18, 95%CI: 1.09-1.28] and after delivery [OR=1.30, 95%CI: 1.08-1.55]), and these associations still kept significant after trim and fill. For AML, paternal smoking was not statistically associated with the risk in all exposure time-windows. Conclusions. Our review supported that paternal smoking increases the risk of childhood ALL. Further studies are needed to investigate the discrepancy of smoking effect between parents in aspect of childhood leukemia incidence.

# A111

PARENTAL SUBFECUNDITY AND EPILEPSY IN THE CHILD – A COHORT STUDY BASED ON THE AARHUS BIRTH COHORT. Kettner LO\*, Ramlau-Hansen CH, Kesmodel US, Bay B, Henriksen TB (Perinatal Epidemiology Research Unit, Department of Paediatrics, Aarhus University Hospital, Denmark)

Background Studies indicate that children conceived by fertility treatment may be at increased risk of epilepsy. However, whether this risk is due to the treatment or may be due to characteristics of the subfecund couple is unknown. Objective To investigate the association between parental subfecundity and epilepsy in the child. Methods This cohort study included all live-born singletons from the Aarhus Birth Cohort between 1995 and 2013. In a questionnaire, the mothers reported on time to pregnancy as a measure of fecundity, fertility treatment and maternal characteristics. Couples with a time to pregnancy of more than 12 months were categorized as infertile. By linkage to the Danish National Patient and Prescription Register. children with epilepsy were identified until December 2013. Data was analyzed using Cox proportional hazards regression adjusting for potential confounders, including maternal age, body mass index, education, smoking status and maternal diagnosis of epilepsy. Results A total of 60,434 singletons were included; 469 (0.8 %) children had epilepsy. Preliminary results indicate no increased risk of epilepsy in children of untreated, infertile couples, compared with children of couples with a time to pregnancy of 0 to 5 months (hazard ratio 1.22 (0.83-1.79)). Similar results were found if the couples received fertility treatment (hazard ratio 1.10 (0.76-1.61)). Conclusion Preliminary results indicate that children of subfecund couples have no increased risk of epilepsy in childhood.

CONTRIBUTION OF INFLUENZA VIRUSES TO MEDICALLY-ATTENDED ACUTE RESPIRATORY ILLNESSES IN YOUNG CHILDREN: A SYSTEMATIC REVIEW AND META-

**ANALYSIS**. Sarah A Buchan\*, Travis S Hottes, Jeff C Kwong (Dalla Lana School of Public Health, University of Toronto, Toronto, ON; Public Health Ontario, Toronto, ON; Institute for Clinical Evaluative Sciences, Toronto, ON)

Background The burden of disease in children attributable to influenza is difficult to quantify given the similarity of symptoms caused by infection due to influenza or other viruses. We aimed to systematically review the evidence to determine the proportion of healthy children presenting for healthcare services with an acute respiratory illness (ARI) who have laboratoryconfirmed seasonal influenza. Methods & Findings We searched OVID MEDLINE, EMBASE, SCOPUS (from inception to 2014) and references of included articles. We included studies that used polymerase chain reaction methods to test for influenza in healthy children aged <5 years who presented with an ARI for healthcare services in high-income countries. Seventeen 17 studies covering 12 different influenza seasons were included in the review and meta-analysis. A pooled proportion of influenza positivity was calculated overall to be 20% (95%CI 15-25), using the Inverse Variance Heterogeneity method in MetaXL. A Random Effects model was also used to compare positivity estimates obtained through different methods and was calculated to be 26% (95%CI 22-31) with a prediction interval of 8-49%. Subgroup analyses were performed by season, region, setting, age group, and vaccination status, given the considerable amount of heterogeneity (I2=91%). Children aged 2-5 years had significantly higher influenza positivity compared to children aged <2 years (34% vs 16%). Conclusions This study is a first step in understanding what proportion of ARI is attributable to influenza virus infection in pediatric populations in high-income countries. However, more work is needed to understand the large amount of variability in this estimate.

# A113

COMPARATIVE SAFETY OF IN UTERO EXPOSURE TO ATAZANAVIR VERSUS NON-ATAZANAVIR CONTAINING REGIMENS ON NEURODEVELOPMENT IN HIV EXPOSED BUT UNINFECTED INFANTS. Caniglia EC\* (Harvard T.H. Chan School of Public Health, Boston, MA), Patel K, Huo Y, Kapetanovic S, Rich K, Sirois P, Williams P, Hernán MA, Seage G for the Pediatric HIV/AIDS Cohort

Objective: To evaluate the safety of in utero exposure to atazanavir and neurodevelopment in HIV-exposed but uninfected (HEU) infants age 9-15 months. Methods: HEU infants enrolled in the PHACS SMARTT study, at least 9 months of age, of HIV-infected mothers who were not on antiretrovirals (ARVs) at their last antepartum menstrual period were included in the analysis. We ascertained whether the first ARV regimen initiated in pregnancy contained atazanavir and evaluated neurodevelopment at 9-15 months using the Bayley Scales of Infant and Toddler Development-Third Edition (Baylev-III). We estimated mean differences for each Baylev-III domain for atazanavir versus non-atazanavir regimens by trimester of ARV initiation. Results: 146 and 671 HEU infants were exposed to atazanavir and non-atazanavir regimens in utero, respectively. 575 infants completed the Bayley-III assessment. The adjusted mean difference (95% CI) in domain score for exposure to atazanavir compared to non-atazanavir regimens initiated in the first trimester was -1.37 (-5.95, 3.21) for cognitive, -3.34 (-7.76, 1.07) for language, -2.40 (-7.25, 2.45) for motor, 0.53 (-5.72, 6.78) for social-emotional, and -0.88 (-5.19, 3.43) for general adaptive. The respective mean differences (95% CIs) for regimens initiated in the second or third trimester were 0.74 (-2.79, 4.27), -2.83 (-5.68, 0.02), 0.75 (-2.37, 3.87), -5.67 (-9.21, -2.13), and -2.24 (-5.60, 1.12). Conclusions: We found no evidence for an effect of in utero exposure to atazanavir regimens initiated early in pregnancy on neurodevelopment. However, exposure to atazanavir regimens initiated later in pregnancy may result in lower language and social-emotional scores at 9-15 months.

# SEXUAL ORIENTATION DISPARITIES IN HUMAN PAPILLOMAVIRUS VACCINATION.

Charlton BM\*, Kahn JA, Spiegelman D, Missmer SA, Austin SB (Boston Children's Hospital & Harvard Medical School, Boston, MA)

Compared to heterosexuals, sexual minority (i.e., lesbian and bisexual) adolescents are an increased risk for acquiring the human papillomavirus (HPV). Since we know sexual minorities are less likely to get preventive medical services (e.g., Pap tests), we hypothesize they may also be underutilizing the HPV vaccine. We used multivariable regression with prospective data gathered from 4,598 females aged 26 to 32 in the Growing Up Today Study, a cohort of offspring from the Nurses' Health Study II. When stratified by sexual orientation, 26% of completely heterosexuals (N=1,217/4,665), 28% of mostly heterosexuals (N=299/1,066), 18% of bisexuals (N=23/132), and 20% of lesbians (N=16/83) reported having =>1 dose. After adjusting for age, race, and geographic region, bisexuals remained significantly less likely to have been vaccinated (risk ratio, 95% confidence intervals: 0.63 [0.43, 0.93]) compared to completely heterosexuals. There was no significant difference in vaccination among mostly heterosexuals (1.07 [0.96, 1.19]) or lesbians (0.74 [0.47, 1.17]) compared to completely heterosexuals. Nearly all participants who reported having the vaccine, regardless of their sexual orientation, had completed the three dose series rather than simply initiating it with either one or two doses. Among girls and young women across the United States, the HPV vaccine is profoundly underutilized. Despite being at increased risk for acquiring the HPV virus, bisexual females in this study were significantly less likely to have been vaccinated compared to their heterosexual peers. Public health efforts need to address the vaccine underutilization across the population while being aware of the disparity by sexual orientation.

# A115

RACIAL DIFFERENCES IN PRETERM NEONATAL OUTCOMES. Epps NM\*; Wallace M; Mendola P; Chen Z; Smarr M; Hinkle SN; Zhu Y; Kim S; Grantz KL (NICHD) A higher proportion of Black women experience fetal and perinatal losses than other races or ethnicities among preterm deliveries. Less is known about racial differences in neonatal morbidity which would be helpful for clinical counseling. Our analysis was based on 19,870 nonanomalous, singleton, live-born preterm deliveries (<37 weeks' gestation) among White (n=9,029), Black (n=6,952), and Hispanic (n=3,889) mothers in the Consortium on Safe Labor (2002-2008). We used log-Poisson models with generalized estimating equations to estimate the relative risk (RR) and 95% confidence interval (CI) for respiratory distress syndrome (RDS). sepsis, periventricular/intraventricular hemorrhage (PVH/IVH), and neonatal death. Whites were the reference group. Analyses were adjusted for site, maternal demographics, health behaviors, and pre-existing medical conditions. Both Black and Hispanic preterm infants had a 1% increased risk for neonatal death (Black RR=1.01, Cl=1.01, 1.02; Hispanic RR=1.01, Cl=1.00, 1.01) and increased risk for sepsis (Black RR=1.04, CI=1.03, 1.05; Hispanic RR=1.02, CI=1.01, 1.03), while they experienced a significantly lower risk for RDS (Black RR=0.98, CI = 0.97, 1.00; Hispanic RR=0.97, CI=0.96, 0.98). Black infants were more likely to have PVH/IVH (RR=1.01, CI= 1.00, 1.01) but there was no difference between Hispanics and Whites. Analyses restricted to births at <34 and <32 weeks yielded similar findings although with less precision. Our findings from a modern obstetrical cohort support the literature that suggests neonatal death is more common among Black and Hispanic infants compared with White infants but racial differences in morbidities did not necessarily follow the same pattern.

# **Plenary Session 1**

# Tuesday, June 16th 8:15 - 9:30 am

# Determinants of fertility



RACIAL DISPARITIES IN VISITING A DOCTOR FOR HELP GETTING PREGNANT: A REPORT FROM THE FUCHSIA WOMEN'S STUDY. Chin HB\*, Howards PP, Kramer MR, Mertens AC, Spencer JB (Rollins School of Public Health, Emory University, Atlanta, GA) Fertility counseling and treatment can help women achieve their desired family size, however, disparities exist in the utilization of this type of medical care. This study examines the persistence of a racial disparity in seeking medical help for becoming pregnant after controlling for mediating pathways. We used data from the FUCHSIA Women's Study, a population-based study of fertility outcomes among 1073 women of reproductive age (22-45 years). Self-reported race in the study population included: 29% black, 66% white, and 5% other races. Overall, 28% of women reported infertility with similar prevalence by race. We fit log binomial models to quantify the magnitude of the racial difference in reported care seeking after adjustment for hypothesized mediators (education, income, place of residence, comfort with assisted reproductive technology, reproductive conditions, and sexually transmitted infections) using inverse probability weighting. In the total cohort, compared with white women, black women were less likely to have a visit [adjusted risk ratio (aRR) = 0.57, 95% confidence interval (CI): 0.41, 0.80] and this association remained among the subgroup of women who reported infertility [aRR = 0.75, 95% CI: 0.56, 0.99]. Among women who visited the doctor, black women waited twice as long on average before seeking help compared with white women. There were notable racial differences in visiting a doctor for help getting pregnant in this study even though reports of infertility were similar by race. These differences identify an area for improved provider patient communication on available infertility services such as counseling on specific treatment options.

# THE IMPACT OF PRECONCEPTION MATERNAL SELF-REPORTED STRESS ON FECUNDABILITY. Akhter S, Kerber RA, Kong M, Taylor KC\* (University of Louisville, Louisville, KY)

Recent studies have indicated a possible association between maternal stress (either selfreported or as measured by biomarkers) and reduced fecundability, but results have been inconsistent. This study evaluated the effects of pre-conception self-reported stress on fecundability in a prospective pregnancy study, the Mount Sinai Study of Woman Office Workers (N=405). Women recorded stress on a scale from 1 to 4 (low to high) and covariates such as age, alcohol consumption, smoking, and unprotected intercourse in a daily diary for 12 cycles or until pregnant. Age, weight, height, pregnancy intention (yes/no), and other variables were collected at baseline. The mean stress levels for each cycle were calculated for the entire cycle, the ovulatory window, and the implantation window. Windows were estimated by counting days until the start of the subsequent cycle (days -18 to -14 for the ovulatory window; days -12 to -5 for the implantation window). Pregnancy was determined by hCG assays on two consecutive days when the next menstrual cycle was expected (N=135 pregnancies). Discrete survival analysis was used to estimate associations between self-reported stress and fecundability (cycles until pregnancy) adjusting for age, body mass index, alcohol, frequency of unprotected intercourse, and pregnancy intention. Higher stress during the ovulatory window was significantly associated with reduced fecundability (FOR=0.65; 95%CI 0.50-0.87; p=0.003); attenuated trends were seen for the entire cycle (FOR=0.76; 95% CI 0.57-1.01) and the implantation window (FOR=0.86; 95%Cl 0.65-1.13). These data support the notion that perceived stress impacts fecundability, and the effect may vary across the menstrual cycle.

**SERUM CAFFEINE AND PARAXANTHINE AND MENSTRUAL CYCLE FUNCTION**. Schliep KC,\* Wactawski-Wende J, Perkins NJ, Zarek SM, Radin RG, Mitchell EM, Sjaarda LA, Mumford SL (Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Rockville, MD, USA)

Despite common female counsel to reduce caffeine intake while attempting to conceive, few studies have evaluated the impact of caffeine on menstrual cycle function, and no previous studies have assessed biologic dose via repeated, well-timed measurements. Participants (n = 259) were followed for up to 2 menstrual cycles and provided fasting blood specimens for caffeine and hormonal assessment at up to 8 visits per cycle. Linear mixed models estimated associations between serum caffeine biomarkers and reproductive hormones while Poisson regression with robust error variance assessed relative risk (RR) of sporadic anovulation. The highest (median: 4.02 µmol/L) versus lowest (median: 0.18 µmol/L) serum caffeine tertile was significantly associated with lower total (-3.9%; 95% confidence interval [CI]: -6.8 to -1.0) and free testosterone (-4.9%; 95% CI: -7.7 to -2.0) after adjusting for age, race, percent body fat, daily vigorous exercise, perceived stress, and total energy and alcohol intake. A reduced adjusted RR for anovulation was found for the highest versus lowest tertile of caffeine and paraxanthine (RR: 0.41, 95% CI: 0.18, 0.90; RR: 0.42, 95% CI 0.19, 0.92, respectively). Further adjustment for self-reported coffee intake did not alter testosterone findings but did attenuate the results for serum caffeine and paraxanthine and anovulation (RR 0.44, 95% CI: 0.19, 1.09; RR: 0.47, 95% CI: 0.21, 1.08, respectively). Moderate caffeine intake may be associated with improved menstrual cycle function, but further research is needed to establish whether other components in coffee (e.g., polyphenols) may be contributing to the effect.

**ESTROGEN USE IS ASSOCIATED WITH INCREASED 25-HYDROXY VITAMIN D.** Harmon QE,\* Umbach DM, Baird DD (National Institute of Environmental Health Sciences, Epidemiology Branch, Research Triangle Park, NC)

Vitamin D has been associated with a range of reproductive health outcomes. Interestingly, several small studies suggested that use of oral contraceptive pills is associated with elevated levels of 25-hydroxy-Vitamin D (25(OH)D). We explored the association between current use of hormonal contraception and serum 25(OH)D levels in 1660 young black women (24-34 years old) from Detroit, MI enrolled in the Study of Lifestyle, Environment & Fibroids (SELF). We constructed a predictive model that accounted for season using a cosinor function and included dietary intake of Vitamin D, supplement use, behavioral factors, measured skin reflectance and use of contraception; we explored confounding and residual confounding by supplement use and other behaviors associated with choice of contraception. Levels of Vitamin D were low with 70% of women below the 20ng/ml level recommended by IOM. Supplement use and current use of an estrogen-containing contraceptive had the largest magnitude of effect on 25(OH)D. Use of an estrogen-containing contraceptive was associated with a 21% (95% CI: 15-28) increase in 25(OH)D levels. In young women, exogenous estrogen was associated with increased levels Vitamin D. This result raises several mechanistic and methodologic questions. Depending on the mechanism of action, natural fluctuations in endogenous estrogen may also result in changing levels of 25(OH)D. These natural fluctuations may impact clinical decision making and point to possible disease pathways. For other health outcomes, exogenous sources of estrogen should be considered as potential confounders. Further work to elucidate the association between both exogenous and endogenous estrogen and 25(OH)D is warranted.

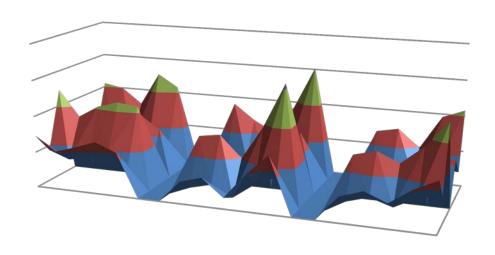
THE EFFECTS OF PRECONCEPTION LOW DOSE ASPIRIN TREATMENT ON CLINICAL PREGNANCY AND LIVE BIRTH: THE IMPACT OF INFLAMMATORY STATUS. L Sjaarda\*, E Mitchell, SL Mumford, R Radin, S Zarek, K Schliep, T Plowden, R Kalwerisky, N Perkins, J Stanford, J Wactawski-Wende, J Townsend, A Lynch, L Lesher, D Faraggi, N Galai, R Silver, EF Schisterman\* (Epidemiology Branch, Division of Intramural Population Health Research, NICHD, Bethesda, MD, USA)

The effects of low dose aspirin (LDA) on reproductive outcomes in women have varied among studies. Recently, preconception LDA (81mg) was reported to increase fecundability and live birth rates relative to placebo in a subset of women with a history of one recent (prior 12 months) pregnancy loss in the EAGeR randomized trial. However, the mechanisms of LDA's effects remain uncertain, and there is a need to better identify women who may benefit from treatment. We assessed high-sensitivity C-reactive protein (CRP), a marker of systemic inflammatory status, measured at baseline, in relation to subsequent clinical pregnancy, live birth, and pregnancy loss in 1184 women. Log-binomial models with robust variance assessed the association between log-transformed CRP and pregnancy outcomes, adjusted for age, BMI, race, and income. Women were divided into lower (≤1.65 mg/L, n=685) and higher (>1.65, n=499) CRP levels based on optimal cut-point analysis. LDA treatment increased clinical pregnancy in women with higher (RR: 1.19; 95%CI: 1.03, 1.38), but not lower (RR: 1.03; 95%CI: 0.94, 1.14) CRP at baseline. Likewise, LDA treatment was associated with increased live birth in women with higher (RR: 1.23; 95%CI: 1.02,1.48), but not lower (RR: 1.02; 95%CI: 0.90,1.17) CRP. There was no impact of LDA on pregnancy loss in either group. Thus, modifying inflammation may be a mechanism explaining LDA's previously observed effects on improving pregnancy and live birth rates in certain women. Higher CRP in women with a history of pregnancy loss may indicate a systemic inflammatory milieu amendable to improvement with preconception LDA treatment.

## **Plenary Session 2**

## Tuesday June 16th 10:00 – 11:15 am

## Advanced Methods in Perinatal Epidemiology



THE NICHD FETAL GROWTH STUDIES: TWIN TRAJECTORIES. Grantz KL\*, Grewal J, Albert PS, Wapner RJ, D'Alton ME, Sciscione AC, Grobman WA, Wing DA, Owen J, Newman R, Chien EK, Kim S, Zhang C, Buck Louis GM, Hediger ML (Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Rockville, MD, USA)

Our objective was to compare fetal growth trajectories in dichorionic twins to optimal trajectories in singletons, as few such studies in twins exist. A prospective cohort of 171 women with dichorionic twin gestations was recruited from 8 sites (2012-2013). After an initial sonogram at 11w0d-13w6d, randomization occurred to one of two serial 2D/3D ultrasonology schedules (maximum number=7). Growth curves were estimated using linear mixed models with cubic splines, and percentiles per week then compared between singletons and twins, and whether they varied by racial/ethnic group, after adjustment for age, race/ethnicity height, weight, parity, employment, marital status, insurance, income, and education. The median estimated fetal weight (EFW) for the twins became smaller than that of the singletons starting at 31 weeks and continuing through 39 weeks. At 35 weeks, the 10th, 50th, 90th EFW percentiles for twins were 1980g, 2383g, 2867g and for singletons 2131g, 2521g, 2982g (P<0.001), respectively. The abdominal circumference and biparietal diameter were also significantly smaller in twins from 31-39 weeks and from 32-37 weeks, respectively. Conversely, both the head circumference between 18 and 22 weeks, humerus length between 13-15 weeks, and femur length between 12-14 weeks were significantly larger for twins. We observed a racial interaction, where EFW differences between twins and singletons were stronger in Whites (P<0.001). The differences between twin and singleton trajectories, which are suggestive of a more asymmetric growth pattern in twin gestations, suggest that the intrauterine environment may become less capable of sustaining optimal growth in twin fetuses manifesting around 31 weeks.

THE REPORTING OF STABILIZED AND RISK-ADJUSTED RATES OF STILLBIRTH AND NEONATAL DEATH IN THE UNITED KINGDOM: MBRRACE-UK. BN Manktelow\* (University of Leicester, UK), LK Smith, TA Evans, ES Draper, UK), DJ Field, JJ Kurinczuk, on behalf of MBRRACE-UK

Background: The routine collection, analysis and reporting of perinatal death is vital in order to facilitate improvements in obstetric and neonatal care. From 2013 information on all late fetal losses, stillbirths and neonatal deaths in the United Kingdom (UK) has been collected by MBRRACE-UK. Methods: MBRRACE-UK data, together with individual-level data on all UK births, enables for the first time the calculation of UK-wide case-mix adjusted mortality rates. This was undertaken using an approach based on the CMS 'Hospital Compare' methodology. A mixed effects logistic regression model was developed comprising fixed terms for baby and mother characteristics (destational age, socio-economic status, mother's age, ethnicity, sex of baby, multiple birth) and a random term for local government area (n=217). The SMR was estimated for each area by the ratio of predicted to expected outcomes, which was then multiplied by the national average to obtain a stabilized and risk-adjusted rate. Areas were identified as potential outliers if the probability of their rate being over 10% greater than the national average was >0.5. Results: In 2013 there were 780211 births, with 3173 stillbirths (4.07/1000 births) and 1334 neonatal deaths (1.72/1000 live births). The ranges of case-mix adjusted rates for the local government areas were 3.77-4.56 per 1000 births for stillbirths (1 potential outlier), 1.46-2.11 per 1000 live births for neonatal death (13 potential outliers). Conclusions: This methodology provides robust information to support the delivery of high quality care, and is vital to monitoring changes over time and to local, national and international comparisons.

**GEOGRAPHIC VARIATION IN INFANT MORTALITY DISPARITIES IN THE U.S.** Rossen LM\*, Khan D, Schoendorf KC\* (Infant, Child, and Women's Health Statistics Branch, Office of Analysis and Epidemiology, National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, MD)

The large disparity in mortality between black and white infants in the U.S. persists despite decades of research examining determinants of these inequities. Prior studies of infant mortality disparities have been limited to large metropolitan areas for which stable estimates of infant mortality rates (IMRs) by race can be determined, leaving much of the U.S. unexplored. The objective of this analysis was to describe geographic variation in county-level racial disparities in IMRs across the 48 contiguous U.S. states using national linked birth and infant death period files (2004–2011). Bayesian shared component models were implemented in WinBUGS, accounting for the spatially correlated structure of the data and borrowing strength across both spatial units and racial groups. County-level variation in IMRs common to both white and black infants and county-level variation unique to black infants were explored. Black infants had higher IMRs than white infants in all counties, but there was geographic variation in the magnitude of both relative and absolute disparities. The mean difference between black and white IMRs was 5.80 per 1,000 (interquartile range 3.86 to 7.55 per 1,000), while IMRs for black infants were 2.1 times higher than for white infants (interquartile range 1.92 to 2.26). Most (95%) of the county-level variation in IMRs for black infants was shared with white infants. Recognizing the extent to which county-level variation in infant mortality rates may be shared by both black and white infants may inform efforts to redress inequities and reduce the burden of infant mortality in the U.S.

HIGH MATERNAL BMI IN EARLY PREGNANCY AND RISK OF INFANT MORTALITY – A POPULATION-BASED SIBLING STUDY IN SWEDEN. Lindam AP\*, Johansson S, Stephansson O and Cnattingius S. (Clinical Epidemiology Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden)

Introduction: Previous studies have reported that high body mass index (BMI) in early pregnancy is a risk factor for infant mortality, but familial confounding is a concern. We investigated mother's BMI and infant mortality risk in a case-control study, using both mothersibling controls and population (non-related) controls. Methods: We included all primipara women with live-born singleton infants in Sweden between 1992 and 2011, who also had a sister giving birth to her first infant within this period. Cases were infants who died during the first year of life. Mothers of cases were matched to their sister with live first born infant closest birth in time of the case infant. Population controls were surviving infants of women who did not have a sister having an infant death. We analyzed the association between BMI and infant mortality with logistic regression and adjusted for the mother's age, height, smoking habits. education and calendar time. Results: We identified 573 cases of infant mortality with 573 sister controls and 210,551 population controls. Women with low or normal BMI (<25) were used as reference. Using mother sibling controls, the OR (95% CI) of infant mortality increased with BMI as follows: BMI 25-30: 1.34 (0.90-2.01); BMI 30-35: 2.01 (1.13-3.57); and BMI >35: 11.2 (3.26-38.56). Using population controls, the ORs (95% CI) were: BMI 25-30: 1.22 (0.97-1.54); BMI 30-35: 1.87 (1.34-2.61), and BMI >35: 3.57 (2.41-5.29). Conclusions: High BMI increases risk of infant mortality independent of maternal genetic factors or early environment.

ACCOUNTING FOR THE RELATIVE SEVERITY OF ADVERSE EVENTS IN COMPOSITE PERINATAL OUTCOMES. Hutcheon JA\*, Bodnar LM, Platt RW (University of British Columbia, Vancouver, Canada)

Background: In perinatal research, multiple adverse events are often combined to create a single, composite outcome. Although components may differ in their severity (e.g., transient tachypnea vs. stillbirth), composite outcomes are usually weighted equally. Scoring tools for assigning points according to event severity have been published, but are challenging to incorporate into standard statistical analyses. Objectives: To outline a novel, regression-based method to account for the relative severity of components in composite outcomes, and to apply this approach to estimate maternal risks following planned vaginal birth after Cesarean (VBAC) versus planned Cesarean delivery. Methods: Low-risk women with a previous Cesarean in the 2011 Nationwide Inpatient Sample were included (n=100,371). A composite of maternal complications (including death, uterine rupture, transfusion, and perineal tears) was created and scored using the previously-published Adverse Outcome Index. Odds ratios (OR) for planned VBAC were estimated using logistic regression, with more severe outcomes up-weighted using frequency weights and bootstrapped confidence intervals. Results: In unweighted regression, planned VBAC was associated with increased risk of the composite maternal outcome (OR=2.6 [95% CI: 2.4-2.9]). After weighting components to account for their relative severity, the magnitude of risk was diminished considerably (weighted OR=1.4 [95% CI: 1.3-1.6]). Conclusion: Our approach to account for event severity in composite outcomes is easy to implement and produces results that better reflect the risk-benefit trade-offs associated with perinatal care decisions.

Poster Session B

Tuesday, June 16th

12:00 pm – 1:30 pm



# B1 TRAFFIC-RELATED AIR POLLUTION, NEIGHBORHOOD SOCIOECONOMIC FACTORS AND NEURAL TUBE DEFECTS IN THE SAN JOAQUIN VALLEY OF CALIFORNIA. Amy M.

Padula\*, Wei Yang, Suzan L. Carmichael, Ira B. Tager, Frederick Lurmann, S. Katharine Hammond, Gary M. Shaw (University of California, Berkeley, Berkeley, CA) Neural tube defects, including spina bifida and anencephaly, are one of the most common types of birth defects. Environmental pollutants and socioeconomic factors have been associated with neural tube defects. The potential impact of interaction between ambient air pollution and neighborhood socioeconomic factors on the risks of neural tube defects is not well understood. We investigated whether associations between traffic-related air pollutant exposure in early gestation and neural tube defects were modified by neighborhood socioeconomic factors in the San Joaquin Valley of California, 1997-2006. Five pollutant exposures, three outcomes and 9 neighborhood socioeconomic factors were included for a total of 135 investigated associations. Estimates were adjusted for maternal race-ethnicity, education, body mass index and multivitamin use. We present below odds ratios whose accompanying confidence intervals do not include 1 and a chi-square test of homogeneity p-value <0.05. We observed increased odds of spina bifida comparing the highest to lowest quartile of particulate matter <10 micrometers (PM10) among those living in a neighborhood with: a) median household income of less than \$30,000 per year (OR=3.9; 95% CI: 1.3, 12.1); and b) more than 30% with less than or equal to a high school education (OR 2.7; 95% CI: 1.1, 6.2). Among women who lived in higher SES categories, there was no association between PM10 and neural tube defects. When analyzing both case types together, these odds were attenuated. Our results demonstrate effect modification by neighborhood socioeconomic factors in the association of fine particulate matter and spina bifida in California.

### B2

ECONOMIC EVALUATION OF THE COST TO HOSPITALS OF NEWBORN SCREENING FOR CRITICAL CONGENITAL HEART DISEASE. Reeder MR\*, Kim J, Nance AE, Krikov S, Feldkamp ML, Randall H, Botto LD (University of Utah, Salt Lake City, UT) The purpose of this study was to estimate the costs associated with performing pulse oximetry screening for detection of critical congenital heart disease (CCHD) at two Utah hospitals. Pilot newborn CCHD screening was conducted in two Utah hospitals from May 2013-July 2014. A time and motion study was conducted at each site's newborn nursery in February 2014 to estimate the time needed to perform CCHD screening and identify potential factors influencing its variations. A questionnaire was used to estimate labor and equipment costs. A total of 53 CCHD screens were observed. Screens at site A were mostly performed by medical assistants (95%) using disposable probes (100%); screens at site B were mostly performed by certified nursing assistants (90%) using reusable probes (90%). Among first screens only (n=47), the median screen time for both sites combined was 8.6 minutes (range: 3.2-23.2), with no significant difference in screening time between sites. The overall cost (\$ in 2014) of screening ranged from \$2.58 at site B, to \$24.55 at site A, with nearly 90% of the cost at site A due to the use of disposable probes. At site B, reusable probes accounted for 3% of total cost, with labor contributing the largest percentage (90%). These study results indicate that pulse oximetry screening for detection of CCHD was not time intensive; however, there was a large discrepancy in total cost to screen, largely due to the type of oximeter and probe used.

MATERNAL AMBIENT AIR POLLUTION EXPOSURE IN PRECONCEPTION AND EARLY GESTATION AND OFFSPRING CONGENITAL OROFACIAL DEFECTS. Zhu Y\*, Zhang C, Wallace M, Grantz KL, Liu D, Mendola P (Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Rockville, MD)

Maternal air pollution exposure has been related to congenital malformations but the literature is equivocal. Potential chronic preconception effects have not been studied. The associations of air pollutant exposure during 3 months preconception and weeks 3-8 of gestation with orofacial defects were estimated. Among 188,012 eligible live/stillborn births from the Consortium on Safe Labor (2002–2008), 63/90 had isolated/non-isolated cleft palate and 159/194 had isolated/non-isolated cleft lip with/without palate. Air pollution exposures were estimated using a modified Community Multiscale Air Quality model. We performed logistic regression analyses with generalized estimating equations adjusted for region and maternal demographic, lifestyle and clinical factors. During the 3 months preconception window, positive associations were observed between carbon monoxide (CO) exposure and isolated cleft palate [odds ratio (OR)=2.24; 95% confidence interval (CI): 1.21, 4.16) per interguartile range increasel, particulate matter diameter ≤10 µm and isolated cleft palate (OR=1.72; 95% CI: 1.12, 2.66), and sulfur dioxide and isolated cleft lip (OR=1.93; 95% CI: 1.16, 3.21). Similar results were observed for non-isolated oral clefts. During gestational weeks 3-8, average exposures to CO, nitrogen oxides (NOx) and particulate matter diameter ≤2.5 µm (PM2.5) were associated with increased odds of isolated/non-isolated cleft palate while CO was also positively associated with nonisolated cleft lip (OR=1.47; 95% CI: 1.01, 2.12). Furthermore, weekly analyses revealed that positive associations of NOx and PM2.5 with cleft palate were prominent from weeks 3-6 and 3-5, respectively. In conclusion, positive associations between air pollutants and orofacial defects were observed with stronger associations appearing during early organogenesis.

### **B4** ASSESSMENT OF DIFFERENCES IN ACADEMIC OUTCOMES AMONG CHILDREN WITH **CONGENITAL HEART DISEASE.** Knight JH\*, Drews-Botsch C, Kramer MR, Mahle WT, Williams B, Oster ME (Rollins School of Public Health, Emory University, Atlanta, GA) Congenital heart disease (CHD) is the most common type of birth defect, and survival in this population has dramatically improved. Understanding the long-term impact of CHD will help ensure optimal health and quality of life for those affected. However, types of defects and other clinical characteristics are likely to result in different outcomes in these children. This study compared failure rates on standardized tests and special education use in children with single ventricle, critical two-ventricle CHD (surgery before age 1), and non-critical CHD. The study population included survivors without Down or DiGeorge Syndrome who were born in 1998-2002 and surgically treated at Children's Healthcare of Atlanta. Clinical data were successfully linked to 3rd grade education records for 428 (53%) children. More than one fourth of survivors were receiving special education services (29% of those with non-critical CHD, 28% with critical two ventricle, and 23% with single ventricle). The proportion of children failing the standardized test was highest (26%) in math and lowest (8%) for reading. Although there were no significant differences in subject-specific failure rates, generally, those with non-critical CHD had the highest rates and those with single ventricle, the lowest. After controlling for defect type, a greater number of surgeries and being male increased the odds of failure and receiving special education services. These results suggest a high risk of failure on standardized tests and enrollment in special education for all children surgically treated for congenital heart disease regardless of the type of defect.

INTERACTION BETWEEN MTHFR 677C>T AND PERICONCEPTIONAL FOLIC ACID SUPPLEMENTATION IN THE RISK OF HYPOSPADIAS. E Dokter, I van Rooij, C Wijers, B Franke, JJ van der Biezen, W Feitz, L. van der Zanden, N Roeleveld\* (Department for Health Evidence / Department of Pediatrics, Radboud Institute for Health Sciences, Radboud university medical centre, Nijmegen, The Netherlands)

Background: Hypospadias is a congenital malformation of the penis with the meatus located on the ventral side. Both environmental factors and genetic predisposition are believed to play a role in the pathogenesis. As adequate folate levels are essential during embryogenesis but are reduced by the C677T polymorphism in the methylenetetrahydrofolate reductase (MTHFR) gene, we studied the role of maternal periconceptional use of folic acid supplements and the mother and child MTHFR C677T polymorphism in the etiology of hypospadias. Methods: We conducted a case-control study among 914 nonsyndromic hypospadias cases and 711 population-based controls from the AGORA (Aetiologic research into Genetic and Occupational/environmental Risk factors for Anomalies in children) data- and biobank, born between 1990 and 2012. Information on folic acid use was derived from maternal questionnaires and DNA from mother and child was used to assess the MTHFR C677T polymorphism using Tagman assays. In the analyses, we assumed a dominant effect of the polymorphism. Results: Preliminary univariable analyses showed a small protective effect of folic acid supplements on the risk of hypospadias (OR=0.8, 95%CI: 0.6-1.0). No associations were found for mother or child MTHFR C677T polymorphisms (both OR=1.1; 95%CI: 0.9-1.4). However, lack of folic acid supplement use in combination with carrying the MTHFR C677T polymorphism increased the risk of hypospadias (child: OR=1.5; 95%CI: 1.1-2.1, mother: OR=1.5, 95%CI: 1.1-2.2). Conclusion: This study showed an increased risk of hypospadias when no folic acid supplements were used and mother or child carried the MTHFR C677T polymorphism.

### **B6**

DETECTION BIAS IN THE PRENATAL DIAGNOSIS OF MALFORMATIONS AMONG SSRI EXPOSED WOMEN. Anna M. Modest\* Martha M. Werler; Carla Van Bennekom, Allen A. Mitchell (Department of Epidemiology, Boston University School of Public Health, Boston, MA) Background: Selective serotonin reuptake inhibitors (SSRIs) in pregnancy have been inconsistently associated with birth defects, particularly cardiac defects. If exposure to SSRIs prompted efforts to identify defects through rigorous prenatal ultrasound (US) screening, detection bias may account for positive associations. Objectives: Determine whether SSRI exposure in pregnancy is associated with higher proportions of structural defects being identified by US. Methods: For 1998-2014, we studied all mothers of babies with malformations from the Slone Birth Defects Study, a case-control study of malformed and non-malformed infants in North America. Women were interviewed within 6 months after delivery about medication use, illnesses, and prenatal care. Those who received fertility treatment, had seizures, diabetes, multiple births, or unknown SSRI exposure status were excluded. Since information on negative ultrasounds was not available, we compared, among SSRI-exposed and unexposed pregnancies, the proportions of structural malformations that were identified by US. Log-binomial regression was used to estimate the RR and 95% CI. Results: Among 15,632 mothers of malformed infants, 680 (4.4%) were exposed to an SSRI. For all defects, after adjustment for maternal age, race, center of birth, and year of baby's birth, prenatal diagnosis was not associated with SSRI exposure (aRR 1.0, 95% CI 0.95-1.1). When defects were grouped according to organ system, no associations were observed. Of particular interest, the aRR for cardiac defects was 1.0 (0.91-1.1). Conclusion: We saw no evidence that US-detected defects were more common among SSRI-exposed babies, suggesting that detection bias resulting from SSRI exposure was unlikely to explain observed associations.

## THE ROLE OF PREVIOUS MISCARRIAGES AND SINGLE NUCLEOTIDE POLYMORPHISMS IN DEVELOPMENTAL GENES IN THE ETIOLOGY OF ANORECTAL

**MALFORMATIONS**. R van de Putte, C Wijers, I de Blaauw, C Marcelis, C Sloots, A Brooks, P Broens, H Brunner, L van der Zanden, I van Rooij,N Roeleveld\* (Department for Health Evidence / Department of Pediatrics, Radboud Institute for Health Sciences, Radboud university medical centre, Nijmegen, The Netherlands)

Background: Anorectal malformations (ARM) are birth defects of the gastrointestinal tract, often combined with multiple other congenital anomalies. The etiology is likely to involve both environmental and genetic factors. Having had previous miscarriages seems to be a risk factor for birth defects and genetic factors may be a cause of miscarriages. Therefore, we studied associations between ARM and known polymorphisms in the developmental genes BMP4 and GLI2 and previous miscarriages as well as their GxE interaction. Methods: We performed a case-control study in a Caucasian population of 431 nonsyndromic ARM cases and 661 population-based controls derived from the AGORA (Aetiologic research on Genetic and Occupational/ environmental Risk factors for Anomalies in children) data- and biobank. Genotyping of the children's DNA was done by PCR and guestionnaires were used for information on miscarriages. Results: The SNP rs17563 in BMP4 was not associated with ARM, but we found associations with rs3738880 in GLI2, especially in ARM patients with multiple congenital anomalies (homozygous GG genotype: OR=2.1; 95%CI: 1.2-3.7). A 4-fold increased risk was found for homozygous variant genotypes of both genes (OR=4.1; 95%CI: 1.0-17.8). Among control mothers, 19% reported a previous miscarriage versus 25% of case mothers (OR=1.4; 95%Cl 1.1-2.0). We could not show a clear gene-environment interaction. Conclusion: We found independent associations between ARM and previous miscarriages and the variant in GLI2, consistent with a multifactorial etiology, and a gene-gene interaction between BMP4 and GLI2, both downstream genes in the Sonic Hedgehog (SHH) pathway, which is involved in several important developmental processes.

#### **B8**

## RARE CODING VARIANTS AND THE RISK OF CONGENITAL ANORECTAL MALFORMATIONS: AN EXOME CHIP ASSOCIATION STUDY. C Wijers, H Reutter, J Goeman,

S Vermeulen, T Galesloot, E Jenetzky, L Kiemeney, I de Blaauw, H Brunner, I van Rooij, N Roeleveld\* (Department for Health Evidence / Department of Pediatrics, Radboud Institute for Health Sciences, Radboud university medical centre, Nijmegen, The Netherlands)

Background: Anorectal malformations (ARM) are rare congenital malformations and knowledge on their etiology is scarce. Previous genetic studies on ARM mainly focused on candidate genes but did not yield any substantial evidence. Therefore, hypothesis-generating approaches seem valuable to acquire new knowledge. Methods: We performed genotyping of 598 Caucasian ARM cases and 1,931 population-based controls using the Illumina Human Exome BeadChip, which contains ~250K rare coding variants. Patients were derived from the AGORA (Aetiologic research on Genetic and Occupational/ environmental Risk factors for Anomalies in children) data- and biobank in the Netherlands and the German Network for Congenital Uro-REctal malformations (CURE-Net) and controls from the Nijmegen Biomedical Study (NBS). In total, 558 cases, 1,886 controls and 241,177 markers passed all quality control steps and were included in single variant and gene-based analyses. Statistically significant results were technically validated and replicated in additional Caucasian and Han Chinese cases and controls using the molecular inversion probe (MIP) technique. Results: All variants with minor allele frequencies >0.4% were tested and 55 variants reached statistical significance. However, only three variants in the CLCN1, LRBA, and ZNF423 genes could be validated and none were replicated. The gene-based analyses did not lead to new insights either. Conclusion: We found no evidence for strong associations between ARM and rare coding variants captured by the HumanExome BeadChip. Future studies need larger sample sizes to identify common and rare variants with small to moderate effects, while stratifying on phenotypically homogenous groups of ARM patients. Therefore, international collaboration is essential.

DIET QUALITY, OBESITY, AND BIRTH DEFECTS. Carmichael SL\*, Yang W, Gilboa S, Ailes E, Correa A, Botto L, Feldkamp M, Shaw GM (Stanford University, Stanford, CA) Maternal obesity and low diet quality are both associated with increased risks of specific birth defects. We examined whether risks of 16 birth defect phenotypes were higher than expected in the presence of obesity and low diet quality, based on relative excess risk due to interaction (RERI). Analyses included mothers of 13,523 cases and 8,617 population-based nonmalformed controls born 1997-2009 and interviewed for the National Birth Defects Prevention Study. We examined 16 phenotypes for which preliminary data suggested an association with body mass index or diet quality. We used logistic regression to generate odds ratios (ORs) adjusted for maternal age, race-ethnicity, education, parity, energy intake, and periconceptional alcohol consumption, smoking, or vitamin/mineral supplement intake. We compared risks among women who were obese and had diet quality in the lowest quartile: women with only one of these risk factors (2 groups); and women with neither (reference). ORs for women with both risk factors were highest for 13/16 studied phenotypes. For 8/9 non-heart phenotypes, ORs ranged from 1.3-2.1; for gastroschisis, the OR was 0.2 (driven by its protective association with obesity); and for 7 heart phenotypes, ORs ranged from 1.3-2.0. For most of these comparisons, 95% confidence intervals (CI) excluded 1.0. Most RERIs were positive but small (<0.5), with CIs that included zero. These findings provide evidence for the hypothesis of highest birth defect risks among offspring to women who are obese and have low diet quality but minimal evidence for an interaction of these factors in their contribution to risk.

### B10

DIETARY INFLAMMATORY INDEX DURING PREGNANCY AND EARLY CHILDHOOD: ASSOCIATIONS WITH MID-CHILDHOOD ADIPOSITY AND INSULIN RESISTANCE. Sen S\*, Rifas-Shiman SL, Shivappa N, Wirth MD, Hebert JR, Gold DR, Gillman MW, Oken E (Pediatric Newborn Medicine. Brigham and Women's Hospital. Boston. MA) Background: A pro-inflammatory diet in adults has been linked with adverse cardiometabolic outcomes. The impact of such a diet in pregnancy and childhood on child health outcomes has not been investigated. Objective: Examine associations of Dietary Inflammatory Index (DII) in pregnancy and early childhood (EC) (3-5 y) with BMI z-score and cardiometabolic markers (insulin, triglycerides, systolic BP) in mid-childhood (MC) (6-10 y). Methods: We included 929 mother-child pairs in Project Viva, a pre-birth cohort in MA. We calculated DII, a predictor of dietary inflammatory potential, from food frequency questionnaires. We used multivariable linear regression models. Results: Mean (SD) DII was -2.6 (1.4) in pregnancy and 0.28 (0.70) at EC; a higher score indicates a more pro-inflammatory diet. In MC, mean (SD) BMI-z was 0.42 (0.97). Pregnancy DII was associated with higher MC BMI-z (β [per 1 unit increase in DII] 0.08 higher BMI-z; 95% CI 0.03, 0.12), and insulin (β 0.57 uU/ml; 0.22, 0.92), but not SBP (β 0.26mmHg; -0.13, 0.65) or TG (β -1.1mg/dL; -3.4, 1.2) after adjustment for age and sex. Associations were attenuated after adjusting for maternal socio-demographics and pre-pregnancy BMI: BMIz 0.02 (-0.02, 0.07), and insulin 0.32 (-0.05, 0.70), respectively. DII in EC was associated with MC BMIz (β 0.10; 0.01, 0.20) but not with insulin (β -0.29; -1.03, 0.46), SBP (β 0.07; -0.80, 0.93) or TG (β -0.6; -3.8, 2.6) after adjusting for the above covariates. Conclusions: Dietary inflammatory potential in pregnancy and early childhood may contribute to higher adiposity and insulin resistance in mid-childhood.

**PRENATAL USE OF ACETAMINOPHEN AND CHILDHOOD INTELLIGENCE QUOTIENT (IQ): A DANISH NATIONAL BIRTH COHORT STUDY**. Liew Z\*, Ritz B, Virk J, Arah OA, Olsen J (Department of Epidemiology, Fielding School of Public Health, University of California-Los Angeles, Los Angeles, CA)

Acetaminophen (paracetamol) is the most commonly used pain and fever medication during pregnancy and may influence early brain development by interfering with maternal hormones. Recently, we reported a positive link between maternal use of acetaminophen during pregnancy and risk of attention deficit hyperactivity disorders (ADHD) in the Danish National Birth Cohort (DNBC). We now examined the association between prenatal acetaminophen use and childhood IQ. Between 2003 and 2008, a sub-cohort of 1,782 mothers and their 5-year-old children from the DNBC participated in a neuropsychological assessment of cognitive ability including the IQ tests (Wechsler Primary and Preschool Scales of Intelligence-Revised). Information on acetaminophen use was collected prospectively in 3 computer-assisted telephone interviews with the mother during pregnancy and at 6 months postpartum. We used multiple linear regression to estimate the mean difference between prenatal acetaminophen use and child IQ adjusted for a set of important confounders including parental education, maternal IQ, and indications of acetaminophen use. We found that children whose mothers used acetaminophen during pregnancy had a reduction of full scale IQ of -1.22 points (95% CI -2.38, -0.06) and performance IQ of -1.61 points (95% CI -3.01, -0.11), but no difference in verbal IQ, compared to children whose mothers did not use acetaminophen during gestation. Effect estimates were stronger in boys than girls. We also conducted sensitivity analysis for selection bias. Our results suggest that prenatal acetaminophen use may result in lower full IQ and performance IQ scores in children at age five in the DNBC.

### **B12**

LIPOPROTEIN PARTICLE SUBCLASSES IN RELATION TO ENDOGENOUS REPRODUCTIVE HORMONES. Zarek SM\*, Browne RW, Ye A, Wactawski-Wende J, Sjaarda LA, Schliep KC, DeCherney AH, Schisterman EF, Mumford SL (National Institutes of Health, Bethesda, MD)

Background: Premenopausal women benefit from the cardio-protective effects of estrogen on traditional cholesterol levels, but little is known about the association of lipoprotein particle subclass distributions and endogenous reproductive hormone levels. Methods: Regularly menstruating women (n= 259), aged 18–44 years, were followed for up to two complete menstrual cycles. Generalized linear mixed models, adjusted for age and BMI, were used to assess the association between lipoprotein particle subclasses, measured by hydrogen1 nuclear magnetic resonance (H1 NMR) during the mid-luteal phase, and cumulative exposure (calculated as the area under the curve) to endogenous free estrogen, progesterone, FSH and LH, at up to eight times per cycle, with timing of menstrual cycle phase assisted by fertility monitors. Results: Cumulative exposure to free estrogen was associated with a significant decrement (2-3%, p <0.05), in total, medium, and large very-low density lipoprotein (VLDL) particles, with pronounced associations among women less than age 35 (interaction p<0.05). Cumulative progesterone exposure was associated with a significant decrement in total and large high density lipoprotein (HDL) particles (2% and 1-6% respectively, p <0.05). There were no significant associations between reproductive hormones and low density lipoprotein (LDL) particles. Conclusion: We report novel findings of the association of cumulative free estrogen exposure and a consistent decrement in VLDL particle subclasses, particularly in premenopausal women below 35 years. These data suggest an alternative cardio-protective role of estrogen in younger women, given the known atherogenic potential of VLDL, particularly large VLDL particles.

IS MATERNAL ADHERENCE TO A MEDITERRANEAN DIET ASSOCIATED INFANT DNA METHYLATION PATTERNS AT BIRTH?. S Gonzalez-Nahm\*, C Hoyo, V Hogan (Department of Maternal and Child Health, University of North Carolina at Chapel Hill) Maternal diet during pregnancy may influence maternal and fetal health and may contribute to the in-utero development of disease, but evidence looking at infant outcomes is scarce. We assessed associations between maternal adherence to a Mediterranean diet pattern (MD) on infant DNA methylation at seven differentially methylated regions (DMR) measured at birth using data on 621 women participating in the Newborn Epigenetic Study (NEST) with first trimester food frequency questionnaire data. DMRs were chosen based on their links to growth or obesity. A 10 component MD score was constructed based on above median g/1000 kcals of fruit, vegetables, fish, dairy products, whole grains, nuts, legumes, mono-saturated fat ratio, and below median intakes of processed and unprocessed meats. Associations between dietary intakes and infant DNA methylation were assessed using logistic models adjusted for maternal race/ethnicity, age, education, gestational diabetes, pre-pregnancy BMI, parity, child gender, gestational age, gestational weight gain, and delivery route. Women with high MD adherence were more likely to be non-Hispanic White and have a higher socioeconomic status. Preliminary results show that mean infant DNA methylation at 6 of the 7 DMRs tested did not significantly differ among women with high MD adherence compared to low adherence. DNA methylation at the paternally expressed gene 3 (PEG3) DMR was lower in infants with greater maternal MD adherence compared with those with low adherence (OR 0.54, 95% CI: 0.31, 0.97). Results suggest that maternal diet during pregnancy may affect the in-utero development of risk factors for obesity later in life.

### B14 SOCIOECONOMIC DISADVANTAGE. GESTATIONAL I

SOCIOECONOMIC DISADVANTAGE, GESTATIONAL IMMUNE ACTIVITY, AND NEURODEVELOPMENT IN EARLY CHILDHOOD. Gilman SE\*, Hornig M, Hahn J, Cherkerzian S, Goldstein JM (Harvard TH Chan School of Public Health)

Gestational immune activity is hypothesized to play a key role in fetal development, particularly neurodevelopment, and is responsive to aspects of the maternal environment. Here we test if socioeconomic disadvantage is associated with differences in gestational immune activity, and whether such differences impair offspring neurodevelopment. Concentrations of inflammatory cytokines in mid-gestation maternal serum (interleukin [IL]-6, IL-8, IL-10, IL-1β, and tumor necrosis factor [TNF]-α) were assayed from 1,494 participants in the New England cohorts of the Collaborative Perinatal Project, and were investigated in relation to the level of maternal socioeconomic disadvantage and their impact on neurologic abnormalities in offspring at ages 4 months and 1 year. We found that median concentrations of IL-8 were significantly lower in the most disadvantage pregnancies (-1.53 pg/mL on the log scale; 95% confidence interval: -1.81, -1.25). Offspring of these pregnancies had significantly higher risks of neurologic abnormalities at 4 months (odds ratio (OR)=4.61; CI=2.84, 7.48) and 1 year (OR=2.05; CI=1.08, 3.90). This was partly due to fetal exposure to lower maternal IL-8, which predicted higher risks of neurologic abnormalities at both 4 months (OR=7.67; CI=4.05, 14.49) and 1 year (OR=2.92; CI=1.46, 5.87). These findings support the involvement of gestational immune activity in fetal neurodevelopment, which, we speculate, is dysregulated in the context of maternal economic hardship, and demonstrates one pathway through which maternal social disadvantage affects poorer neurobehavioral outcomes in her offspring.

EPIGENOME-WIDE AND TRANSCRIPTOME-WIDE ANALYSES REVEAL GESTATIONAL DIABETES IS ASSOCIATED WITH ALTERATIONS IN THE HUMAN LEUKOCYTE ANTIGEN COMPLEX. Binder AM, LaRocca J, Lesseur C, Marsit C, Michels KB\* (Harvard Medical School, Boston, MA)

Gestational diabetes mellitus (GDM) affects approximately 18% of pregnancies in the United States and increases the risk of adverse health outcomes in the offspring. These adult disease propensities may be set by anatomical and molecular alterations in the placenta associated with GDM. To assess the mechanistic aspects of fetal programming, we measured genome-wide methylation (Infinium HumanMethylation450 Beadchips) and expression (Affymetrix Transcriptome Microarrays) in placental tissue of 41 GDM cases and 41 matched pregnancies without maternal complications from the Harvard Epigenetic Birth Cohort. Specific transcriptional and epigenetic perturbations associated with GDM status included alterations in the major histocompatibility complex (MHC) region, which were validated in an independent cohort, the Rhode Island Child Health Study. Gene ontology enrichment among gene regulation influenced by GDM revealed an over-representation of immune response pathways among differential expression, reflecting these coordinated changes in the MHC region. Our study represents the largest investigation of transcriptomic and methylomic differences associated with GDM, providing comprehensive insight into the molecular basis of GDM induced fetal (re)programming.

### **B16**

SEXUALLY DIMORPHIC INFLUENCE OF FIRST TRIMESTER PHTHALATE AND PHENOL EXPOSURE ON THE REGULATION OF GENES IMPLICATED IN METABOLISM AND CELLULAR ORGANIZATION IN HUMAN PLACENTA. Binder AM, LaRocca J, Michels KB\* (Harvard Medical School, Boston, MA)

Prenatal exposure to endocrine disrupting chemicals (EDCs) may disrupt normal hormone homeostasis during critical windows of structural and functional development, shaping adult disease susceptibilities. Phthalates and phenols are two classes of suspected EDCs that are of significant concern due to their ubiquitous human exposure and potential detrimental health effects. EDC exposure has been suspected to induce changes in placental physiology. potentially contributing to the intrauterine programing of these phenotypes. To investigate this etiology, we assessed genome-wide changes in methylation and gene expression in 171 human placentas associated with first trimester urinary metabolites of 11 phthalates and 8 phenols, modeling site-specific methylation and expression was modeled as a function of each metabolite. These associations were assessed separately in the placentas of males and females due to potential effect modification by sex-specific patterns of methylation associated with cell growth and differentiation. We identified changes in methylation and expression among genes implicated in metabolism and cellular organization for both males and females. However, the specific EDCs with the greatest influence on these pathways varied by sex, and between methylation and expression patterns. This study represents the first investigation into the influence of phenols and phthalates on genome-wide regulation in human placental tissue. Notably, our study provides novel evidence for the molecular basis of the impact of prenatal phthalate and phenol exposure on human placental function which may have long-lasting implications.

SEX DIFFERENCES IN FETAL-PLACENTAL PROTEINS FLUCTUATE BY MATERNAL RACE, AGE, WEIGHT AND BY GESTATIONAL AGE. Adibi JJ\*, Lee MK, Saha SR, Boscardin WJ, Apfel A, Currier RJ (University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA)

Objective. To test the stability of sex differences in placental-fetal proteins at the population level. Methods. We used population-level prenatal serum screening data for the State of California from 2009 – 2012 (1.1 million serum samples) to estimate fetal sex differences in 5 placental-fetal hormones and their fluctuations by maternal factors. Analyte values were modeled by multivariate linear regression to estimate predicted means for women carrying female and male fetuses. Ratios of female to male predicted means were used to assess the magnitude of the sex differences. Results. Human chorionic gonadotropin, dimeric inhibin and pregnancy associated plasma protein A were higher in the case of a female by 11, 9 and 2% respectively (p<0.0001). Alpha feto-protein was 5% higher in male fetuses (p<0.0001). There were small (1-6%, p<0.05) fluctuations in the sex differences by maternal race, weight, and age. In two cases, the sex difference was reversed. In African-American women, pregnancy associated plasma protein A was 2% higher when carrying male fetuses; as opposed to Asian women in which pregnancy associated plasma protein A was 6% higher when carrying females (p<0.0001). Unconjugated estriol shifted from 3% higher in female fetuses to 3% higher in male fetuses between 15 and 20 weeks gestation (p<0.0001). Conclusions. Within a wellenumerated, diverse U.S. population, sex differences in placental hormones overall were stable. Small fluctuations and reversal within population subgroups may be relevant to environmental and physiologic contributions to fetal outcomes and obstetric complications and can be probed further using these types of clinical data.

### **B18**

# PRENATAL TRIPTAN EXPOSURE, MIGRAINE HEADACHE, AND BEHAVIORAL CHANGE OVER TIME: RESULTS FROM THE NORWEGIAN MOTHER AND CHILD COHORT STUDY.

ME Wood\*, KL Lapane (University of Massachusetts Medical School, Worcester, MA) HME Nordeng (University of Oslo) JA Frazier (University of Massachusetts Medical School) Background Triptans are migraine medications with high affinity for serotonin 1B/D receptors. which are important for fetal brain programming. No studies to date have examined different developmental trajectories associated with triptan exposure. Methods The Norwegian Mother and Child Cohort Study includes more than 100000 women recruited during pregnancy. Data are collected through questionnaires and linkage to birth registries. This study included 101625 live singleton births without major malformations. 53547 were present at the 18 or 36 month post-partum follow-up, of which 516 (1%) used triptans during pregnancy, 1051 used triptans prior to pregnancy only, 4333 had migraines without triptan use, and 47643 with no history of migraine or triptan use. The Child Behavior Checklist (CBCL) internalizing and externalizing scales were the outcome measures. We used mixed models to examine the change over time for each group, reported as the change in z-score (β) with 95% confidence intervals (CI). Results Children born to pre-pregnancy and in-pregnancy triptan users had similar rate of increase in externalizing (βpreg 0.10, 95% CI 0.00 to 0.21 and βpp 0.12, 95% CI 0.04 to 0.19) and internalizing (βpreg 0.09, 95% CI -0.02 to 0.19 and βpp 0.15, 95% CI 0.08 to 0.23) symptoms, compared to population comparison. While rate of change was similar for triptan using groups, those exposed prenatally had higher scores at 18 months, indicating more problems. Conclusion Migraine headache but not triptan exposure influences developmental trajectory, however, children prenatally exposed to triptans start out with more behavioral problems. Continued longitudinal assessment is needed.

## GESTATIONAL WEIGHT GAIN IS ASSOCIATED WITH HIGH BIRTH WEIGHT BUT NOT OVERWEIGHT DURING CHILDHOOD IN A NATIONALLY-REPRESENTATIVE,

**LONGITUDINAL STUDY**. Leonard SA\*, Petito LC, Rehkopf DH, Ritchie LD, Abrams B (Division of Epidemiology, University of California, Berkeley, CA)

Concerns about the rising prevalence of obesity and health risks linked to high gestational weight gain (GWG) prompted the Institute of Medicine to revise GWG recommendations in 2009 to include specific, limited weight ranges for overweight and obese women. Based on these revisions and to expand on the limited understanding of GWG and offspring obesity, we examined data from the National Longitudinal Study of Youth 1979: an ongoing, nationallyrepresentative study that enrolled adolescent participants in 1979 and female participants' children starting in 1986. Our study sample of full-term singleton births included 7,670 children and 4.241 mothers. We categorized GWG using the Institute of Medicine recommendations and analyzed its association with high birth weight (≥ 4,000 g) and child overweight (BMI ≥ 85th percentile for age and sex) at ages 3, 8, and 15 y. We estimated logistic regression models with standardized sampling weights and generalized estimating equation estimators to adjust for clustering of children in families. In unadjusted analyses, excessive GWG was significantly associated with higher odds of high birth weight and overweight throughout childhood. Adjustment for confounders nullified effect measures for child overweight but not high birth weight (OR=1.55; 95% CI: 1.24, 1.93), with significant confounders including race/ethnicity, prepregnancy BMI, maternal employment, maternal smoking, parity, and year of birth. Similar results were found in sensitivity analyses using birth weight ≥ 4,500 g and BMI ≥ 95th percentile. These findings add to the inconsistent evidence of an association between GWG and offspring body weight outcomes.

### **B20**

# PRE-PREGNANCY BODY MASS INDEX, GESTATIONAL WEIGHT GAIN, AND OFFSPRING EXTERNALIZING BEHAVIOR PROBLEMS AMONG EARLY ADOLESCENTS. Kim H,

Leonard SA\*, Deardorff J, Petito LC, Abrams B (Division of Epidemiology, UC Berkeley School of Public Health, Berkeley CA)

Increasing attention has been paid to how maternal pregnancy-related factors influence offspring behavioral outcomes, as a number of studies have found a link between prepregnancy body mass index (BMI) and child behavior problems. However, the long-term effects of pre-pregnancy obesity and gestational weight gain (GWG) have not been investigated among older children. This study focused on 10 to 11 year old children to test this relationship. We used a nationally representative sample (n=3,615) from the National Longitudinal Survey of Youth 1979 (NLSY79) and their children's (NLSY79-Child and Young Adults) data. Pre-pregnancy BMI and GWG guidelines from the Institute of Medicine were our primary exposure variables. Our outcome variable was mother-rated children's externalizing problem scores from the Behavior Problems Index questionnaire. Scores ≥90th percentile were defined as "clinically significant" based on prior literature. We performed multivariable logistic regression with custom sampling weights. Children whose mothers were obese before pregnancy had higher odds of having externalizing problems compared to those whose mothers were normal weight (OR=1.65, 95% CI: 1.22, 2.24). In addition, inadequate GWG was marginally associated with higher odds of externalizing problems in children (OR=1.37, 95% CI: 1.004, 1.87) compared to recommended GWG, after adjusting for child, maternal, and family background factors. Our results highlight that maintaining healthy weight before and during pregnancy is crucial for child health.

**GENETIC ASSOCIATIONS FOR HYPOSPADIAS: REVIEW OF CURRENT KNOWLEDGE AND REPLICATION**. L van der Zanden, N van Leeuwen, R Makkinje, W Feitz, I van Rooij, N Roeleveld\* (Department for Health Evidence, Radboud Institute for Health Sciences, Radboud university medical center, Nijmegen, The Netherlands)

Background: Hypospadias is a common congenital malformation of the male external genitalia with a multifactorial etiology. Several single nucleotide polymorphisms (SNPs) have been associated with hypospadias, but replication is often lacking. Therefore, we identified all genetic associations reported for hypospadias and tried to replicate the most promising ones. Methods: After a thorough literature search and SNP selection, we genotyped 816 Caucasian nonsyndromic hypospadias patients and 668 population-based controls derived from the AGORA (Aetiologic research on Genetic and Occupational/ environmental Risk factors for Anomalies in children) data- and biobank in the Netherlands, using TagMan assays, Results: When excluding studies using microarrays performed after our SNP selection, 36 polymorphisms in DGKK and 67 polymorphisms in 16 other genes were identified. DGKK was already successfully studied in our cohort previously. In the other genes, 52 polymorphisms were examined only once and 15 more than once. Many of these were found not to be associated with hypospadias, had a minor allele frequency <2% in the Caucasian population, or were repeats or deletions, while four SNPs had already been replicated unsuccessfully in our cohort. Therefore, we selected seven SNPs in the genes HSD17B3, ESR1, ESR2, ATF3 and MAMLD1 for this replication study. None of these SNPs was associated with hypospadias in our study populaton, with the possible exception of rs944050 in ESR2 (OR 1.5, 95%CI: 1.0-2.3). Conclusions: The results from genetic association studies on hypospadias vary considerably between populations, which hampers identification of polymorphisms that truly increase the risk.

### **B22**

RACIAL DISPARITIES IN PRETERM BIRTH: DO MOTHER'S GESTATIONAL AGE AT BIRTH AND NEIGHBORHOOD SOCIAL AND ECONOMIC FACTORS MATTER? Ncube CN\*, Burke JG, Enquobahrie DA, Ye F, Marx J, Reiber GE, Voorhees R, Albert SM (University of Washington, Seattle, WA)

Rates of preterm birth (PTB) have fluctuated over time but disparities between non-Hispanic (NH) black and white women have remained largely unchanged. Research has historically focused on maternal health behaviors/characteristics, but has not fully explained these disparities; social context as a possible predictor has increased over the years. Some researchers report mothers born prematurely are more likely to deliver premature infants. The mechanism postulated is fetal programming that predisposes the mother to poor pregnancy outcomes. The objective of this study was to explore the role of mothers' gestational age (weeks) at her birth (MGA), along with transgenerational racial (0%≤low<13%, 13%≤medium<50%, and 50%≤high≤100% NH black residents) and economic (0%≤low<34% and 34%≤high≤100% low income households) neighborhood composition on infants' risk of PTB. Covariates were mother's race, socioeconomic status (SES), marital status, Medicaid, and childhood SES. This study involved 6,592 linked infant-mother birth records. Multinomial logistic regression was used to model the PTB subgroups of late PTB (LPTB), 34-36 weeks, and early PTB (EPTB), <34 weeks, relative to term births, ≥37 weeks. Racial disparities in LPTB (RR: 1.25, 95%CI: 0.90-1.75) and EPTB (RR: 0.83, 95%CI: 0.46-1.50) were fully explained by the factors examined in the models. Longer MGA reduced the odds of LPTB relative to term birth (RR: 0.93, 95%CI: 0.89-0.98). On the other hand, exposure to high neighborhood poverty both at the mothers' birth and the infants' birth was a significant predictors of EPTB (RR: 3.08, 95%CI: 1.50-6.33). Findings suggest that MGA and generational neighborhood poverty are significant predictors of PTB subgroups.

### MATERNAL METABOLIC CONDITIONS ASSOCIATED WITH AUTISM-SPECIFIC

**MATERNAL AUTOANTIBODIES**. Krakowiak P\*, Walker CK, Hertz-Picciotto I, Van de Water J (University of California. Davis)

Background: Mothers of children with autism spectrum disorder (ASD) are more likely, than mothers of typically developing (TD) children, to have pregnancies complicated by metabolic conditions (MCs) including diabetes (type 2 or gestational), chronic hypertension, preeclampsia, and/or obesity. Recent findings from several research groups suggest that approximately 23% of mothers whose child has ASD produce specific patterns of autoantibodies to fetal brain proteins that have been detected in <1% of mothers of TD children. The biological mechanisms underlying the development of these ASD-specific maternal autoantibodies are poorly understood. MCs are characterized by sustained low-grade inflammation and insulin resistance. Chronic inflammation during pregnancy might create an unstable immune environment that is susceptible to generating maternal antibodies that are reactive to fetal brain proteins. Objectives: This study examines whether these ASD-specific maternal autoantibodies are associated with MCs during gestation. Methods: This study included 225 mothers enrolled in the CHARGE (Childhood Autism Risk from Genetics and the Environment) Study whose child (2-5 years old) had a diagnosis of ASD confirmed on both Autism Diagnostic Interview-Revised (ADI-R) and Autism Diagnostic Observation Schedule (ADOS). Maternal blood specimens collected at study enrollment were analyzed for autoantibodies. MCs during pregnancy were ascertained from medical records or structured telephone interview with the mother and included pre-pregnancy body mass index (BMI) >30, gestational and type 2 diabetes, chronic hypertension, and preeclampsia. Autism severity was measured using calibrated ADOS scores. We conducted log-linear regression analyses (Poisson regression with robust error variance) to examine associations between maternal MCs and the presence of ASD-specific maternal autoantibodies. The strength of association was measured by prevalence ratio (PR) and 95% confidence interval (CI). Results: Fortyfour (19.6%) out of 225 mothers had ASD-specific autoantibodies to fetal brain proteins. Mothers with and without autoantibodies did not differ with respect to age, parity, or inter-pregnancy interval. Diabetes and preeclampsia were more common among mothers who had autoantibodies than those who did not (diabetes: 13.6% vs. 7.2%; preeclampsia: 15.9% vs. 9.4%) although these differences did not reach statistical significance. However, when we restricted to mothers of children with severe symptoms (autism severity score ≥7; 28 mothers with and 116 without autoantibodies), those with diabetes were 3.6 times more likely to have autoantibodies relative to mothers without MCs and with a BMI <25 (21.4% vs. 8.6%; PR=3.6; 95% CI 1.4, 9.7). Similarly, mothers who developed preeclampsia were nearly 3 times more likely to have autoantibodies (17.9% vs. 9.5%; PR=3.0; 95% Cl 1.1, 8.6). Maternal obesity was not associated with an increased likelihood of autoantibodies. Conclusions: The biological mechanisms that lead mothers to become sensitized to fetal brain proteins are not yet understood. These preliminary findings suggest that MCs during pregnancy, particularly diabetes and preeclampsia, may be associated with ASD-specific maternal autoantibodies. Given that MCs are more prevalent in mothers of children with ASD than mothers of TD children, and these conditions are characterized by dysregulated immune responses (e.g., chronic inflammation, autoantibodies to other proteins), these findings reveal a plausible mechanism for production of ASD-specific autoantibodies that warrants further investigation.

### **B24**

### INTAKE OF CAFFEINATED BEVERAGES AND FECUNDABILITY IN A PRECONCEPTION

**COHORT**. AK Wesselink\*, LA Wise, S Mahalingaiah, KJ Rothman, EM Mikkelsen, EE Hatch (Boston University School of Public Health, Boston, MA)

Caffeine is an adenosine receptor agonist that may influence fertility potential by affecting ovulation or other menstrual characteristics. We studied the relation between preconception caffeine intake and fecundability in Pregnancy Study Online (PRESTO), a cohort of pregnancy planners. Frequency of coffee, tea, soda, and energy drink intake was self-reported at baseline. Outcome data were updated every 8 weeks until clinically-recognized pregnancy, fertility treatment, loss to follow-up, or end of observation (12 months). We restricted analyses to women who had been trying to conceive for ≤6 cycles at study entry. Adjusted fecundability ratios (FR) and 95% CIs were estimated using a proportional probabilities model. Over 60% of daily caffeine intake among 1,367 women was from coffee consumption. Compared with <100 mg/day of caffeine, FRs for 100-199, 200-299, and 300+ mg/day at baseline were 1.01 (CI: 0.88, 1.16), 1.04 (CI: 0.84, 1.27), and 1.25 (CI: 0.92, 1.69), respectively. FRs for 1 and 2+ servings/day of coffee, compared with 0 servings/day, were 1.28 (CI: 0.99, 1.67) and 1.32 (CI: 0.88, 2.00), respectively. High intake of other caffeinated beverages was rare, resulting in imprecise FR estimates. We found a suggestion of reduced fecundability among women who consumed the most caffeinated tea, herbal tea, caffeinated soda, and sugar-sweetened soda. Energy drink intake was weakly associated with fecundability. Results were consistent when we stratified by attempt time at study entry (0-2 cycles vs. 3-6 cycles). Our findings do not support the hypothesis that caffeine or coffee intake causes reduced fecundability.

# SERUM 25-HYDROXYVITAMIN D (25(OH)D) AND MENSTRUAL CYCLE CHARACTERISTICS. Jukic AM\*, Upson K, Harmon QE, Baird DD. (Epidemiology Branch, NIEHS, Durham, NC 27709)

In animals, diet-induced vitamin D deficiency results in ovarian cycle disturbances, but human data are lacking. We examined 25(OH)D and menstrual cycle characteristics in 1696 African-American women, aged 23-34. In primary analyses, we excluded 594 women who either had no menstrual cycles in the past year or were on a medication that affects cycles. Participants reported their typical cycle length and problems with menstrual pain over the past year. Serum 25(OH)D, measured by chemiluminescence immunoassay, was used to estimate a seasonallyadjusted yearly average for each woman. We used polytomous logistic regression to estimate the association of 25(OH)D with cycle lengths categorized as "short" (<27 days, N=373), "long" (≥35 days, N=55), "normal" (27-34 days, N=623), or "too irregular to estimate" (N=51). The median 25(OH)D level was 15 ng/mL (IQR: 11-20). After adjustment, a doubling of 25(OH)D was associated with about half the odds of long cycles (OR(95%CI)): 0.54(0.33, 0.89), p=0.02). Increasing 25(OH)D was also associated with a lower odds of menstrual pain interfering with daily life "a lot," but this association was weakened when adjusting for smoking (p=0.14). In a secondary analysis, adjusted for ever smoking, women with a history of clinician-diagnosed vitamin D deficiency (N=223) were more likely to have reported using a hormonal contraceptive to treat either irregular cycles (OR(CI): 1.5(1.1, 2.0), p=0.009) or menstrual pain (OR(CI): 1.6(1.1, 2.3), p=0.008). These findings suggest that vitamin D influences the ovarian cycle in humans. Further research should investigate whether vitamin D is on the causal pathway between smoking and menstrual pain.

### **B26**

ANTI-MÜLLERIAN HORMONE IS NOT ASSOCIATED WITH FECUNDABILITY. Zarek SM\*, Mitchell EM, Sjaarda LA, Silver RM, Wactawski-Wende J, Townsend JM, Lynch AM, Lesher LL, Stanford JB, Galai N, Faraggi D, Schliep KC, Plowden TP, Radin RG, Kalwerisky RA, Perkins NJ, DeCherney AH, Mumford SL, Schisterman EF (National Institutes of Health, Bethesda, MD) Background: The impact of anti-Müllerian hormone (AMH), a marker of ovarian reserve, on fecundability in fertile women is understudied. Methods: Fertile women (n=1228) attempting pregnancy with one to two prior pregnancy losses participated. Preconception AMH levels were categorized as low (<1.25 ng/mL), normal (referent group, 1.25 to 4.0 ng/mL), and high (>4.0 ng/mL) based on clinically relevant cut-points. Cox proportional hazard regression models assessed fecundability odds ratios (FOR), adjusting for age and BMI and accounting for left truncation and right censoring. Analyses were repeated within three domains of reproductive history, stratified across 1) history of 1 or 2 prior pregnancy losses, 2) time since most recent loss of  $\leq 1$  or  $\geq 1$  vear, and 3) history of 0 or  $\geq 1$  prior live birth. Results: There were no significant associations observed between AMH level and fecundability among women with 1 (Low AMH: FOR, 0.98, 95% CI 0.7, 1.3; High AMH: FOR 1.13, 95% CI 0.9, 1.4) or 2 (Low: FOR, 1.14, CI 0.8, 1.7; High: FOR 1.04, CI 0.8, 1.4) prior pregnancy losses. Similarly, no associations were observed when women were stratified by time since most recent loss or by history of live birth. with the exception of a marginally higher fecundability in women with higher vs. normal AMH (FOR 1.16, CI 0.9, 1.4) among women with a pregnancy loss within ≤1 year. Conclusion: In fertile women with a history of pregnancy loss, AMH was not consistently associated with fecundability.

PRENATAL EXPOSURE TO MATERNAL STRESS FOLLOWING BEREAVEMENT AND INFERTILITY IN THE OFFSPRING: A POPULATION-BASED COHORT STUDY. Plana-Ripoll O\*, Olsen J, Kesmodel US, Parner ET, Li J and Basso O (Section of Epidemiology, Aarhus University, Denmark)

INTRODUCTION About 10 to 15% of couples experience fertility problems. Despite substantial progress in diagnosing and treating infertility, we have a limited knowledge of its risk factors. Recent research suggests that prenatal exposures may be important. Maternal stress, through hormonal disturbance in fetal life, could result in reduced offspring fertility. Here, we report preliminary findings on the association between prenatal stress due to maternal bereavement and indicators of infertility in a large cohort. METHODS All infants born in Denmark between 1973 and 2008 (N=2,396,859) were included in this population-based study. Infants were considered prenatally exposed if their mothers had lost the partner, a sibling, or a parent during pregnancy or the year before. The outcome was defined using the National Hospitalization Register as the composite endpoint: (i) congenital malformation of genital organs, infertility and testicular cancer for males; (ii) congenital malformations of genital organs, infertility, endometriosis, and polycystic ovary syndrome for females. Data were analyzed, stratified by sex, using Cox Proportional Hazards models adjusted for potential confounders. RESULTS A total of 43,009 individuals (1.8%) were considered exposed and 98,564 (4.11%) had the composite outcome during follow-up. The HR [95% CI] of infertility for exposed compared to unexposed was 1.10 [1.03-1.16] for males and 1.09 [0.99-1.21] for females. CONCLUSIONS These preliminary results suggest a modest association between prenatal stress and later infertility. Further analyses will include loss of a child as a source of maternal bereavement, infertility outcomes from the Infertility and Prescription registries, as well as a sibling analysis.

### **B28**

EARLY SECONDARY AMENORRHEA AND PREGNANCY IN WOMEN DIAGNOSED WITH SYSTEMIC LUPUS ERYTHEMATOUS DURING THEIR REPRODUCTIVE YEARS: AN ANALYSIS USING THE GOAL STUDY. Knight JH\*, Howards PP, Spencer JB, Tsagaris KC, Lim SS (Rollins School of Public Health, Emory University, Atlanta, GA) Systemic lupus erythematosus (SLE) disproportionately affects women and often develops during their reproductive years. Research suggests that some women who receive cyclophosphamide as treatment for SLE experience earlier decline in menstrual function, but reproductive outcomes among women with SLE who have not taken this drug are less well understood. This study aims to better understand the relation between SLE and reproduction by assessing early secondary amenorrhea and pregnancy in women treated with and without cyclophosphamide. Female SLE patients, ages 20-40 at time of diagnosis, who were 40 years or older at the time of the survey were included in this analysis (n=187). Participants in the GOAL study were asked about their reproductive histories including early secondary amenorrhea, defined as loss of menstruation before age 40. Women who were not treated with cyclophosphamide had an increased prevalence of early secondary amenorrhea compared with population estimates, 13% compared with 1-5%. Factors associated with early secondary amenorrhea in women not treated with cyclophosphamide were marital status and receipt of a kidney transplant. Treatment with cyclophosphamide doubled the prevalence after adjustment for patient characteristics. Over 90% of women reported being pregnant at least once, and about 83% of these had a child, but the majority of pregnancies occurred before diagnosis. SLE may affect women's reproductive health even if they are not treated with cyclophosphamide. Better understanding of other factors related to reproductive outcomes in this population will improve clinicians' and patients' abilities to make treatment and family planning decisions.

PRE-CONCEPTION LOW-DOSE ASPIRIN AND SEX RATIO: THE EAGER TRIAL. Radin RG\*, Mumford SL, Silver R, Lesher L, Galai N, Faraggi D, Wactawski-Wende J, Townsend JM, Lynch AM, Simhan HN, Sjaarda LA, Perkins NJ, Zarek SM, Plowden TC, Mitchell E, Schliep KC, Kalwerisky R, Schisterman EF (NICHD, Bethesda, MD)

Overactive endometrial inflammation is observed in women with recurrent miscarriage. Disordered inflammation may be exacerbated by the male embryo, which has more active metabolism and provokes greater oxidative stress and immune activation. Thus, low-dose aspirin (LDA), an anti-inflammatory drug, may alter the sex ratio among women with a history of pregnancy loss. We assessed the sex ratio at birth and approximate sex ratio at implantation in a preconception randomized trial of LDA vs. placebo. Participants were age 18-40 with 1-2 pregnancy losses. We estimated the intention-to-treat (ITT) RR and 95% CI for a live-born male. The RR for pregnancy with male offspring included karvotypes of losses (n=48). When restricting to ultrasound-confirmed pregnancies and live births, respectively, we adjusted with stabilized inverse-probability-of-treatment weighting. A sensitivity analysis examined bias from the pregnancy losses with unknown offspring sex (n=85). The ITT RR for live-born male, LDA vs. placebo, was 1.31 (1.07-1.60) among 1,078 women who completed follow-up and 1.23 (1.03-1.46) among 595 live births (sex ratio at birth). The RR for pregnancy with male offspring among 728 ultrasound-confirmed pregnancies was 1.22 (1.02-1.45); in the sensitivity analysis, RRs were 1.15-1.17 and statistically significant, indicating that missing karyotype data on pregnancy losses produced little bias. Among women with the inflammatory biomarker Creactive protein>1.65 mg/L at randomization, the ITT RR=1.79 (1.24-2.58) vs. 1.07 (0.84-1.37) among women with values<1.65 mg/L (P-interaction=0.02). Preconception LDA was associated with an increased sex ratio. LDA may have modulated decidual inflammation that was exacerbated by the male embryo.

### **B30**

SUGAR-SWEETENED SODA CONSUMPTION AND MALE FECUNDABILITY. JJ Michiel\*, LA Wise, AK Wesselink, KA Hahn, EM Mikkelsen, KJ Rothman, EE Hatch (Boston University) Sugar-sweetened beverage intake has been associated with a variety of adverse health outcomes, including poorer sperm motility, but its effect on male fecundability has not been examined. We assessed the association between weekly sugar-sweetened soda (SSS) intake and fecundability among male participants of the Pregnancy Study Online (PRESTO), a North American web-based preconception cohort study. At baseline, men reported detailed data on demographics, medical history, and lifestyle and behavioral factors, including their intake of SSS and diet soda. Men were linked with their female partners, and pregnancy status was updated every 8 weeks for up to 12 months or until clinically-recognized pregnancy. Fecundability ratios (FR) and 95% CI were derived from proportional probabilities models, controlling multiple covariates including race/ethnicity, education, smoking status and BMI. Analyses were restricted to 469 couples who had been trying to conceive for ≤6 cycles at study entry. Intakes of SSS and diet soda were determined by summing total weekly soda intake (bottles/cans per week). FRs for SSS intake of 1, 2-7 and ≥8 bottles/cans per week versus no intake were 1.16 (CI: 0.85-1.57), 0.87 (0.68-1.12) and 0.65 (CI: 0.40-1.07), respectively. FRs for diet soda intake of 1, 2-7 and ≥8 bottles/cans per week versus no intake were 1.22 (CI: 0.87-1.71), 1.15 (CI: 0.88-1.49) and 1.03 (CI: 0.69-1.52), respectively. Our study is the first to examine the association between SSS intake and male fecundability. Preliminary findings on SSS agree with studies of sperm parameters. Future analyses will look at additional types of sugar-sweetened beverages, including juice.

# B31 NOVEL BACTERIAL VAGINOSIS-ASSOCIATED ORGANISMS MEDIATE THE RELATIONSHIP BETWEEN VAGINAL DOUCHING AND PELVIC INFLAMMATORY

DISEASE. Gondwe T\*, Ness RB, Totten PA, Astete S, Ferris M, Tang G, Norori J, Gold M, Martin DH, Haggerty CL (University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA) Background: Vaginal douching is associated with an increased risk of bacterial vaginosis (BV), the result of aerobic and anaerobic vaginal microorganism overgrowth. As BV has been associated with pelvic inflammatory disease (PID), we sought to determine whether the relationship between vaginal douching and PID is mediated by select, novel BV-associated organisms. Methods: We conducted multiple logistic regression to identify risk factors for endometrial infection with ≥ 1 BV-associated organism (among Atopobium vaginae, BVassociated bacterium 1 (BVAB1), and Sneathia (Leptotrichia) amnionii and sanguinegens). We then examined whether endometrial infection mediated the association between vaginal douching (≥ 2 times in the past month) and histologically confirmed PID (≥5 neutrophils and/or ≥2 plasma cells in endometrial stroma). Microbes were assessed by targeted polymerase chain reaction among archived specimens from 609 women with clinically suspected PID in the PID Evaluation and Clinical Health (PEACH) study. To measure mediation effects, we used a modified Sobel test for binary variables. Results: Factors significantly associated with endometrial infection with ≥ 1 of the BV-associated organisms in the multivariate model were being African-American (adjusted odds ratio (aOR) 2.2, 95% CI 1.5-3.4), unmarried (aOR 1.8, 95% CI 1.0-3.2), less than high school education (aOR 1.8, 95% CI 1.2-2.8), and vaginal douching (aOR 2.1, 95% CI 1.2-3.8). Endometrial infection with ≥ 1 BV-associated organisms was found to mediate the relationship between vaginal douching and PID (Sobel test of mediation: p-value=0.04), Conclusions: Endometrial infection by novel BV-associated organisms is on the causal pathway in the relationship between vaginal douching and PID.

### **B32**

# THE ASSOCIATION BETWEEN HORMONAL CONTRACEPTION AND BREASTFEEDING DURATION. Houk K\*, Stuebe AM, Chetwynd E, Bryant AG, Muddana A, Yourkavitch J (Gillings School of Global Public Health, University of North Carolina at Chapel Hill)

The benefits of breastfeeding for mothers and infants are well established. However, few rigorous studies have been conducted to determine the effect of hormonal contraceptives on milk supply and early breastfeeding cessation. Given the importance of postpartum contraception for improving birth spacing and reducing unplanned pregnancies, the association between hormonal contraceptives and disrupted lactation requires further investigation. We analyzed data from the Infant Feeding Practices Study II (IFPS II), a longitudinal survey of U.S. mothers with information on both contraceptive use and infant feeding outcomes. Using Cox proportional hazards models, we assessed duration of any and exclusive breastfeeding for women taking hormonal contraceptives at three months compared with those not taking hormonal contraceptives, adjusted for prenatal breastfeeding intention. Significant differences in prenatal intended breastfeeding duration were observed by contraceptive type: women using a low dose minipill had longer intended duration, whereas women using higher dose combined oral contraceptives (COCs) or Depo-Provera had shorter intended duration compared with women not using a hormonal method. While women taking the minipill had no significantly increased hazard of stopping breastfeeding at three months compared with women not using a hormonal method, the hazards for women taking COCs or Depo-Provera were significantly higher: 1.40 (1.10-1.78) for any breastfeeding and 1.74 (1.21-2.50) for exclusive breastfeeding among women on COCs, and 1.55 (1.03-2.31) for any breastfeeding and 1.31 (0.65-2.66) for exclusive breastfeeding for women on Depo-Provera. These results indicate an association between some forms of hormonal contraception and lower breastfeeding duration, highlighting a need for further research.

**EVALUATING THE IMPACT OF INFORMATIVE CLUSTER SIZE IN A STUDY OF** PREGNANCY OUTCOMES FOLLOWING INTRAUTERINE INSEMINATION. \*Peck JD, Stoner JA, Duong NQ, Craig LB (University of Oklahoma Health Sciences Center, Oklahoma City, OK) Studies of infertility treatment outcomes usually include patients who experience multiple treatment cycles. Correlation introduced by repeated observations within the same patient is typically ignored, avoided by restricting analyses to the first cycle, or addressed by using generalized estimating equation (GEE) methods to account for clustering. Because the number of repeated cycles may be influenced by prior outcomes, failure to account for informative cluster size may bias observed associations. We evaluate the impact of informative cluster size on associations between patient characteristics and pregnancy outcome following treatment with intrauterine insemination (IUI). Our cohort includes 719 patients undergoing 2221 IUI treatment cycles at a university-based clinic from 2007-2012. GEE methods were used to fit modified Poisson regression models, with a log link function, that included categorical age, race/ethnicity, and body mass index as independent factors and pregnancy (serum quantitative human chorionic gonadotropin >10 mIU/mL) as the outcome of interest. All IUI cycles were analyzed to compare unweighted GEE with cluster-weighted GEE (CWGEE) models accounting for informative cluster size by weighting the GEE score equation by the inverse of the number of IUI cycles for each patient. The CWGEE approach reduced the influence of individuals with a greater number of cycles, resulting in modified estimates of observed associations and/or statistical significance for all characteristics examined (e.g., for age>40 vs. age<35, unweighted GEE risk ratio (RR)=0.56 (95%CI 0.39-0.82) and CWGEE RR=0.62 (95%CI 0.37-1.04)). Thus, informative cluster size may be an important source of bias in studies of IUI and assisted reproductive technology.

### **B34**

DAIRY INTAKE AND FECUNDABILITY IN TWO PRECONCEPTION COHORT STUDIES. LA Wise\*, AK Wesselink, EM Mikkelsen, KA Hahn, KJ Rothman, KL Tucker, VK Knudsen, EE Hatch (Boston University School of Public Health, Boston, MA)
A 2007 study of female nurses reported that high-fat dairy intake was associated with reduced risk of ovulatory infertility. We evaluated the relation of dairy intake to fecundability in two

preconception cohort studies: Snart Foraeldre (SF) in Denmark and Pregnancy Study Online (PRESTO) in North America. In both cohorts, female pregnancy planners completed a validated food frequency questionnaire at baseline. Total, high-fat, and low-fat dairy in cup equivalents/day (PRESTO) and grams/day (SF) were calculated based on reported frequencies. average serving sizes, and standard recipes for mixed foods. Outcome data were updated every 8 weeks for up to 12 months or until clinically-recognized pregnancy. Analyses were restricted to 2.022 women attempting pregnancy for ≤6 cycles at study entry. Fecundability ratios (FR) and 95% CIs were estimated using a proportional probabilities model adjusted for age, education, BMI, physical activity, smoking, multivitamin use, total energy, and race/ethnicity (PRESTO only). Among 1,117 PRESTO participants, FRs for total dairy intake of 1, 2, ≥3 vs. <1 servings/day were 0.99 (Cl: 0.85-1.17), 0.85 (Cl: 0.65-1.10), and 1.41 (Cl: 1.00-1.99), respectively. Among 905 SF participants, FRs for total dairy intake of 300-449, 450-599, and ≥600 vs. <300 g/day were 1.13 (Cl: 0.94-1.37), 1.09 (Cl: 0.88-1.35, and 1.34 (Cl: 1.08-1.66), respectively. Intake of high-fat dairy was not appreciably related to fecundability in either cohort, but low-fat dairy was associated with increased fecundability in SF (≥400 vs. <100 g/day, FR=1.40, CI: 0.93-2.11). Our findings support the hypothesis that high levels of dairy intake improve fertility, but do not support an association between high-fat dairy and fertility. Results for low-fat dairy were inconsistent. Future analyses will involve examination of dairy subtypes (yogurt, cheese) and micronutrients (calcium, phosphorus, lactose).

**DIETARY FAT AND TIME-TO-PREGNANCY**. Tucker KL, Wise LA, Saklani S, Knudsen VK, Mikkelsen EM, Riis AH, Wesselink AK\*, Hahn KA, Rothman KJ, Hatch EE (Boston University School of Public Health, Boston, MA)

The Nurses' Health Study reported that trans fat intake, but not intake of other fats, was associated with increased risk of ovulatory infertility. We evaluated the relation of total, saturated (SAT), monounsaturated (MONO), polyunsaturated (POLY) and trans fatty acid (FA) intakes to fecundability in two preconception cohort studies: Snart Foraeldre (SF) in Denmark and PRESTO in North America. Female pregnancy planners completed a validated food frequency questionnaire at baseline. Outcome data were updated every 8 weeks for up to 12 months or until clinically-recognized pregnancy. Fecundability ratios (FR) and 95% CIs were estimated using proportional probabilities models, adjusted for age, parity, last contraceptive used, education, income, marital status, BMI, physical activity, smoking, and total energy intake. Models were run adjusting for total fat (to interpret relative proportion of each FA subtype) and adjusting for remaining FA (to interpret increases in each FA subtype, holding the rest constant). Among 949 PRESTO participants, there was little association with total fat. MONO and POLY tended to be associated with higher fecundability, while SAT was associated with lower fecundability, but CIs were wide. Trans FA intake was associated with lower fecundability. Relative to <1.3% energy from trans FA, FRs for quartiles with median intakes of 1.4, 1.7 and 2.2% energy from trans fat were 0.81 (Cl: 0.66-0.99), 0.65 (Cl: 0.43-0.98), and 0.53 (Cl: 0.28-0.97), respectively, adjusting total fat and were similar adjusting remaining fat. Among 905 SF participants, FRs for quartiles (median 0.5, 0.6, 0.8% vs. <0.5% energy from trans fat) were 0.94 (CI: 0.75-1.18), 0.88 (CI: 0.56-1.39), and 0.83 (CI: 0.42-1.64), respectively, showing the same trend as in PRESTO. Trans fat intake was lower in Denmark than in the US, which may explain the weaker FRs. Our findings support the hypothesis that higher trans fat intake reduces fertility.

### **B36**

SUBSTANCE USE AND HEALTH DISPARITIES IN HERPES SIMPLEX VIRUS TYPE 2. BD Taylor\*, NM DeGenna, M Perez, P Zhang (Texas A&M Health Science Center, College Station, TX)

Objective: Herpes simplex virus type 2 (HSV-2) is a prevalent sexually transmitted infection that disproportionately affects women and racial minorities. HSV-2 can increase the risk of HIV and infected women have a risk for vertical transmission during pregnancy. Although HSV-2 is linked to several behavioral factors including substance use, it is unknown if HSV-2 risk profiles are consistent across racial/ethnic groups in young adults. Our objective was to explore associations between substance use, race/ethnicity and HSV-2 in a nationally representative population. Methods: We obtained data from 3.436 individuals aged 18-25 who were assayed for HSV-2 antibody from the National Health and Nutrition Examination Survey 2005-2012 cycles. Recreational drug use (marijuana, cocaine, heroin, and methamphetamine) and sexual behavior (sexual debut and multiple sexual partners) were determined using audio computerassisted self-interview. Associations between drug use and HSV-2 were examined using weighted logistic regression adjusting for race/ethnicity, age, gender and sexual behavior. Results: Consistent with other studies, female gender, black race, and early sexual debut were associated with HSV-2 in multivariable models. After adjustments, we found that marijuana use was associated with HSV-2 [odds ratio (OR) 2.8, 95% confidence interval (CI) 1.8-4.5]. There was a significant interaction between race/ethnicity and drug use (p=0.0085). Conclusions: Among young adults, marijuana use, female gender, non-Hispanic black race, and early sexual debut were associated with HSV-2. However, these associations showed some variability among racial/ethnic groups. This is consistent with syndemic theory that health disparities should be examined within analytical frameworks that consider multiple, overlapping categories of risk.

### STRESS AND PRETERM BIRTH: MULTIPLE DOMAINS AND POINTS IN THE LIFE-

**COURSE**. Margerison-Zilko CE, Strutz KL\*, Li Y, Holzman CB (Michigan State University, East Lansing, MI)

Despite proliferative literature investigating "stress" and preterm birth (PTB), few studies consider stressors across multiple domains or life-course periods. We examined multiple stressors in childhood, adulthood, and around the time of pregnancy and PTB. Data were from Pregnancy Outcomes and Community Health (POUCH, 1998-2004), a Michigan pregnancy cohort enrolling women in the 16th-27th week of pregnancy (n=2,559). We assessed stressors during childhood, adulthood, and in the previous 6 months via questionnaire; domains included abuse/witnessing violence (hereafter "abuse"), loss, economic stress, and substance abuse. Stressors during childhood and adulthood were coded as: childhood only, adulthood only, both childhood/adulthood, or neither (reference). Our main outcome was preterm birth (<37 weeks gestation), further categorized as early (≤34 weeks) or late (35-36 weeks) and medically indicated or spontaneous. Our sample was 79% white/other and 21% African American, and mean (SD) age was 27.9(5.1). Stressors in the previous 6 months were not associated with PTB. Abuse during both childhood/adulthood was associated with increased adjusted odds of PTB (aOR 1.3, 95%Cl 0.9,1.9), with a stronger, significant effect among white/other women (aOR 1.6, 95%CI 1.1,2.5). Among all women, abuse in childhood only was associated with late PTB (aOR 1.5, 95%CI 1.0,2.2) while abuse in both childhood/adulthood was associated with early PTB (aOR 1.6, 95%CI 0.9,2.7). Exposure to abuse during childhood and adulthood may increase risk of PTB, with stronger effects among white women, and timing of exposure may differentially affect early vs. late PTB. Improved understanding of these pathways linking stress and PTB may help interrupt them.

### **B38**

### RECENT TRENDS IN GESTATIONAL AGE, FETAL GROWTH AND NEONATAL

**MORTALITY/MORBIDITY IN CANADA**. K.S. Joseph\*, Shiliang Liu, Amy Metcalfe, Sarka Lisonkova, Paromita Deb-Rinker, Reg Sauve, Michael S. Kramer, for the Canadian Perinatal Surveillance System (Public Health Agency of Canada)

Background: Rates of obstetric intervention in Canada have decreased since 2004, when iatrogenic early delivery was responsible for a peak in late preterm and early term birth. We examined temporal trends in gestational age, fetal growth and neonatal mortality/morbidity between 2003 and 2012. Methods: Data on all singleton live births (n=2,560,253) between 33 and 43 weeks in Canada (excluding Quebec) were obtained from the Canadian Institute for Health Information. Small- and large-for-gestational age (SGA; LGA) live births were identified using the Intergrowth-21st standard. Gestational age-specific incidence of birth and composite neonatal mortality/morbidity (i.e., seizures, assisted ventilation or birth asphyxia) was quantified using the fetuses-at-risk approach. Results: Between 2003-04 and 2011-12, live births decreased at 33 weeks (RR 0.93, 95% CI 0.87-0.99) but increased at 37 weeks (RR 1.04, 95% CI 1.02-1.05), 38 weeks (RR 1.12, 95% CI 1.11-1.13), 39 weeks (RR 1.22, 95% CI 1.21-1.23) and 41 weeks (RR 1.37, 95% CI 1.29-1.46). SGA<3rd centile (RR 0.88, 95% CI 0.85-0.92), LGA>97th centile (RR 0.89, 95% CI 0.88-0.90), and neonatal deaths (RR 0.88, 95% CI 0.77-1.01) decreased, while composite neonatal mortality/morbidity (RR 1.01, 95% CI 0.98-1.05) remained unchanged. Changes in neonatal mortality/morbidity occurred at 34 weeks (RR 0.83, 95% CI 0.71-0.95), 37 weeks (RR 1.17, 95% CI 1.03-1.32), 39 weeks (RR 1.18, 95% CI 1.08-1.28) and 40 weeks (RR 1.11, 95% CI 1.04-1.20). Conclusion: Reductions in neonatal mortality and changes in gestational age-specific neonatal mortality/morbidity likely reflect the effect of changes in obstetric intervention at late preterm and term gestation.

THE TIP OF THE ICEBERG: THE PROBLEM OF MISSING DATA IN RACIAL DISPARITIES **OF PRETERM BIRTH**. Sapra KJ\*, Ahrens KA, Chaurasia AK, Hutcheon JA (Eunice Kennedy Shriver National Institute of Child Health and Human Development, Rockville, MD) Epidemiologic studies estimating the effects of preconception risk factors typically compare risks among pregnancies resulting in live births. Excluding pregnancies ending in induced termination may introduce selection bias. We estimated the black-white disparity in preterm birth (PTB) among live births only and after imputing pregnancy outcomes (spontaneous termination, preterm birth, full-term birth) for induced terminations. We used New York City registry records of 1.6 million live births and spontaneous and induced terminations to non-Hispanic white and black women, 2000-2012. We multiply imputed outcomes for induced terminations based on maternal characteristics (race, age, marital status, US/foreign born, parity, payer). Black-white odds of PTB (<37 weeks) was estimated using logistic regression among live births only (complete case analysis) and after multiple imputation. For black and white women, respectively, 56% and 19% of pregnancies ended in induced termination and 13% and 8% of births were preterm. Characteristics associated with PTB were also associated with induced termination (black race, unmarried, US-born). In the complete case analysis, PTB odds were higher in black than white women (OR: 1.73, 95% CI: 1.71-1.75). After imputation, PTB disparity was modestly higher (OR: 1.77, 95% CI: 1.75-1.80). When induced termination rate in white women was weighted to mirror that in black women, PTB disparity was similar to complete case analysis (OR: 1.72, 95%CI: 1.69-1.76). While black-white disparity in PTB among live births is not strikingly different from results following imputation of pregnancy outcomes for induced terminations, our findings highlight PTB risk is influenced by who becomes and remains pregnant.

### **B40**

SMALL FOR GESTATIONAL AGE AND FETOPLACENTAL FETAL RATIO INDEX
COMPARATIVE ACCURACY ASSESSMENT FOR EARLY NEONATAL DEATH. Miguel Angel
Luque-Fernandez\*, Cande V. Ananth, Michelle A. Williams\* (Department of Epidemiology,
Harvard T.H. Chan School of Public Health, Boston, MA)
Background: Small for gestational age (SGA) defines all small infants at birth as intrauterine

Background: Small for gestational age (SGA) defines all small infants at birth as intrauterine growth restricted (IUGR) without distinguishing between those who are constitutionally small from those who are pathologically small. IUGR is highly predictive of early neonatal death (END). We have argued that the fetoplacental ratio index (FPRI), defined as birth weight to placental weight ratio, is an indicator of true IUGR. We compared accuracy of FPRI and SGA as predictors of END. Methods: We completed a diagnostic-accuracy study using data from the US National Collaborative Perinatal Project. We included 39,324 singleton live infants >28 gestation weeks. SGA was defined as a birthweight z-score for gestational age and fetal sex <10th centile. We fitted parametric logit models to derive the area under the curve (AUC) of ROC curves for SGA and FPRI. Models were adjusted for maternal pre-pregnancy body mass index, parity, age, race and infant sex. Results: In total, 361 END cases were reported representing an incidence of 9.2 cases per 1,000 infants (95%CI:8.2, 10.2). FPRI presented higher AUC than SGA (0.80 vs. 0.64, p-value<0.001). FPRI accuracy was good for preterm infants with an AUC:0.84 (95%CI: 0.81, 0.87) and poor among term infants (AUC:0.63, 95%CI:0.58, 0.68). Conclusions: The FPRI demonstrated good accuracy as predictor of END among all infants, and particularly among preterm infants. In low and middle income settings, where ultrasound during pregnancy is not routinely used to identify IUGR, the FPRI at birth may offer a good clinical measure useful for predicting a high risk of END among preterm infants.

DEPRESSIVE SYMPTOMOLOGY, PHYSICAL HEALTH, AND PRETERM BIRTH (PTB) AMONG BLACK WOMEN: THE LIFE-COURSE INFLUENCES ON FETAL ENVIRONMENTS STUDY. Slaughter-Acey, JC\*, Ekshyyan, O, Caldwell CH, Dailey R, Giurgescu, C, Misra, DP (Drexel University College of Nursing & Health Profession, Philadelphia, PA) We sought to examine the relationship between severe depressive symptoms during pregnancy and the rate of preterm birth (PTB) while controlling for women's overall physical health. Data were obtained from a cohort of 1410 Black women in Detroit, Michigan metropolitan area (71% response rate; 16.4% PTB) using maternal interviews and medical record abstraction. The Center for Epidemiologic Studies Depression Scale (CES-D) was used to measure depressive symptomology; women reported how often during the past week they experienced depressive symptoms using a 4-point Likert scale (0-"rarely" to 3-"most or all of the time", range: 0-60). Women were asked to report their overall physical health as excellent, very good, good, fair, or poor. Modified Poisson regression models were used to calculate unadjusted and adjusted prevalence ratios (PR) with 95% confidence intervals (CI). Approximately 20% of women had severe depressive symptoms (score >23). Unadjusted results showed both severe depressive symptoms (PR=1.61, 95% CI: 1.24-2.09) and a lower physical health rating [fair/poor vs. excellent/very good: PR=1.56, 95% CI: 1.14-2.11 were significantly associated with the rate of PTB. Even after adjusting for overall physical health (p=0.01), demographics (maternal age, p=0.07; education, p=0.82; and financial situation, p=0.76), and smoking during pregnancy (p=0.84), prenatal care utilization (p<0.001) and stress (p=0.09); women with severe depressive symptoms were 1.69 times (95% CI: 1.22 - 2.35) more likely to have a PTB than women with mild or moderate depressive symptomology. Our findings suggest that depressive symptoms may affect PTB through multiple pathways.

### **B42**

improve pregnancy outcomes.

MATERNAL DIETARY PATTERNS DURING PREGNANCY AND PRETERM BIRTH. CL Martin\*, D Sotres-Alvarez, AM Siega-Riz (UNC Chapel Hill, Chapel Hill, NC) Preterm birth is one of the leading causes of neonatal morbidity in the United States. Despite decades of research, the etiology is largely unknown. To examine the association between maternal dietary patterns during pregnancy and preterm birth, we used data from the Pregnancy, Infection, and Nutrition (PIN) study (n=3,143). Diet was assessed using a food frequency questionnaire. Patterns were derived using factor analysis and the Dietary Approaches to Stop Hypertension (DASH) eating plan. Associations between dietary patterns and preterm birth were assessed using logistic regression. Four dietary patterns evolved from factor analysis characterized by high intakes of: 1) fruits, vegetables, low fat dairy, high fiber and fortified cereals, non-fried chicken and fish, and wheat bread: 2) beans, corn. French fries. hamburgers, potatoes, fried chicken, mixed dishes, and ice cream; 3) collard greens, coleslaw, red and processed meats, cornbread, whole milk, and Vitamin C-rich drinks; and 4) shellfish, pizza, salty snacks, and refined grains. High adherence to a diet characterized by collard greens, coleslaw, red and processed meats, etc. was associated with a 59% increase in odds of preterm birth (Quartile 4 vs. Quartile 1 adjusted OR: 1.59; 95% CI: 1.10-2.30). Greater adherence to the DASH diet was associated with decreased odds of preterm birth compared to women in the lowest quartile (Quartile 4 vs. Quartile 1 adjusted OR: 0.64; 95% CI: 0.45-0.92). In our study, diet quality during pregnancy is associated with preterm birth and effective periconceptional and early prenatal dietary counseling promoting healthy dietary intake could

PROBABILITY OF LIVE BIRTH BEFORE 28 WEEKS OF GESTATION AFTER DETECTION OF FETAL GROWTH RESTRICTION: A POPULATION STUDY IN FRANCE. I Monier\* and J Zeitlin for the EPIPAGE 2 Study Group (Obstetrical, Perinatal and Pediatric Epidemiology Research Team, Center for Epidemiology and Biostatistics, INSERM U1153, Paris, FRANCE) Objective: Few studies have documented the effects of early antenatal detection of fetal growth restriction (FGR) on obstetric management, pregnancy and neonatal outcomes. We investigated the probability of extremely preterm live birth after detection of FGR before 28 weeks of gestation age (GA). Methods: Data come from the EPIPAGE 2 study, a population-based prospective study of very preterm births in France in 2011. We included singleton fetuses without severe congenital anomalies born between 22 and 27 weeks of GA and detected with FGR, based on ultrasound measurements. We studied four outcomes: termination of pregnancy (TOP), stillbirth, live birth and survival to discharge home. Results: Out of 1616 singletons born between 22 and 27 weeks, 16.6% were detected antenatally with FGR. In 16% of these cases, a TOP was carried out, 28.5% were fetal deaths and 55.5% were live born. The probability of live birth was 25%, 37%, 29% and 61% when detection occurred at 22, 23, 24 and 25 weeks GA respectively versus 95% and 94% at 26 and 27 weeks. Survival after live birth was 60% before 26 weeks GA and 67% between 26 and 27 weeks. However, survival was 22% versus 63% respectively if terminations and stillbirth were considered. Conclusion: There is a thresholdeffect associated with the probability of live birth and survival after early detection of FGR at 26 weeks GA in France. Cross-cohort comparisons of the impact of antenatal detection of FGR on neonatal outcomes must consider differences in practices for managing FGR.

### **B44**

## DOES INFANT SEX PREDICT EARLY BIRTH DIFFERENTLY IN INFANTS OF BLACK AND WHITE PARENTS? McGill University, Montreal, QC, Canada

Although more boys than girls are born preterm, previous reports suggest that little or no preterm male excess is seen in Black infants. I examined the association between male sex and birth before 34 completed weeks in singleton US infants born between 2004 and 2008 to White and Black parents, taking father's race into consideration. After "cleaning" gestational age, there were 15,138,553 live births for analysis. Of these, 63.4% had two White parents (WW), 1.9% had a White mother and a Black father (WB), 0.6% had a Black mother and a White father (BW), and 8.9% had two Black parents. The percent of birth before 34 weeks (VPTB) was 1.6, 2.3, 3.0, and 3.9 in WW, WB, BW and BB infants, respectively. Male sex was associated with an OR of 1.20 (95% CI: 1.19, 1.21) for VPTB in WW babies, 1.15 (1.10, 1.20) in WB babies, 1.09 (1.02, 1.16) in BW babies, and 1.02 (1.00, 1.03) in BB babies. Among these very preterm infants, the percent of neonatal death was 10.1, 10.5, 12.6, and 12.5 in WW, WB, BW, and BB babies, respectively. Being male was more strongly associated with neonatal death when the mother was Black. These results corroborate previous findings that male sex is more weakly associated with preterm birth in Blacks, and suggest a possible role of father's race. In Blacks, male sex was less predictive of birth before 34 weeks, but was more strongly associated with neonatal death, especially when the mother was Black.

# UNRAVELING THE "HISPANIC PARADOX": DISPARITIES IN DELIVERY CHARACTERISTICS AND BIRTH OUTCOMES BY HISPANIC ETHNIC SUBGROUPS. KL

Downes\*(University of Maryland, Department of Family Science, College Park, MD) The "Hispanic Paradox" is well-documented, but recent studies have noted variation by ethnic subgroups and nativity. The purpose of this study was to compare delivery characteristics and birth outcomes among Mexican, Puerto Rican and Cuban ethnic subgroups, in contrast to non-Hispanic white women. The 2013 national vital statistics were used to examine cesarean delivery (CD) and induction/augmentation of labor, low birth weight, preterm birth, prolonged ventilation, neonatal intensive care unit (NICU) admission and use of surfactants among the specified groups. Group comparisons were performed with chi-square tests. A total of 2,752,742 births were available within the specified groups: Mexican (19.8%), Puerto Rican (2.5%), Cuban (0.7%), and non-Hispanic white (77.1%). Compared to white women. CD was higher among Cuban (32.0% vs 48.2%, p<0.001) and Puerto Rican women (32.0% vs 34.2%, p<0.001), but lower among Mexican women (32.0% vs 30.9%, p<0.001). Compared to white women, preterm birth was higher among both Puerto Rican (10.2% vs 13.0%, p<0.001) and Cuban women (10.2% vs 14.2%, p<0.001). The pattern of group differences remained after stratifying by nativity, but foreign-born women of all Hispanic ethnic subgroups tend to have more favorable birth outcomes compared to women in the same subgroups that are born within the U.S. The "Hispanic Paradox" is not a uniform phenomenon. Women who identify as Puerto Rican or Cuban may represent a higher risk subgroup; additional studies are needed to more fully understand the nature of these differences and the underlying mechanisms.

### **B46**

# DOES NEIGHBORHOOD RACIAL SEGREGATION INFLUENCE PRETERM BIRTH ACROSS THE LIFE COURSE? AN APPLICATION OF MARGINAL STRUCTURAL MODELS.. TL

Osypuk\*, NM Schmidt, R Kehm, R Platt, DP Misra. (University of Minnesota, Minneapolis, MN 55454)

Racial residential segregation and neighborhood racial composition are linked to birth outcomes. However few studies focus on preterm birth (PTB), and most evidence is based on cross-sectional evidence at time of the birth. We leverage data from the Life-course Influences on Fetal Environments (LIFE) study, of 394 Black women who gave birth 2009-2011 in a Detroit-area hospital, linked to survey data from their mothers (the grandmothers). We use medical records, survey data, and geocoded residential histories linked to historical Census data (1970-2010), to reconstruct women's earlier life course. We test whether neighborhood racial composition, census tract % black (dichotomized at 75%), at various times, is associated with PTB (birth before 37th completed week of gestation), using marginal structural models/inverse probability weights in Poisson regression. Such methods accommodate timevarying exposures, and covariates that are simultaneously confounders and mediators. We model time-varying exposures (tract % black) and covariates at 4 times: woman's own birth, age 10, age 18, and her child's birth. Covariates include body weight, 5 SES socioeconomic-status measures, tract % poverty, and 4 confounders at childbirth. After testing different life course models, we find support for a trigger effect; living in high (vs. low) % black neighborhoods at the time of her child's birth is associated with 89% higher PTB risk (RR= 1.89, 95%CI: 1.14-3.12). Yet segregation other time periods is not associated with PTB. Our results suggest that neighborhood segregation is most relevant for PTB at the time of the birth as opposed to at earlier life course periods.

### SEX-SPECIFIC ASSOCIATIONS OF PLACENTAL CADMIUM AND INFANT BIRTH SIZE.

Hensley MD\*, Tadesse MG, Mohanty AF, Williams MA, Enquobahrie DA (University of Washington, Seattle, WA)

Background: Higher maternal urinary cadmium (Cd) has been associated with reduced fetal growth, particularly among females. The effect of maternal Cd burden on the fetus may involve the placenta, a major component of the intrauterine environment. The placenta bioaccumulates Cd and serves as an efficient but imperfect barrier to fetal Cd exposure. We investigated infant sex-specific associations of placental Cd and birthweight. Methods: Placental samples were collected at delivery from participants (N=544) of a pregnancy cohort. Placental Cd was measured using Agilent 7500 ICP-MS. Information on birth weight was abstracted from medical records. Participants were categorized into infant-sex specific placental Cd quartiles. Multivariable linear regression models were used to examine associations between placental Cd and birth weight, adjusted for maternal age, race/ethnicity, body mass index, preeclampsia, gestational diabetes, and smoking history. Results: Medians of placental Cd for male and female infants were 0.0037ng/mg and 0.0034ng/mg, respectively. Among males, infants in the upper quartiles for placental Cd had 360.5g (quartile 2), 148.9g (quartile 3), and 372.9g (quartile 4) lower birth weights, compared with infants in the lowest quartile (trend p-value=0.017). We did not observe similar associations among female infants. Corresponding estimates for quartiles 2, 3, and 4, compared with quartile 1, were -2.4g, -184.0g, and 25.5g (trend pvalue=0.746). Conclusions: Placental Cd is inversely associated with birth weight among male infants, but not female infants. This contrasts with previous reports of urinary Cd-birth weight associations among females. Inconsistencies between these associations and underlying mechanisms are potential areas of future research.

### **B48**

**GLYCEMIA IN PREGNANCY AND GESTATIONAL AGE AND FETAL SIZE AT BIRTH**. SL Rifas-Shiman\*, MF Hivert, EM Eggleston, K Kleinman, RL Smith, S Norris, MW Gillman (Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA) How to screen for gestational diabetes (GDM), which is increasing worldwide, is controversial. Many now favor a 1-step-75g OGTT over the 2-step-50g glycemic challenge (GCT) followed by 100g OGTT among those who "failed" GCT. Among 2067 mother-child pairs in the pre-birth cohort Project Viva, we examined associations of 2nd trimester glycemia, in 4 categories from the 2-step approach, with gestational age and size at birth. We used multivariable linear and logistic regression, adjusted for socio-demographics and pre-pregnancy BMI. Mean(SD) BMI was 24.8(5.5); 67% were white. 5.7% had GDM (failed >2/4 OGTT cutpoints), 3.1% had impaired glucose tolerance (IGT; failed 1 OGTT cutpoint), 8.7% had isolated hyperglycemia (IH; failed GCT/normal OGTT) and 82.5% had normal glucose. Mean(SD) GA was 39.5wk(1.7) and BW/GA-z-score was 0.17(0.97); 6.6% were preterm (<37wk) and 13.6% were large-forgestational-age (LGA). Compared with normoglycemic mothers, offspring of GDM mothers had shorter GA (β -0.64wk; 95%CI -0.97,-0.32) and higher risk of preterm (OR 1.69; 0.91,3.15). Estimates for IGT and IH were β -0.03wk (-0.45,0.40) and OR 0.74 (0.23,2.42) and 0.03wk (-0.23,0.28) and 0.96 (0.49,1.89), respectively. GDM was associated with higher BW/GA-z (B 0.27; 0.10,0.45) and LGA (OR 1.99; 1.15,3.46). Estimates for IGT and IH were β 0.16 (-0.07,0.39) and OR 1.40 (0.70,2.81) and 0.21 (0.07,0.35) and 1.59 (1.04,2.43), respectively. In summary, GDM was associated with fetal overgrowth and higher risk of preterm delivery, IH with fetal overgrowth, and IGT with neither. These findings suggest that 2-step GDM-screening may reveal subtle difference in risk of preterm birth and altered fetal growth.

MATERNAL OBESITY AND FETAL GROWTH: FINDINGS FROM THE NICHD FETAL GROWTH STUDIES. Cuilin Zhang\*, Paul S. Albert, Jagteshwar Grewal, Anthony Sciscione, Deborah A. Wing, William Grobman, Roger Newman, Ronald Wapner, Mary E. D'Alton, Daniel Skupski, Angela Ranzini, John Owen, Edward K. Chien, Sabrina Craigo, Mary L. Hediger, Sungduk Kim, Katherine L. Grantz, Germaine M. Buck Louis (Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Rockville, MD, USA)

Despite the escalating prevalence of pre-gravid obesity, systematic data regarding its effect on fetal growth, especially in the absence of major chronic diseases, are sparse. We aimed to investigate this effect and determine whether it varies by racial/ethnic groups in a prospective cohort of 441 healthy obese (pre-pregnancy BMI 30-45kg/m2) women, without chronic diseases such as hypertension and diabetes, and 2.161 healthy non-obese women, all with singleton pregnancies recruited from 12 centers (2010-2013). Women were enrolled at 8w0d-13w6d and randomized among four 2D/3D ultrasonology schedules (in the 2nd and 3rd trimesters) for longitudinal fetal measures. Growth curves were estimated using linear mixed models with cubic splines. Median differences at each gestational week between obese and non-obese cohorts were examined using likelihood ratio and Wald tests after the adjustment for maternal characteristics. The median bone (humerus and femur) length, estimated fetal weight (EFW), and abdominal circumference (AC) for obese women became greater than the non-obese cohort's at 20, 29 and 38 gestational weeks, respectively. For example, median EFW and AC at 38 weeks for obese vs. non-obese women was 3217 vs. 3146 grams, and 342 vs. 339 mm, respectively (P < 0.05). Race/ethnicity significantly modified the association with bone length, EFW, AC and head circumference (HC). For instance, median HC was significantly larger in obese cohort than the non-obese only among whites during 32 - 39 weeks. In conclusion, fetal growth differs between the pregnancies of healthy obese and non-obese women, and such differences vary in timing of onset and by race/ethnicity.

### **B50**

NEWBORN BIRTH WEIGHT FOR GESTATIONAL AGE IN CANADA BASED ON THE INTERGROWTH-21ST STANDARD. Shiliang Liu,\* Amy Metcalfe, Juan Andrés León, Reg Sauve, Michael S. Kramer, K.S. Joseph

Background: The INTERGROWTH-21st project recently published an international standard for newborn size using a rigorous methodology. We examined the frequency of small and large birth-weight-for-gestational age live births and associated neonatal mortality/morbidity rates using this standard. Methods: Data on all singleton live births in Canada (excluding Quebec) between 2002 and 2012 were obtained from the Canadian Institute for Health Information. including gestational age (obstetric estimate), birth weight, diagnoses and interventions. We classified live births between 33 and 43 weeks gestation into birth weight centile categories and quantified associated rates of composite neonatal mortality/morbidity (i.e., seizures, assisted ventilation rates or birth asphyxia). Results: Of 2,753,817 singleton live births, 0.87% (95% CI 0.86-0.88), 2.6% (95% CI 2.6-2.6), 14.2% (95% CI 14.1-14.2) and 9.6% (95% CI 9.6-9.6) were categorized as being in the <3rd, 3rd to <10th, >90th to 97th and >97th centiles, respectively. Composite neonatal mortality/morbidity rates were 46.4 (95% CI 43.8-49.1) per 1000 live births in the <3rd centile category, 23.0 (95% CI 22.0-24.2) at 3rd to <10th, 14.2 (95% CI 13.9-14.5) at 10th to 50th, 11.5 (95% CI 11.3-11.7) at 50th to 90th, 10.7 (95% CI 10.4-11.0) at >90th to 97th and 12.9 (95% CI 12.5-13.4) in the >97th centile category. Conclusion: Neonatal mortality/morbidity patterns were as expected. The surprisingly low rates of live births <10th centile and high rates of live births >90thth centile imply the need to re-evaluate fetal growth status in populations, and ensure adequate obstetric management and neonatal care.

LOW BIRTH WEIGHT AMONG DETAILED RACIAL AND ETHNIC GROUPS BY MATERNAL COUNTRY OF ORIGIN. PD Wartko\*, E Wong, DA Enquobahrie (University of Washington School of Public Health, Seattle, WA)

Background: Disparities in low birth weight (LBW) incidence by racial/ethnic group are well known. However, the extent of differences in LBW by maternal country/region of origin within racial/ethnic groups in the Pacific Northwest is not known. Methods: We conducted a population-based study of LBW using 122,393 live birth records from King County, Washington from 2008-2012. We assessed risk for LBW (<2,500 g) by mother's country/region of origin (birthplace) categorized using the United Nation's Millennium Development Goals Regional Groupings within racial/ethnic groups (Asian, black, Native Hawaiian/Pacific Islander, and white). Risk was estimated using odds ratios (ORs) and 95% confidence intervals (CIs) from multivariable logistic regression, adjusted for demographic and reproductive characteristics. Results: Compared with white women, black and Asian women had a 1.93-fold (95% CI:1.76-2.11) and 1.60-fold (95% CI:1.50-1.72) higher risk of having a LBW infant, respectively. Women from Sub-Saharan Africa were less likely to have a LBW infant than US-born blacks (OR 0.62, 95% CI:0.52-0.74). Risk of LBW was lower for women from Eastern Asia, compared with USborn Asians (OR 0.75, 95% CI 0.64, 0.89). LBW was more likely in women from Southern Asia and South-Eastern Asia than in US-born Asians (OR 1.22, 95% CI:1.04-1.44 and OR 1.29, 95% CI:1.07-1.55, respectively). Conclusions: We found that incidence of low birth weight differed in King County, Washington by country/region of origin within racial groups, particularly among blacks and Asians. Factors contributing to these differences, such as weathering, are potential areas of research for planning and implementing interventions to improve LBW incidence.

### **B52**

DOES GESTATIONAL AGE AT BIRTH MEDIATE THE RELATIONSHIP BETWEEN MATERNAL SMOKING DURING PREGNANCY AND NEONATAL DEATH? . Seaward AVC\*,

Basso O, Kaufman JS, Platt RW (McGill University, Montreal, Canada) An intermediate variable lies on the causal pathway between exposure and outcome. Previously, the standard method for identifying direct and indirect effects was through conditioning on the intermediate, but biases can arise from this conditioning. The objective of this preliminary study was to determine if gestational age at birth (GA) mediates the relationship between maternal smoking during pregnancy and neonatal death, using the US Vital Statistics 2006 birth cohort linked birth/infant death dataset. Singleton live births with no reported congenital anomalies were included in final analyses (n=4,038,603). Maternal smoking during pregnancy was classified as never smoker vs. smoker. GA was classified as term (≥37 weeks) vs. preterm (<37 weeks). Neonatal death was defined as infant death <28 days. Log-Poisson regression models were used to estimate the total effect of maternal smoking on neonatal death and the direct effect by conventional methods. Log-Poisson marginal structural models with inverse probability weighting were used to estimate the controlled direct effect (setting GA to term). All models were adjusted for maternal age, race, marital status, and medical risk factors. The total effect of smoking on neonatal death, the direct effect estimated by standard methods and the controlled direct effect estimated using MSMs were all very similar (adjusted risk ratio 0.998, 95% CI: 0.997, 0.998). Results from this study suggest that preterm birth does not mediate the effect of maternal smoking on neonatal death; however, future studies should focus on modeling gestational age at different cut-offs as well as the impact of unmeasured confounding.

INVESTIGATING THE CHANGING TIDE IN US PRETERM BIRTH RATES: AN AGE-PERIOD-COHORT ANALYSIS. Miles GL\*, Wilder JR, Chapman DA (University of North Carolina Chapel Hill Gillings School of Global Public Health)

After steadily increasing for several decades, the rate of preterm birth (live birth at <37 completed weeks gestation) in the US began to decline in 2006. We sought to determine whether this trend reversal can be explained by birth cohort effects. Using 1985-2013 US natality data, we conducted an age-period-cohort analysis of preterm delivery among first births to white and black mothers (N=41,013,331) using the median polish method. This method isolates cohort effects by removing the effects of age and period from contingency table data through a series of iterative steps. Delivery years and maternal ages were collapsed into 5-year groups producing 12 synthetic birth cohorts (e.g. 1940-1944, 1945-1949...1995-1999). The median polish residuals were regressed on birth cohort indicators to produce relative estimates of cohort effects (prevalence ratios and 95% confidence intervals) using the 1960-1964 birth cohort as a reference. Strong effects of both age and period (year of delivery) on the prevalence of preterm birth were observed across both races in stratified analysis. Compared to the referent cohort, the 1940-1944 birth cohort of white women were more likely to have a first birth result from a preterm delivery (1.11 [1.05, 1.18]). In contrast, earlier cohorts of nulliparous black women were less likely to deliver preterm (1940-1944: 0.79 [0.73, 0.85]; 1945-1949: 0.94 [0.89, 0.99]; 1950-1954: 0.95 [0.91, 0.99]). These findings point to racial differences in the effect of birth cohort prior to 1955, but do not provide evidence that recent trends in preterm birth are due to cohort effects.

### **B54**

ANTI-MÜLLERIAN HORMONE IS NOT ASSOCIATED WITH PREGNANCY LOSS. Zarek SM\*, Mitchell EM, Sjaarda LA, Silver RM, Wactawski-Wende J, Townsend JM, Lynch AM, Lesher LL, Stanford JB, Galai N, Faraggi D, Schliep KC, Plowden TP, Radin RG, Kalwerisky RA, Perkins NJ, DeCherney AH, Mumford SL, Schisterman EF (National Institutes of Health, Bethesda, MD) Background: The association of anti-Müllerian hormone (AMH), a marker of ovarian reserve. and pregnancy loss is understudied. Methods: Fertile women (n=1228) attempting pregnancy with one to two prior pregnancy losses participated. Preconception AMH levels were categorized as low (<1.25 ng/mL), normal (referent group, 1.25 to 4.0 ng/mL), and high (>4.0 ng/mL) based on clinically relevant cut-points. Log binomial model with robust variance assessed RR for pregnancy loss (prevalence 12%), adjusting for age and BMI. Analyses were repeated within three domains of reproductive history, stratified across 1) history of 1 or 2 prior pregnancy losses, 2) time since most recent loss of ≤ 1 or >1 year, and 3) history of 0 or ≥1 prior live birth. Results: There were no significant associations observed between low or high versus normal AMH levels and pregnancy loss among women with 1 (Low AMH: RR, 1.14, 95% CI 0.7, 1.8; High AMH: RR 1.09, 95% CI 0.8, 1.5) or 2 (Low: RR, 1.44, CI 0.8, 2.3; High: RR 1.06, CI 0.6, 1.7) prior pregnancy losses. Similarly, no associations were observed when women were stratified by time since most recent loss or by history of live birth, with the exception of a higher risk of pregnancy loss with low versus normal AMH (RR 1.39, CI 1.1, 1.9) among women with a history of 2 prior pregnancy losses and/or at least one prior live birth. Conclusion: In fertile women with a history of loss, AMH was not consistently associated with risk of subsequent pregnancy loss.

**PATERNAL EDUCATION AND BIRTH OUTCOMES IN CANADA**. Shapiro GD\*, Kramer MS, Kaufman JS, Bushnik T, Sheppard AJ, Wilkins R, Tjepkema M, Yang S (McGill University, Montreal)

Background: Research on predictors of adverse birth outcomes has focused on maternal characteristics. Less is known about the role of paternal factors. Paternal education is an important socioeconomic marker that may predict birth outcomes over and above maternal socioeconomic indicators. Objective: To measure the role of paternal education in the prediction of preterm birth (PTB), small-for-gestational-age (SGA) birth, stillbirth and infant mortality in Canada, controlling for maternal characteristics. Methods: We analyzed the 2006 Canadian Birth-Census Cohort, a cohort of births between May 2004 and May 2006 created by linking Canadian birth/infant death registration data with a 20% sample completing the 2006 Canadian census. Paternal education level was taken from the census and categorized as less than high school, completed high school, some university, or completed university degree or higher. Birth outcomes were obtained from the birth registration data. Binomial regression was used to estimate risk ratios and 95% CIs for adverse birth outcomes associated with paternal education, after controlling for maternal education, age, marital status, parity, ethnicity, nativity and household income. Results: 135,426 births were included in the cohort, with data on paternal education available for 117,012 (86%). Comparing the highest to the lowest education category, adjusted RRs (95% CI) were 0.90 (0.82-0.97) for PTB, 0.91 (0.84-0.99) for SGA birth, 0.57 (0.40-0.80) for stillbirth and 0.62 (0.42-0.91) for infant mortality. Conclusions: Our study suggests that paternal education predicts adverse birth outcomes, independently from maternal characteristics.

### **B56**

**DOES GESTATIONAL AGE REPORTED ON THE FETAL DEATH CERTIFICATE PROVIDE AN ESTIMATE OF THE GESTATIONAL AGE AT DEATH?** Christiansen-Lindquist L\*, Hogue CJR, Silver RM, Parker CB, Dudley DJ, Coustan DR, Koch MA, Kramer MR, Reddy UM, Saade GR, Willinger M

OBJECTIVE: To determine whether gestational age reported on fetal death certificates (GA FDC) estimates the gestational age at death (GA Death), and whether differences between these values vary by maternal and delivery characteristics. METHODS: Singleton stillbirths enrolled in the Stillbirth Collaborative Research Network's (SCRN) case-control study of stillbirth in Georgia and Utah were linked to fetal death certificates. GA\_FDC was compared to SCRN's algorithm-derived estimate of GA\_Death. The difference between these values was categorized, and chi-square and ANOVA tests were used to determine whether the distribution of these categories varied by maternal and delivery characteristics. RESULTS: The difference between GA FDC and GA Death was 0 or 1 week for 36% and 30% of stillbirths, respectively. In 18.5% of the cases, GA FDC overestimated GA Death by 2 or more weeks (range: 2-17). This difference was not associated with county of residence, maternal age, race/ethnicity, or when the death occurred relative to labor initiation. This difference was associated with the gestational age at delivery (as reported by SCRN), such that losses delivered between 20 and 27 weeks' gestation were more likely to have GA FDC overestimate GA Death, and losses delivered after 27 weeks' gestation were more likely to have GA FDC underestimate GA\_Death. CONCLUSIONS: The lack of association between the difference between GA\_FDC and GA Death and the timing of the death relative to labor initiation suggests that dating of all stillbirths needs improvement. These improvements will benefit families, physicians, and researchers by aiding investigations into cause(s) of death, management of subsequent pregnancies, and improving stillbirth surveillance.

TWINS LESS FREQUENT THAN EXPECTED AMONG MALE BIRTHS IN RISK AVERSE POPULATIONS.. Deborah Karasek\*, Julia Goodman, Alison Gemmill, April Falconi (University of California, Berkeley, CA), Terry Hartig (Uppsala University, Uppsala, Sweden) Aristotle Magganas, Ralph Catalano (University of California, Berkeley, CA) Male twin gestations exhibit higher incidence of fetal morbidity and mortality than singleton gestations. From an evolutionary perspective, the relatively high rates of infant and child mortality among male twins born into threatening environments reduce the fitness of these gestations, making them more vulnerable to fetal loss. Women do not perceive choosing to spontaneously abort gestations although the outcome may result from estimates, made without awareness, of the risks of continuing a pregnancy. Here we examine whether the non-conscious decisional biology of gestation can be linked to conscious risk aversion. We test this speculation by measuring the association between household surveys in Sweden that gauge financial risk aversion in the population and the frequency of twins among live male births. We use timeseries regression methods to estimate our suspected associations and Box-Jenkins modeling to ensure that autocorrelation does not confound the estimation or reduce its efficiency. We find, consistent with theory, that financial risk aversion in the population correlates inversely with the odds of a twin among Swedish males born two months later. The odds of a twin among males falls by approximately 3.5% two months after unexpectedly great risk aversion in the population. This work implies that economic downturn or other shocks that affect population risk aversion carry implications for fetal loss in vulnerable pregnancies.

### **B58**

**BED-SHARING IN THE TEXAS-MEXICO BORDER REGION**. JA McDonald\*, L Zhu, A Amatya (New Mexico State University, Las Cruces, NM)

INTRODUCTION: Parental-infant bedsharing is associated with increased risk of Sudden Infant Death Syndrome (SIDS); the American Academy of Pediatrics (AAP) has recommended against the practice since 2005. SIDS risk is lower, however, among Hispanic/Latino infants than other infants, while bedsharing is more common. Moreover, because breastfeeding and other healthy behaviors are also associated with bedsharing, the AAP recommendation is controversial. In Hispanic communities along the Texas-Mexico border, efforts to increase breastfeeding are underway, yet little is known about the prevalence of bedsharing and its relationship with breastfeeding and related factors. OBJECTIVES: To determine the prevalence of infant bedsharing by Hispanic mothers in Texas-Mexico border counties and identify behavioral and demographic factors that are associated with it. METHODS: Data from 2009-2010 Texas Pregnancy Risk Assessment Monitoring System were used to measure the weighted frequency of bedsharing and 20 covariates among 516 Hispanic respondents in Mexico border counties. We used unadjusted and adjusted ORs to measure the associations. Interactions between important covariates were tested. RESULTS: Always/often bedsharing was reported by 41.3% (35.0-47.7) of women. In unadjusted analyses, only ORs for low income, recent smoking, not drinking and current breastfeeding were significantly elevated (2.3-2.9;p<.05). After adjustment, women not drinking had higher odds of bedsharing than drinking women (OR=2.2;1.2-4.3) and women who breastfed and smoked had especially high odds compared to women who did neither (OR=35.3;8.7-142.9). CONCLUSION: Given the high prevalence of bedsharing and the known benefits of breastfeeding, stopping bedsharing to prevent SIDS might have unintended consequences. Focusing on smoking prevention may be more important in this population.

**PREGNANCY LOSS AMONG US WOMEN: 1991-2011.** Branum AM, Ahrens KA, Rossen LM (Reproductive Statistics Branch, Division of Vital Statistics, National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, MD)

Pregnancy loss can take a physical and emotional toll on women and their families. Etiologies are often elusive and valid population estimates of pregnancy loss are important for public health and related research efforts; however, descriptions of pregnancy loss from a populationbased sample of US women are lacking. We examined self-reported data on early (<12 weeks) and late (12+ weeks) pregnancy loss for over 23,000 pregnancies occurring during 1991-2011, as reported in the 2006-2010 and 2011-2013 National Survey of Family Growth among women 15-44 years at the time of interview. For the 2006-2010 respondents, after adjusting for maternal age and marital status at the time of pregnancy, 18.7% (SE: 0.7) of pregnancies resulted in pregnancy loss; for the 2011-2013 respondents 19.8% (SE: 0.9) resulted in loss (p=0.35). Risk of pregnancy loss differed by age (p<0.0001) and poverty level (p<0.0001) with women aged 35-44 reporting the highest loss (28.1%, SE: 1.5) as well as those living at 400% or greater percentage of poverty level (26.8%, SE: 1.6). Risks differed by race (p=0.0001) and were lowest among Hispanic women (14.4%, SE: 0.9). After adjusting for maternal age, marital status at the time of pregnancy, education, poverty level, race, and gravidity, there was a slight but significant increase in reported pregnancy loss over time from 1991-2011 (RR=1.02, 95% CI: 1.01, 1.03); which was concurrent with an increase in early pregnancy loss (RR=1.02, 95% CI: 1.01, 1.04). There was no significant increase in late pregnancy loss observed. Further exploration of these trends is warranted.

### **B60**

**GESTATIONAL WEIGHT GAIN AND RISK OF STILLBIRTH IN A POPULATION-BASED COHORT.** Freese KE\*, Abrams B, Hutcheon JA, Parisi SM, Bodnar LM (University of Pittsburgh, PA)

When the Institute of Medicine published revised gestational weight gain (GWG) guidelines in 2009, little was known about whether maternal weight gain was associated with fetal death. Our objective was to describe the relationship between GWG and the incidence of stillbirth in a population-based cohort. We used records from all births and fetal deaths in Pennsylvania from 2006-2011 (n=835,972). Stillbirth was defined as intrauterine fetal death at ≥20 weeks' gestation. Weight gain was classified based on BMI- and gestational-age-specific z-score charts. We classified GWG as a gestational age- and BMI-specific z-score, categorized as <-1, -1 to +1, or >+1 standard deviation (SD). Multivariable logistic regression models were used to assess the association between GWG and stillbirth by BMI category, while adjusting for maternal race/ethnicity, smoking, education, and other confounders. The overall risk of stillbirth was 5.3 per 1,000 births, and increased as BMI rose from normal weight (4.3/1,000) to obese class 3 (9.4/ 1.000), GWG z-score <-1SD was associated with an increased risk of stillbirth compared with z-score -1 to 1 SD among underweight (adjusted OR (95% CI): 2.2 (1.5, 3.3)), normal weight (1.7 (1.5, 1.9)), overweight (1.4 (1.2, 1.6)), obese class 1 (1.3 (1.1, 1.7)) and obese class 3 (1.7 (1.1, 2.5)). The threshold for -1SD corresponded to 10kg, 11kg, 9kg, 5kg, and -2kg in these respective BMI categories. GWG >+1SD was not significantly associated with stillbirth in any BMI group. These results suggest that stillbirth should be considered an important outcome when determining optimal GWG recommendations.

PREGNANCY LOSS ASSOCIATED WITH FIRST TRIMESTER NAUSEA AND VOMITING. SN Hinkle\*, SL Mumford, EF Schisterman, EM Mitchell, LA Sjaarda, KC Schliep, NJ Perkins, RG Radin, RM Silver, LL Lesher, JM Townsend, AM Lynch, J Wactawski-Wende, N Galai, D Faraggi, KL Grantz (Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH, Bethesda, MD) Nausea and vomiting during pregnancy have been associated with a reduced risk for pregnancy loss. However, prior studies may be subject to selection bias due to late enrollment missing early losses. In a preconception cohort of women with 1-2 prior losses (EAGeR; n=784), we evaluated the association between first trimester nausea and vomiting and pregnancy loss. Nausea and vomiting were self-reported in daily diaries during gestational weeks 2-5 (n=388) and/or by questionnaire at ~12 weeks regarding symptoms in the past 4 weeks (n=563). Ageadjusted log-binomial regression was used with multiple imputation for missing exposure to account for potential selection bias due to truncation. Pregnancy outcome was available for all women, with 189 (24.1%) having a loss. Nausea or vomiting were less common at 2-5 (n=178, 44.3%), but common at 12 weeks (n=508, 90.2%). Women who reported nausea only [RR=1.00 (95%CI 0.63; 1.58); RR=0.73 (95% CI 0.31, 1.72)] or vomiting [RR=0.96 (0.44, 2.08); [RR=0.53 (0.23, 1.23)] at 2-5 or 12 weeks were not at an increased risk for loss compared to neither. respectively. Sensitivity analyses assessed informative nausea/vomiting missingness (no missing outcome); 100% and 92% of RRs were not significant for 2-5 or 12 weeks, respectively. In this preconception cohort, early nausea or vomiting was not associated with loss, and symptoms later in the first trimester are unlikely to be significantly associated with loss. Future preconception studies with more frequent symptom assessment to reduce truncation bias will provide a more conclusive understanding of the consequences of nausea or vomiting after 5 weeks.

### **B62**

PREPREGNANCY OBESITY AND RISK OF STILLBIRTH. Carmichael SL\*, Blumenfeld YJ, Mayo J, Wei E, Gould JB, Stevenson DK, Shaw GM, on behalf of the March of Dimes Prematurity Research Center at Stanford University School of Medicine (Stanford University, Stanford, CA)

We examined the association of maternal obesity with risk of stillbirth, focusing on whether the pattern of results varied by gestational age or maternal race-ethnicity or parity. Analyses included 4,012 stillbirths and 1,121,234 liveborn infants delivered in California from 2007-2010. We excluded stillbirths due to congenital anomalies and women with hypertensive disorders or diabetes, to focus on fetuses and women without these known contributing conditions. We used Poisson regression to estimate relative risks (RR) and 95% confidence intervals (CI). Separate models were run for stillbirths delivered at 20-23, 24-27, 28-31, 32-36, 37-41 weeks, relative to liveborn deliveries at 37-41 weeks. For stillbirth at 20-23 weeks, RRs were elevated for all raceethnicity and parity groups. The RR for a 20-unit change in BMI (which reflects the approximate BMI difference between a normal weight and an Obese III woman) was 3.5 (95% CI 2.2, 5.6) for nulliparous white women and ranged from 1.8 to 5.0 for other sub-groups. At 24-27 weeks, the association was significant (p<0.05) only for multiparous non-Hispanic whites: at 28-31 weeks. for multiparous whites and nulliparous whites and blacks; at 32-36 weeks, for multiparous whites and nulliparous blacks; and at 37-41 weeks, for all groups except nulliparous blacks. The pattern of results was similar when restricted to stillbirths due to unknown causes and somewhat stronger when restricted to stillbirths attributable to obstetric causes. In conclusion, increased risks were observed across all gestational ages, and some evidence of heterogeneity of the associations was observed by race-ethnicity and parity.

**EXPLORING INFANT SLEEP ENVIRONMENTS AMONG MOTHERS**. Shah DA\*, Raines-Milenkov AL, Habiba NM, Middlemiss W, Roane BM, Bowman WP (University of North Texas Health Science Center, Fort Worth, TX)

Background: Mothers receive postnatal education for infant care before hospital discharge and from a pediatrician. However, it may not be sufficient to educate parents on the importance of a safe sleep environment. A safe sleep environment includes: always placing infant on the back to sleep, having a separate sleep place for the infant, removing all objects from sleep space, and avoiding infant's exposure to smoking. Methods: In-person surveys were administered by research personnel to mothers 18 years or older with infants aged 2 weeks to 3 months during their UNTHSC-Pediatric Outpatient Clinic visits. Results: Of 103 mothers, 46 (44.7%) mothers surveyed were Hispanic, 28 (27.2%) were White/Caucasian, and 18 (17.5%) were Black/African-American. Our survey showed that 73 (70.9%) infants started sleeping in a crib in mother's room; however, 38 (36.9%) slept in mother's bed at some point during the night and 26 (25.2%) infants usually awoke in mother's bed. About a quarter of mothers, 25 (24.3%) put their baby to sleep on either side or prone position. Few of infants, 11 (10.7%) slept with a pillow, or bumpers. Most of mothers, 86 (83.5%) reported that no one is allowed to smoke anywhere inside their home. Conclusions: Understanding parents' practices related to their infant sleep environment can contribute to the creation of targeted patient education on the importance of safe sleep environment for newborns. Pediatricians should address the risk of bed-sharing, prone and side sleep positions, inconsistent sleep environment and having objects in infants sleep space with their patients.

### **B64**

EARLY GESTATIONAL WEIGHT GAIN IS ASSOCIATED WITH GESTATIONAL

HYPERTENSION. Lujing Zhan, Jihong Liu\*, Bo Cai, Anwar T. Merchant, Xuemei Sui (Department of Epidemiology and Biostatistics, University of South Carolina, Columbia, SC) Gestational hypertension, the most common complication during pregnancy, has increased 1.8 times from 1987 to 2004. Findings on the association between gestational weight gain (GWG) and gestational hypertension are inconsistent. Our study investigated the association between the trajectories of GWG during early pregnancy (8-20 weeks gestation) and the subsequent development of gestational hypertension and blood pressure change. Data came from women in 1988 the National Maternal and Infant Health Survey (N=3,332). Linear mixed models and generalized equation models with Poisson regression were used to explore the associations. Using latent class growth model we identified four distinct GWG trajectories in early pregnancy: low growth (2.3%), low normal growth (39.7%), normal growth (48.2%), and high growth (9.9%) groups. Women in high growth group had 1.7 mmHg increases in systolic blood pressure (95% CI: (0.9, 2.6)), and 0.9 mmHg increases in diastolic blood pressure (95% CI: (0.2, 1.7)), compared to women in normal growth group. In contrast, women in low growth group were protected from subsequent systolic blood pressure (mean difference: -1.67, 95% CI: (-3.2, -0.1)) and diastolic blood pressure increases (mean difference: -1.22, 95% CI: (-2.5, 0.1)). Women in high growth group also had higher risk of gestational hypertension (RR: 2.0, 95% CI: 1.4, 2.9) compared to those in normal growth group. These associations were independently of weight gain after 20 weeks' gestation. These results suggest that appropriate weight management in early pregnancy holds promise to control blood pressure and reduce the risk of pregnancyinduced hypertension.

ASSOCIATIONS OF MATERNAL CADMIUM BODY BURDEN WITH TRIMESTER-SPECIFIC BLOOD PRESSURE IN PREGNANCY. Osorio-Yáñez C\*, Gelaye B, Miller RS, Enquobahrie DA, Qiu C, Williams MA (Department of Epidemiology, Harvard T.H. Chan School of Public Health; Center for Perinatal Studies, Swedish Medical Center)

Background: Previous studies revealed associations of urinary Cd (U-Cd), a chronic exposure biomarker, with blood pressure in non-pregnant adults. However, the evidence regarding trimester-specific blood pressure in pregnancy and U-Cd is scarce and needs to be addressed. Methods: We evaluated whether maternal body burden of Cd is associated with trimesterspecific blood pressure. We randomly selected 757 women from the Omega Cohort. Creatinine (Cr)-corrected Cd in maternal clean-catch spot urine samples was quantified by inductively coupled plasma mass spectrometry. Systolic (SBP) and diastolic blood pressure (DBP) were determined twice at first, second and third trimesters of pregnancy employing standard protocols. Trimester-specific, mean arterial pressure (MAP) was also calculated. Urinary Cd quartiles (≤0.12, 0.13-0.32, 0.33-0.49 and ≥0.5 µg/g Cr) were used in unadjusted, adjusted and stratified multivariable linear regression models. Results: In unadjusted linear regression models, women had reduced SBP (-2.0; 95% CI: -3.85,-0.53 mmHg) and DBP (-1.7; 95% CI:-3.19,-0.32 mmHg) with greater quartile of U-Cd in the second and third trimester of pregnancy. respectively. Third trimester MAP was significantly reduced among those the highest U-Cd quartile (-1.64; 95% CI:-3.16,-0.18 mmHg) in the third trimester. In multivariable regression models adjusted for maternal age, race, family history of diabetes and BMI, the decrease in second trimester SBP, DBP and MAP remained statistically significantly associated with the highest U-Cd quartile. Associations are modified by maternal overweight/obesity and calcium status. Conclusions: Our findings suggest are consistent with findings from some other studies which report reduced blood pressure values with relatively highly Cd body burden.

### **B66**

HYPERTENSIVE DISORDERS IN PREGNANCY AND THE RISK OF INCIDENT CARDIOVASCULAR DISEASE: THE IMPACT OF TIME-VARYING CONFOUNDING. Grandi SM\*, Eberg M, Platt RW, Vallée-Pouliot K, Arel R, Basso O, Filion KB (McGill University, Montreal, QC,) Background: Previous studies have suggested an increased risk of later cardiovascular disease (CVD) in women diagnosed with hypertensive disorders in pregnancy. However, the effect of time-varying confounders on this association has not been investigated. Methods: We used the Clinical Practice Research Datalink to define a population-based cohort study of 156,967 women, aged 15-45 years, with a first pregnancy. Hypertensive disorders were defined using clinical diagnoses, blood pressure values, and medication prescriptions between 20 weeks gestation and 6 weeks postpartum. The primary outcome was a diagnosis of CVD. To account for time-varying confounders, marginal structural Cox models (MSM) with weights estimated as the product of the probability of exposure history, of pregnancy based on previous history, and of censoring, were used. We also performed an analysis analogous to intention-to-treat (ITT) by using the pregnancy that resulted in cohort entry to define each woman's exposure status; no time-varying confounders were considered in this analysis. To assess the impact of time-varying confounding on the association of interest, the results of the MSM and ITT analyses were compared. Sensitivity analyses were performed to assess the influence of weight truncation and exclusion of subjects with extreme weights on our MSM estimates. Results: Our MSM analysis resulted in a HR of 2.7 (95% CI 2.2, 3.3) for incident CVD. Sensitivity analyses resulted in similar estimates compared to the primary MSM analyses. The results of the ITT analysis were similar to the weighted results (HR 2.4, 95% CI 2.0, 3.0). Conclusions: The similar estimates obtained with the MSM analysis (which accounted for time-varying confounding and the cumulative effect of exposure) and the ITT analysis (which measured the one-time effect) suggests that downstream confounding over multiple pregnancies did not impact the association of interest.

ASSOCIATION OF PROVIDER ADVICE AND PREGNANCY WEIGHT GAIN IN A PREDOMINANTLY HISPANIC POPULATION. Liu J\*, Whitaker KM, Yu SM, Chao SM, Lu MC. (University of South Carolina, Columbia, SC)

Objectives: To determine the accuracy of provider advised weight gain according to the Institute of Medicine (IOM's) guidelines and its association with women's weight gain during pregnancy. Methods: Data came from the 2007 Los Angeles Mommy and Baby study (n=3,402). The 1990 IOM guidelines on gestational weight gain were used to define whether the provider's advice on weight gain and women's weight gain was below, within, or above the guidelines. Provider advice was based by maternal self-report after delivery. Multinomial logistic regression was used. Results: Forty-two percent reported receiving weight gain advice from a health care provider within IOM guidelines, 16.5% received advice being below and 10% above the recommended amount, and an additional 13.5% reported the discussion but did not report the recommended weight gain amount. Women who reported provider advice on weight gain being less than the recommendation were 1.6 times (95% CI: 1.2, 2.0) more likely to gain less than the IOM recommended amount. Women who reported provider advice being more than the IOM recommended range were 1.8 times (95% CI: 1.3, 2.6) more likely to gain above the guidelines. Overweight and obese women were more likely to gain above the guidelines, and Hispanics, foreign-born women, and underweight women were less likely to gain above the recommended range. Conclusions: There is a need for more women to receive accurate advice on gestational weight gain from their prenatal care providers. Intervention strategies are needed to educate providers about IOM guidelines and about how to counsel gestational weight gain.

### **B68**

ASSOCIATION OF POOR SUBJECTIVE SLEEP QUALITY AND SLEEP PATTERNS WITH SUICIDAL IDEATION AMONG PREGNANT WOMEN. B Gelaye\*, YV Barrios, Q Zhong, MB Rondon, CPC Borba, SE Sanchez, DC Henderson, MA Williams (Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA)

Objective: To examine the independent and joint relationships of poor subjective sleep quality. and depression with suicidal ideation among pregnant women. Methods: A cross-sectional study was conducted among 641 pregnant women attending prenatal care clinics in Lima, Peru. Antepartum depression and suicidal ideation were assessed using Patient Health Questionnaire-9 (PHQ-9) scale. Antepartum sleep quality was assessed using Pittsburgh Sleep Quality Index (PSQI). Logistic regression procedures were performed to estimate odds ratios (aOR) and 95% confidence intervals (95% CI) adjusted for confounders. Results: Overall, the prevalence of suicidal ideation in this cohort was 16.8% and poor sleep quality was more common among women endorsing suicidal ideation as compared to their counterparts who did not (47.2%vs.24.8%, p<0.001). After adjustment for confounders including maternal depression, poor sleep quality (defined using the recommended criteria of PSQI global score of >5vs.≤5) was associated with a 1.7-fold increased odds of suicidal ideation (aOR=1.67; 95%CI 1.02-2.71). When assessed as a continuous variable, each 1-unit increase in the global PSQI score resulted in an 18% increase in odds for suicidal ideation, even after adjusting for depression (aOR=1.18; 95%CI 1.08-1.28). Women with both poor sleep quality and depression had a 3.5fold increased odds of suicidal ideation (aOR=3.48; 95%Cl 1.96-6.18) as compared with those who had neither risk factor. Conclusion: Poor subjective sleep quality was associated with increased odds of suicidal ideation. Replication of these findings may promote investments in studies designed to examine the efficacy of sleep-focused interventions to treat pregnant women with sleep disorders and suicidal ideation.

TRENDS IN MEAN GESTATIONAL AGE AT TIME OF PREGNANCY AWARENESS. A

Branum\*, K Ahrens (Reproductive Statistics Branch, Division of Vital Statistics, National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, MD) Early pregnancy detection is important for improving pregnancy outcomes as the first trimester is a critical window of development; however, there has been no description of national trends and characteristics of gestational age at time of pregnancy awareness among US women. We examined self-reported data on gestational age at time of pregnancy awareness from the 1995 through 2011-2013 National Survey of Family Growth among women 15-44 years who reported at least one pregnancy in the 5 years prior to interview. Gestational age at pregnancy awareness (continuous) was assessed by race/Hispanic origin, age at pregnancy, gravidity, pregnancy intendedness, education, income, and prenatal care. Among all women, ageadjusted mean gestational age at pregnancy awareness did not change linearly over time but decreased between 1995 and 2002 (5.8 to 5.4 weeks, p<0.01) and increased between 2002 and 2011-2013 (5.4 to 5.7 weeks, p<0.01). Mean gestational age at pregnancy awareness was greater among women 15-19 compared to women 20-24, 25-29, 30-44 (6.5, 5.9, 5.3, 5.0 weeks, respectively, all p<0.01), women who were non-Hispanic black and Hispanic compared to non-Hispanic white (6.2 and 5.8, respectively, vs. 5.2, all p<0.01), women having their first pregnancy compared to those having their second or higher (5.8 vs. 5.3, p<0.01), and for unwanted pregnancies versus those that were intended (6.1 vs. 5.1, p<0.01). These patterns were consistent over time. In recent years, mean gestational age at awareness of pregnancy has increased slightly but remains later among certain groups of women who are more likely to have adverse birth outcomes.

### **B70**

HOSPITAL-LEVEL VARIATION IN THE USE OF CESAREAN DELIVERY FOR DYSTOCIA ACROSS THREE CANADIAN PROVINCES. Riddell CA\*, Hutcheon JA, Kaufman JS (McGill University, Montreal, QC)

Objective The objective of this study was to quantify the extent to which choice of hospital alters a woman's risk of having a cesarean delivery for the diagnosis of labour dystocia. Methods Provincial perinatal databases containing obstetrical chart records from mothers delivering between 2008 and 2012 in Ontario, Alberta, and British Columbia, Canada, were pooled for analysis. We examined nulliparous women who delivered singletons in cephalic position at term gestation, underwent labour, and did not have pre-labour indications for cesarean delivery. A mixed effects logistic model was used to model cesarean delivery as a function of maternal risk factors (maternal age, pre-existing comorbidities, and gestational conditions), province, year of delivery, and a random intercept for hospital. We estimated the variation in the hospital-level random effect and calculated hospital-level standardized cesarean delivery rates for dystocia. Results 387.933 women delivering across 170 hospitals were analyzed, of whom 12.7% had a cesarean delivery for the indication of dystocia. The variance of the random effect was estimated to be 0.20 (standard error: 0.02), implying a significant variation in risk of having a dystocia-related cesarean delivery after accounting for differences in maternal risk factors included in the model. The standardized cesarean delivery rates for dystocia ranged from 5.1% to 32.1%, with a median rate of 15.1% and inter-quartile range of 11.2% to 18.5%. Conclusions We found that a woman's risk of having a cesarean delivery for the indication of dystocia is affected by the hospital where she delivers, above and beyond her individual risk factors.

COMPARISON OF HEALTHCARE UTILIZATION ACROSS RACE/ETHNICITY IN PREGNANT AND NON-PREGNANT WOMEN OF CHILD-BEARING AGE. Amyx M,\* Xiong X, Xie Y, and Buekens P (Tulane University School of Public Health and Tropical Medicine, New Orleans, LA)

To examine patterns of healthcare utilization (e.g., location, number of doctor visits, and insurance type) among different racial/ethnic groups of childbearing age (15-44 years old) women, we analyzed data from the National Health and Nutrition Examination Survey (NHANES) from 2005-2010, including 432 pregnant and 3175 non-pregnant women of childbearing age. The proportion of women reporting particular locations used, number of doctor visits, and insurance types was estimated by race/ethnicity, stratified by pregnancy status. The Rao-Scott x2statistic was used to compare proportions of each characteristic by race/ethnicity. In both pregnant and non-pregnant women, statistically significant differences were found for all three variables (p<0.05). Non-Hispanic white (NHW) women (5.1% pregnant and 29.6% nonpregnant) were least likely to report only 0-1 doctor's visits in the past year compared to minority women (26.6% and 51.0% for Mexican-American and 19.3% and 33.4% for non-Hispanic black [NHB], respectively). NHW women were also less likely to report having no insurance (7.7% and 17.1%) compared to NHB (10.7% and 25.2%) and Mexican-American women (39.4% and 52.6%). While the majority of both pregnant and non-pregnant NHB (73.0% and 69.7%) and NHW women (79.7% and 79.2%) reported receiving healthcare at a doctor's office or HMO, the majority of pregnant Mexican-American women received care at a clinic or health center (60.5%), while the majority of non-pregnant Mexican-American women received care at a doctor's office or HMO (52.4%). In conclusion, overall, both pregnant and non-pregnant NHW women reported better healthcare utilization compared to minority women.

### **B72**

### NUTRITIONAL IMBALANCE IN PREGNANT WOMAN ON OPIOID MAINTENANCE

**THERAPY**. S Shrestha\*, HL Gutierrez, L Garrison, P Pribis, JM Stephen, LN Bakhireva. (University of New Mexico Health Sciences Center, Albuquerque, NM) As prescription opioid abuse has reached epidemic proportions in the U.S., opioid abuse and dependency among pregnant women are also rising. Nutrition and dietary supplementation might be important modifiable risk factors among pregnant women on opioid-maintenance therapy (OMT). The objective of this study was to compare nutritional status of opioiddependent pregnant women (n=24) on OMT to healthy controls (n=15) in a prospective cohort study at the University of New Mexico. Dietary assessment was conducted using the Block Brief 2000 Food Frequency Questionnaire which evaluated the participants' diet for a 30-day period before delivery. Mean age at recruitment was 27±5.5 years and pre-pregnancy weight 143.3±29.6 lbs. with no differences between the groups (p>0.05). Compared to controls, OMT group had significantly higher total energy intake (1.981.3±666.1 vs. 2.769.8±1.523.5 kcal. p=0.03) and higher intake of carbohydrates (225±80.9 vs. 328±163.9 g, p=0.01). Analysis of micronutrient intake showed that subjects in both groups had adequate daily intake of thiamine, riboflavin, vitamin B6, B12, C, D, K and calcium. However, compared to controls, OMT group showed significantly lower intake of beta-carotene (6,054.6±3,849.6 vs. 3,587.3±3,303.9 µg. p=0.05), vitamin K (274.5±199.2 vs. 129.4±145 µg, p=0.02), supplemental vitamin D (432.4±91.5 vs. 351.2±139.8 IU, p=0.03), and supplemental iron (40.6±31.5 vs. 20.8±17.5 mg, p=0.03). Both groups had inadequate intake of folate (456±156.1 vs. 516.5±243.1 µg) and iron (15.4±6.7 vs. 20.1±11.3 mg), but the differences between the groups were nonsignificant(p>0.05). These results demonstrate nutritional imbalance and micronutrient deficiencies among pregnant women on OMT, suggesting a need for public health intervention.

DIAGNOSIS OF POSTPARTUM DIABETES AFTER PHARMACOLOGICAL TREATMENT FOR GESTATIONAL DIABETES, 2001 TO 2011. Landi SN\*, Camelo Castillo W, Boggess K, Conover MM, Jonsson Funk M (University of North Carolina, Chapel Hill NC) Gestational diabetes mellitus (GDM) is a prevalent pregnancy complication in the U.S. for which pharmacological treatment with glyburide or insulin may be required. Despite being off-label, glyburide use is frequent and more common than injectable insulin in recent years. However, glyburide's comparative impact on maternal health has not been adequately assessed. We identified pregnant women aged 15 to 50 who received glyburide or insulin treatment for GDM in Truven Health Analytics' MarketScan database from 2001 to 2011 (n=5238). Women were followed two years postpartum to identify incident cases of type 2 diabetes, defined as ≥ 2 outpatient or ≥ 1 inpatient relevant ICD-9 codes (250.xx). We estimated risk ratios and 95% confidence intervals using log-binomial regression to compare diagnosis outcomes between glyburide and insulin users, adjusting for age, region, calendar year, and claims for obesity diagnosis. Over half of women received glyburide for GDM during their pregnancy (n=2764, 52.8%). Overall, 364 (7.0%) women were diagnosed with type 2 diabetes within two years postpartum; 53.9% were previously treated with insulin, and 46.2% were previously treated with alyburide. Women receiving glyburide treatment were 22% less likely to be diagnosed with type 2 diabetes in the two years after delivery (adjRR=0.78 [95% CI 0.63, 0.96]) as compared with women receiving insulin treatment. The lower risk of type 2 diabetes among those treated with glyburide may be attributed to residual confounding or differences in utilization of health services during the postpartum period. Characterization of clinical surveillance in pharmacologically-treated women with GDM requires further exploration.

### **B74**

ANTENATAL MATERNITY LEAVE AND CHILDBIRTH USING THE FIRST BABY STUDY: A PROPENSITY SCORE ANALYSIS. J Goodman\* (UC Berkeley, Berkeley, CA) K Kjerulff (Penn State University, Hershey, PA)

Background: Prior studies suggest that taking antenatal maternity leave (ANL) reduces the risk of adverse obstetric outcomes, presumably by allowing pregnant women time to rest and prepare for childbirth. The small literature examining this relationship suffers from several important limitations: small sample size; imprecise measurement of ANL; and failure to adequately address selection bias. Methods: With data from the First Baby Study, a longitudinal cohort study of nulliparous women who gave birth to singletons in Pennsylvania hospitals (N = 3,006), I examine the effects of ANL on maternal health among employed women who did not deliver preterm. I use propensity score matching to reduce potential selection bias. Exposure was leave taken before delivery in days. Primary outcomes were labor induction, labor duration, pain during labor and use of pain-reducing medication, mode of delivery, satisfaction with childbirth, breastfeeding initiation, and postpartum depression. I conduct subgroup analyses for full- and part-time employed women. Preliminary results: In unmatched analyses adjusting for potential confounders, women who stopped working more than one day before delivery had increased likelihood of using epidural analgesia (adjusted odds ratio [AOR] = 1.54; p = 0.004), delivering by Cesarean section (any [AOR = 1.51; p < 0.001] and unplanned [AOR = 1.33; p = 0.022]), and had labor lasting 1.66 hours longer (p = 0.001) than women who did not stop working before delivery. However, initial propensity score analyses indicate that leave-takers and non-leave-takers differ significantly. I will report results from propensity score matched multivariable regression analyses and subgroup analyses.

TEMPORAL TRENDS IN OBSTETRIC TRAUMA AND SURGERY FOR PELVIC FLOOR DISORDERS: AGE-PERIOD-COHORT ANALYSIS. S Lisonkova\*, I Chen, G Muraca-Muir, GW Cundiff, KS Joseph (University of British Columbia, BC, Canada)

Objective: Obstetric trauma during childbirth is a major risk factor for urinary and fecal incontinence and pelvic organ prolapse. We carried out a population-based study to explore the association between the trauma during childbirth and pelvic floor disorders. Methods: We examined age-specific temporal trends in vaginal and cesarean delivery, obstetric trauma, and surgery for urinary and fecal incontinence and pelvic organ prolapse in Washington state, USA, between 1987 and 2009. Cases of obstetric trauma (including 3rd and 4th degree perineal tears, high vaginal lacerations, and inversion of the uterus) and surgery for pelvic floor disorders were identified among all hospitalizations. Temporal trends and age-period-cohort analyses were used to quantify the experience of women born between 1920 and 1980. Results: Cesarean delivery rates increased, vaginal delivery rates remained stable and instrumental vaginal delivery rates declined between 1987 and 2009. Obstetric trauma decreased from 6.7 in 1987 to 2.5 per 1,000 women aged 15-44 years in 2009 (P<0.001). Surgery for pelvic organ prolapse decreased from 2.1 in 1987 to 1.4 per 1000 women aged 20-84 years in 2009 (P<0.001); a similar trend was observed in surgery for urinary incontinence (from 1.4 to 0.8 per 1,000, P<0.001). Obstetric trauma rates in 1987-99 were strongly correlated with rates of surgery for pelvic organ prolapse in 1997-2009 (correlation coefficient=0.93, P<0.001). Conclusion: Temporal increases in cesarean delivery and concomitant declines in instrumental vaginal delivery have resulted in significant declines in obstetric trauma and consequent reductions in surgery for urinary incontinence and pelvic organ prolapse.

### **B76**

DOES MILK CONSUMPTION DURING PREGNANCY AFFECT THE RISK OF GESTATIONAL DIABETES MELLITUS?. Song-Ying Shen, Jian-Rong He, Min-Shan Lu, Ming-Yang Yuan, Nian-Nian Chen, Lan Qiu, Cui-Yue Hu, Wei-Dong Li, Jin-Hua Lu, Yu Liu, Kar Keung Cheng, Hui-Min Xia, Xiu Qiu\* (Division of Birth Cohort Study, Guangzhou Women and Children's Medical Centre, Guangzhou Medical University, Guangzhou, China)

Background: Pregnant women are usually advised to increase milk consumption. However, evidence concerning effects of milk consumption on pregnancy health was sparse, especially from non-Western areas. We aimed to investigate the relationship between milk consumption during pregnancy and the risk of gestational diabetes mellitus (GDM) in a Chinese population. Methods: Pregnant women were recruited from an ongoing study, the Born in Guangzhou Cohort Study between February 2012 and December 2014. A total of 4270 women who had information on milk consumption (including fluid milk, milk powder and yogurt) at 24-27 weeks of gestation and GDM diagnosis were included. The relationship between milk consumption and the risk of GDM was evaluated using logistic regression model, adjusted for maternal age, prepregnancy BMI, parity and passive smoking. Results: The prevalence of habitual intake (≥1 servings/week) for fluid milk, milk powder and yogurt were 72.1%, 58.8% and 64.4%, respectively. Intakes of milk powder and yogurt were not significantly associated with the risk of GDM. However, compared to those consumed <1 serving/week, women consumed ≥14 servings/week of fluid milk had a marginally significant and elevated risk [OR (95% CI), 1.47 (0.99, 2.19)]. Increased consumptions of combined milk (a sum of fluid milk and milk powder) also elevated the risk of GDM [OR (95% CI), 1.47 (1.01, 2.12) and 1.71 (1.12, 2.60) for 1-13 and ≥14 servings/week, respectively]. Conclusions: Our results suggest that higher consumption of fluid milk and milk powder could increase GDM risk. This finding may be useful in dietary counseling during pregnancy.

SERIAL ASSESSMENTS OF CERVICAL FUNNELING AND THE RISK OF PRETERM BIRTH AMONG WOMEN WITH A PRIOR PRETERM BIRTH. Q Li, R Newman, S Sullivan, EY Chang, K Willan (Medical University of South Carolina, Charleston, SC)

Objective: To evaluate whether cervical funneling in the second trimester is associated with the increased risk of preterm birth (PTB) among women with a prior PTB. Study Design: We performed a secondary analysis of a multi-center prospective cohort study (Preterm Prediction Study) of the NICHD Maternal-Fetal Medicine Units Network. We included 236 African American and White mothers with at least one prior spontaneous PTB < 37 weeks. Cervical length and funneling were assessed at 22-24 and 26-29 weeks\' gestation. Adjusted relative risk (RR) and confidence intervals (CI) were estimated in multivariate analyses. Results: PTB rate was 24.6%. Forty seven (19%) had funneling at either one or both visits and delivered earlier than 189 women without funneling at either visit (36.9±3.4 weeks vs 38.2±2.3 weeks: P=0.01). The progression from absent to present funneling at the second assessment was associated with earlier delivery (-1.2 weeks; CI: -2.3 to -0.1), while funneling at both scans was associated with the earliest delivery (-1.8 weeks; CI: -3.4 to -0.2). When cervical lengths were more than 25 mm (n=205), the presence of funneling was associated with a significantly higher risk for PTB (45.2% vs 18.4%; RR: 3.4; CI: 1.4-8.2). When cervical lengths were less than 25 mm (n=31), cervical funneling was not associated with an earlier week at delivery (36.4±3.9 vs 36.5±3.2; P=0.94) or increased PTB risk (RR: 2.2; CI: 0.4-12.3). Conclusion: Cervical funneling identified in the second-trimester was significantly associated with PTB and earlier gestational age at delivery among mothers with a cervical length>25 mm.

### **B78**

**DISPARITIES IN ROUTINE CERVICAL LENGTH SCREENING WITH TRANSVAGINAL ULTRASOUND**. Haviland MJ\*, Shainker SA, Hacker MR, Burris HH (Beth Israel Deaconess Medical Center, Boston, MA)

Objective: To determine if race and ethnicity is associated with the risk of 1) missed transvaginal cervical length screening or 2) a composite outcome of missed or late screening. Study Design: This was a retrospective cohort study of nulliparous women with singleton gestations and a fetal anatomy ultrasound from 16-24 weeks' gestation at our institution from January, 2012 to November, 2013. We calculated the risk ratio (RR) and 95% confidence interval (CI) for missed cervical length screening and a composite outcome of missed or late screening at ≥20 weeks' gestation, with log-binomial regression. Results: There were 2967 women who met eligibility criteria. Their mean (SD) age was 31.7 (5.4) years; 1256 (42.3%) were white, 600 (20.2%) were Asian, 485 (16.4%) were black, 191 (6.4%) were Hispanic and 435 (14.7%) were other/unknown race or ethnicity. Among these women, 779 (26.3%) did not receive cervical length screening and 192 (6.5%) received late screening. Unadjusted analysis suggested that black (RR: 1.1; 95% CI: 0.92-1.3) and Hispanic (RR: 1.2: 95% CI: 0.94-1.5) women were more likely to miss screening than white women. Similarly, Black (RR: 1.3; 95% CI: 1.1-1.5) and Hispanic (RR: 1.2; 95% CI: 1.01-1.5) women were more likely to miss screening or be screened late than white women. Adjusting for maternal age and insurance status did not attenuate these associations. Conclusions: Our findings suggest that black and Hispanic women may be more likely to have missed opportunities for cervical length screening or be screened later in gestation.

MATERNAL EARLY PREGNANCY SERUM METABOLITES AND RISK OF GESTATIONAL DIABETES MELLITUS. DA Enquobahrie\*, M Denis, MG Tadesse, B Gelaye, H Ressom, MA Williams (University of Washington, Seattle, WA)

Background: Metabolites represent cellular functions and can provide important insights into gestational diabetes mellitus (GDM) pathogenesis. However, only a handful, mostly small, GDM metabolomics studies exist. Few were conducted in early pregnancy and none evaluated joint metabolite profiles, limiting assessment of metabolite interactions underlying GDM. We investigated maternal early pregnancy serum metabolites and subsequent risk of GDM. Methods: We identified 178 GDM cases and 180 controls among participants of the Omega study, a pregnancy cohort study. Information on participant characteristics and GDM diagnosis was collected using in-person interviews and medical record abstraction, respectively. Early pregnancy (~16 weeks gestation) serum samples were used for non-targeted metabolite profiling using a gas chromatography-mass spectrometry platform. Lasso regression was used to select a set of metabolites that are jointly associated with GDM case-control status. We evaluated predictive performance of the set of selected metabolites using a receiver operating characteristics curve and area under the curve (AUC). Functional relationships of identified metabolites were examined using pathway analytic tools. Results: A set of 20 metabolites (fatty acids, sugars/alcohol, amino acids, and organic acids) differentiated GDM cases from controls. Fold changes of relative abundance for these metabolites ranged from 1.47 (linoleic acid) to 0.88 (urea). Selected metabolites participate in solute-carrier-mediated transmembrane transport. Addition of selected metabolites to the set of well-known GDM risk factors improved the AUC significantly (0.71 to 0.87, p-value=3.97e-07). Conclusions: A combination of maternal early pregnancy serum metabolites predicts GDM risk. Replication of findings may have implications for design of GDM prevention or early diagnosis protocols.

### **B80**

DENTAL CLEANING DURING PREGNANCY AND ASSOCIATED CHARACTERISTICS AMONG WOMEN WITH LIVE BORN INFANTS IN 5 STATES. Le BT\*. D'Angelo DV. Ahluwalia I, Thornton-Evans G, Lin M (Centers for Disease Control and Prevention, Atlanta, GA) Oral health is important to general health and well-being, and is increasingly being recognized as a factor that may adversely affect women's health during pregnancy. However, oral health is often overlooked as an essential part of comprehensive prenatal care for pregnant women. Data from the 2011 Pregnancy Risk Assessment Monitoring System (PRAMS) were used to describe women who had a dental cleaning while they were pregnant. PRAMS is a state- and populationbased surveillance system designed to collect data on maternal experiences before, during, and after pregnancy. Data were analyzed from five states (n=6603) that asked women about dental care during pregnancy and had weighted response rates ≥65%. Logistic regression for survey data, incorporating backward selection for modeling, was used to assess relationships (adjusted odds ratios [OR] and 95% confidence intervals [CI]) between women's characteristics and dental cleaning during pregnancy. Results indicate that 54.5% of respondents reported not having a dental cleaning during pregnancy. Odds of not obtaining dental cleaning were higher among women who were <25 years (OR=1.6, CI=1.2-2.3), white (vs. Hispanic, OR=1.9, CI=1.1-3.1), and did not receive dental cleaning in the 12 months before pregnancy (OR=12.5, CI=9.8-16.0). Given the high prevalence of women who reported they did not obtain a dental cleaning during pregnancy, findings suggest that dental cleaning needs to be emphasized as part of comprehensive prenatal care. Furthermore, dental cleaning should be encouraged in women prior to getting pregnant. Efforts to increase dental cleaning during pregnancy should focus on women who are younger, white, and uninsured.

CIRCADIAN RHYTHMS: CLOCK GENES GENETIC RISK SCORES AND RISK OF PLACENTAL ABRUPTION. C Qiu\*, B Gelaye, M Denis, MG Tadesse, MA Luque Fernandez, DA Enquobahrie, CV Ananth, MA Williams (Center for Perinatal Studies, Swedish Medical Center, Seattle, WA)

Background: The circadian clock plays an important role in several aspects of female reproductive biology, including ovulation, embryonic implantation, and parturition. However, evidence linking circadian clock-related genes to pregnancy outcomes has been inconsistent. We have previously reported findings suggesting a diurnal circadian periodicity among placental abruption (PA). We sought to examine whether variations in single nucleotide polymorphisms (SNPs) of circadian clock genes is associated with PA. Methods: Maternal blood samples were collected from 470 PA case and 473 control participants in the Peruvian Abruptio Placentae Epidemiology study. Genotyping was performed using the Illumina's Cardio-Metabochip platform. We examined 119 SNPs in 13 candidate genes known to control circadian rhythms (e.g., CRY2, ARNTL, RORA). Univariate and penalized logistic regression models were fit to estimate odds ratios. We also examined the combined effect of multiple SNPs on PA risk using weighted genetic risk scores (WGRS). Results: A common SNP (minor allele frequency=23%) in the RORA gene (rs2899663) was associated with a 21% reduced risk in PA (p<0.05). Participants in the highest quartile for WGRS had a 5.13-fold (95%CI: 5.8-12.56) higher odds of PA as compared to participants in the lowest quartile. The odds of PA increased with increasing values of the WGSR (p-value for trend < 0.001). Conclusions: Genetic variants in circadian rhythm genes (clock genes) may contribute to PA risk. Larger studies are needed to confirm these findings and to further elucidate the pathogenesis of this important clinical complication of pregnancy.

### **B82**

**EARLY POSTPARTUM DEPRESSIVE SYMPTOMS IN IMMIGRANT AND US-BORN WOMEN IN NEW YORK CITY**. Simons HR\*, Thorpe LE, Jones HE, Janevic T, Beam Dowd J. (Planned Parenthood Federation of America, New York, NY)

Background: Studies conducted outside of the US have found a higher prevalence of postpartum depression in immigrant than native-born women. US studies have been less consistent but have used convenience samples and lacked comparison groups. Objectives: To compare prevalence and risk factors for early postpartum depressive symptomatology between immigrant and US-born women in New York City (NYC). Methods: In a cross-sectional analysis of NYC Pregnancy Risk Assessment Monitoring System data (2009¬¬-2010), we used logbinomial regression to assess the association between nativity and postpartum depressive symptomatology and to determine whether age, race/ethnicity, and education modified this association. Among immigrant women, we assessed the relationship between exposure to the US (e.g. time since and timing of migration) and postpartum depressive symptomatology. Results: Prevalence of postpartum depressive symptoms was comparable between immigrant and US-born women (adjusted Prevalence Ratio [aPR]=1.08, 95% CI 0.74-1.58), but varied by race/ethnicity and education. Non-Hispanic White immigrant women were at elevated risk compared to their US-born counterparts (aPR=2.46, 95% CI 1.27-4.77; interaction contrast [IC]White v. Black=-0.11, P=0.01; ratio of prevalence ratios [RPR] White v. Black=0.22, 95% CI 0.08–0.61), as were immigrant women with high school degrees or more compared to their USborn counterparts (aPR=1.73; 95% CI 0.95-3.14; IC=-0.09, P=0.01; RPR=0.35; 95% CI 0.14-0.88). There was a slightly elevated, non-significant risk of depressive symptomatology among immigrant women with greater compared to less exposure to the US. Conclusions: Routine screening and referral to culturally appropriate support/treatment might be offered to subgroups of immigrant women.

**REASSESSING DURATION OF THE SECOND STAGE OF LABOR.** Grantz KL\*, Sundaram R, Hinkle SN, Berghella V, Hoffman MK, Ma L, Lu Z, Reddy UM (Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Rockville, MD, USA)

Increased second stage of labor duration, the time from 10 cm to delivery, is associated with increased risk of maternal and neonatal morbidity. We sought to determine the second stage duration wherein the chance of vaginal delivery was outweighed by increased morbidity risk. In the Consortium on Safe Labor (12 U.S. sites, 2002-2008) we analyzed singleton, live, vertex deliveries ≥36 weeks without prior cesarean (n=43,810 nulliparas; n=59,605 multiparas). For each parity and epidural status, hazard rates indicating risk for the outcome at a given duration, were calculated for spontaneous vaginal delivery (SVD) versus risk of composite morbidities (maternal, neonatal and maternal or neonatal), and then combined in bivariate survival models. The hazard for SVD versus either maternal or neonatal morbidity crossed at 2.6 and 2.4 hours for nulliparas, and 1.4 and 2.3 hours for multiparas with and without an epidural, respectively. For nulliparas with an epidural who were to labor past 3 hours (current guidelines), 60.0% and 51.2% of women would develop a maternal or neonatal morbidity, respectively, but only 16.0% would successfully have a SVD. Extending second stage by just 1 additional hour would result in 5.4% of SVD occurring during that hour with a 3-fold increase in maternal (15.9%) or neonatal (15.2%) morbidities. Crossing times for SVD and any morbidity occurred slightly earlier than current recommended guidelines for women with an epidural, but slightly later for women without epidural. We provide data for counseling to balance chances of SVD versus morbidity with increasing duration of second stage.

### **B84**

**ESTIMATED GESTATIONAL WEIGHT GAIN TOGETHER WITH BIOCHEMICALLY-CONFIRMED SMOKING CESSATION**. Rockhill KM\*, England LJ, Tong VT, Sharma AJ (Centers for Disease Control and Prevention, Atlanta, GA)

Though smoking cessation during pregnancy improves birth outcomes, the potential for additional maternal weight gain associated with cessation can be a barrier to quitting. Few studies have quantified the additional weight gain due to cessation during pregnancy. Data came from a large, prospective randomized control trial, the Smoking Cessation in Pregnancy project (1987-1991), which evaluated the effect of brief cessation counseling on smoking cessation by the last trimester. Cessation was biochemically confirmed using urine cotinine concentration. Pre-pregnancy weight was self-reported, and gestational weight was measured at last prenatal care visit. We estimated the mean difference in gestational weight gain between biochemically-confirmed quitters and continuing smokers among women delivering full-term infants in both intervention arms using multivariable linear regression. We accounted for correlation by clinic and controlled for confounders. We also assessed the percentage of women who gained within recommended 2009 Institute of Medicine weight gain guidelines based on pre-pregnancy body mass index. Of 2,610 women, on average those who guit smoking by the end of pregnancy gained 34.1 pounds (SD: 0.78) compared to continued smokers 29.2 pounds (SD: 0.65; p-for-difference < 0.001). A lower percentage of quitters compared to smokers had inadequate gain (11.2% versus 28.2%) and a greater percentage had excess gain (56.9% versus 37.8%) (chi-square p<0.001). Women who quit smoking during pregnancy gained on average five pounds more than continuing smokers. Providers should continue to stress the importance of smoking cessation; however, smokers who guit during pregnancy may need additional support to ensure gestational weight gain is within recommendations.

ASSOCIATION OF ENDOMETRIAL HYPERPLASIA OR CANCER WITH A HISTORY OF GESTATIONAL DIABETES- RESULTS FROM A POPULATION-BASED STUDY IN WASHINGTON STATE, 1987-2013. PD Wartko\*, TL Beck, BA Mueller, SD Reed, SE Hawes (University of Washington School of Public Health, Seattle, WA)

Background: Excess circulating insulin may contribute to endometrial cancer (EC) development - some, but not all, studies suggest increased risk of EC in women with type 2 diabetes mellitus. We investigated the association of gestational diabetes mellitus (GDM) with EC and its precursor, endometrial hyperplasia (EH). Methods: We conducted a population-based casecontrol study of women in Washington State with a live birth or fetal death record from 1987-2013. Cases were women with a hospital discharge record of EH/EC after delivery (n=591). Controls were selected from remaining deliveries, frequency matched 10:1 with cases on delivery year and age (n=6036). Logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs). ORs were adjusted for maternal race/ethnicity, the only confounder identified. Results: EH/EC was associated with a history of GDM (OR 1.64, 95% CI 1.14-2.36), and this association held when restricting to EC cases (OR 1.77, 95% CI 1.12-2.78). Adjustment for BMI, available from 1992-2013, attenuated the ORs to 1.14 for EH/EC (95% CI 0.72-1.80) and 1.21 for EC alone (95% CI 0.66-2.23). Conclusions: This exploratory study suggests an association of EH/EC with GDM, possibly through the hyperinsulinemia pathway. Future research focusing on the role of obesity will help elucidate the etiology of EH/EC. If women with GDM have increased EH/EC risk, they may warrant closer monitoring.

### **B86**

RACIAL/ETHNIC DIFFERENCES IN CUMULATIVE NEIGHBORHOOD DEPRIVATION AND GESTATIONAL WEIGHT GAIN. Headen I\*, Mujahid MM, Abrams B (University of California, Berkeley)

Healthy gestational weight gain (GWG) is associated with numerous health outcomes. A woman's environment may affect GWG, but data on neighborhood environments and GWG are sparse and mainly focus on cross-sectional measures. To contribute knowledge about chronic exposure, we investigated the association between cumulative neighborhood socioeconomic deprivation (NDI) in relation to GWG and whether results varied by race/ethnicity in the 1979 National Longitudinal Survey of Youth (N=1716 mothers; 2382 singleton births between 1990-2000). Cumulative NDI was calculated using census tract-level socioeconomic indicators for woman's tract of residence from 1979 (baseline) to the year she gave birth. Inadequate and excessive GWG were categorized using 2009 Institute of Medicine guidelines. We estimated relative risks for exposure and GWG using log-linear multivariable models, adjusting for maternal age, socioeconomic status, race/ethnicity, marital status, parity, immigration status, infant's birth year, region of birth, and selected maternal residential characteristics. Interactions between exposure and race/ethnicity were retained if p<0.10. Cumulative NDI was not associated with GWG in the full population model (RR: 1.12; 95% CI: 0.97-1.30), but interaction by race/ethnicity was significant. Cumulative NDI increased risk of inadequate GWG for white women (RR: 1.35; 95% CI: 1.07-1.69) decreased risk for Latina women (RR: 0.64; 95% CI: 0.50-0.82), and was unassociated in Black women. In this study, prolonged exposure to adverse neighborhood environments had different implications for adverse GWG outcomes by race. Future work should continue to consider length of exposure in exploring how neighborhood environments contribute to adverse GWG, especially for racial/ethnic subgroups.

CONSTRUCTION OF A PRECONCEPTION COHORT OF LOW-INCOME WOMEN USING SAFETY NET ELECTRONIC HEALTH RECORDS: THE ADVANCE PRECONCEPTION OBESITY COHORT. Boone-Heinonen J,\* O'Malley JP, Tillotson CJ, Cottrell EK, Gaudino JA, Laurie M, Paul L, Mayer K, Potter J, McBurnie MA, Gold R, DeVoe JE (Oregon Health & Science University, Portland, OR)

Background: Preconception health is a critical determinant of women's life course health and disease risk in the next generation. Yet, collecting preconception data on women followed into pregnancy is challenging, especially for low-income populations. Methods: We constructed a cohort of girls and women using electronic health record data from the PCORNet ADVANCE Clinical Data Research Network, a national network of Federally-Qualified Health Centers serving over 1 million safety net patients across the U.S. The cohort includes patients who were 15-45 years of age and had at least one valid, non-pregnancy Body Mass Index (BMI) measure in 2012-2014. We characterized the cohort with respect to pregnancy, pre-pregnancy obesity (≥95th percentile CDC growth charts [<20 years]; BMI≥30 kg/m2 [≥20 years]) and severe obesity (≥20% greater than 95th percentile; BMI>35) among teenagers (<18 years) and adults. Results: The cohort includes 30,528 teenage girls and 238,436 women and is racially/ethnically diverse (e.g., 12.4% Black, 29.3% Hispanic). 7.6% of women and 2.1% of teenage girls were pregnant at any point in 2012-2014. Among these patients, 34.5% had a pre-pregnancy BMI measure in 2012-2014; 29.0%, 18.4% and 14.8% were overweight, obese, or severely obese. Pre-pregnancy obesity prevalence was highest in Black (38.0%) and Hispanic (35.6%) women. Conclusions: Women in the ADVANCE Preconception Obesity Cohort carry a high burden of pre-pregnancy obesity. This large cohort provides unique opportunities for data linkage to birth outcomes, following women and children over time, and studying determinants and consequences of adverse preconception health in low-income girls and women.

### **B88**

OUT-OF-HOSPITAL BIRTH IN OREGON: EXAMINING OUTCOMES BY PLANNED PLACE OF DELIVERY, ACCOUNTING FOR HOSPITAL TRANSFERS. JM Snowden\*, E Tilden, J Snyder, B Quigley, AB Caughey, YW Cheng (OHSU, Portland, OR)

Background: The rate of planned out-of-hospital birth has increased in recent years in the United States. At the national level there is no way to disaggregate hospital births between those that were planned to occur at the hospital and those that were not. Methods: This was a population-based retrospective cohort study of all Oregon births between 2012 and 2013, analyzing vital statistics data. We compared perinatal outcomes by planned birth setting (out-ofhospital compared to in-hospital). We used new data from the Oregon birth certificate that enable disaggregation of hospital births between planned hospital births and out-of-hospital-tohospital transfers. Outcomes included perinatal morbidity/mortality, maternal morbidity, and obstetric procedures. Results: Planned out-of-hospital birth was associated with an increased rate of perinatal death (3.9 per thousand as compared to 1.8 per thousand, P=0.003), a difference that was not detected using standard birth certificate data on birth setting (1.9 per thousand for both settings, P=0.97). Planned out-of-hospital birth was also associated with higher odds of neonatal seizures and lower odds of neonatal intensive care unit admission. Planned out-of-hospital birth was strongly predictive of unassisted vaginal delivery (93.8%, as compared to 71.9% in planned hospital births, P<0.001) and decreased odds of obstetric procedures. Conclusions: Perinatal mortality was greater in planned out-of-hospital birth, a finding that may be historically underappreciated due to the impact of misclassification of intended birth setting in US vital statistics. More comprehensive vital statistics data collection would provide women and their families with more accurate information to guide their choice on birth setting.

PRECONCEPTION EXPOSURES TO PERSISTENT ORGANIC POLLUTANTS AND GRAVID CONDITIONS. Smarr MM\*. Zhang C. Grantz KL. Sundaram R. Maisog JM. Kannan K. Buck Louis GM. (Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Rockville, MD, USA) Persistent organic pollutants (POPs) have recently been associated with an increased risk of diabetes, hypertension and metabolic syndrome in the general population, but data are sparse for their association with gravid conditions such as gestational diabetes mellitus (GDM) and hypertension (GH). A prospective cohort of 258 women whose preconception serum concentrations of 9 organochlorine (OC) pesticides and 10 polybrominated diphenyl ethers (PBDEs) were quantified and with hCG confirmed pregnancies reaching ≥24 weeks gestation were followed to delivery with ongoing capture of physician diagnosed GDM (11%) and GH (10%). Chemical concentrations were natural log-transformed and standardized by their standard deviation (SD) to aid interpretation of the findings. Separate models were run for each chemical. Multiple logistic regression models were first adjusted for serum lipids and also age, body mass index, race, and smoking. Final models also adjusted for the sum of the remaining POPs in each chemical class to account for serum concentrations of chemically similar compounds. Women's serum concentrations of PBDE-153 was associated with an increased odds of GDM (OR= 1.38, 95% CI: 1.03 - 1.86) per SD increase in concentration, in adjusted models without the \( \subseteq \) of remaining PBDEs. A higher odds of GH was observed for the organochlorine pesticide gamma-hexachlorocyclohexane in both adjusted models with and without the ∑ of remaining organochlorine pesticides, (OR= 1.40, 95% CI: 1.01 – 1.93) and (OR= 1.41, 95% CI: 1.01 – 1.96), respectively. Our findings suggest a positive association between select preconception POPs and a greater odds of gravid diseases.

### **B90**

**INFANT FEEDING PRACTICES BY MODE OF CONCEPTION**. Kara A. Michels; Sunni L. Mumford; Rajeshwari Sundaram; Erin Bell; Scott Bello; Edwina Yeung (Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Rockville, MD)

Background: Differences in infant feeding practices between parents conceiving with and without fertility treatments are poorly described. Feeding may be influenced by socioeconomic differences or differences in birth outcomes that may influence growth and nutritional needs. Methods: The Upstate KIDS cohort enrolled mothers delivering live births in upstate New York between 2008-2010 and sampled on fertility treatment exposure. Parents reported feeding practices such as provision of breast milk, solid foods, and formula at 4, 8, and 12 months postpartum. Generalized estimating equations were used to compare odds for each feeding practice by mode of conception, after adjusting for maternal age, body mass index, education, marital status, and private insurance status and paternal age, race, and education. Results: Among 4,332 infants (singletons and a randomly selected infant from twin sets), 1,273 (29%) were conceived with fertility treatments. Compared to mothers not conceiving with treatments. mothers who used treatments were less likely to breast feed at 8 (OR 0.74, 95%CI 0.62, 0.87) and 12 months postpartum (OR 0.66, 95%CI 0.53, 0.83); more likely to initiate solid foods by 8 months (OR 2.84, 95%CI 1.52, 5.30); and more likely to provide formula at 4 (OR 1.17, 95%CI 1.00, 1.36), 8 (OR 1.42, 95%CI 1.17, 1.73), and 12 months (OR 1.25, 95%CI 1.05, 1.48). Conclusions: Infants conceived with fertility treatments are less likely to be breast fed and more likely to be introduced to other forms of nutrition in infancy. This may be due to difficulties breast feeding, social beliefs, or physician recommendations.

LEVERAGING "BIG DATA" FOR OBESITY RESEARCH IN LOW-INCOME INFANTS AND CHILDREN: THE ADVANCE EARLY LIFE COHORT. Boone-Heinonen J,\* O'Malley JP, Tillotson CJ, Cottrell EK, Gaudino JA, Amafah A, Rivom ML, Mayer K, McBurnie MA, Gold R, DeVoe JE (Oregon Health & Science University, Portland, OR) BACKGROUND: Early life is a critical period in obesity etiology. Low income populations have high risk of adverse early life exposures and later disease, but are understudied due to challenges in recruitment and follow-up in longitudinal research. METHODS: We constructed a cohort of infants and young children using electronic health record data from the PCORNet ADVANCE Clinical Data Research Network, a national network of Federally-Qualified Health Centers serving over 1 million safety net patients across the US. This cohort includes patients 0-5 years of age who had at least one valid Body Mass Index measure in 2012-2014. We calculated prevalence of obesity (≥95% percentile. WHO [0-2 vrs] or CDC [>2 vrs] growth curves) and severe obesity (≥20% greater than 95th percentile). RESULTS: The cohort includes 98,312 infants and young children and is racially/ethnically diverse (e.g., 14.0% Black, 45.3% Hispanic). Among patients 0 to <6, 6 to <12, and 12 to <24 months, 5.3, 12.1, and 20.2% had elevated weight-for-length, respectively. Among children 2-5 years, 15.0% were obese, compared to <11% nationally. Severe obesity prevalence in our cohort was 1.8% overall, 2.6% in Hispanics, and 3.8% in Native Hawaiians/Pacific Islanders. Nearly 70% of children had ≥2 BMI measures. Among 4-5 year olds, 74% had BMI measures at least 2 years apart. CONCLUSIONS: ADVANCE's data repository is a powerful resource for identifying and characterizing this Early Life Cohort. It offers unique and critically important opportunities to identify and mitigate early life determinants of obesity in this large population of hard-to-reach children.

### **B92**

RESPIRATORY DISTRESS SYNDROME IN MODERATELY PRETERM INFANTS AND RISK OF EPILEPSY: A POPULATION-BASED STUDY. Sandra Kruchov Thygesen\*, Morten Olsen, Lars Pedersen, John Rosendahl Østergaard, Henrik Toft Sørensen (Department of Clinical Epidemiology, Aarhus University Hospital, Denmark) Background: Infant respiratory distress syndrome (IRDS) is a common respiratory disorder among preterm infants. Known morbidities include among others, intracerebral hemorrhage. However, data on long-term morbidity are sparse. Objectives: To examine the association between IRDS in moderately preterm infants and epilepsy in young adults. Methods: We conducted this population-based cohort study using individual-level data linkage among nationwide registries. The Danish Medical Birth Registry allowed us to identify all live infants born between 32 and 36 weeks of gestation during January 1, 1978 to December 31, 2009 in Denmark. Using the Danish National Registry of Patients covering all Danish hospitals, we then identified all infants diagnosed with IRDS in the same period. We computed the cumulative incidence proportion of epilepsy at age 15 with death as competing risk. Using Cox's proportional hazards regression, we computed hazard ratios comparing children with an IRDS diagnosis to those without adjusted for covariates including sex, birth year, gestational age, 5minute Apgar score, multiplicity, and maternal age. We also stratified by these covariates. Results: We identified 96,120 children born during 32-36 weeks of gestation. Among these, 6,516 had an IRDS diagnosis as infants. The cumulative incidence of epilepsy by age 15 in IRDS patients was 2.0% (95% confidence interval (CI): 1.9%-2.1%). After adjustment, the corresponding hazard ratio was 1.3 (95% CI: 1.1-1.5). Conclusion: The risk of epilepsy is increased for children born during 32 to 36 weeks of gestation and diagnosed with IRDS compared to children without the IRDS diagnosis.

**5-MINUTE APGAR SCORE AS A MARKER FOR DEVELOPMENTAL VULNERABILITY AT 5 YEARS OF AGE**. Neda Razaz\* W. Thomas Boyce, Marni Brownell, Douglas Jutte, Helen
Tremlett, Ruth Ann Marrie, KS Joseph (School of Population and Public Health, Faculty of Medicine, University of British Columbia, Vancouver, Canada)

Background: The Apgar score has been examined in relation to various health outcomes, but its association with childhood developmental outcomes remains unclear. We assessed the relationship between 5-minute Apgar scores and developmental vulnerability at 5 years of age. Methods: We conducted a population-based retrospective cohort study in Manitoba, Canada. All children born between 1999 and 2006 at term gestation, with a documented 5-minute Apgar score and a completed Early Development Instrument (EDI) assessment at age 5 were included. Logistic regression was used to assess the association between Apgar score and vulnerability on each domain of the EDI. Results: The majority (81.5%) of children in the study (n=33,883) had a 5-minute Appar score of 9; 1% of children had a score <7, 11.9% had scores of 7 or 8 and 5.6% had a score of 10. Children with Appar scores <10 had higher odds of vulnerability on the physical domain at age 5 years compared with children with a score of 10 (adjusted odds ratio [aOR] for an Apgar of 9=1.23, 95% CI 1.05-1.44). Similarly, children with Apgar scores of <10 were more vulnerable on the emotional domain (aOR for an Apgar of 9=1.20, 95% CI 1.03-1.41). Nevertheless, the Apgar-based prognostic model had a poor sensitivity for physical vulnerability (19%, 95% CI 18-20%). Conclusion: The risk of developmental vulnerability at 5 years of age is inversely associated with the 5-minute Apgar score across its entire range, and the score can serve as a population-level indicator of developmental risk.

### **B94**

THE ASSOCIATION BETWEEN PARENTAL PERCEPTIONS OF BODY NORMS AND CHILD'S RISK OF T2DM. S Fernando\*, K Fulda S Franks N Habiba (UNT Health Science Center, Fort Worth, TX)

Background: The growing rate of type 2 diabetes mellitus (T2DM) in children presents a critical public health problem. This study examined the association between parental perceptions of weight norms and child's risk of T2DM. Methods: Data were obtained from 290 10-14 year olds in North Central Texas participating in a study examining risk for T2DM. Parental perceptions of norms were measured using three questions: "Most people who are important to me think that children who are chubby look cute," "My child is not overweight; he or she is at the correct healthy weight compared to other children I know" and "Most people have children who are underweight compared to my child". Associations were assessed using logistic regression models controlled for race, gender and age. Results: Among 290 subjects, 5.7% were Caucasian, 15.4% were African-American, and 78.9% were Hispanic. Mean age was 11.87±1.4, while 50.3% of subjects were female. A higher perception of an overweight child had increased odds of being high risk for T2DM (1.749 OR, 95% CI: 1.518-2.016). Perception of a chubby child as cute had slightly increased odds of being high risk for T2DM (1.022 OR, 95% CI: 0.897-1.165). Finally, perceiving other children as underweight in comparison had increased odds of being high risk for T2DM (1.203 OR, 95% CI: 1.064-1.361). Conclusions: Results from this study suggest that parental perception of body norms is associated with T2DM risk. Educating parents on body norms and healthy behaviors may lead to a reduction in their child's risk for T2DM.

## PEDIATRIC HOSPITALIZATION FOLLOWING SPONTANEOUS VERSUS MEDICALLY INDICATED LATE PRETERM BIRTH IN NEWFOUNDLAND AND LABRADOR. CE Wright (Newfoundland and Labrador Centre for Health Information)

Background: A recent analysis of neonatal outcomes in children born late preterm (between 34 and 36 weeks' completed gestation) found higher rates of adverse health outcomes in children born following induced labor or Caesarean without labor, compared to those born following spontaneous preterm labor. We sought to determine whether differences in hospitalization outcomes by delivery method among children born late preterm persist beyond the neonatal period. Methods: A retrospective cohort analysis was performed using linked birth and hospitalization records for children born at 34-36 weeks' completed gestation in Newfoundland and Labrador between 1996 and 2005 (N=2038). Rates of hospitalization at ages 28 days to 5 years, repeat hospitalization within 1 year of an initial pediatric hospitalization, and average length of hospital stay in children born following induced labor or Caesarean without labor were compared to outcomes in children born following spontaneous preterm labor. Results: Compared to children born following spontaneous preterm labor, children born following induced preterm labor had slightly higher rates of hospitalization at ages 28 days to 5 years (RR 1.05, 95% CI 1.00-1.11), but pediatric hospitalization rates were not significantly higher for children born by Caesarean section or following any medically indicated preterm delivery. Rates of repeat hospitalization and average length of stay also did not differ significantly between delivery groups. Conclusion: Overall pediatric hospitalization outcomes show few significant differences by method of delivery in children born late preterm. It remains to be determined whether differences in individual disease outcomes are observed beyond the neonatal period.

### **B96**

## PREGNANCY INTENTION AT CONCEPTION AND SUBSEQUENT BREASTFEEDING AMONG MOTHERS AGED 15-44 IN THE UNITED STATES. Febo-Vazquez I\*, Martinez G (National Center for Health Statistics, CDC, Hyattsville, MD)

The long term benefits of breastfeeding have been well documented, as have several demographic and behavioral factors that may play a role in the initiation of breastfeeding; however, less is known about the association of pregnancy intentions and breastfeeding. Using nationally representative data on women aged 15-44 from the 2006-2010 National Survey of Family Growth (NSFG), we assessed the association between pregnancy intention at conception and breastfeeding initiation and duration. We analyzed women's most recent pregnancies ending in live births (n=3,049) and found that a lower percentage of women with unintended births initiated breastfeeding compared with those with intended births (61% vs 73%, respectively, p<0.0001). As expected from prior studies, women who initiated breastfeeding were more likely to be white, older, married, and of higher education. In the multivariate analyses, women with unintended pregnancies were less likely to initiate breastfeeding (OR=0.69; 95% CI, 0.51-0.94) compared with women with intended pregnancies after controlling for race and Hispanic origin/nativity, and age at birth. No differences in breastfeeding initiation by pregnancy intention were observed after adding levels of education to the model. In terms of breastfeeding duration, we found that women with an unintended pregnancy were less likely to still be breastfeeding after 6 months (OR=0.71; 95% CI, 0.53-0.94) compared with women who had an intended pregnancy but this was no longer significant after controlling for socio-demographic characteristics (OR=0.96; 95% CI, 0.68-1.31). Pregnancy intendedness appears to not be associated with breastfeeding initiation and breastfeeding duration after controlling for demographic factors.

COMPLEMENTARY FEEDING CHOICES AMONG PARTICIPANTS IN THE HEALTHY MOMS STUDY, A RANDOMIZED TRIAL TO LIMIT GESTATIONAL WEIGHT GAIN IN OBESE PREGNANT WOMEN. Eckhardt CL\*, Vesco KK, Karanja N, Leo M, Smith KS, Stevens VJ (Portland State University, Portland, OR)

The Healthy Moms behavioral intervention randomized trial was effective in its primary goal of reducing gestational weight gain in obese pregnant women. The intervention included components on dietary modification, food preparation, and infant feeding. We explored whether complementary feeding practices differed by intervention group, as a secondary outcome of interest. Obese pregnant women (n=114) were recruited at <20 weeks gestation from Kaiser Permanente Northwest HMO patients. Controls received one-time dietary advice and standard care. The intervention group received a weekly behavioral intervention. We analyzed data from 9 months (n=85: 44 control, 41 intervention) and 12 months postpartum (n=77: 41 control, 36 intervention). Previous work revealed no differences by group in breastfeeding practices. We focused on the introduction of fruits and vegetables, sugar-sweetened beverages, and processed foods. At 9 months, we found no differences by group in the mean number of fruits and vegetables (from a list of 8) provided (6.0±1.9 overall), in the proportion of children receiving sugar-sweetened beverages (21% overall), nor in the proportion of children (67% overall) who had tried any of 8 listed common processed foods. Similar results were seen at 12 months, although the proportion of children that had tried any listed processed foods tended to be higher in the control v. the intervention group (30% v. 14%, p=0.10), indicating a possible intervention effect that did not reach statistical significance due to small sample size. Behavioral interventions targeting pregnant mothers may have intergenerational impacts and should include long-term follow up of participants and their children.

### **B98**

THE SOUTH CAROLINA CEREBRAL PALSY PROJECT. Q Li\*, R Newman, N Paneth, H Kirby, JE Vena, S Kinsman, RS Kirby (Medical University of South Carolina) Cerebral Palsy (CP) is a relatively common and severe motor disability in which genetics, pregnancy and perinatal events play a role, and there is a suggestion of a higher prevalence in the US. A CP prevalence of 3.1 to 3.6 per 1,000 8-year old children was recently found by the CDC in Alabama, Georgia, Wisconsin and Missouri, figures much higher than the rate of 1.5 – 2 per 1,000 live births found in several European registries and older data from California. We attempted to ascertain all cases of CP diagnosed in South Carolina from 1996 to 2013. We identified 2,641 children up to age 4 years with a CP diagnosis by searching linked records from the Department of Disabilities and Special Needs (DDSN 429 cases), Hospital Discharge Files (805 cases), and Medicaid files (2,510 cases) using the International Classification of Diseases, Ninth Revision, Clinical Modification codes 343.0 - 343.9. DDSN serves any South Carolinian meeting the disability requirements, while a CP diagnosis qualifies a child for the Supplemental Security Income Program and the child is then eligible for the Medicaid program. The prevalence of CP was 2.7/1,000 live births. Among twins, CP prevalence was 6.0/1,000 births. Birth prior to 32 weeks was found in 28.1% (695) of 2,475 singletons and in 65.1% (69) of 106 twins. Birth below 1,500 g was found in 25.9% (641) of singletons and 67.0% (71) of twins. This study joins recent CDC research in finding a CP prevalence in the US above 2.5/1,000 live births.

POLYFLUORINATED COMPOUNDS AND INDICATORS OF IMMUNE FUNCTION IN CHILDREN AGED 12 – 19 YEARS: NHANES. Stein CR\*, McGovern KJ, Pajak AM, Wolff MS (Mount Sinai School of Medicine, New York, NY)

Polyfluorinated compounds (PFCs) are widely used as surface treatment chemicals to create oil, stain, grease, and water repellent coatings on carpet, textiles, leather, and paper. Measurable levels of several PFCs have been universally detected in human sera and also found in amniotic fluid, maternal and umbilical cord blood, and breast milk. Toxicological studies identified immunotoxic effects of PFCs. Epidemiological evidence of PFC exposure and immune perturbation is limited and mixed. To further explore this association we examined PFC serum concentration among 12 to 19 year old children in relation to measles, mumps, and rubella antibody titers in NHANES 1999 - 2000 and 2003 - 2004 (n=1191) and allergic conditions and allergic sensitization in NHANES 2005 – 2006 (n=640). In a survey-weighted linear regression model containing PFOS, PFOA, PFHxS, and PFNA that was adjusted for age, sex, and race/ethnicity, a doubling of PFHxS serum concentration was associated with a 1.4% decrease (95% CI -2.7, -0.1) in measles titers. A doubling of PFOS was associated with a 0.3% decrease (95% CI -0.5, -0.1) in mumps titers. It is unclear if either of these reductions in titer levels are substantively meaningful. There was no association between any PFC and rubella titers. In a survey-weighted logistic regression model containing PFOS, PFOA, PFHxS, and PFNA that was adjusted for age, sex, race/ethnicity, body mass index, and serum cotinine, the overall pattern was of no association between PFC concentration and prevalent asthma, allergies, or allergic sensitization. In this cross-sectional analysis the association between PFCs and immune function remains mixed.

### **B100**

ASSOCIATION OF PRETERM BIRTH WITH BOTH AUTISM SPECTRUM DISORDER AND DEVELOPMENTAL DISABILITIES. JL Daniels\*, E Rubenstein , C Cordero, CJ Newschaffer, BY Park, L Croen, D Fallin, S Levy, J Pinto-Martin, L Schieve, D Schendel, G Windham (University of North Carolina at Chapel Hill)

Preterm birth and low birth weight have been associated with increased risk of autism spectrum disorder (ASD) and other developmental disabilities (DD). Improved understanding of these associations may help target early intervention and direct etiologic research. We investigate preterm birth and small size for gestational age (SGA) in relation to neurodevelopment at ages 3-5 years in the Study to Explore Early Development (SEED), a case-control study of children born in six U.S. sites, 2003-2006. Gestational age, birth weight, and covariates were obtained from birth records, medical records, and maternal interview. Logistic regression was used to compare the odds of preterm birth (< 37 weeks completed gestation) and SGA (birth weight below the 10th percentile for gestational age among term births) for 598 children with clinicconfirmed ASD and 852 children with non-ASD DDs to 787 non-ASD children randomly sampled from the population (POP), controlling for child's sex, birth order, and maternal age, body mass index, race, and ethnicity. ASD was associated with both preterm birth (Adjusted Odds Ratio (OR) 1.8, 95% Confidence Interval (CI) 1.2, 2.8) and SGA (OR 1.8; CI: 1.1, 2.6). DD was similarly associated with preterm birth (OR 3.6; CI 2.5, 5.2) and SGA (OR 1.9; CI: 1.3, 2.9). Associations were not modified by maternal age or body mass index. Both ASD and DD were more strongly associated with very preterm birth (<32 weeks completed gestation). We will further assess the specificity of observed associations among phenotypic subgroups of ASD and investigate potential antecedents of preterm delivery.

RACIAL DIFFERENCES IN CROSSING GROWTH PERCENTILES IN INFANCY AND RISK OF CHILDHOOD OBESITY. \*SS Hawkins, SL Rifas-Shiman, MW Gillman, and EM Taveras (Boston College, Chestnut Hill, MA)

Upward crossing of major weight-for-length (WFL) percentiles in infancy is associated with later obesity. However, little is known of how these associations differ by race, a variable often poorly measured in clinical databases. We used data from the CENTURY Study, a longitudinal clinical database of well-child visits linked to each child's birth certificate, which contains race of the mom. We examined associations of ever crossing upwards ≥2 (v. <2) major WFL percentiles in the first 24 months of life with obesity at age 5 (age- and sex-specific body mass index ≥95th percentile) for white and black children. We included 12,033 children with percentile crossing data in all 4 six-month periods in the 1st 24 months (1-6, 6-12, 12-18, 18-24) and BMI data at 5 years. We used logistic regression models, adjusted for sex, age and year at outcome assessment, and stratified by race. Among white children, 63% crossed upwards ≥2 major WFL percentiles and 12% were obese v. 7% obese among <2 crossings. Among black children, 64% crossed upwards ≥2 major WFL percentiles and 24% were obese v. 9% obese among <2 crossings. Black children (OR 3.11, 95% CI 2.17-4.47) who had ever crossed upwards ≥2 major WFL percentiles had a higher odds of obesity at age 5 than white children (1.84, 1.59-2.12) (interaction p=0.01). These results suggest that rapid weight gain in infancy is more deleterious among black than white children and highlights advantages of linking databases to identify racial differences in risk factors for obesity.

### B102

FEMALE DISADVANTAGE IN VERY YOUNG IMMIGRANT CHILDREN'S HEALTH CARE USE: A SYSTEMATIC REVIEW. Pulver A\*, Urquia M, Ramraj C (Department of Epidemiology, Dalla Lana School of Public Health, University of Toronto, Toronto, Canada) Background: Son-preference in several world regions culminates in higher mortality, inadequate immunization, and less frequent health care use for young girls compared to boys. Higher male to female birth ratios among immigrant groups from such regions, including India, Pakistan and China, imply that gender bias persists after immigration to high-income countries. It is unknown if such bias may affect parents' health care decisions for their children. Objective: To review the literature regarding gender disparities in health care use among young immigrant children. Methods: A systematic review of the literature in Medline, Embase, PsycINFO and Scopus databases identified studies reporting gender-specific estimates of health care use of immigrant children 0-5 years. We retrieved 1547 titles, 103 were given full-text reviews, and 12 met inclusion/exclusion criteria. Data extraction was duplicated and a quality assessment tool was applied to each included study. Results: Greater use of acute health services and some routine care including immunizations and medications was observed for immigrant boys. No consistent gender differences were found for primary care. Select US studies demonstrated higher health care use from physician exams and health expenditures among immigrant females than immigrant males. The absence of gender-based analysis and the neglect of acculturation factors were noted. Discussion: Patterns indicate that health care use among young immigrant children may be gendered, however studies are lacking. Gender-based analysis may be important for studying immigrant children's health care. Studies are important to help health care providers identify immigrant families who may have children with unmet health care needs.

IS EARLY PRENATAL VITAMIN D STATUS ASSOCIATED WITH SOCIAL AND EMOTIONAL **DEVELOPMENT AMONG INFANTS?** D Chawla\*, JL Daniels, BF Fuemmeler, SE Benjamin Neelon, C Hoyo, S Murphy (University of North Carolina, Chapel Hill, NC) Many pregnant women in the United States have insufficient vitamin D, but the impact on infant development is unclear. We investigated the association between early prenatal serum 25hydroxyvitamin D [25(OH)D] concentration and children's social and emotional development in the Newborn Epigenetic Study, a prospective study of pregnancies from 2009 to 2011 in Durham, North Carolina. We measured 25(OH)D concentrations in 1st or 2nd trimester serum samples and characterized vitamin D as deficient, insufficient, or sufficient based on Institute of Medicine recommendations. Covariates were derived from maternal questionnaires. Mothers completed the Infant Toddler Social-Emotional Development Assessment when children were 12-24 months of age. We used multivariable linear regression to obtain betas and 95% confidence intervals for the association between 25(OH)D and internalizing and externalizing behaviors, adjusted for maternal age, education, parity, smoking, marital status, pre-pregnancy BMI, and infant gender. We investigated effect modification by race. Of the 224 mother-infant pairs with complete data, 19% of mothers were vitamin D deficient and 48% were vitamin D insufficient. Only 8% of black women had sufficient vitamin D compared to 57% of white and Hispanic women. Mean developmental scores were similar by race. Overall, Vitamin D was not associated with social emotional development; but, vitamin D deficiency and insufficiency among black mothers were associated with reduced mean internalizing scores (β = -0.33, 95%) CI: -0.56, -0.10) and ( $\beta = -0.28$ , 95% CI: -0.51, -0.06), respectively. Though imprecise, preliminary results warrant further investigation regarding a role for prenatal vitamin D and children's early emotional development.

### B104

THE ASSOCIATION BETWEEN PARENTAL BELIEF IN SELF-SUFFICIENCY AND CHILD'S RISK OF T2DM. S Fernando, K Fulda S Franks N Habiba (UNT Health Science Center, Fort Worth, TX)

Background: The growing rate of type 2 diabetes mellitus (T2DM) in children presents a crucial public health concern. This study examined the association between parental belief in selfsufficiency and child's risk of T2DM. Methods: Data were obtained from 290 10-14 year olds in North Central Texas participating in a study examining risk for T2DM. Questions on parental self-sufficiency were measured using three questions, including "Getting sick just happens to children," "The only way I can make my child stay healthy is to do what other people tell me to do" and "I can do many things to fight illness in my child". Associations were assessed using logistic regression models controlled for race, gender and age. Results: Among 290 subjects, 5.7% were Caucasian, 15.4% were African-American, and 78.9% were Hispanic. The mean age was 11.87±1.4, while 50.3% of subjects were female. Increased perception of the inevitability of sickness had increased odds of being high risk for T2DM (1.122 OR, 95% CI: 1.01-1.380). Increased belief that a child's health is affected by others' actions had slightly increased odds of being high risk for T2DM (1.257 OR, 95% CI: 1.007-1.631). Finally, belief in the ability to fight illness in a child had decreased odds of being high risk for T2DM (0.764 OR, 95% CI: 0.591-0.987). Conclusions: Results from this study suggests that parental belief in self-sufficiency is associated with T2DM risk. Improving a parent/guardian's belief in self-sufficiency may lead to a reduction in their child's risk for T2DM.

**TRIVALENT INACTIVATED INFLUENZA VACCINE DURING PREGNANCY AND RISK FOR ADVERSE INFANT DEVELOPMENT**. Avalos LA\*, Ferber J, Zerbo O, Naleway A, Kauffman T, Bulkley J, Li DK. (Kaiser Permanente Northern California, Division of Research, Oakland, CA 94612)

Concerns by pregnant women regarding the safety of the influenza vaccination remain a barrier to uptake, despite the demonstrated efficacy of reducing severe influenza infections in pregnant women and their newborns. The purpose of this study is to assess the risk of trivalent influenza vaccination (TIV) during pregnancy on early infant development. We conducted a multi-site cohort study of pregnant women receiving prenatal care from Kaiser Permanente Northern California (KPNC) and Northwest (KPNW) and followed them and their newborns until six months post-delivery during the 2010-2011 and 2011-2012 influenza seasons. Information on TIV during pregnancy was ascertained from medical records and self-report (if participant was vaccinated outside the health plan). We include 1458 mother-infant pairs (847 from KPNC, 611 from KPNW) in which the mother completed the Ages and Stages Questionnaire-3 (ASQ) for their 6 month infant. No differences were found in early infant development for infants of vaccinated women compared to un-vaccinated women with regard to Communication (93% were on schedule vs. 93%, p=0.641) (vaccinated vs. un-vaccinated, respectively), Gross Motor (89% vs. 89%, p=0.621), Fine Motor (91% vs. 92%, p=0.273), Problem Solving (94% vs. 93%, p=.615), and Personal-Social (90% vs. 87%, p=0.081). Our findings persisted after adjusting for potential confounders. Our preliminary findings suggest TIV exposure during gestation does not adversely impact early infant development.

### **B106**

**DIABETES DECREASES THE DURATION OF BREASTFEEDING IN AFRICAN AMERICAN WOMEN**. Chetwynd EM\*, Stuebe AM, Troester M, Palmer JR (University of North Carolina at Chapel Hill)

Limited research from predominantly white populations suggests that women who have type 2 diabetes wean earlier than those without diabetes. African American women are disproportionately affected by type 2 diabetes as well as having lower rates of breastfeeding. We examined the relation between pre-pregnancy diabetes and breast feeding duration in African American (AA) women in data from the Black Women's Health Study, a large cohort of AA women followed since 1995. There were 3404 participants who gave birth for the first time between 1997 and 2009. After examining covariates for health behaviors, demographics, and metabolic poor health, our multivariable hazard model included terms for family history of diabetes, age, vigorous exercise, and body mass index (BMI) prior to pregnancy; other demographic, health behavior, and metabolic factors did not meet criteria for confounding. Survival curves demonstrated a markedly reduced duration of breastfeeding in diabetic women (crude HR 0.48, 95% CI 0.39, 0.60), The HR was only slightly attenuated in a fully adjusted model (HR 0.56, 95% CI 0.45, 0.70). Survival curves stratified by obesity (BMI >30) indicated that the association was present both among obese (HR 0.40, 95% CI 0.31, 0.50) and nonobese women (HR 0.58, 95% CI 0.46, 0.73). The findings support the hypothesis that prepregnancy diabetes is associated with a shorter duration of breastfeeding and suggest that the relation is not explained by the greater prevalence of obesity in diabetic women.

HEARING LOSS AND EAR INFECTIONS FROM BIRTH THROUGH FIRST GRADE: THE U.S. EARLY CHILDHOOD LONGITUDINAL STUDY-KINDERGARTEN CLASS OF 2010–11 (ECLS-K:2011). Hoffman HJ\*, Li C-M, Themann CL

Objective: To describe associations between ear infections and hearing loss from birth through spring of first grade. Methods: ECLS-K:2011 children (n=13,399) were drawn from a national sample of public and private schools, both full- and part-day kindergarten classes in 2010–11. Information on medically-diagnosed ear infections (Els), hearing loss, and health history, was reported by parents; additional information was provided by teachers, schools, and daycare providers. Trained examiners administered age-appropriate assessments of intellectual development and hearing in school settings. Logistic regression models were statisticallyadjusted for covariates using national sampling weights. Results: Before age 2, 39.6% had 1+ Els. By kindergarten, 66.8% had 1+ Els; by spring of first grade 80.3%. Before age 2, 90.2% of Els were treated with antibiotics, 14.7% ear drops, 13.0% surgically-implanted ear tubes (ETs), 2.3% 'watch/wait' (multiple treatments occurred); Els from kindergarten-to-spring first grade, 72.1% antibiotics, 21.1% ear drops, 3.6% ear tubes, 10.1% 'watch/wait'. Most common diagnoses for children referred for hearing trouble were 'middle-ear fluid' and 'acute/chronic ear infection'. Hearing loss prevalence was 1.2% if no Els reported, 2.9% with Els (without ETs), and 10.9% with ETs. Hearing loss was associated with EIs (without ETs), odds ratio (OR)=2.2, 95% confidence interval (CI): 1.0-4.9, while ETs increased the risk, OR=7.5, 95%CI: 3.4-16.6, in multivariable models adjusted for parents' education, insurance, children's sex, race, plurality, birth weight, birth complications/NICU, breastfeeding, and overall health. Conclusion: Hearing loss in early primary grades is associated with Els and risk is 3-fold higher for children treated with ETs.

### **B108**

A LONGITUDINAL ANALYSIS OF EAR INFECTION AND HEARING IMPAIRMENT IN PRE-SCHOOL AGED CHILDREN: THE U.S. EARLY CHILDHOOD LONGITUDINAL STUDY-BIRTH COHORT: 2001. Li C-M, Hoffman HJ\*

Objective: To estimate prevalence of ear infections (Els) and hearing impairment (HI) and impact of Els on HI in a nationally-representative study of early childhood. Methods: The ECLS-B is a longitudinal study of 2001 U.S. births. Parent interviews and brief exams were completed at 9 months (N=10,688 infants), 2 years (N=9,835), 4 years (N=8,903), and upon kindergarten entry (N=6,856). HI was doctors' diagnosis of child's hearing difficulty or deafness. Exposure was parents' or caregivers' report of medically-diagnosed Els. Multivariable logistic regression was used to model the effect of preceding EIs on subsequent HI, while adjusting for covariates using national sampling weights. Adjusted odds ratios (aOR) and 95% confidence intervals (CI) are reported. Results: Period-specific prevalence of 1+ medically-diagnosed Els from birth-9 months was 41.4%: 46.6%. 9 months-2 years: 48.7%. 2-4 years: 20.8%. 4 years-kindergarten. Period-specific prevalence of HI was 0.6%, birth-9 months; 1.1%, 9 months-2 years; 1.6%, 2-4 years; 1.2%, 4 years-kindergarten. Multivariable logistic regression showed HI at kindergarten. entry was significantly associated with EI at 2-4 years (aOR=4.75, 95%CI: 1.83-12.37), at 4 years-kindergarten entry (aOR=5.55, 95%CI: 2.73-11.30), from birth-4 years (aOR=5.46, 95%CI: 1.51-19.81), and from birth-kindergarten entry (aOR=5.13, 95%CI: 1.27-20.67) after adjusting for sex, race/ethnicity, birth weight, newborn medical problems, breastfeeding, family poverty, health insurance, health status, child care, mother's education, and geographic region. Conclusion: Preceding Els have significant impact on subsequent HI in preschool-aged children. Special attention and follow-up are needed for pre-school aged children with Els.

PARENTAL PERCEPTIONS OF ALTERNATIVE PEDIATRIC HEALTHCARE VENUES IN GREATER NEW ORLEANS. Morrison FJR\*, Rabito FA, Smith SM, Carlson JC (Tulane University School of Public Health and Tropical Medicine, Department of Epidemiology, New Orleans, LA)

Introduction: Differential access has contributed to racial disparities in health outcomes. In post-Katrina New Orleans, use of mobile and school-based venues were prioritized. This survey aims to assess the perceived quality of these novel venues. Methods: This ongoing survey has been administered at health/community fairs around New Orleans since June 2014. Questions include pragmatics, skills, expectations, and marginalization components of the Barriers to Care Questionnaire (BCQ), using a Likert scale from 0 (big problem) to 100 (not a problem). Parents completed questionnaires for one child. Results: Preliminary results in this primarily African-American study population of 34 suggest most children had access to primary care (97%), and received care from the same physician for over 1 year (88%). Children were mainly seen at private (77%) or community (21%) clinics. Among the one-third with chronic conditions, 71% felt they had access to care for all their conditions, while 14% had none. Chronic care was mainly provided exclusively by specialists (44%) or PCPs (33%), but sometimes in combination. Those who utilized mobile, school, or community clinics scored these clinics higher than those who had not on all four BCQ components. Clinics scored lowest on pragmatics (means 72-77) and marginalization (means 67-79) among non-users. Overall, mobile clinics scored highest among both groups, while users scored community and non-users scored school based clinics lowest. Conclusion: Access to care is not perceived to be a problem in New Orleans. Non-users of novel venues (school, community, and mobile clinics) were most concerned about pragmatics (logistical, cost) and marginalization (negative experiences) in these facilities.

### **B110**

## **COCOONING TO PROTECT INFANTS FROM PERTUSSIS: POLICY ADHERENCE.** JR Wilder\*, DS Lauderdale (University of Chicago)

Background: Pertussis rates have steadily increased, with a significant shift in morbidity towards infants 6 months and younger, who are too young to have completed the vaccination series. In 2006, the Centers for Disease Control and Prevention and the Advisory Committee on Immunization Practices recommended cocooning, the immunization of infants' close contacts who cannot be protected through immunization. Purpose: To assess adherence to cocooning by determining the proportion of mothers and fathers who received a Tdap vaccine since the 2006 cocooning recommendations and to determine factors predicting parental vaccination. Methods: Data from adults and children participating in the National Health Interview Survey (2010-2012) were examined. Log binomial regression was used to assess predictors of parental vaccination with- and without adjustment for parental socio-demographic characteristics and seasonal flu vaccination. Results: Twenty-two percent of parents with children born since 2006 received a Tdap vaccination. Fathers' rate of Tdap coverage was lower than mothers (19.4% vs. 24.7%). Non-Hispanic Blacks and Hispanics Tdap coverage was lower than non-Hispanic Whites coverage (16.2% and 10.8% vs. 28.4%). While Tdap coverage among parents rose significantly from 2010 to 2012, there is an increasing gap in coverage between mothers and fathers, with a greater gap in coverage for more recent births. Conclusion: While Tdap coverage has increased among parents six years after cocooning recommendations were issued, it stills remains low, highlighting the need for greater awareness among parents and physicians. Disparities in Tdap coverage highlight the need for greater efforts aimed at fathers and minority parents.

## CHARACTERISTICS OF CHILDREN IN MEDICAID MANAGED CARE AND MEDICAID FEE FOR SERVICE. Patricia Lloyd\*, Alan E. Simon, Jennifer Parker

Medicaid claims have been used to characterize utilization patterns of child Medicaid beneficiaries. However, because states are increasingly adopting Medicaid managed care plans, analyses of children in Medicaid based only on claims for enrollees in Fee for Service (FFS) programs may not apply to the general Medicaid population. We use the 2003-2005 National Health Interview Survey linked to 2003-2005 Medicaid Analytic eXtract files to examine associations between sociodemographic, health, and geographic characteristics of children aged 0-17 years and enrollment in Medicaid FFS compared to a comprehensive managed care (CMC) program. Additional analyses of age-specific health outcomes were performed on a subset of children aged 6-17 years. We used chi-square tests to assess associations and provided 95% confidence intervals for point prevalence estimates. Higher percentages of children in CMC compared to FFS were non-Hispanic white, lived under the 100% federal poverty level, had excellent/very good health, lived in the Northeast and West, and lived in large central metro areas. No significant differences were observed by sex, age, and asthma diagnoses between children enrolled in CMC and FFS. Among children age 6-17 years, higher percentages of children enrolled in FFS compared to children in CMC were diagnosed with learning disabilities or developmental delay, and attention deficit hyperactivity disorder. Researchers using data from children enrolled only in Medicaid FFS programs to describe children enrolled in Medicaid should understand differences between children enrolled in CMC and FFS. Generalization of study results from FFS claims may depend on the outcomes examined.

#### **B112**

## ENGAGING MEN TO PROMOTE AND SUPPORT EXCLUSIVE BREASTFEEDING: A REVIEW OF USAID'S CHILD SURVIVAL AND HEALTH GRANTS PROGRAM 2003 - 2013. JM Yourkavitch\*, J Alvey, DM Prosnitz, MH Labbok, JC Thomas (University of North Carolina,

JM Yourkavitch\*, J Alvey, DM Prosnitz, MH Labbok, JC Thomas (University of North Carolina Chapel Hill, NC)

Mothers need support to exclusively breastfeed but the most effective method in different contexts remains largely unknown. The role of men in promoting and supporting exclusive breastfeeding has not been systematically evaluated at the community level in different countries. USAID's Child Survival and Health Grants Program supported community-based breastfeeding promotion and support efforts. We examined the mean exclusive breastfeeding prevalence difference in project areas where men were engaged in breastfeeding promotion and support (0.27; 95% CI: 0.24 – 0.30; n=27) to the prevalence difference where men were not engaged (0.20: 95% CI: 0.11 - 0.29: n=22). In sub-Saharan Africa the prevalence difference was 0.39 (95% Cl 0.25 - 0.53; n=14) where men were engaged vs. 0.28 (95% Cl 0.15 - 0.41;n=11) where they were not. Other regions had no difference or too few projects to analyze separately. To examine policy implications further, we used logistic regression adjusting for population size and region to examine the relationship between male engagement categorized by intensity (for example, one-to-one counseling is high intensity compared to a health fair which is low intensity) and post intervention prevalence higher than the median value. There was a slight increase in the odds of post-intervention exclusive breastfeeding prevalence higher than 0.72 where there was high-intensity male engagement compared to no male engagement (OR: 1.02; 95% C.I. 0.27 – 3.96). Our small sample size did not support a robust multivariable analysis with male engagement categories; however, our analyses suggest higher exclusive breastfeeding prevalence where men were engaged compared to where they were not.

## **Plenary Session 3**

# Tuesday, June 16th 2:00 – 3:15 pm

## Translational Obstetric Epidemiology



**BLOOD PRESSURE DURING PREGNANCY AND RISK OF HYPERTENSION LATER IN LIFE: A LONGITUDINAL STUDY OF POUCHMOMS.** GL Dunietz\*, KL Strutz, C Holzman, Y Tian, D Todem, B Bullen, J Catov (Department of Epidemiology and Biostatistics, Michigan State University)

Hypertensive disorders in pregnancy carry a long-term risk of cardiovascular disease (CVD) for women. However, future hypertension (HTN) status among pregnant women with moderately elevated blood pressure (MEBP), who do not meet criteria for hypertensive disorders, is unknown. We examined the risk of later HTN among pregnant women with MEBP or gestational hypertensive disorders (GHD) compared to normotensive women. Data are from the Pregnancy Outcomes and Community Health (POUCH) study, which enrolled pregnant women from 5 Michigan communities (1998-2004). We included 667 women with gestational BP measurements who participated in the POUCHMoms follow-up 7-15 years later. MEBP was defined as systolic BP (SBP) ≥120 or diastolic BP (DBP) ≥80 among pregnant women, without a hypertensive disorder. Weighted multinomial logistic regression models were run to estimate odds of MEBP or HTN at follow-up. Adjusted models controlled for maternal prenatal confounders and time between pregnancy and follow-up. Women meeting the MEBP criteria (59.6%) had significantly higher odds of HTN at follow-up (aOR=2.8; 95%CI:1.4-5.5). These trends were seen for MEBP identified prior to 20 weeks, and for MEBP observed due to elevated SBP either alone or combined with elevated DBP. GHD were also associated with increased odds of HTN at follow-up (aOR=17.0; 95%CI:6.1-47.2). All of the above relationships held after accounting for body mass index at follow-up. Moderately elevated blood pressure, particularly SBP, in pregnancy may be a risk factor for future HTN. Pregnancy may be an opportunity to identify women at risk for CVD who would not have been identified otherwise.

CUMULATIVE EXPOSURE TO BLOOD PRESSURE ELEVATIONS AND CORONARY ARTERY CALCIFICATION AMONG WOMEN WITH PRETERM BIRTH. Janet Catov\*, Andrew Althouse, Cora E. Lewis, Kiang J. Liu, Erica Gunderson (University of Pittsburgh School of Medicine, Dept of OB/Gyn/RS)

A history of preterm birth (PTB) confers excess cardiovascular morbidity and mortality for women, but mechanisms linking these conditions are not well understood. Compared to women with term births, those with PTB have higher blood pressure both before and after pregnancy, but the long term effects are unknown. We hypothesized that the cumulative exposure of modest, persistent blood pressure elevations in women with PTB would be associated with coronary artery calcification (CAC) many years after pregnancy. We studied 814 women (51% black) with live births (n=206 delivered preterm <37 weeks; n=608 with term births) between enrollment in the Coronary Artery Risk Development in Young Adults study (age 18-30 years) and 20 years later. Latent class modeling was used to identify blood pressure trajectories using measurements at baseline and at years 2, 5, 7, 10, 15, and 20, which were related to coronary artery calcification (CAC) greater than or equal to 100 Hounsfield units at year 20 according to preterm birth status. Three distinct systolic blood pressure (SBP) trajectories were identified: low-stable (n=451, 55.4%), moderate-stable (n=318, 39.1%), and elevated-increasing (n=45, 5.5%). Women with PTB compared to term births were more likely to be in the elevatedincreasing group (37.3% vs. 4.3%, p<0.0001). Rates of CAC among women in the elevatedincreasing group were higher in those with preterm compared to term births (33.3% vs. 12.5%). After accounting for age, race, education, body mass index and smoking, women with an elevated-increasing SBP trajectory and PTB had a 5.2-times higher risk of CAC compared to those with PTB and a low-stable SBP trajectory (95% CI 1.15, 23.20). In contrast, women with term births and an elevated-increasing SBP trajectory had no excess risk (aOR 1.31 [0.34, 5.44]). Women with PTB were more likely to follow a high risk blood pressure trajectory throughout young adulthood that was associated with excess risk of CAC in middle age. Women with PTB may benefit from blood pressure surveillance after pregnancy.

### MATERNAL DIETARY PATTERNS AND CARDIOMETABOLIC MARKERS DURING

**PREGNANCY**. Martin CL\*, Sotres-Alvarez D, Robinson WR, Daniels JL, Perrin EM, Stuebe AM, Siega-Riz AM (UNC Chapel Hill, Chapel Hill, NC)

Diet during pregnancy is a modifiable factor that may influence offspring adiposity by optimizing levels of cardiometabolic markers. To investigate the association between maternal dietary patterns and cardiometabolic markers (glucose, insulin, insulin resistance (HOMA), triglycerides, and cholesterol) during pregnancy, data from the Pregnancy, Infection, and Nutrition study (2000-2005) was used (n=513). Diet was assessed using a food frequency questionnaire. Patterns were derived using latent class analysis (LCA) and the Dietary Approaches to Stop Hypertension (DASH) index. Three patterns evolved from the LCA characterized by high intakes of: 1) hamburgers, hot dogs, bacon, French fries, fried chicken, white bread, and soft drinks; 2) some vegetables, fruit juice, refined grains, mixed dishes, processed meat, and empty calorie foods; and 3) fruits, vegetables, whole grains, low fat dairy, breakfast bars, and water. DASH index was based on eight components (fruits, vegetables, nuts and legumes, low fat dairy, whole grains, sodium, red and processed meat, and sweetened beverages) and scores categorized into tertiles. Linear regression was used to examine associations between patterns and cardiometabolic markers. After adjusting for potential confounders, DASH Tertile 3 (higher dietary quality) was associated with 10% decrease in the geometric mean of triglycerides compared to Tertile 1. The LCA pattern characterized by high intakes of fruits, vegetables, whole grains, etc. was associated with 11% and 12% decrease in the geometric mean of insulin and HOMA, respectively. Our results provide evidence that maternal diet quality affects offspring health. Scalable interventions are needed to help women adapt healthier dietary patterns during pregnancy.

CAN DECLINING PREGNANCY HYPERTENSION RATES BE EXPLAINED BY INCREASING PLANNED DELIVERIES? Roberts CL,\* Algert CS, Patterson JA, Morris JM, Ford JB. (Clinical and Population Perinatal Health Research, Kolling Institute, University of Sydney, Australia) Background: Pregnancy hypertension rates have declined in Europe, Canada and Australia, despite increasing rates of obesity, nulliparity and maternal age. As most pregnancy hypertension occurs at term (85-90%), the aim of this study was to determine whether increases in planned deliveries explain at least part of the decline. Method: Data were obtained from linked birth and hospital records for >1.16M deliveries in Australia 2001-2012. Pregnancy hypertension included gestational hypertension, preeclampsia and eclampsia, and planned delivery included labour induction and prelabour caesarean section. Annual gestational agespecific pregnancy hypertension rates were determined among pregnancies-at-risk and assessed using chi-square for trend (P<0.001). Multivariable logistic regression predictive models for pregnancy hypertension were developed using 2 years of data (2001-2 for forecasting: 2011-12 for backcasting) and the results applied to the data from other years to produce predicted trends (both forward and backward) that accounted for the actual trends in maternal factors. Results: The overall pregnancy hypertension rate declined from 9.9% to 7.7% (P<0.001). Contemporaneously, increasing planned deliveries led to a decline in deliveries ≥39 weeks (73.7% to 68.7%) and an increase at 37-38 weeks (19.8% to 24.5%). Gestational agespecific pregnancy hypertension rates declined from 38 weeks onwards, most steeply at ≥41 weeks. Based on changes in the prevalence of maternal risk factors, the pregnancy hypertension rate was predicted to increase by 7% (forecasting) to 26% (backcasting). Conclusions: The rate of pregnancy hypertension has decreased in Australia. An overall increase in early planned delivery explained much of the observed decline in pregnancy hypertension rates.

WHAT WAS THE IMPACT OF OREGON'S HARD-STOP POLICY TO LIMIT ELECTIVE EARLY-TERM DELIVERIES? Quigley BP\*, Snowden JM, Darney BG, Muoto I, Caughey AB (Oregon Health and Science University, Portland, OR)

Risk of adverse neonatal and maternal outcomes varies across the term period, with infants born early term (37 or 38 weeks' gestation) at increased risk for negative health outcomes. In 2011, Oregon implemented a Hard-Stop policy across the state to limit elective deliveries (induction and cesarean) before 39 weeks' gestation. We used Oregon vital statistics data to compare rates of obstetric interventions from 2008 - 2013 before and after 2011. We used multivariable models to compare maternal and neonatal outcomes before and after policy implementation. Outcomes examined included perinatal lacerations, maternal intensive care unit admission, maternal blood transfusion, chorioamnionitis, operative vaginal delivery, stillbirth, infant death, neonatal intensive care unit admission, Appar scores, and meconium. Between 2008-2010 there were 33,560 elective deliveries (~11,187/year) in the state of Oregon. Between 2012-2013 (2011 wash out year) there were 19,553 elective deliveries (~9,777/year). Implementation of the Hard-Stop policy was associated with lower odds of early elective inductions (adjusted odds ratio [aOR], 95% confidence interval [CI]: 0.62, 0.59 - 0.66) and cesarean deliveries (aOR, 95% CI: 0.64, 0.59 - 0.70). The policy was associated with significantly higher odds of maternal blood transfusion for full-term births (aOR, 95% CI: 1.40, 1.14 - 1.72) and chorioamnionitis for all births (aOR, 95% CI: 1.90, 1.76 - 2.06). The Oregon Hard-stop policy was successful in reducing early elective inductions and cesareans. The odds of important outcomes – blood transfusion and chorioamnionitis – were higher following the policy. Re-evaluation of the assumed positive health effects of limiting early elective interventions is needed.

## **Plenary Session 4**

## Tuesday, June 16th 4:15 – 5:30 pm

## Origins of Pediatric Diseases



**AUTISM, PESTICIDES AND GENE EXPRESSION.** I. Hertz-Picciotto,\* Blythe Durbin-Johnson, Lora Delwiche

Autism is a complex neurobehavioral disorder affecting 1-2% of children. Pesticides have been associated with autism and cognitive impairments, but their mechanisms are poorly understood. Children ages 2-5 years with autism spectrum disorder (ASD), and typical development (TD) were enrolled in the CHARGE (Childhood Autism Risks from Genetics and Environment) Study beginning in 2003. Diagnoses were confirmed or changed by trained clinicians using gold standard instruments assessing ASD, cognitive skills, and adaptive function. Extensive interviews collected sociodemographic and environmental exposure information, including household application of pesticides. Blood samples were collected, including PAX tubes for RNA sequencing. We examined associations between gene expression in the child at ages 2-5 years and household use of pesticide sprays and foggers during pregnancy (6 or more months vs. never) in ASD cases and TD controls separately. In ASD children, of the 32 most significant genes (unadjusted p-values <0.001), all but one was up-regulated in those exposed to pesticides, and 1/4th were found in annotated toxico- and pharmaco-genomic databases to also be differentially expressed in association with organophosphate pesticides. Of the top ten, two have been associated with thyroid dyshormonogenesis and two with Parkinson's Disease. In contrast, among TD controls, about ½ of the 32 most significant genes were downregulated, many fewer were significant in the CHARGE sample or associated with other pesticides in annotated genomic databases. These differential patterns in cases vs. controls for associations between prenatal pesticides and child's gene expression provide clues about potential geneenvironment interactions in the etiology of ASD.

MEASURING ESTROGEN RESPONSE IN VAGINAL AND URETHRAL EPITHELIAL CELLS OF INFANTS: A STUDY OF SOY-BASED INFANT FORMULA FEEDING. M Adgent\*, D Umbach, B Zemel, A Kelly, J Schall, E Ford, W Rogan, V Stallings (National Institute of Environmental Health Sciences)

Soybeans contain isoflavone compounds that are estrogenic. Infants who are exclusively fed soy-based formula are exposed to high levels of isoflavones, but their physiologic response to this estrogenic exposure is uncharacterized. Here, we apply a classic marker of estrogen response in adult women, cytological evaluation of urogenital epithelial cells, to a study of sovfed infants. Methods: We analyzed urogenital epithelial cells from 283 infants, all fed either breast milk (BF) (n=70), cow's milk formula (CMF) (n=111), or soy formula (SF) (n=102) since birth. Cells were collected through non-invasive urethral or vaginal swabs at birth and at 2-4 week intervals until 28 (boys) or 36 (girls) weeks of age. We assigned each sample a Maturation Index (MI) using standard gynecologic methods (Pap smear), where higher scores suggest more estrogenization. We used restricted cubic splines to estimate MI trajectories with increasing age, by feeding group. Results: Demographic characteristics differed between breast- and formula-fed infants, but not between CMF and SF infants. For SF girls, the MI trajectory was above and increasingly divergent with age from the trajectory of both CMF (p=0.02) and BF girls (p=0.01). SF boys demonstrated higher MI than CMF or BF boys until approximately 20 weeks, but all converged thereafter (p=0.08 vs. CMF; p=0.11 vs. BF). No difference in MI was observed between CMF and BF infants of either sex. Conclusions: Consistent with an estrogen response, soy formula feeding is associated with elevated MI in vaginal and, transiently, male urethral tissue. The long-term significance of these effects is unknown.

**DETERMINANTS OF MENTAL HEALTH DISORDERS IN CHILDREN OF PARENTS WITH PARENTAL MULTIPLE SCLEROSIS.** Neda Razaz\*, Martin Guhn (University of British Columbia, Vancouver, Canada) W. Thomas Boyce (University of California, San Francisco, USA) Ruth Ann Marrie (University of Manitoba, Winnipeg, Canada) KS Joseph (University of British Columbia, Vancouver, Canada)

Purpose: Early-life stressors can have harmful effects on the social and emotional functioning of children. We examined the incidence and determinants of mental health disorders in children with and without a parent with multiple sclerosis (MS). Methods: We carried out a retrospective matched cohort study in British Columbia, Canada, using linked population-based education and health databases. Children who were born between 1993 and 2011, with an MS parent, were compared with age-matched children whose parents did not have MS. The outcome of interest was the diagnosis of a mental health disorders in children (typically anxiety or depression). Cox regression was used to estimate adjusted hazard ratios (aHR) and 95% confidence intervals (CI). Results: Overall, 935 children with an MS parent and 3209 children of parents without MS formed the study cohort. Rates of mental health disorders were similar in children with (4.7%) and without (4.0%) an MS parent. However, mental health disorders affected more MS parents compared with parents without MS (42.6% vs. 24.7%, p<0.001). Parental mental health and sex of the MS affected parent modified the relationship between parental MS and mental health disorders in children. The incidence of mental health disorders in children whose mother had MS was 53% higher than the matched comparison cohort (aHR:1.53, 95%CI:1.08-2.18) and 85% higher for those who had a parent with mental health problems (HR:1.85, 95%CI:1.12-3.07). Conclusion: Maternal MS and mental health comorbidity in parents with MS increased the risk of mental health disorders in children compared with children of parents without MS.

ASSOCIATIONS OF PRE- AND POSTNATAL WEIGHT GAIN WITH BODY COMPOSITION AND CARDIOMETABOLIC RISK DURING MID-CHILDHOOD IN PROJECT VIVA. Perng W\*, Hajj H, Belfort MB, Rifas-Shiman SL, Gillman MW, and Oken E (Michigan State University Department of Epidemiology & Biostatistics)

Aims: Excess weight gain during pre- and postnatal periods may increase risk for later obesity and metabolic dysfunction. However, the combined effects of fetal and postnatal weight gain patterns on future cardiometabolic health are not well-established. Methods: We included 963 participants from Project Viva, a US pre-birth cohort. Using linear regression, we examined relations of BMI z-score (BMIZ) change during four postnatal periods (birth-6mo, 6mo-1y, 1-2y, 2-3y) with mid-childhood adiposity (DXA total fat, BMIZ, DXA trunk fat, waist circumference) and metabolic risk (HOMA-IR, leptin, adiponectin, CRP, IL-6), within tertiles of birthweight-forgestational-age ('fetal growth'). In multivariable analysis, we adjusted for child age, sex, race, breastfeeding duration, maternal education, continuous fetal growth, and BMIZ change in previous periods. All metabolic biomarkers were natural log-transformed. Results: Children were 6.6-10.7y; 50% were male. The combination of higher fetal and higher postnatal BMIZ gain, especially from 2-3y, corresponded with greater mid-childhood adiposity. Among infants in the highest fetal growth tertile, each unit of BMIZ gain corresponded with greater childhood total fat mass: 0.85 kg (95% CI: 0.33, 1.38) for 0-6mo, 0.06 kg (-0.79, 0.90) for 6mo-1y, 0.99 kg (0.28, 1.70) for 1-2y, and 1.37 kg (0.51, 2.23) for 2-3y. We observed similar trends with other adiposity indicators. For metabolic outcomes, higher BMIZ gain from birth-6mo correlated with greater inflammation among children with highest fetal growth (CRP: 0.34 [0.06, 0.62]; IL-6: 0.19 [0.05, 0.34]), whereas 6mo-1y BMIZ gain was related to insulin resistance (HOMA-IR: 0.42 [0.18, 0.67]) and higher leptin (0.34 [0.12, 0.56]) among those with lowest fetal growth. Conclusions: Larger babies who grow rapidly during early infancy and the toddler years appear to be at risk for excess adiposity and inflammation during mid-childhood.

### CESAREAN DELIVERY AND CHILDHOOD ASTHMA INCIDENCE IN A BIRTH COHORT.

Flak AL\*, Strickland MJ, Klein M, Hansen C, Drews-Botsch CD, Darrow LA (Emory University, Atlanta, GA)

Background: Mounting evidence suggests that delivery by cesarean section may influence asthma development. Two previous studies indicate this association is stronger among girls. Methods: We examined the association between cesarean delivery and childhood asthma among 17,075 children born between 2000 and 2010 enrolled in Kaiser Permanente Georgia; a subgroup of the Kaiser Air Pollution and Pediatric Asthma (KAPPA) Study cohort linked to mothers and birth records. Electronic medical records were used for classification of incident asthma, defined as 1 asthma diagnosis and 1 asthma-related medication dispensing after the first year of life. Binomial linear regression with generalized estimating equations, to account for correlation between siblings in the cohort, were used to estimate risk differences (RD) for incident asthma at ages 2 through 8. Results: In preliminary analyses, cesarean delivery was positively associated with cumulative asthma incidence at follow-up ages 4 through 7. In comparison to vaginal delivery, cesarean delivery was associated with an absolute 3 percent increase in risk of asthma by age 5 (RD (95% CI) 0.0293 (0.0038, 0.0548)) in a model controlling for child sex, race, ethnicity, low birthweight, birth year, maternal asthma, maternal education, and maternal age. In stratified models, the association was stronger among females (RD (95% CI) female 0.0381 (0.0029, 0.0732), male 0.0187 (-0.0171, 0.0546)). Associations were strongest at follow-up ages 5 and 6, but showed similar trends at all follow-up ages. Conclusion: These results align with limited previous findings that the association between mode of delivery and childhood asthma may be stronger among girls.

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