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ABSTRACTS

Plenary Session

Oral Presentations

EXTERNAL VALIDATION OF PREDICTION MODELS FOR RISK OF CESAREAN DELIVERY AFTER LABOR INDUCTION

Valery Danilack, Jennifer Hutcheon, David Savitz

Clinical prediction models for the risk of cesarean delivery after labor induction have focused on clinical characteristics at the time of induction. There is a need to more accurately predict cesarean delivery earlier in pregnancy, when clinicians are considering whether to induce labor. Previously, we developed two prediction models, one for pregnancies with medically indicated or preterm induction and a second for pregnancies with non-medically indicated term induction. Using discharge data linked to birth certificate data from a single hospital not in the original cohort, we studied 55,830 deliveries occurring 2004-2012. Applying the same exclusions as in the original cohort, we restricted the sample to 39,921 singleton liveborn deliveries between 34-42 weeks' gestation and without prior cesarean delivery, placenta previa, cephalopelvic disproportion, nonvertex presentation, or uterine abnormalities. Among 9,362 labor inductions, there were 1,786 cesarean deliveries (19%). The original medically indicated or preterm model contained the following predictors: maternal race, maternal age, parity, obesity, fibroids, high station, and excessive fetal growth; and used a predicted probability cut-off of 0.250 to best balance sensitivity and specificity. The area under the curve (AUC) in the external validation cohort using the same predictors was 0.725 (versus 0.769 in the original cohort), with sensitivity=68% and specificity=65%. The non-medically indicated term model contained these predictors: maternal race, maternal age, parity, obesity, fibroids, herpes, gestational age and excessive fetal growth; and used a predicted probability cut-off of 0.078. The AUC in the external validation cohort was 0.824 (versus 0.819 in the original), with sensitivity=87% and specificity=70%. This external validation of our two prediction models for cesarean delivery after labor induction suggests that our models are broadly suitable to inform clinical decisions about induction.

PATTERNS OF GESTATIONAL WEIGHT GAIN IN EARLY PREGNANCY AND RISK OF GESTATIONAL DIABETES MELLITUS

Sarah C. MacDonald, Lisa M. Bodnar, Katherine P. Himes, Jennifer A. Hutcheon

Background: Despite a call to study the effect of weight gain pattern on the development of gestational diabetes mellitus (GDM), few studies have correctly adjusted for the independent effects of gain after the first trimester. The objective of this study was to use a conditional percentile approach to model the independent association between first and second trimester weight gain trajectories and the development of GDM. **Methods:** Women delivering singleton infants from 1998-2010 at Magee-Womens Hospital in Pittsburgh, (n=124,590) were sampled using a case-cohort design. Weight gain trajectories in the first and second trimesters of pregnancy were modelled using conditional weight gain percentiles, and multivariable logistic regression assessed the independent associations of the trajectory with GDM. Associations were studied separately according to pre-pregnancy body mass index category. **Results:** The final cohort included 806 women with GDM and 4,819 randomly-sampled deliveries without GDM. In normal-weight women, every one standard deviation increase in weight gain in the first trimester above a woman's predicted gain was associated with a 24% increased odds of GDM [95% CI: 1.0, 1.6], while higher than predicted weight gain in the second trimester was not (OR: 1.1 [95% CI: 0.9, 1.3]). This pattern was similar in obese class I and obese class II but not in overweight and obese class III women. **Conclusions:** An upward weight gain trajectory in the first trimester was positively associated with GDM for women of most pre-pregnancy BMI categories. Second trimester weight gain trajectory was not significantly associated with GDM for any group.

INSULIN-LIKE GROWTH FACTOR AXIS AND GESTATIONAL DIABETES: A LONGITUDINAL AND PROSPECTIVE STUDY IN A MULTIRACIAL PREGNANT COHORT

Yeyi Zhu

Insulin-like growth factor (IGF)-axis may be implicated in glucose metabolism and homeostasis. Data on longitudinal changes in IGF-axis biomarkers throughout pregnancy and their roles in gestational diabetes (GDM) development are lacking. We prospectively investigated the roles of IGF-I and IGF binding proteins (IGFBP)-2 and -3 in the etiology of GDM. In a nested case-control study within the NICHD Fetal Growth Study, 107 GDM cases were identified by medical records and matched 1:2 to non-GDM controls on age, race/ethnicity, and gestational week (GW) at blood draw. Plasma levels of IGF-I, IGFBP-2, and IGFBP-3 were measured at GW 8-13, 16-22, 24-29, and 34-37. Conditional logistic regression was used, adjusting for major risk factors including pre-pregnancy body mass index. Overall, levels of IGF-I and IGFBP-3 and IGF-I/IGFBP-3 ratio increased, whereas IGFBP-2 decreased across gestation among both cases and controls. Before GDM diagnosis, the mean levels of IGF-I and IGF-I/IGFBP-3 ratio were significantly higher whereas IGFBP-2 was significantly lower in cases than controls. Specifically at GW 8-13, IGF-I and the IGF-I/IGFBP-3 ratio were increased approximately 3-fold in cases (odds ratio = 2.93 [95% confidence interval (CI) 1.18-7.30], 3.31 [CI 1.10-9.98], respectively) and IGFBP-2 was decreased 96% (odds ratio = 0.04 [CI 0.01-0.16]) comparing the highest vs. lowest quartiles. IGFBP-3 was not associated with GDM risk. Similar results were observed at GW 16-22. Further, IGFBP-2 significantly improved the prediction of GDM over conventional risk factors and plasma glucose levels (area under the curve: 0.71 vs. 0.62 at GW 8-13, P = 0.001; 0.72 vs. 0.68 at GW 16-22, P = 0.021). Findings suggest a potential important role of the IGF-axis in the etiology of GDM, with dysregulation underway as early as GW 8-13. IGFBP-2, free of postprandial fluctuation, may serve as a convenient and early predictor for GDM, on top of conventional risk factors and plasma glucose levels.

A LOW-INTENSITY INTERVENTION IMPLEMENTED AT THE HEALTH SYSTEM LEVEL IMPROVES GESTATIONAL WEIGHT GAIN AMONG WOMEN WITH GESTATIONAL DIABETES: THE GESTATIONAL DIABETES EFFECTS ON MOMS TRIAL

Monique Hedderson, Susan Brown, Samantha Ehrlich, Ailin Tsai, Charles Quesenberry, Yvonne Crites, Assiamira Ferrara

Gestational weight gain (GWG) above the Institute of Medicine (IOM) guidelines and gestational diabetes (GDM) are both risk factors for short and long term complications, including macrosomia and obesity in the mothers and their offspring. This study was a cluster randomized controlled trial of 44 medical facilities (including 2,280 women with GDM) in Kaiser Permanente Northern California, randomized to an intervention or usual care. The pregnancy intervention included a mailed tailored letter specifying a goal for total GWG by the end of pregnancy, based on the lower end of the guidelines, except for underweight women who were recommended to gain the mid-point of the guidelines. The letter sent shortly after the GDM diagnosis, explained that GDM increases diabetes risk, described how weight management can aid in prevention, and provided healthy eating and physical activity tips. The primary outcomes were the proportion that met the study goal for total gestational weight gain and the proportion meeting the IOM guidelines for rate of GWG from the GDM diagnosis to the end of pregnancy. Women in medical facilities assigned to the intervention had a 20% higher odds of meeting the IOM total weight gain goals (odds ratio (OR): 1.21; 95% Confidence Interval (CI): 0.98-1.49) and a significant 35% higher odds of meeting the IOM rate of GWG guidelines (OR: 1.35, 95% CI: 1.05-1.72) from the time of GDM diagnosis to delivery. The odds of meeting the IOM rate of GWG guidelines was 80% higher for women whose BMI was less than 25.0 before pregnancy (OR: 1.79; 95% CI: 1.10-2.92) compared with 20% for women who were overweight or obese (OR: 1.22; 95% CI: 0.95-1.56). A low-intensity intervention consisting of a tailored mailed letter from the woman's health care system improved GWG among women with GDM. The potentially synergistic adverse effects of GDM and excess GWG makes developing interventions to improve weight gain during pregnancy among women with GDM particularly important.

MATERNAL AND CHILD POLYMORPHISMS IN NITRIC OXIDE AND CARBON MONOXIDE SIGNALING PATHWAYS AND PREECLAMPSIA IN THE NORWEGIAN MOTHER AND CHILD COHORT

Anna Bauer, Stephanie Engel, Min Shi, Clarice Weinberg, Christy Avery, Andrew Olshan, Quaker Harmon, Tracy Manuck, Kari Klungsoyr, Lill Trogstad, Per Magnus

Background: Preeclampsia is a severe pregnancy complication, defined by hypertension and proteinuria after 20 weeks gestation. The etiology is incompletely understood, but aberrant placentation is hypothesized to play a critical role. Family-based studies have demonstrated a genetic component; however, genome-wide association studies and candidate gene studies have found few consistent associations. The influence of child genetics has been understudied, and no studies have jointly assessed maternal and child genetics. We used a maternal-child dyad design in the Norwegian Mother and Child Birth Cohort to disentangle maternal and child genetic associations with preeclampsia. **Methods:** We conducted a nested case-control study of 2,011 dyads (1,076 case-mother; 935 control-mother). Preeclampsia was validated on all cases and controls. Maternal blood was collected during pregnancy and cord blood collected at birth. We selected 1,518 single nucleotide polymorphisms (SNPs) with minor allele frequency >5% from 66 genes in the nitric oxide and carbon monoxide signaling pathways. We used log-linear Poisson regression models and likelihood ratio tests to assess maternal and child effects. **Results:** A maternal intronic SNP in estrogen receptor 1 (ESR1) was associated with a reduced risk of preeclampsia (rs1569788, relative risk [RR]=0.64, 95% CI: 0.52-0.78). Additionally, one child synonymous SNP in adenylate cyclase 8 (ADCY8) was associated with an increased risk (rs12547243, RR=1.42, 95% CI: 1.20-1.69). All results remained significant after Bonferroni correction for multiple testing ($p < 3.29 \times 10^{-5}$). Additional analyses by preeclampsia subtypes and severity will be presented. **Conclusions:** We found an association of maternal ESR1 with preeclampsia, confirming similar findings in other populations. Additionally, we found a novel association of a child SNP in ADCY8 with preeclampsia. These results underscore the importance of considering both maternal and child genotype.

TIME-VARYING CONFOUNDING OF THE ASSOCIATION BETWEEN PERFLUOROALKYL ACIDS AND TIME TO PREGNANCY: AN EXAMPLE FROM THE DANISH NATIONAL BIRTH COHORT

Cathrine Carlsen Bach, Niels Bjerregård Matthiesen, Jørn Olsen, Tine Brink Henriksen

Background: Previous studies have investigated the associations between levels of perfluoroalkyl acids (PFAAs) in women and time to pregnancy (TTP). Inconsistent results may be explained by differences in whether and how studies conditioned on parity. We used causal directed acyclic graphs (DAGs) to evaluate the causal structure of the association and exemplified the approach in a sample of Danish women. **Methods:** According to our DAGs, studies including parous women may be confounded by factors related to previous pregnancies as well as the interpregnancy interval. To test this hypothesis, we included 638 nulliparous women and 613 parous women from the Danish National Birth Cohort who provided a blood sample and reported their TTP during early pregnancy. By the use of discrete-time survival analyses we estimated the associations between quartiles of plasma PFAAs, including perfluorooctane sulfonate and perfluorooctanoate (PFOA), and TTP, adjusted for potential confounders. **Results:** In nulliparous women, we found no association between PFAA levels and TTP [e.g. for PFOA: fecundability ratio (95 % confidence interval) 0.92 (0.73; 1.15), highest versus lowest quartile]. In parous women, higher PFAA levels were associated with longer TTP [e.g. for PFOA: fecundability ratio (95 % confidence interval) 0.63 (0.47; 0.86), highest versus lowest quartile]. Adjusted for interpregnancy interval, these associations were attenuated. **Conclusions:** The associations between PFAAs and TTP in parous women could be due to confounding by factors related to previous pregnancies and the duration of the interpregnancy interval. In studies of the association between PFAA levels measured during pregnancy and TTP, restriction to nulliparous women may minimize such bias. These issues may also apply to other chemicals with properties similar to PFAAs i.e. sharing the same or similar pharmacokinetic structures (accumulation in the body and excretion during pregnancy and breastfeeding).

OZONE EXPOSURE IN THE WEEK PRIOR TO DELIVERY ASSOCIATED WITH THE RISK OF STILLBIRTH

Pauline Mendola, Maeve Wallace, Sandie Ha, Danping Liu, Yeyi Zhu, Anna Pollack, Sung Soo Kim, Seth Sherman, Katherine Grantz

Both chronic air pollution exposure and acute exposures in the days prior to delivery have been examined in relation to stillbirth, but only in a small number of studies with inconsistent findings. We examined the risk of stillbirth in a retrospective cohort of 223,375 singleton deliveries, ≥ 23 weeks of gestation, from 12 clinical sites across the United States. Average exposure to criteria air pollutants was calculated using modified Community Multiscale Air Quality models for the day of delivery and each of the seven days prior, whole pregnancy, first and second trimester. Poisson regression models using generalized estimating equations estimated the relative risk (RR) of stillbirth and 95% confidence intervals (CI) in relation to an interquartile increase in pollutant in single and multi-pollutant models adjusted for age, race, parity, smoking, alcohol, pre-pregnancy body mass index, insurance, marital status, hypertension, diabetes, season of conception, birth year and study site. We observed 992 stillbirths during the study period (0.4%). Ozone (O3) was associated with a 14-21% increased risk on days 2, 3 and 5 -7 prior to delivery in single pollutant models and these findings persisted in multi-pollutant models for days 5 (RR= 1.24, CI=1.08-1.43) and 6 (RR=1.19, CI=1.04-1.36). Particulate matter (PM) <2.5 microns was associated with risk in the day 1 multi-pollutant model (RR=1.15, CI=1.01-1.31) but this was non-significant in the single pollutant model. First trimester O3 increased risk only in the single pollutant model (RR=1.17, CI=1.01-1.36). First trimester exposures to sulfur dioxide and carbon monoxide were inversely associated with risk. Whole pregnancy and second trimester averages were not related to risk of stillbirth and no significant associations were observed for exposure to nitrogen oxides or PM < 10 microns. This large cohort with rich clinical data suggests that O3 may have both an early pregnancy and acute relation to stillbirth.

DIETARY VITAMIN B12 AND B6 INTAKES AND MENSTRUAL CYCLE FUNCTION IN THE BIOCYCLE STUDY

Ellen Chaljub, Jean Wactawski-Wende, Keewan Kim, Kara Michels, James Mills, Sunni Mumford

Background: Vitamin B12 deficiency is associated with infertility, especially in women undergoing in vitro fertilization, and is hypothesized to act by disrupting one-carbon metabolism. Less is understood regarding the role of B vitamins among healthy women. Thus, we investigated associations between dietary vitamin B12 and B6 intakes and menstrual function among healthy, regularly menstruating women. **Methods:** We measured reproductive hormones (including estrogen, progesterone, luteinizing and follicle-stimulating hormone, sex hormone-binding globulin, and testosterone) ≤ 8 times per cycle, across 2 menstrual cycles among 259 women in the BioCycle Study. Homocysteine was measured ≤ 3 times per cycle. Dietary vitamin B12 and B6 intakes were assessed ≤ 4 times per cycle using 24-hour dietary recalls. Intakes were evaluated by tertiles and by the recommended dietary allowance (RDA). Linear mixed models were used to determine associations between vitamins and reproductive hormones and generalized linear models were used to determine associations with risk of anovulation. All models were adjusted for age, race, body mass index, physical activity, energy, protein and dietary fiber intakes, and percentage of energy from fat. **Results:** Women with B12 intakes above the RDA had lower homocysteine concentrations compared to women with intakes below the RDA (β -0.53, 95% confidence interval [CI] -0.91, -0.16), though no differences were observed in hormone concentrations. High B12 intakes were associated with a decreased risk of anovulation, (adjusted risk ratio, aRR 0.98, CI 0.97, 1.00; per 10 $\mu\text{g/mL}$), as was B6 intakes (aRR 0.99, CI 0.98, 1.00, tertile 3 vs. tertile 1). **Conclusion:** Vitamin B12 intakes above the RDA were associated with lower homocysteine concentrations and increases in B12 and B6 intakes were suggestive of a decreased risk of anovulation. Future studies are needed to further understand the role of B vitamins involved in one-carbon metabolism and reproduction.

EFFECT OF PRECONCEPTION-INITIATED LOW DOSE ASPIRIN THERAPY ON C-REACTIVE PROTEIN THROUGHOUT PREGNANCY: THE EAGER TRIAL

Lindsey Sjaarda, Rose Radin, Robert Silver, Emily Mitchell, Sunni Mumford, Brian Wilcox, Noya Galai, Neil Perkins, Jean Wactawski-Wende, Joseph Stanford, Enrique Schisterman

In pregnancy, inflammation is linked to adverse outcomes such as gestational diabetes and preeclampsia. We also recently observed lower pregnancy and live birth rates in women with higher inflammation, as indicated by C-reactive protein (CRP) prior to conception, which were restored by daily low-dose aspirin (LDA) in a randomized, placebo-controlled trial. Here, we examined the effect of LDA on CRP concentrations throughout pregnancy, stratified by baseline (pre-pregnancy, pre-intervention) CRP tertile (low:<0.70 mg/L; mid:0.70- <1.95 mg/L; high:≥1.95 mg/L). For women achieving clinical pregnancy, serum CRP was also measured at gestational weeks 8, 20, and 36. After excluding withdrawals and acutely elevated baseline CRP (>10mg/L), 680 women were analyzed using generalized estimating equations. Inverse probability weights adjusted for potential bias from post-randomization restriction to pregnant women. LDA lowered CRP throughout pregnancy in the high-CRP group (P=0.03), but not in the low- (P=0.32) or mid-CRP (P=0.87) groups. To further evaluate the relationship of these findings to adiposity, the high-CRP group was stratified by BMI (<25 vs. ≥25 kg/m²). Within the high-baseline CRP tertile, LDA was associated with lower CRP throughout pregnancy in lean (P=0.04), but not overweight/obese women (P=0.66). Indeed, lean women in the high-baseline CRP tertile on LDA had CRP levels at 36 weeks' gestation (geometric mean 4.2 mg/L, 95%CI 3.2, 5.5) similar to their baseline level (3.6 mg/L), and lower than CRP among lean women assigned to placebo and overweight/obese women in both treatment groups (all >6.0 mg/L) at week 36. These findings suggest that the effect of LDA on ameliorating excess inflammation through pregnancy may be strongest in lean women with higher pre-pregnancy CRP. Larger studies should next assess the effect of LDA on preventing inflammation-related adverse outcomes during pregnancy, such as preeclampsia, according to pre-pregnancy inflammation status.

P2.6-p

CONTRIBUTION OF IMPROVED SURVEILLANCE TO TEMPORAL INCREASES IN MATERNAL MORTALITY IN THE UNITED STATES

K.S. Joseph, Sarka Lisonkova, Giulia Muraca, Neda Razaz, Yasser Sabr, Azar Mehrabadi, Enrique Schisterman

Background: Maternal death rates in the United States have increased 4-fold in recent decades. We carried out a study to quantify the contribution of improved surveillance to this apparent increase in maternal mortality. **Methods:** Data on maternal deaths and live births in each state from 1993 to 2014 were obtained from the mortality and birth files of the United States. Maternal deaths were modeled using ecological random intercept Poisson regression with state-year as the unit of analysis (n=1020). Crude temporal trends were contrasted with trends adjusted for improvements in surveillance i.e., the introduction of a pregnancy question on death certificates, International Classification of Diseases (ICD-10) coding, and the standard pregnancy checkbox on death certificates. Analyses were also carried out by underlying cause of death with a focus on new ICD-10 codes. **Results:** Maternal mortality ratios increased from 7.91 in 1993-94 to 28.6 per 100,000 live births in 2013-14 (rate ratio [RR] 3.62, 95% CI 3.31-3.95). Adjustment for improvements in surveillance abolished this increase (RR 1.56, 95% CI 0.96-2.56). Between 1999 and 2014, deaths due to preeclampsia decreased from 1.92 to 0.58 (RR 0.44, 95% CI 0.32-60), while those due to complications of labour and delivery decreased from 1.52 to 0.65 per 100,000 live births (RR 0.47, 95% CI 0.35-0.65). Deaths from 3 causes with new pregnancy chapter codes in ICD-10 increased: between 1999 and 2014 deaths from obstetric causes >42 days and <1 year after delivery (ICD-10 O96) increased from 0.13 to 6.39, deaths from other specified maternal diseases (ICD-10 O99) increased from 1.11 to 6.87, and deaths from other specified pregnancy-related conditions (ICD-10 O26.8) increased from 0.23 to 5.27 per 100,000 live births. Exclusion of deaths from these 3 causes abolished the temporal increase in maternal deaths. **Interpretation:** The recent increase in maternal mortality rates in the United States is an artifact of surveillance bias.

POOR SLEEP HYGIENE, PREGNANCY DISCOMFORTS AND DEPRESSIVE SYMPTOMS ARE ASSOCIATED WITH SLEEP DISTURBANCES IN EARLY PREGNANCY

Deborah Da Costa, Kaberi Dasgupta, Jane Su, Anna Denis, Rebecca Wickett, Michael Raptis, Phyllis Zelkowitz

Poor quality sleep has been associated with increased risk of perinatal depression and pregnancy complications. Sleep disturbances have mostly been examined in late pregnancy and the postpartum, with little known about their pattern in early pregnancy. This study aimed to identify sociodemographic, health-related, lifestyle, and psychosocial factors associated with poor sleep quality in pregnant women during early pregnancy. A total of 457 women (mean age = 33.1 years, ± 4.6 years) completed standardized on-line self-report questionnaires measuring demographic factors, pregnancy-related physical symptoms (i.e. back in, nausea), sleep hygiene, physical activity, health status, pregnancy-related stress and depressive symptoms during the late first or early second trimester of pregnancy (mean gestational weeks 14.2, ± 1.4). Sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI). Multiple linear regression was used to examine factors associated with poorer sleep quality. The mean global PSQI score was 6.0 (±2.8) and self-reported sleep duration was 7.7 hours (±3.3). The prevalence of poor sleep quality defined as PSQI > 5 was 47.8% (n=219). Multiparity (β = -0.17, 95% CI [-0.42, -0.54]), greater severity of pregnancy-related symptoms (β = 0.31, 95% CI [0.14, 0.24]), poorer sleep hygiene (β = 0.20, 95% CI [0.06, 0.14]), poorer self-reported health status (β = -0.19, 95% CI [-0.97, -0.38]), and greater depressive symptoms (β = 0.13, 95% CI [0.03, 0.15]) were associated with poorer sleep quality. Age, household income, physical activity level, pre-pregnancy body mass index, and pregnancy-specific stress were not associated to poor sleep quality. Sleep disturbance is common during early pregnancy. Given that sleep quality is likely to worsen over the course of pregnancy and/or following childbirth, ongoing screening and interventions aimed at alleviating pregnancy-related discomforts, depressed mood and sleep hygiene counseling are recommended.

P2.7-p

VARIATIONS IN SEVERE MATERNAL MORBIDITY IN CANADA ASSOCIATED WITH MATERNAL BIRTHPLACE

Marcelo Urquia

Background There is large variation in the risk of maternal mortality and severe maternal morbidity (SMM) worldwide. Because of selective migration processes, immigrants may not be representative of their source populations. Variations in severe maternal morbidity according to immigrants' birthplace are not well documented. **Methods** We analyzed 1,252,543 in-hospital deliveries of Ontario residents discharged between April 1, 2002 and March 31 2012. The main outcome measure was a Canadian composite indicator of SMM. The top 10 most common conditions were also evaluated. Maternal country of birth and other immigration characteristics were objectively assessed through a linkage with official immigration records. We used generalized linear models to assess associations according to maternal birthplace. **Results** Overall, immigrant women (N=335,544) did not differ from Canadian-born women (n=916,999) in the risk of SMM (12.1 versus 12.0 per 1000 deliveries, respectively). However, SMM varied substantially according to maternal region of birth, from 9.2/1000 among immigrants from western countries to 23.0/1000 among those from Sub-Saharan Africa. Even larger disparities were found where immigrants were categorized by their specific countries of birth. Compared to Canadian-born women, women from Nigeria, Congo, and Haiti had at least twice the risk of SMM, even after adjustment for covariates, followed by women from the Philippines and Vietnam. The top contributing condition was postpartum hemorrhage involving blood transfusion, accounting for about 1 in 4 cases among most groups, with the notable exception of HIV, which was the most common diagnosis among immigrants from Sub-Saharan Africa. After removing HIV cases, disparities in SMM were attenuated but did not disappear. Sickle cell anemia was an important contributor to the risk of SMM among Caribbean women but not among other groups. **Conclusion** There are sizeable variations in SMM and their components among immigrants to Canada.

P2.8-p

UNDERSTANDING SUPPORTIVE NEIGHBORHOOD ENVIRONMENTS FOR PREGNANCY: AN APPLICATION OF LATENT CLASS ANALYSIS

Irene Headen, Barbara Laraia

Neighborhood factors are associated with adverse health outcomes in pregnant women. However, few studies have jointly classified neighborhoods using multiple characteristics of the physical, social, and resource environment in order to understand cumulative exposure to neighborhood risks germane to supporting a healthy pregnancy. We investigated patterns of neighborhood risk in a population of low-income pregnant women. We linked 205 geocoded addresses to external data sources to measure four neighborhood domains: food environment, walkability, crime and traffic safety, and socioeconomic deprivation. We used latent class analysis (LCA) to identify underlying “types” of neighborhoods from these domains. We fit a set of LCA models with a range of class solutions and determined the best-fitting model using appropriate fit statistics. We then used multinomial logistic regression to look at associations between neighborhood type and demographic (race, income, education) and maternal (age, parity) factors. We identified six neighborhood types. Two poor neighborhood types (type1 n=48; type2 n=42) were fairly safe, but differed in having supportive food environments and walkability. One “lower-middle income” neighborhood type (n=16) had a fairly supportive overall environment across food, safety, and walkability. Two “mixed income” neighborhood types (type4 n=39; type5 n=28), in which women experienced all levels of deprivation, had supportive food environments but differed on walkability and safety. One “split-income” neighborhood type (n=32), in which women experienced either very high or very low deprivation, was walkable but fairly unsafe and had a poor food environment. Maternal and demographic characteristics were not associated with neighborhood type. Our analysis suggests that jointly characterizing neighborhoods across multiple characteristics of the environment can identify differential patterns of cumulative neighborhood risk experienced by pregnant women.

P3.1

LOW CARB DIETS: ARE THEY COUNTER TO THE SUCCESS OF FOLIC ACID FORTIFICATION?

Tania Desrosiers, Anna Maria Siega-Riz, Bridget Mosley, Charlotte Hobbs, Robert Meyer

Folic acid (FA) fortification has significantly reduced the prevalence of neural tube defects (NTDs) in the US. The popularity of “low carb” diets raises concern that women who intentionally avoid carbohydrates (CHO) – thereby consuming fewer fortified foods – may not have adequate FA intake and thus be at higher risk of an NTD-affected pregnancy. To assess the impact of CHO intake on dietary FA and NTDs, we analyzed data from the National Birth Defects Prevention Study from 1,740 mothers of infants, stillbirths and terminations with NTDs, and 9,545 mothers of live born infants without a birth defect conceived between 1998 and 2011. Usual diet in the year before conception was ascertained using a modified Willet Food Frequency Questionnaire. FA and CHO from food and beverages were estimated using the USDA National Nutrient Database. We defined restricted CHO intake as ≤ 5 th percentile among control mothers (96.5g). Maternal characteristics of interest included age, race/ethnicity, education, nativity, smoking, alcohol use, and pregnancy intent. We estimated the association between restricted CHO intake and NTDs using logistic regression, and assessed effect measure modification by FA supplement use, BMI, and pre-pregnancy diabetes. Women with restricted intake were more likely to be older, non-Hispanic white, born in the US, completed high school, and used alcohol during pregnancy. Estimated mean intake of dietary FA among women with restricted CHO was less than half that of other women ($p < 0.01$), and women with restricted CHO had modestly increased odds of delivering an infant with any NTD (adjusted OR = 1.38; 95% CI = [1.10-1.74]; 102 exposed cases), anencephaly (1.50 [1.02-2.23]; 32), or spina bifida (1.32 [1.02-1.80]; 61). This is the first study to specifically examine the effect of restricted CHO intake on NTD risk among pregnancies conceived post-fortification, and suggests that low carb diets may be counter to the success of folic acid fortification in the US.

P2.9-p

MATERNAL PHYSICAL ABUSE IN CHILDHOOD IS ASSOCIATED WITH OFFSPRING OVERWEIGHT AND OBESITY IN EARLY CHILDHOOD

Lucia Petito, Stephanie Leonard, David Rehkopf, Lorrene Ritchie, Barbara Abrams

Adverse childhood experiences (ACE) have recently been associated with high gestational weight gain (GWG), and high GWG has been associated with child obesity. We hypothesized that maternal ACE exposures are associated with offspring obesity, partially mediated by high GWG. Our study included 4,771 mother-child pairs from the National Longitudinal Survey of Youth (1979-2012). We used log-linear regression models that accounted for the complex survey design to estimate the associations of three maternal ACE measures (physical abuse, mental illness in the household, and alcohol abuse in the household) with the outcomes: ever obese or ever overweight/obese at ages 2-5 years, 6-11 years, or 12-19 years old. For significant associations, we then estimated the total direct effect by adding GWG (measured with z-scores standardized for gestational duration) to the adjusted regression model. Next, we estimated the natural direct effect by allowing GWG in the model to vary as it would in the absence of the exposure. After adjusting for other early life exposures, a history of physical abuse was associated with increased risk of obesity (RR=1.24, 95% confidence interval (CI): 1.01, 1.53) and overweight/obesity (RR=1.14, 95% CI: 0.99, 1.31) in 2-5 year olds. There were no associations for other ACE exposures or age groups and mediation by GWG was not significant. In this large, diverse study sample, physical abuse in childhood was associated with offspring overweight and obesity in early childhood, and GWG did not mediate the associations.

P3.2

MATERNAL ANTIBODIES TO COMMON HERPES VIRUSES AND GASTROSCHISIS RISK IN OFFSPRING

Martha Werler, Samantha Parker, Klaus Hedman

Gastroschisis risk is highest in offspring of young women and is increasing in prevalence, suggesting that exposures which are increasingly common among younger females may be causal. Infections with viruses in the herpes family remain in the body in perpetuity and can reactivate in response to stressors. Epstein-Barr virus (EBV), herpes simplex viruses (HSV), and cytomegalovirus (CMV) are common and risk of infection during the earlier childbearing years has been increasing over time for some of them. The Finnish Maternity Cohort, Congenital Malformation, and Medical Birth registers (1987-2012) were linked for this nested case-control study of gastroschisis and age-matched controls. Maternal serum samples collected in early pregnancy were used to measure levels of antibody (immunoglobulin, Ig) to EBV viral capsid antigen, HSV-1 and -2, and CMV. Conditional logistic regression models were used to estimate odds ratios (OR) and 95% confidence intervals for Ig levels. High IgG indicates ‘past’ infection and high IgM indicates ‘recent’ infection. Reactivations are less clearly identified because both IgM and IgG can be high. For EBV, ORs for both ‘recent’ and ‘past’ infections were elevated: 2.16 (0.97-4.79) and 2.16 (0.82-5.70), respectively. For HSV, ‘past’ infection with either type 1 or 2 (test is non-specific) suggested an increased risk; the OR was 1.94 (0.74-5.12). ‘Past’ infection with HSV-2 increased gastroschisis risk (OR: 2.48, 1.50-4.10). ‘Past’ HSV-1, ‘past’ CMV, and ‘recent’ CMV infections were not associated with increased gastroschisis risk. Observed associations with both indicators of recent and past EBV and HSV infections suggest reactivations may be risk factors for gastroschisis.

P3.3

CHILDHOOD ADIPOSITY AND FERTILITY DIFFICULTIES: THE BOGALUSA HEART STUDY

Marni Jacobs, Lydia Bazzano, Gabriella Pridjian, Emily Harville

Obesity in adulthood is associated with infertility; however, little attention has been paid to childhood obesity. We sought to examine the association between childhood adiposity and adult fertility among 1,061 women participating in a long-term follow-up study of childhood cardiovascular risk factors and reproductive outcomes. Women were classified as normal/overweight/obese for age by body mass index (BMI) and subscapular and triceps skinfold (SSSF, TRSF) thickness in childhood (age ≤ 18); associations with self-reported fertility difficulties were estimated using log-binomial regression. Controlling for race, education, smoking, current BMI, and income, participants who were obese between ages 9 – 12 were more likely to report any fertility difficulties (adjusted relative risk (aRR) = 1.82, 95% confidence interval (CI) 1.17 – 2.82) and inability to get pregnant when trying (aRR = 1.94, 95% CI 1.22 – 3.08), as were those obese prior to age 9 (aRR = 1.76, 95% CI 1.04 – 2.97). Ever being overweight or obese prior to age 12 also led to increased risk of inability to get pregnant when trying (aRR 1.44, 95% CI 1.03 – 2.03) and any fertility difficulties (aRR 1.42, 95% CI 1.03 – 1.95). Women with a high SSSF measure prior to age 12 were more likely to report ever receiving help getting pregnant (aRR = 2.16, 95% CI 1.15 – 4.06), inability to get pregnant when trying (aRR = 1.46, 95% CI 1.05 – 2.04) and any fertility difficulties (aRR = 1.56, 95% CI 1.13 – 2.14). Participants who were obese and had very high SSSF measures in childhood also had fewer total pregnancies and live-births. Results for TRSF were similar but attenuated. Effects persisted excluding women with polycystic ovarian syndrome (PCOS). Findings from the present study support an association between childhood adiposity and fertility difficulties in adulthood, not solely driven by development of PCOS, providing additional incentive to promote healthy weight maintenance in childhood.

P3.5

BORDERLINE NEONATAL THYROID STIMULATING HORMONE LEVELS AND EDUCATIONAL AND DEVELOPMENT OUTCOMES: A POPULATION-BASED RECORD-LINKAGE STUDY

Samantha Lain, Jason Bentley, Veronica Wiley, Michelle Jack, Christine Roberts, Bridget Wilcken, Natasha Nassar,

Background: Congenital hypothyroidism (CH) causes intellectual delay unless identified and effectively treated soon after birth. Newborn screening (NBS) has virtually eliminated significant CH-associated intellectual disability. There remains clinical uncertainty about infants with thyroid stimulating hormone (TSH) levels below current NBS cut-points. Aim: To evaluate the association between neonatal TSH levels and educational and developmental outcomes. Methods: We conducted a population-based record-linkage study of infants undergoing NBS from 1994-2008 in New South Wales, Australia, with subsequent assessments of childhood development or school performance. Multivariable logistic regression was used to account for potential confounders. Results: 503,706 infants had a newborn TSH result that linked to a developmental or educational outcome. As newborn TSH levels increase, from the 75-80th centile, the risk of having a poor neurodevelopmental outcome increased until the 99.95th centile. Infants with a newborn TSH >99.95th centile, likely to have diagnosed and treated CH, had similar results to infants with a TSH <75th centile. Infants with a newborn TSH result between 99.5th-99.9th centile were more likely to have special needs (adjusted odds ratio (aOR) 1.68, 95% confidence interval (95%CI) 1.23-2.30), poor numeracy performance (aOR 1.57, 95%CI 1.29-1.90) and poor development (aOR 1.52, 95%CI 1.20-1.93). Conclusions: This large study has shown that there is an association between newborn TSH levels below the current NBS thresholds of many countries and poor education and developmental outcomes, requiring further investigation.

P3.4

DO BENEFICIAL EFFECTS OF BREASTFEEDING ON CHILD NEUROCOGNITIVE FUNCTION PERSIST IN ADOLESCENCE? EVIDENCE FROM A CLUSTER-RANDOMIZED TRIAL

Seungmi Yang, Richard Martin, Emily Oken, Mikhail Hameza, Glen Doniger, Shimon Amit, Rita Patel, Jennifer Thompson, Konstantin Vilchuck, Natalia Bogdanovich, George Davey Smith, Michael Kramer

Background Evidence on the long-term causal effect of breastfeeding on neurocognitive development is inconclusive and is based almost exclusively on observational studies. Our aim was to evaluate whether the neurocognitive benefits of breastfeeding we observed at age 6.5 years in a cluster-randomized trial of a breastfeeding promotion intervention would persist at age 16 years. Methods At 16-year follow-up of the Promotion of Breastfeeding Intervention Trial (PROBIT), we measured neurocognitive function using a computer-based, self-administered test battery in 13,416 participants. We estimated cluster-adjusted mean differences in seven different cognitive domain scores and in a global cognitive function score between the two randomized (intervention vs. control) groups by intent-to-treat (ITT) analysis. We also estimated cluster- and confounder-adjusted mean differences by instrumental variable (IV) analysis to estimate the causal effects of breastfeeding by accounting for “noncompliance” with the randomized intervention. Results In ITT analyses, the intervention to promote prolonged and exclusive breastfeeding yielded no significant mean differences in any of the neurocognitive scores. In the IV analysis adjusted for clustering and potential confounders, children who were exclusively breastfed for >3 (vs <3) months had a 3.6-point (95% CI: 0.05, 7.2) higher mean verbal function score, consistent with results we observed at age 6.5 years. Conclusions Overall, the beneficial effects of breastfeeding on neurocognitive function appeared to diminish by age 16. More prolonged and exclusive breastfeeding was associated with increased verbal ability at age 16 years, but to a lesser degree than at age 6.5 years.

P4.1

FETAL GROWTH VELOCITY AND IMPROVEMENT OF THE PRECISION OF SONOGRAPHIC BIRTHWEIGHT ESTIMATION

Katherine Grantz, Sungduk Kim, William Grobman, Roger Newman, John Owen, Daniel Skupski, Jagteshwar Grewal, Ed Chien, Deborah Wing, Ronald Wapner, Angela Ranzini, Stefanie Hinkle, Karin Fuchs, Mary Hedi-ger, Germaine Buck Louis, Paul Albert

Error in ultrasound estimated fetal weight (EFW) prediction of birthweight (BW) has clinical implications such as timing of delivery for fetal undergrowth or decision for cesarean due to suspected macrosomia. We examined whether the addition of fetal growth velocity (FGV), i.e., the estimated fetal growth rate (g/wk) between two ultrasound scans, compared to a single assessment of EFW improves prediction of BW and of small- or large-for-gestational age (SGA or LGA) births. In the NICHD Fetal Growth Studies–Singletons, a prospective cohort of 2,802 singleton pregnancies (studied from 2009 to 2013), a multivariable regression with the EFW at visit 3 (EFW3, GA=32.0 \pm 1.5 wk) was used to estimate BW and compared with a regression that also included FGV between visit 2 (EFW2, GA=27.1 \pm 2.1 wk) and visit 3. Fetal growth velocity from EFW2 to EFW3 was linearly, significantly and independently associated with BW (P<.0001). The 25th, 50th and 75th percentiles for growth velocity between the two visits were 146g/wk, 170g/wk, and 199g/wk, respectively. BW (g) was estimated by the equation: -4324.2 + 0.138*(EFW3) + 3.728*(FGV) + 172.094*(Birth GA). Using the median EFW3 (1860g) for illustration, the predicted BW at the median GA at birth (39.4 wk) was 3265g, 3354g, and 3460g for the 25th, 50th, and 75th percentiles of velocity. The estimated BW prediction error was 7% less with inclusion of growth velocity compared with the model based on EFW3 alone. The BW prediction errors were \pm 357g and \pm 371g (P<0.0001) for the models with and without velocity, respectively. The accuracy in prediction of SGA was improved by 5.0% when FGV between the 2nd and 3rd visit was included in the model, with a 2.1% improvement for LGA (P<0.0001 for both). Integrating fetal growth velocity into a BW estimating formula improves the precision of BW, SGA and LGA prediction. Decreasing error in BW prediction has potential to advance clinical intervention decisions that rely on EFW.

ON NEONATAL MORTALITY AND THE GESTATIONAL-AGE PARADOX: PRENATAL PATHOLOGY AS AN UNMEASURED CONFOUNDER

Quaker Harmon, Olga Basso, Clarice Weinberg, Allen Wilcox

The calculation of gestational-age-specific neonatal mortality is contentious for perinatal epidemiologists. The conventional approach calculates gestational-age-specific risk as deaths among neonates born at a given gestational age. With a “fetuses-at-risk” approach, risk is instead based on deaths among all who were in utero at the given gestational age. We construct a simulation that demonstrates that both approaches are flawed for studying etiology. In our construction, causes of neonatal death arise from two distinct sets of mechanisms: One originates in fetal life, and comprises intrauterine pathologies (such as birth defects) that can kill either the fetus or the newborn. The other comprises factors that are birth-dependent – mainly complications of immaturity, but also including complications that present during or after delivery. The risk sets corresponding to those two sources of mortality are distinct: intrauterine pathologies develop among fetuses prenatally, while birth-dependent problems develop only later. The contributions of the two sources to neonatal mortality cannot be distinguished. Moreover, intrauterine pathologies confound the relation between gestational age and neonatal mortality by causing both early birth and neonatal death. We generate simulations that admix the two sources of neonatal death, and replicate the so-called gestational-age paradox (in which neonatal mortality at preterm weeks is lower in the higher-risk category, due to collider-stratification bias). Simulations also illustrate that, in calculating gestational-age-specific risk, neither denominator (fetuses or newborns) allows etiologic interpretation of effects of prenatal exposures. Valid etiologic inference is achievable by foregoing stratification on gestational age and simply including all live births in the denominator.

INTERGENERATIONAL POVERTY AND RACIAL-ETHNIC DISPARITIES IN RISK OF PRETERM BIRTH

Michelle Pearl, Jennifer Ahern, Alan Hubbard, Barbara Laraia, Raymond Lum, Martin Kharrazi

BACKGROUND: Preterm birth varies dramatically by race, however proximal measures of the social environment have limited ability to explain these disparities. This study leverages an intergenerational linked cohort from birth, prenatal and newborn screening records to characterize life course exposure to poverty and its impact on birth outcomes. **METHODS:** Records for births between 1997-2011 were linked to birth and screening records for mothers who were themselves born in California since 1982, yielding 138,002 white, 56,562 black, and 303,995 Hispanic mothers. Addresses from birth and newborn screening records were geocoded to obtain census tract poverty levels, with greater than 20% poverty categorized as high poverty. Preterm birth (<37 weeks gestation; PTB) was derived from prenatal records where available. The marginal risk difference (RD) accounting for confounders was estimated under various permutations of early life and adult exposure to poverty for each race-ethnicity. **RESULTS:** Relative to low life course poverty, the RD of living in sustained high poverty was .008 (95% confidence interval [.002, .015]), .011 (.004, .017), and .007 (.004, .009), for white, black and Hispanic mothers, respectively. For white and black mothers, the RDs for high poverty in early life (RD=.007 [.003, .011] and RD=.008 [.003, .013], respectively) were larger than RDs for high poverty in adulthood (RD=.004 [.001, .008] and RD=.005 [.000, .010] respectively); the opposite trend was observed among Hispanic mothers (RD=.002 [.000, .004] and RD=.007 [.005, .009]). Racial-ethnic disparities in PTB under low life course poverty are lower than observed disparities (.027 vs. .035 for blacks and .012 vs. .014 for Hispanics, compared to whites). **CONCLUSION:** Early life and sustained exposure to neighborhood poverty may impact future risk of delivering preterm, but do not fully explain racial-ethnic disparities.

THE GESTATIONAL VAGINAL MICROBIOME AND SPONTANEOUS PRETERM BIRTH AMONG NULLIPAROUS AFRICAN AMERICAN WOMEN

Deborah Nelson, Shin Hakdong, Jingwei Wu, Maria Dominguez-Bello

Spontaneous preterm birth (SPTB) is a substantial health burden for both pregnant mothers and their neonates. Early markers to identify pregnant women at high risk for SPTB have been limited. Recent attention has focused on examining the role and importance of characterizing the vaginal microbiota during pregnancy to predict risk of SPTB. Given racial differences in vaginal ecology and the important role of prior SPTB in the risk of SPTB, it is important to examine these relations among a select group of nulliparous, African American pregnant women. We examined the diversity and structure of the bacterial vaginal microbiota during early pregnancy and compared 27 African American nulliparous women who delivered at term (38 weeks gestation or later) and 13 African American nulliparous women who delivered preterm (<37 weeks gestation). Samples were taken at one of two points in gestation, either prior to 16 weeks or between 20-24 weeks. The V4 region of 16S rRNA gene were amplified and sequenced with Illumina MiSeq platform. Among women who delivered preterm compared to women who delivered at term, we found lower bacterial diversity at 20-24 weeks of gestation, with lower abundance of family Coriobacteriaceae, Sneathia, Prevotella, and Aerococcus among women delivering preterm. The mean Shannon Diversity Index was also lower among the group of women delivering preterm compared to term (2.06 + 1.72 and 2.63 + 1.25). Phylogenetic Diversity and Chao1 indicated a marginally significant difference with lower diversity in the vaginal microbiota of women who delivered preterm compared to term (p=0.07 and p=0.06, respectively). The difference in vaginal diversity between the groups was greatest in the samples collected prior to 16 weeks although this difference was not statistically significant (p-value=0.24). This study suggests that different vaginal gestational microbiota in pregnancy may be related to preterm delivery.

THE CONTRIBUTION OF FATHER'S LIFELONG SOCIOECONOMIC POSITION TO AFRICAN-AMERICAN MOTHER'S BIRTH OUTCOME: A POPULATION-BASED STUDY.

James Collins

Background. Published studies have rarely considered the contribution of paternal factors to the racial disparity in birth outcome. **Objective.** To determine the extent to which paternal lifelong socioeconomic position (SEP) is a risk factor for low birth weight (< 2500g, LBW) among African-American women. **Methods.** Stratified and multilevel logistic regression analyses were performed on an Illinois transgenerational dataset of African-American infants (1989-1991), their mothers (1956-1976), and fathers (1956-1976) with appended U.S. census income information. The neighborhood incomes of father's place of residence at the time of his birth and at the time of his infant's birth were used to measure of lifelong SEP. **Results.** In Cook County IL, infants born to fathers (n=356) with a lifelong residence in high-income neighborhoods had a LBW rate of only 5.6%. In contrast, infants born to fathers with an early-life (n=1,446), adulthood (n=805), or lifelong (n=4,673) residence in low-income neighborhoods had LBW rates of 10.0%, 11.3%, and 10.4%, respectively; RR= 1.8 (1.1-2.8), 2.0 (1.3-3.2), and 1.9 (1.2-2.9), respectively. Most striking, these associations tended to persist across maternal biologic and demographic status. In multilevel logistic regression models, the adjusted (controlling for maternal birth weight, age, education, and marital status) OR of LBW for infants born to fathers with an early-life, adulthood, or lifelong residence in low (compared to lifelong residence in high) income neighborhoods equaled 1.8 (1.1-3.0), 2.0 (1.2-3.3), 1.7 (1.1-2.7) respectively. The Population Attributable Risk of LBW for paternal lifelong low SEP was 40%. **Conclusions.** Low paternal SEP is a novel risk factor for infant LBW independent of African-American women's demographic characteristics. This finding strongly suggests that policy makers should address the contribution of father's lifelong SEP to the racial disparity in adverse birth outcome.

Poster Session A

DISCUSSIONS BETWEEN PARENTS AND PROVIDERS ON TRANSITION TO ADULT HEALTH CARE FOR ADOLESCENTS WITH PEDIATRIC HEART DISEASE, NATIONAL SURVEY OF CHILDREN WITH SPECIAL HEALTH CARE NEEDS, 2009-2010

Karrie Finn, Sherry Farr, Matthew Oster, Margaret Honein

Children with heart disease require lifelong care. A smooth transition from pediatric to adult care may decrease risk for morbidity and mortality. Little is known about the prevalence and predictors of transition-related discussions between parents of children with heart disease and the child's healthcare providers. Using self-reported, population-based data from the 2009-2010 National Survey of Children with Special Health Care Needs, our aim was to assess the prevalence and predictors of transition-related discussions between providers and parents of children 12 to 17 years of age with special health care needs (CSHCN) and heart disease. Logistic regression was used to generate adjusted prevalence ratios (aPR) for demographic characteristics and transition-related discussions. All calculations used weights to generate population-based estimates. Of the 758 interviews of CSHCN with heart disease (representing 220,000 individuals nationally), 52% were female, 65% were white, 37% had medical homes, and 60% had private insurance. Less than half of parents of CSHCN with heart disease reported discussing with providers their child's health insurance as an adult (25.4%), eventual shift to adult care (22.3%), and adult healthcare needs (47.5%). Among parents who did not have discussions, up to 67% reported desiring one. Having a child 16-17 years of age, compared to 12-13 years, was associated with discussing future health insurance (aPR 1.9, 95% CI [1.2, 3.1]), a shift to adult care (aPR 2.2, 95% CI [1.2, 4.0]), and adult healthcare needs (aPR 1.4, 95% CI [1.0, 1.9]). Having a medical home was associated with discussing future health insurance (aPR 1.8, 95% CI [1.3, 2.6]) and other adult healthcare needs (aPR 1.4, 95% CI [1.1, 1.8]). Less than half of parents of CSHCN with heart disease reported discussions with healthcare providers around transition to care for their children, despite evidence that a substantial percentage would find transition-planning beneficial.

CONGENITAL HEART DEFECTS AND ACADEMIC ACHIEVEMENT IN A NATIONWIDE COHORT OF 458,318 DANISH CHILDREN

Niels Matthiesen

Background: Congenital heart defects (CHD) are the most common birth defects, present in up to 1 % of all children. Over the last decades survival has improved immensely, but concurrently it has become clear that up to 50 % of the children present with abnormal neurodevelopment. Nonetheless, the impact of CHD on the academic achievement of the children remains widely unknown. Methods: We identified a nationwide cohort of 458,318 liveborn Danish children, 1997-2005. CHD was present in 3201 children. Academic achievement was assessed by mandatory national public school tests of reading and mathematics. CHD and potential confounders were identified in national registries. We estimated standardized mean test score differences by random effects linear mixed models adjusted for potential confounders, comparing children with CHD to the general population. Results: Overall, in CHD the standardized mean difference in reading was -0.10 (95%CI -0.13, -0.07). The results were similar in the subdomains language comprehension, decoding, and reading comprehension. Regarding mathematics, the estimate was -0.11 (95%CI -0.14, -0.07). The results were similar in the subdomains numbers and algebra, geometry, and applied mathematics. Several subgroups of CHD were associated with discretely lower scores in both reading and mathematics. The subgroup with the lowest scores was hypoplastic left heart syndrome [language comprehension -0.50 (95%CI -0.97, -0.02), decoding -0.85 (95%CI -1.36, -0.34), reading comprehension -0.43 (95%CI -0.93, 0.06), and mathematics -0.63 (95%CI -1.17, -0.08)]. Conclusion: Children with CHD constitute a distinct population prone to impaired neurodevelopment, including poor academic achievement. The heterogeneity of the academic achievements within subtypes of CHD was striking; some subtypes of CHD were associated with discrete difficulties while several other subtypes, e.g. hypoplastic left heart syndrome, were associated with markedly poorer academic achievement.

RISK COMPARISON FOR PRENATAL USE OF DIFFERENT ANALGESICS AND SELECTED BIRTH DEFECTS

Julia Interrante, Elizabeth Ailes, Jennifer Lind, Marlene Anderka, Marcia Feldkamp, Martha Werler, Suzanne Gilboa, Margaret Honein, Cheryl Broussard

Background: Previous research suggests that the use of opioid analgesics during early pregnancy increases the risk for certain birth defects while the use of acetaminophen is not associated with an increase in risk. However, use of analgesic medications have not been compared to each other with respect to risk for birth defects. Methods: We analyzed cases and controls (birth years 1997-2011) who participated in the National Birth Defects Prevention Study, a population-based, multi-site study, to examine associations between self-reported maternal analgesic use from 1 month before to 3 months after conception (periconceptional period) and 15 selected birth defects. We compared periconceptional use of nonsteroidal anti-inflammatory drugs (NSAIDs) and/or opioids to use of acetaminophen alone. Results: Among 40,091 mothers, 81% reported use of analgesic medications at any time in pregnancy, with 56% reporting use in the periconceptional period. Of the 16,478 case and 5,951 control mothers reporting periconceptional analgesic use, 48% of case (54% of control) mothers reported using acetaminophen as the only analgesic, 48% (42%) NSAIDs, 2% (2%) opioids, and 2% (1%) NSAIDs and opioids. After adjusting for maternal age, race/ethnicity, obesity, parity, smoking, alcohol consumption, periconceptional antibiotic use, study location, and time-to-interview, NSAIDs were statistically significantly associated with 3 of 8 heart defects (range of adjusted odds ratios (aORs): 1.3-1.4) and 6 of 7 non-heart defects (aORs: 1.3-1.6); opioids were associated with 3 of 8 heart defects (aORs: 1.7-2.2); NSAIDs and opioids were associated with 2 of 8 heart defects (aORs: 2.6-2.9) and 3 of 7 non-heart defects (aORs: 1.5-2.8) evaluated. Conclusions: Compared to periconceptional use of acetaminophen, use of NSAIDs and/or opioids appears to pose a greater risk of selected birth defects. Additional studies comparing the relative fetal safety of individual analgesics within these classes are needed.

USE OF INTRACYTOPLASMIC SPERM INJECTION AND BIRTH OUTCOMES IN WOMEN WHO CONCEIVED BY IN VITRO FERTILIZATION

Xu Xiong, Richard Dickey, Pierre Buekens, Jeffrey Shaffer, Gabriella Pridjian

Objective: Intracytoplasmic sperm injection (ICSI) was introduced to improve fertilization in couples with male factor infertility. However, use of ICSI for couples without male factor infertility has increased markedly over the last decades without clear evidence of a benefit over conventional in vitro fertilization (IVF). The objectives of this study were to study the frequency of ICSI use and the effect of ICSI on birth outcomes. Methods: A retrospective cohort study was conducted in 141,030 pregnancies resulting from fresh non-donor in vitro fertilization (IVF) cycles using 2006-2010 data from the Society for Assisted Reproductive Technology. Results: The overall frequency of ICSI use was 71.5%, increasing from 68.9% in 2006 to 73.1% in 2010. For women without male factor infertility, 57.0% were conceived by ICSI. Among all ICSI pregnancies, 47.4% was performed in couples without male factor infertility. Compared with conventional IVF, ICSI use was not associated with increased rates of multiple pregnancies, preterm delivery, low birth weight, stillbirth, and neonatal death. However, the risk of birth defects was significantly increased among women conceived by ICSI [3.0% for ICSI vs. 2.5% for conventional IVF; adjusted odds ratio (OR): 1.24 (95% confidence interval: 1.15-1.33)]; and increased in both women conceived by ICSI for male factor infertility [3.2% vs. 2.5%; aOR: 1.38 (1.25-1.52)] and for non-male factor infertility [2.7% vs. 2.5%; aOR: 1.12 (1.03-1.22)]. In women without male factor infertility, ICSI was associated with a significantly increased risk of genetic birth defect compared with conventional IVF [0.32% vs. 0.25%; aOR: 1.31 (1.01-1.71)]. Conclusions: ICSI is associated with an increased risk of birth defects compared with conventional IVF. Given that about half of all ICSI being performed in couples without male factor infertility and the potential detrimental effect of its use, ICSI may be over-used in practice.

PA005

USE OF ANTI-SEPTIC MOUTH RINSE DURING PREGNANCY AND PREGNANCY OUTCOMES: A RANDOMIZED CONTROLLED CLINICAL TRIAL

Xu Xiong, Hong Jiang, Yi Su, Jinxiang Peng, Xiaoling Zhu, Jinhua Wang, Mengqi Chen, Xu Qian

Objective: To determine whether anti-septic mouth rinse intervention reduces adverse pregnancy outcomes in a low-resource rural area. **Methods:** A randomized controlled trial was conducted among pregnant women less than 20 gestational weeks and with periodontal disease in a county level maternal health care hospital of China. Women with periodontal disease were randomized into the intervention (n=232) and control group (n=234). Participants in the intervention group were provided free mouthwash (alcohol- free antimicrobial mouth rinse containing 0.7% cetylpyridinium chloride) throughout the pregnancy and oral health education. Women in the control group only received oral hygiene education. All participants had periodontal re-examination at the 3rd trimester and were followed up to childbirth. The primary outcomes were gestational age and birth weight. **Results:** The general periodontal status of the intervention group at the 3rd trimester was significantly better than the control group (measured by score: 11.26±3.60 vs 11.92±3.01, P=0.04). There was no difference on pregnancy outcomes except premature rupture of membrane between the two groups. Women in the intervention group had a significantly reduced risk of premature rupture of membrane compared with those women in the control group (1.4% vs 5.7%, OR= 0.23, 95% CI: 0.07, 0.84, P=0.03). **Conclusions:** Mouth rinse intervention during pregnancy improved periodontal health condition. The intervention did not lead to the change on gestational age and birth weight, but it reduced the rate of premature rupture of membrane. Further studies are needed to explore the biological mechanism of this association. This trial is registered with Chinese Clinical Trial Registry (ChiCTR): (#ChiCTR-TRC-13003768, URL: <http://www.chictr.org.cn/enindex.aspx>). This study was funded by the UBS Optimal Foundation, Switzerland (GIFTS ID: 6088).

PA007

GENE VARIANTS AS RISK FACTORS FOR GASTROSCHISIS

Amy Padula, Wei Yang, Kathleen Schultz, Lauren Tom, Bin Lin, Suzan Carmichael, Edward Lammer, Gary Shaw

In a population-based case-control study in California of 228 infants, we investigated 84 genetic variants in 23 genes and risk of gastroschisis with regard to maternal age, race/ethnicity, vitamin use and smoking exposure. We hypothesized that genes related to vascular compromise may interact with environmental factors to affect the risk of gastroschisis. Haplotypes were constructed for 75 gene variants using the HaploView program. Risk for gastroschisis associated with each gene variant was calculated for both the homozygotes and the heterozygotes, with the homozygous wildtypes as the referent. Risks were estimated as odds ratios (ORs) with 95% confidence intervals (CIs) by logistic regression. We found 11 gene variants with increased risk and 4 variants with decreased risk of gastroschisis for heterozygous (ORh) or homozygous variants (ORv) genotypes. These included NOS3 (rs1036145) ORh=0.4 (95% CI: 0.2-0.7); NOS3 (rs10277237) ORv=2.7 (95% CI: 1.3-6.0); ADD1 (rs12503220) ORh=2.9 (95% CI: 1.6-5.4), GNB3 C825T (rs5443) ORh=0.2 (95% CI: 0.1-0.5), ORv=0.4 (95% CI: 0.2-0.9); ICAM1 (rs281428) ORv=6.9 (95% CI: 2.1-22.9), ICAM1 (rs3093030) ORv=2.6 (95% CI: 1.2-5.6); ICAM4 (rs281438) ORv=4.9 (95% CI: 1.4-16.6), ICAM5 (rs281417) ORh=2.1 (95% CI: 1.1-4.1), ORv=4.8 (95% CI: 1.7-13.6); ICAM5 (rs281440) ORh=23.7 (95% CI: 5.5-102.5), ORv=20.6 (95% CI: 3.4-124.3); ICAM5 (rs2075741) ORv=2.2 (95% CI: 1.1-4.4); NAT1088 ORv=0.3 (95% CI: 0.1-0.9). There were additional associations between several gene variants and gastroschisis among women aged 20-24 and among mothers with and without vitamin use. In conclusion, NOS3, ADD1, ICAM1, ICAM4 and ICAM5 warrant further investigation in additional populations and with the interaction of additional environmental exposures.

PA006

CHALLENGES IN ESTIMATING HOSPITALIZATION COSTS FOR BIRTH DEFECTS USING ADMINISTRATIVE DATA

Sarah Tinker

Birth defects (BDs) are common, costly, and critical and affect people of all ages. Quantifying costs associated with BDs is challenging because of limitations of administrative data. We used 2013 data from the National In Patient Sample of the Healthcare Cost and Utilization Project, a 20% stratified sample of discharges from non-federal community hospitals, to estimate the cost of BD-associated hospitalizations at all ages using facility fee charges multiplied by cost-to-charge ratios and professional fee ratios. In these data, each hospitalization has one primary discharge diagnosis code and up to 25 secondary diagnosis codes. Using only the primary diagnosis code is likely to result in an underestimate of costs, because delivery itself is often coded as the primary diagnosis for birth hospitalizations and BDs may be an important contributing cause for hospitalizations with other primary codes. Conversely, the use of all diagnosis codes may result in an overestimate of costs because the coded BD may be incidental to the reason for the hospitalization. Further complicating the issue are the high costs associated with preterm birth, which is common among infants born with BDs. The degree to which preterm birth is a consequence of a BD is not well-understood, but including costs associated with preterm delivery may overestimate total costs for BDs. The estimated cost of 2013 BD hospitalizations based on primary diagnosis codes was \$5.2 billion; using all diagnosis codes it was \$24 billion. The total cost when hospitalizations with all diagnosis codes for BD were included, but those with preterm delivery codes were excluded, was \$18.8 billion. Estimates of the cost of BD-associated hospitalizations provide researchers and policy makers with critical information on the impact of BDs on the healthcare system. This knowledge can be used to prioritize prevention, early detection, and care throughout the lifespan.

PA008

CHILD DEVELOPMENTAL OUTCOMES OF BOYS UNDERGOING SURGERY FOR GENITAL ANOMALIES

Francisco Schnerer, Jason Bentley, Andrew Holland, Samantha Lain, Nadia Badawi, Natasha Nassar

Background: Male genital congenital anomalies often require surgery in early life. Whilst surgery may address functional and cosmetic consequences of these anomalies, there has been little assessment on of their impact on childhood development. We investigated early childhood developmental outcomes among boys with genital anomalies. **Methods:** We conducted a population-based study of all boys born in New South Wales, Australia. Boys with a recorded diagnosis of hypospadias, undescended testis or other penile or testicular anomalies requiring surgery were compared to two types of controls: i) boys undergoing elective circumcision and ii) those without any hospitalizations in early childhood. Health information and developmental outcomes was obtained via record linkage of administrative hospital and Australian Early Developmental Census data for 2009 and 2012. Generalized estimating equations were used to evaluate the association between genital anomalies and developmental outcomes in five domains (physical health, emotional maturity, communication and general knowledge, language and cognitive skills; and social competence), taking into account individual and school-level factors. **Results:** A total of 1,117 boys with genital anomalies, 845 undergoing elective circumcision and 26,873 without hospitalizations were included. The mean (SD) age at developmental assessment was 5.5 (0.4) years. There was no difference in the proportion of boys considered developmentally vulnerable on two or more domains (scores <10th centile) between those with genital anomalies (13.2%), circumcision (12.7%) and those without hospitalizations (11.8%; p=0.26). There was no overall association between boys with and without genital anomalies and developmental vulnerability (adjusted odds ratio: 1.12; 95% CI: 0.94-1.33) nor any difference on any individual domain. **Conclusion:** There appear to be no increased risk of poor child developmental outcomes among boys diagnosed with genital anomalies

PA009

MATERNAL FIRST TRIMESTER SERUM LEVELS OF FREE-BETA HUMAN CHORIONIC GONADOTROPIN AND MALE GENITAL ANOMALIES

Francisco Schneuer, Carol Bower, Andrew Holland, Vitomir Tasevski, Sarra Jamieson, Natasha Nassar

Background: Hypospadias and undescended testis (UDT) are the most common male genital anomalies. One plausible etiological pathway is altered release of human chorionic gonadotropin (hCG) as this may impact fetal sex development. We investigated the association between maternal levels of hCG with hypospadias and UDT. **Methods:** Serum levels of free-beta hCG measured in women attending first trimester screening in New South Wales (NSW) and Western Australia (WA), were obtained from laboratory databases and combined with health information via record linkage of laboratory, birth, congenital anomalies and hospital data. Median levels of hCG multiple of the median (MoM) were compared between affected and unaffected boys. Logistic regression was used to evaluate the association between levels of hCG MoM and genital anomalies, and stratified by the presence of placental dysfunction and co-existing anomalies. Where relevant, pooled analysis was conducted. **Results:** There were 12,099 boys from NSW and 10,518 from WA included, of which 90 and 77 had hypospadias; and 107 and 109 UDT, respectively. Compared with unaffected (NSW=0.92 MoM; WA=0.88 MoM), there was no difference in median hCG levels among women with an infant with hypospadias (NSW=0.88 MoM, $p=0.83$; WA=0.84 MoM, $p=0.76$) or UDT (NSW=0.89 MoM, $p=0.54$; WA=0.95 MoM, $p=0.95$). Low (<25thcentile) or high (>75thcentile) levels were not associated with hypospadias or UDT, nor when stratifying by placental dysfunction and co-existing anomalies. There was a tendency for high levels for severe types, although results were imprecise. When combining results, high hCG levels were associated with increased risk of proximal hypospadias (odds ratio (OR) 4.34; 95%CI: 1.08-17.4) and bilateral UDT (OR 2.86; 95%CI: 1.02-8.03). **Conclusions:** Overall, first trimester maternal levels of serum hCG are not a marker for detecting male genital anomalies. However, elevated levels may be indicative of severe cases and should be assessed in future studies.

PA011

ASSOCIATIONS BETWEEN CARDIOVASCULAR BIRTH DEFECTS AND DISINFECTION BY-PRODUCT EXPOSURES IN MASSACHUSETTS

J. Michael Wright

Epidemiological and toxicological studies show that exposure to disinfection by-products (DBPs) in treated water leads to an increased risk of cardiovascular birth defects (CVDs), though epidemiological evidence for specific DBPs is limited. We used a case-control design of all birth defects in Massachusetts from 2000-2004 with complete trihalomethane (THM) and haloacetic acid (HAA) data. We randomly matched each case ($n=904$) to 10 controls ($n=9040$) based on week of conception. We used weight-averaged aggregate first trimester DBP exposures across all quarterly monitoring sample locations linked to individuals based on residence at birth. Adjusted odds ratios (aORs) were calculated for nine cardiac defects in relation to DBP categorical exposures including bromoform (TBM), chloroform (TCM), dibromochloromethane (DBCM), monobromoacetic acid (MBA), dichloroacetic acid (DCA), and trichloroacetic acid (TCA). We detected strong associations for Tetralogy of Fallot and the upper exposure categories for TCA, DCA, and Total HAAs (aOR Range: 3.34-6.51) including exposure-response relationships for DCA and Total HAAs. aORs consistent in magnitude were detected for atrial septal defects and TBM (aOR=1.56; 95% CI: 1.01, 2.43) and other DBPs including DBCM, TCM, and Total THMs (aOR Range: 1.26-1.67). Consistently elevated aORs were detected for ventricular septal defects (VSDs) and every DBP metric except TCM, TCA, and Total HAAs. Associations were also detected for VSDs and TBM (aOR=1.85; 95%CI: 1.20, 2.83), MBA (aOR=1.81; 95%CI: 0.85, 3.84), and DBCM (aOR=1.54; 95%CI: 1.00, 2.37). These findings add to previous epidemiologic studies and meta-analyses that show consistent associations between DBP exposures and CVD risks especially VSDs. This is the first study to develop multi-pollutant adjusted regression models and is only the second study to evaluate brominated DBPs; thus, this work adds some specificity to the potential CVD risks previously noted for Total THMs.

PA010

SCHOOL PERFORMANCE FOR CHILDREN BORN WITH CLEFT LIP OR PALATE: POPULATION-BASED RECORD LINKAGE STUDY

Jane Bell, Camille Raynes-Greenow, Robin Turner, Carol Bower, Alan Dodson, Natasha Nassar

Background: Orofacial clefts (OFC) are among the most common congenital anomalies. Effects on speech, hearing, and appearance can lead to chronic adverse health and developmental outcomes. **Method:** To compare the proportion of children with and without OFC meeting the national minimum standards in WALNA (2002-2007) and NAPLAN (2008-2012) literacy and numeracy tests we conducted a cohort study using linked population-based data. We included all children liveborn in Western Australia (WA), 1980-2010 and registered with OFC on the WA Register of Developmental Anomalies ($n=1,509$); and a random sample of 6,603 children born without OFC, frequency matched 4:1 by year of birth. **Results:** Results were available for 3,238 (89%) children expected to participate. Most students met the national minimum standards in both test programs, in all subjects at each year level. Compared to children without OFC, children with cleft palate only were less likely to meet minimum standards for NAPLAN reading (aOR 0.57; 95%CI 0.34, 0.96) and grammar and punctuation (aOR 0.49; 95%CI 0.32, 0.76), WALNA writing (aOR 0.66; 95%CI 0.47, 0.92), and WALNA and NAPLAN numeracy (aOR 0.64; 95%CI 0.43, 0.95, and aOR 0.47; 95%CI 0.28, 0.82, respectively). Children with cleft lip and palate had significantly lower odds for reaching the spelling standard in NAPLAN tests (aOR 0.52; 95%CI 0.29, 0.94), while children with cleft lip only had similar odds for reaching all minimum standards. **Conclusions:** Children born with OFC, particularly children with cleft palate only, should be monitored to identify learning difficulties and enable early intervention to maximise school attainment and longer term outcomes.

PA012

EXPOSURE TO MATERNAL DIABETES AND EARLY CHILDHOOD DEVELOPMENT

Edwina Yeung

Background: Prenatal influences can have long-lasting impact on neurodevelopment. Diabetes during pregnancy may increase risk of developmental delay due to hypoxia or other fetal responses to maternal hyperglycemia. **Methods:** Upstate KIDS recruited mothers who delivered a newborn between 2008 and 2010 in Upstate New York. The cohort was designed to study the impact of infertility treatment on children's development, which required oversampling on infants reported on birth certificates to be conceived with infertility treatment and inclusion of all twins. Parents completed the Ages and Stages Questionnaire© (ASQ) every 4 to 6 months after birth until age 3 years. The ASQ is a validated screening tool assessing 5 developmental domains. Pre-gestational and gestational diabetes were identified by maternal report, birth certificates, or hospital discharge data. Using data for 3767 singletons and 1056 independent twins, adjusted odds ratios (aOR) and 95% confidence intervals (CI) for failing the ASQ domains were estimated by generalized linear mixed models accounting for maternal age, race, education, insurance, marital status, parity, pregnancy smoking and pre-pregnancy obesity. Weights were applied to account for the sampling design. **Results:** Among 4823 children, 154 (3.2%) and 378 (7.8%) had in utero exposure to pre-gestational or gestational diabetes, respectively. Neither pre-gestational nor gestational diabetes were associated with developmental delays. Further adjustment for dietary supplementation and paternal obesity did not meaningfully alter results. After stratifying by plurality, gestational diabetes was suggestive of being associated with increased risk of fine motor developmental delay among twins (aOR 1.99; 95%CI: 0.97-4.10) but not singletons (1.10; 0.59-2.06). **Conclusions:** Maternal diabetes during pregnancy was generally not associated with early developmental delays in children up to 3 years of age. Few exposed children may have limited power to detect differences.

IMPACT OF MATERNAL OBESITY ON NEONATAL MARKERS OF INFLAMMATION AND IMMUNE RESPONSE

Nikhita Chahal, Alexander McLain, Akhgar Ghassabian, Kara Michels, Erin Bell, David Lawrence, Miranda Broadney, Edwina Yeung

Background: Despite the high prevalence of pre-pregnancy obesity in the United States, the impact of maternal obesity on offspring inflammation is unclear. We examined the effect of pre-pregnancy obesity on neonatal inflammatory and immune responses in a birth cohort. **Methods:** The Upstate KIDS Study (2008-2010) was designed to investigate infertility treatment and child development. Pre-pregnancy body mass index (BMI) was derived from vital records. Inflammatory biomarker and immunoglobulin levels were measured from newborn dried blood spots (NDBSs). An inflammation score was derived from levels of six biomarkers (interleukin-6 (IL6), IL8, IL1-alpha, IL1ra, tumor necrosis factor alpha, c-reactive protein), with a higher score indicating a greater inflammatory response. We examined immunoglobulin (Ig) levels separately. We used generalized estimating equations to examine associations between maternal obesity and biomarker levels in singletons and twins (n=3567), after adjusting for maternal age, race, education, marital status, health insurance, pregnancy vitamins use, pregnancy smoking, paternal BMI, and plurality. Sampling weights were applied to account for study design. **Results:** Twenty-five percent of mothers were obese and 26% were overweight before pregnancy. Inflammation scores did not differ between infants born to obese mothers and those born to normal weight mothers, but elevated IgM levels were detected (adjusted mean difference=0.10, 95%CI: 0.04-0.16). In contrast, infants born to overweight mothers had elevated inflammation scores (adjusted mean difference=0.11, 95%CI: 0.01-0.22; compared to infants of normal weight mothers). However, IgM levels did not differ between these two groups. IgE and IgA levels did not differ among infants. **Conclusions:** Inflammation and immune markers may differ between neonates born to normal weight versus overweight or obese mothers. NDBSs could provide a useful tool for evaluating neonatal responses to prenatal exposures.

PRENATAL ALCOHOL EXPOSURE AND AUTISM SPECTRUM DISORDER IN THE STUDY TO EXPLORE EARLY DEVELOPMENT (SEED)

Alison B Singer, Arthur S Aylsworth, Lisa A Croen, Carolyn DiGuseppi, M Daniele Fallin, Stephen R Hooper, Rebecca E Pretzel, Laura A Schieve, Gayle C Windham, Julie L Daniels

Prenatal alcohol exposure can negatively affect neurodevelopment. We examined the association between prenatal alcohol use and autism spectrum disorder (ASD) in the Study to Explore Early Development, a multi-site case-control study. We included 651 children with ASD, 976 children with non-ASD developmental delay (DD), and 924 general population (POP) children. Mothers reported average drinks per week in each month of pregnancy. For each month, we classified women as non-drinkers, light drinkers (≤ 2 drinks per week), or moderate-high drinkers (≥ 3 drinks per week). We used logistic regression to model associations, adjusting for child gender, household income, and maternal race/ethnicity, education, parity, psychiatric conditions, smoking, and age. Non-Hispanic white, highly educated, and higher income women were more likely to report any drinking. In all months, mothers of children with ASD or DD were less likely to report any drinking than mothers of POP controls. In the first month of pregnancy, light drinking was inversely associated with ASD (adjusted odds ratio (aOR): 0.6, 95% confidence interval (CI): 0.5, 0.9) and DD (aOR: 0.8, CI: 0.6, 1.0), but moderate-heavy drinking was not associated with ASD (aOR: 1.0, CI: 0.6, 1.8) or DD (aOR: 1.0, CI: 0.6, 1.6). In the 2nd month, light drinking was inversely associated with ASD and DD, moderate drinking was positively associated with DD (aOR: 2.5, CI: 1.1, 6.0), and an association between moderate drinking and ASD was suggested (aOR: 1.5, CI: 0.5, 4.4) but estimates were imprecise. We could not evaluate dose past the 2nd month of pregnancy because of sample size constraints. Residual or unmeasured confounding could explain inverse associations with light drinking. We will further assess potential explanatory variables in subsequent analyses. Since alcohol is known to negatively affect neurodevelopment and other infant outcomes, women should not drink alcohol if they are pregnant or might be pregnant.

INFLAMMATORY BIOMARKERS AND EARLY DEVELOPMENT: A LONGITUDINAL STUDY

Akhgar Ghassabian, Rajeshwari Sundaram, Nikhita Chahal, Erin Bell, David Lawrence, Stephen Gilman, Edwina Yeung

Studies of neurodevelopmental disorders suggest that immune system activation is associated with brain abnormalities. However, longitudinal studies on the relationship between inflammatory biomarkers and children's neurodevelopment are sparse and inconclusive. In the Upstate KIDS Study (2008-2010), we assayed 20 biomarkers with possible neuro-inflammatory effects using residual newborn dried blood spots [e.g. interleukin (IL)-8, monocyte chemoattractant protein, c-reactive protein, and plasminogen activator inhibitor type 1 (I-1)]. Mothers reported on their children's development across 5 developmental domains repeatedly until age 3 years using the Ages & Stages Questionnaire (ASQ). Generalized linear mixed models were used to test the association of each biomarker with a child's failing of ASQ (n=3038). Models were adjusted for perinatal risk factors and maternal or child characteristics. If any association existed with overall ASQ fail, the associations between biomarkers and failing each of the 5 domains were further examined. Higher levels of I-1 and platelet-derived growth factor-AA (PDGF-AA) were associated with lower odds of failing any ASQ up to age 3 years [adjusted odds ratio (aOR)=0.71, 95%CI: 0.51-0.98 and aOR=0.97, 95%CI: 0.95-0.99, respectively]. Further analyses indicated that higher I-1 was associated with lower odds of delay in developmental domain of gross motor (aOR=0.54, 95%CI: 0.30-0.96). Higher PDGF-AA was inversely associated with delays in 4 out of 5 ASQ domains including fine motor, gross motor, communication and personal-social functioning. Other biomarkers were not associated with ASQ fail after adjusting for confounders. This supports the results of prior studies demonstrating immune activity is involved in neurodevelopment, but raises the question over the nature of such involvement given the unexpected direction of the associations observed.

PRE-PREGNANCY OBESITY IS ASSOCIATED WITH IMPAIRED CHILD NEURODEVELOPMENT

Elizabeth Widen, Piera Cirillo, Barbara Cohn, Linda Kahn, Katrina Kezios, Pam Factor-Litvak

There is mixed evidence regarding the relationship of maternal prepregnancy body mass index (BMI) and gestational weight gain (GWG) with child neurodevelopment. We examined associations of prepregnancy BMI and GWG with child neurodevelopment at age 9. Subjects were a subgroup of offspring (n=1,814) of the Child Health and Development Studies, a pregnancy cohort enrolled between 1959 and 1967 at the Kaiser Foundation Health Plan in the Oakland, California, area. Prepregnancy BMI was ascertained via self-report during pregnancy and GWG was assessed from prenatal records. At age 9, children were administered a Peabody Picture Vocabulary Test, which is an indicator of verbal intelligence and scholastic aptitude. Multivariable linear regression was used to examine the relationship between BMI category, GWG adherence to 2009 IOM guidelines [(excessive (> IOM), adequate or inadequate (<IOM)], and child standardized Peabody score, adjusting for child sex, age, gestational age at delivery, and birth weight, and maternal income, marital status, race, smoking status, and age. An interaction term between BMI and GWG was included to assess effect measure modification; however, no modification was observed on the additive scale. Before pregnancy, a majority of mothers were normal weight (76.9%), while fewer were overweight (11.3%), underweight (8.7%) and obese (3.1%). Mean GWG was 20.6 \pm 7.8 lb (Mean \pm SD). A majority of mothers had inadequate GWG (69%), while 24.7% of mothers adhered to 2009 IOM Guidelines and 6.3% of mothers showed excessive GWG. Compared to normal weight women, prepregnancy obesity was associated with lower offspring Peabody scores [Estimated β : -3.5 (95% CI: -6.3, -0.74), p=0.01], but not prepregnancy overweight (p=0.1) or underweight (p=0.7). Excessive or inadequate GWG was not associated with child outcomes (all p-values>0.2). In this cohort, prepregnancy obesity was associated with impaired verbal ability and scholastic aptitude in children.

INTERPREGNANCY CHANGE IN MATERNAL BODY MASS INDEX, ADVERSE PREGNANCY OUTCOMES, AND OFFSPRING'S NEURODEVELOPMENT

Xiaona Huo

Abstract Background: Maternal body-mass index (BMI) change between two pregnancies has been associated with pregnancy outcomes particularly in obese women. However, no study has examined the impact of interpregnancy BMI change on long-term neurodevelopment in children. The purpose of our study was to evaluate the effect of interpregnancy BMI change of two consecutive pregnancies on pregnancy outcomes and child neurodevelopment. Methods: Data were obtained from the Collaborative Perinatal Project (CPP), a large prospective cohort study to investigate the perinatal factors on neurological and neurosensory disorders in childhood in the U.S. from 1959 to 1976. Women with first two consecutive singleton pregnancies (N=5972) in CPP were included. The primary outcome was the intelligence quotient (IQ) of the second enrolled children at age 4 and 7 years. The secondary outcomes included preterm birth (gestational age <37 weeks), low birth weight (birth weight <2.5 kg), macrosomia (birth weight \geq 4 kg) and pregnancy-induced hypertension. The relative risks of low IQ in offspring and adverse pregnancy outcomes were estimated using multiple logistic regression models. Findings: Compared with women whose BMI gained 0 to 1 unit, those who gained more than 2 units were at increased risks for offspring low IQ (IQ < 70, adjusted odds ratio [aOR] 1.9, 95% confidence interval [CI] 1.0-3.4), pregnancy-induced hypertension (aOR 1.5, 95% CI 1.2-2.0) and macrosomia (aOR 1.8, 95% CI 1.3-2.5). Women with interpregnancy BMI lost 1 unit or more also had elevated risks for low IQ (aOR 2.1, 95% CI 1.2-3.9), preterm birth (aOR 1.5, 95% CI 1.2-2.0) and low birth weight (aOR 2.1, 95% CI 1.5-2.9) in the second pregnancy. Conclusions: Excessive BMI change between pregnancies is associated an increased risk of adverse pregnancy outcomes. Furthermore, excessive BMI gain or loss between pregnancies was associated with lower offspring child IQ. This association was confirmed in women with normal pregnancy BMI ($18.5 \leq \text{BMI} < 25$) in both pregnancies.

EDUCATIONAL OUTCOMES FOLLOWING CARDIAC PROCEDURE IN THE FIRST YEAR OF LIFE: A POPULATION-BASED RECORD LINKAGE STUDY

Samantha Lain, Claire Lawley, Nadia Badawi, Francisco Schneuer, Christine Roberts, Natasha Nassar

Background: Children requiring cardiac surgery in infancy have been shown to have poor neurodevelopmental outcomes in early childhood, however only a few, small studies have investigated school age educational outcomes. **Aim:** Investigate the educational outcomes for infants who have had a cardiac procedure before age one. **Methods:** We conducted a population-based record linkage study of infants born in New South Wales, Australia, 2001-2005 with corresponding education outcome data (N=260,685). Hospital discharge data was used to identify infants that had a cardiac surgical procedure up to age one and individual data was linked to state-wide birth and National school assessment data to assess perinatal characteristics and school performance in grade 3 (aged 7-9 years). Multivariable logistic regression was used to examine perinatal and perioperative predictors of poor educational outcome amongst children who had a cardiac procedure. **Results:** Of 550 infants undergoing cardiac surgery with relevant educational outcome data, over a quarter (26.8%) performed below the National Minimum Standard (NMS) for reading and 27.6% performed below NMS for numeracy, compared to 6.0% and 5.8%, for children without a cardiac procedure, respectively. When infants with a severe congenital anomaly were excluded (1/4 of children who had cardiac surgery), infants who had a cardiac procedure were still significantly more likely to perform below the NMS for both numeracy (14% vs 5.6%, $p < 0.001$) and reading (12.5% vs 5.9%, $p < 0.001$). Significant predictors of poor educational outcome following cardiac surgery for those without a severe congenital anomaly were; low birthweight, cardiac arrest and/or heart failure during initial cardiac procedure. **Conclusions:** Infants having cardiac surgery in the first year of life are more likely to experience developmental disabilities leading to poor educational outcomes and will require additional resources and support.

THE IMPACT OF FERTILITY TREATMENT ON MOTHER-INFANT BONDING IMPAIRMENT AT 4 MONTH POSTPARTUM: A JAPANESE POPULATION BASED STUDY.

Makiko Sampei, Takeo Fujiwara

Background and Objective Little is known about the impact of fertility treatment on mother-infant relationship. This study examines association between fertility treatment and mother-infant bonding impairment in a population based sample of mothers with 4 month old infants in Japan. **Methods** Women who participated in a 4-months health-checkup program in Aichi prefecture, Japan (n= 6590; response rate, 68%) were asked to a complete a questionnaire including fertility treatment history for the delivered infant and the Mother to Infant Bonding Scale Japanese version (MIBS-J), composed of 2 subscales ("lack of affection" and "anger and rejection"). We used multiple logistic regression to assess the association between fertility treatment history and mother-infant bonding impairment adjusted for maternal, infant and family characteristics. **Results** Women who underwent fertility treatment were 1.22 times more likely to show mother-infant bonding impairment after adjustment for maternal, infant and family covariates (odds ratio [OR] = 1.22; 95% confidence interval [CI]:1.02, 1.47). Further, women with fertility treatment were 1.37 times more likely to show "anger and rejection" (OR = 1.37; 95% CI:1.14, 1.64), while no association was found for "lack of affection" (OR = 1.08; 95% CI:0.90, 1.30). **Discussion& Conclusions** Women underwent fertility treatment were at higher risk on mother-infant bonding impairment, particularly they may show anger and rejection towards their infants. While, they did not show lack of affection towards their infants. Further intervention is needed targeting women with infertility treatment to prevent mother-infant bonding impairment.

DIABETES AND HYPERTENSION IN PREGNANCY IN ASSOCIATION WITH AUTISM SPECTRUM DISORDER IN THE CHILD

Christina Cordero, Gayle Windham, M. Daniele Fallin, Lisa Croen, William Thompson, Laura Schieve, Anna Maria Siega-Riz, Alison Stuebe, Julie Daniels

Background: Previous studies have shown complications of pregnancy, labor, and the neonatal period to be associated with autism spectrum disorder (ASD). However, because specific conditions are relatively rare, multiple conditions have often been examined in aggregate and with inconsistent results. More common complications should be investigated independently in a large sample. **Objectives:** To examine the association between 1) maternal diabetes and 2) maternal hypertension active during pregnancy and development of ASD in the child. **Methods:** Our analysis uses the Study to Explore Early Development (SEED), a multi-site, case-control study. Children born in 2003-2006 were enrolled at 2-5 years of age. Developmental assessment in the clinic was used to classify children into three groups based on presence of ASD (n=702), non-ASD developmental delay (DD; n= 893), or non-ASD controls drawn from the general population (POP; n=982). Diagnoses of any diabetes or hypertensive disorder during pregnancy were identified from prenatal medical records, maternal interviews, and questionnaires. We examined the associations between diabetes or hypertension and case status (ASD and DD groups to POP) using logistic regression models; odds ratios were adjusted (aOR) for maternal age, race/ethnicity, education, smoking during pregnancy, and pre-pregnancy body mass index. Models of hypertension were additionally adjusted for parity and plurality. **Results:** From a sample of 2,577, we identified 234 mothers (9.1%) with diabetes and 389 mothers (15.1%) with hypertension in pregnancy. The crude OR=1.24 (95% confidence interval (CI) 0.87, 1.76) for diabetes was attenuated after adjusting for covariates aOR=0.96 (95% CI 0.66, 1.41). For hypertension, the crude OR=1.68 (95%CI 1.28, 2.22) was also attenuated with adjustment, but remained elevated, aOR=1.42 (95% CI 1.05, 1.93). Associations were slightly stronger when comparing DD vs. POP; diabetes aOR=1.24 (95% CI 0.89, 1.75) and hypertension aOR=1.58 (95% CI 1.19, 2.10). **Conclusions:** Our results show an association between hypertension, but not diabetes, during pregnancy and ASD in the child. In general, most associations between mother's conditions and child outcomes were slightly stronger when examining children with a non-ASD developmental delay.

PA021

GESTATIONAL WEIGHT GAIN AND MATH AND READING ACHIEVEMENT AMONG U.S. CHILDREN

Louisa Smith, Lucia Petito, Alison Cohen, Julianna Deardorff, Barbara Abrams

The 2009 Institute of Medicine report on weight gain in pregnancy raised concern about possible effects on child neurodevelopment. Published findings to date have been mixed, and a variety of weight gain and cognitive measures have been used. We used two measures of gestational weight gain (GWG) to investigate associations with math and reading scores at school age in a nationally representative population: (1) total gestational weight gain categorized according to 2009 IOM recommendations, and (2) weight gain-for-gestational age z-scores categorized as below, within, or above 1 standard deviation from the mean. Children from the National Longitudinal Survey of Youth 1979 Children and Young Adults cohort were given math and reading achievement tests at ages 5-6. The associations between GWG and test scores were analyzed in 5,307 mother-child pairs using survey-adjusted multiple linear regression, controlling for maternal and pregnancy factors. Crude analyses showed lower test scores in both the low and high categories of each GWG measure, compared to the intermediate reference. After controlling for confounders, those associations were attenuated and non-significant using the IOM measure. The adjusted z-score analyses, however, showed smaller but still significant associations with lower math scores. Low gain (z-score < -1) was associated with a difference of -0.07 standard deviation units in math score (95 % CI -.14, -.004), and high gain (z-score > 1) was associated with a difference of -0.14 units (-0.24, -.05). This study shows that inconsistencies in the literature may be due to weight gain measure used. Children of both low and high GWG mothers may be at risk for lower achievement, but risk may be limited to the extremes of the weight gain distribution.

PA023

THE EFFECT OF NEURODEVELOPMENTAL DISABILITY DEFINITION ON INCIDENCE RATES AMONG VERY PRETERM INFANTS

Matthew Haslam, Sarka Lisonkova, Dianne Creighton, Paige Church, Anne Synnes

BACKGROUND: Various criteria are used to define severe neurodevelopmental impairment (SND) and the effect of definition is rarely reported. Our objective was to examine the impact of differences in SND definition on incidence rates and the association with risk factors. **METHODS:** Infants (n=2249) born at 20, retinopathy of prematurity stage ≥3, intraventricular hemorrhage grade ≥3 or periventricular leukomalacia, and late onset sepsis were significant risk factors for both SND definitions. **CONCLUSIONS:** SND incidence varies significantly with the definition criteria. Readers should be cognizant of this effect when making conclusions from the literature. A standardized definition of SND would facilitate direct comparison across global Neonatal Follow-Up Networks.

PA022

METALS PRENATAL LEVELS AND MODIFIED CHECKLIST FOR AUTISM IN TODDLERS: A BIRTH COHORT STUDY FROM ITALY

Fabio Barbone

Introduction. Recently, a unifying model in autism involving zinc-deficiency, copper overload and higher early childhood exposure to neurotoxicants (mercury or lead) has been proposed. To test the hypothesis that lower zinc and zinc/copper ratio in cord blood levels and/or higher mercury prenatal exposure may be associated with failing in the Modified Checklist for Autism in Toddlers (M-CHAT), a mother-child prospective cohort from Trieste, Italy was evaluated at child's age 18 months. **Methods.** This cohort included 900 mothers recruited at 20 months of pregnancy at the only children's hospital. Mercury, zinc, copper and other metals were measured in maternal hair and blood during pregnancy and in umbilical cord blood and breast milk. Maternal intelligence was tested by using Raven's Progressive Matrices. Lifestyle, environmental, and socioeconomic factors were assessed by questionnaires during pregnancy. Preterm births and babies with congenital malformations or severe perinatal problems were excluded. 18 months after delivery the M-CHAT was performed by a psychologist. Cut-off points indicating failure in the M-CHAT were defined according to Robins et al 2001. Metals levels (ng/g) were log2 transformed. Bivariate and multivariate logistic regression models were used to evaluate the association between metal level and M-CHAT failure. **Results.** Respondents were 460/900. Overall prevalence of M-CHAT failure was 21.7% (Males =25%). After adjusting for child's gender, mother's Raven test and home size (a valid predictor of socioeconomic status in Italy), lower cord blood zinc level (p<0.025) and Zn/Cu ratio (p<0.013) were associated with M-CHAT failure. By contrast, mercury level in mother's blood was directly associated with M-CHAT failure in females (p<0.016) but not in males (0.877). **Conclusion.** In this Italian mother-child cohort prenatal zinc, zinc/copper balance and mercury contamination play a role as explanatory variables in positive testing at M-CHAT screening.

PA024

AGE AT MENARCHE IS ASSOCIATED WITH CHILDHOOD RED MEAT AND FATTY FISH INTAKE FREQUENCIES IN OPPOSITE DIRECTIONS

Erica Jansen, Eduardo Villamor, Constanza Marin, Mercedes Mora-Plazas

Background: Early age at menarche is associated with breast cancer risk. Red meat consumption in adolescence predicts breast cancer risk, but it is unknown whether it is also related to earlier menarche. **Objectives:** We studied the association between intake of red meat at ages 5-12 y and age at menarche in a prospective study. **Methods:** We assessed usual diet with a food frequency questionnaire (FFQ) in a group of 456 girls aged 8.4 ± 1.7 years and followed them for a median 5.6 y in Bogota, Colombia. Girls were asked periodically about the occurrence and date of menarche. Median age at menarche was estimated with use of Kaplan-Meier survival probabilities by categories of red meat intake frequency. Cox proportional hazards models were employed to compare the incidence of menarche by red meat intake frequency adjusting for potential sociodemographic and dietary confounders including total energy intake and intake frequency of other animal food groups (dairy, poultry, fresh water fish, tuna/sardines, eggs, and innards). **Results:** Median age at menarche was 12.4 years. After adjustment for total energy intake, maternal parity, and socioeconomic status, red meat intake frequency was inversely associated with age at menarche. Compared to girls with red meat intake <4 times per week, those consuming it ≥2 times per day had an adjusted 64% higher probability of menarche (95% CI= 11% to 141%; P, trend= 0.0009). Incidentally, we found that girls with tuna/sardines intake >1 time per week had a 38% lower probability of menarche (95% CI=10% to 58%; P=0.01) than those with intake <1 time per month. Intake frequency of other animal food groups was not significantly associated with age at menarche. **Conclusion:** Red meat intake frequency during childhood was associated with an earlier age at menarche whereas fatty fish intake frequency was related to a later menarcheal age.

SERUM FOLATE AND MENSTRUAL FUNCTION IN THE BIOCYCLE STUDY

Kara Michels, Torie C. Plowden, Keewan Kim, Ellen N. Chaljub, Jean Wactawski-Wende, Edwina Yeung, Sunni L. Mumford

Background: The impact of folate on menstrual function is unclear, but previous research indicates that higher dietary folate intake is associated with higher luteal progesterone levels and decreased risk of anovulation. We aimed to examine aspects of menstrual function as they relate to serum folate levels. **Methods:** The BioCycle Study prospectively followed 259 reproductive aged women for up to 2 menstrual cycles. Serum folate and reproductive hormone concentrations were measured up to 8 times across each cycle; 24 hour dietary intakes were recalled up to 4 times per cycle. We estimated associations between serum folate and hormones using weighted linear mixed models that adjusted for age, race, body mass index, cigarette use, alcohol use, lagged hormones, and cycle-averaged intakes of total energy and fiber. Modified Poisson regression was used to identify associations between tertiles of cycle-averaged folate and anovulation. **Results:** Increasing serum folate was associated with decreasing follicle stimulating hormone (FSH) at the time of expected ovulation (adjusted percent change=-0.3%; 95% confidence interval (CI) -0.6, 0.0%), as well as increasing luteal-phase progesterone (1.0%; 95% CI 0.4, 1.6%). Folate was not associated with changes in estrogen (0.0%; 95% CI -0.3, 0.2%) or luteinizing hormone. It also was not associated with anovulation (adjusted risk ratio aRR 1.45; 95% CI 0.72, 2.94 for the lowest tertile; aRR 0.96; 95% CI 0.47, 1.97 for the highest tertile, when compared to the middle tertile); nor was there a linear trend across tertiles ($p=0.34$). However, an increasing ratio of serum folate to serum homocysteine at the time of expected ovulation was protective against anovulation (aRR 0.90; 95% CI 0.82, 1.00). **Conclusions:** We found that folate is associated with FSH and progesterone levels, but not with anovulation. Further research is needed to understand if changes in diet or dietary supplements can improve ovulation and subsequently, fertility.

TRACE ELEMENTS IN URINE AND COUPLE FECUNDITY

Sunni Mumford, Patrick Parsons, Rajeshwari Sundaram, Germaine Louis

Background: While some trace elements are essential for normal health and immunity, others are non-essential, and have shown adverse associations with reproductive health. Yet, little is known regarding associations with couple fecundity. Thus, we investigated associations between male and female urinary trace element concentrations and time-to-pregnancy (TTP). **Methods:** We measured concentrations of 21 trace elements in urine at baseline among 501 couples desiring pregnancy and discontinuing contraception. Couples were followed for 12 months or until pregnancy. Fecundability odds ratios (FORs) and 95% confidence intervals (CIs) were estimated adjusting for age, body mass index, race, site, creatinine, supplement use, and smoking, in relation to female, male, and joint couple concentrations. FORs<1 denote a longer TTP. **Results:** There were no differences in urinary trace element concentrations in women between couples who did and did not become pregnant, though median thallium concentrations in men were significantly higher among couples that became pregnant (0.15 vs 0.11 $\mu\text{g/L}$, $P=0.02$). No associations were observed between female trace element concentrations and TTP in either the individual or couple-based models for any of the elements measured. Urinary lead concentrations in men were associated with reduced fecundity (individual model FOR 0.84, 95% CI 0.71, 0.99; joint model FOR 0.83, 95% CI 0.70, 0.99), whereas male urinary concentrations of selenium and barium were marginally associated with increased fecundity (selenium, joint model FOR 1.12, 95% CI 0.95, 1.33; barium joint model FOR 1.09, 95% CI 0.95, 1.26). **Conclusion:** Our results suggest that environmentally relevant concentrations of a spectrum of trace elements were largely not associated with couple fecundity, with the exception of male urinary lead concentrations. These findings corroborate earlier findings for blood lead and suggest that both chronic and acute lead exposures are important for fecundity.

ADJUSTING FOR ABSTINENCE TIME IN SEMEN ANALYSES: SOME CONSIDERATIONS

Kara Michels, Ellen N. Chaljub, Torie C. Plowden, Ya-Ling Lu, Keewan Kim, Sunni Mumford

Sexual abstinence time is of concern in semen analysis as it may influence parameters such as volume, sperm concentration, and motility; samples are often collected after a standardized period of abstinence to increase precision when assessing semen quality. Some studies have additionally included abstinence time in their regression models. However, depending on one's research question, abstinence time may or may not act as a confounder and one must consider the implications of statistically adjusting for abstinence time (or adjusting via selection). Our goal was to identify how abstinence time is handled across studies in leading journals, discuss examples of research questions in which one should avoid adjustment, and identify potential solutions if adjustment is unavoidable. We identified 95 relevant articles that contained the terms "abstinence" or "semen" published between October 2014 and September 2015 within 8 epidemiologic and reproductive journals. Of the included articles, 35% limited abstinence time before semen collection, but did not statistically adjust for it, with WHO guidelines being the most commonly used for restricting semen collection or semen analysis. Statistical adjustment in regression models was observed in 15% of the articles, representing potential unnecessary adjustment. Adjustment for factors that do not act as confounders may introduce bias (e.g., a potential causal path between alcoholism and semen quality may be mediated by abstinence time) or may hurt precision (e.g., when abstinence time is only associated with a logistically modeled outcome). These findings highlight the need to establish an analytic plan after properly defining one's research question and describing associations between abstinence time and the exposure. Avoiding practices which may negatively affect precision or causal interpretation will better allow us to identify factors associated with male fertility.

EFFECTS OF FETAL REDUCTION IN MULTI-FETAL PREGNANCY ON PERINATAL OUTCOMES

Neda Razaz, Tehila Avitan, Tracy Pressey, K.S. Joseph

Background: There is currently insufficient evidence regarding the prognosis of multi-fetal pregnancies reduced to twins or singletons. We compared the perinatal outcomes of deliveries following fetal reduction with the perinatal outcomes of deliveries without fetal reduction. **Methods:** We carried out a retrospective cohort study of all births in British Columbia between 2009 and 2013, using information from a population-based database. Comparisons were made between all women who had a fetal reduction to a twin or a singleton pregnancy with those who did not undergo a fetal reduction procedure. The outcomes of interest were preterm delivery and composite severe neonatal morbidity or perinatal mortality. Generalized estimating equations adjusting for maternal age, parity, pre-pregnancy weight, use of in vitro fertilization and baby's sex were used to estimate odds ratios (OR) and 95% confidence intervals (CI). **Results:** Among 207,273 deliveries, 94 (0.05%) had a fetal reduction. Of these, 53 women delivered twins and 37 delivered singletons. Women who had a fetal reduction were more likely to have conceived with in vitro fertilization (77.6%) compared with those who did not (3.31%). Twins delivered after fetal reduction had lower rates of neonatal morbidity/mortality (OR 0.21, 95% CI 0.09-0.45) compared with unreduced triplets but rates similar to those of twins without a reduction procedure (OR 1.53, 95% CI 0.88-2.64). Singletons delivered after fetal reduction had non-significantly lower rates of neonatal morbidity/mortality than unreduced twins (OR 0.46, 95% CI 0.18-1.21) but significantly higher rates of neonatal morbidity/mortality than singleton pregnancies without a reduction procedure (OR 2.59, 95% CI 1.00-6.71). Rates of preterm birth followed a similar pattern. **Conclusion:** Perinatal outcomes of twins delivered after fetal reduction are better than those of unreduced triplets and similar to those of unreduced twins.

TRIMESTER-SPECIFIC URINARY BISPHENOL-A AND PREGNANCY GLUCOSE LEVELS AMONG WOMEN FROM A FERTILITY CLINIC

Yu-Han Chiu, Tamarra James-Todd, Lidia Mínguez-Alarcón, Jennifer B. Ford, Myra Keller, Carmen Messerlian, John Petrozza, Paige Williams, Russ Hauser

Background: Women treated for infertility are at increased risk of impaired glucose tolerance and gestational diabetes during pregnancy. Studies suggest higher BPA exposure may increase risks of insulin resistance and diabetes in non-pregnant populations, but, the association between BPA and glucose dysregulation in pregnancy is unknown for this high-risk group. **Methods:** A total of 260 women from a fertility clinic participating in the Environment and Reproductive Health Study contributed at least one urine sample during the 1st and 2nd trimesters, delivered a live birth, and had available blood glucose data. Urinary BPA concentrations were quantified by isotope dilution tandem mass spectrometry. Blood glucose levels 1-hour after a 50-gram glucose challenge test were assessed at 24-28 weeks gestation. Trimester-specific urinary BPA concentrations were categorized in quartiles. Linear regression was used to evaluate associations between trimester-specific BPA and continuous blood glucose levels adjusting for age, race/ethnicity, pre-pregnancy body mass index, smoking, education, fetus number, and infertility diagnosis. **Results:** 46 women (18%) had glucose levels ≥ 140 mg/dL according to Carpenter-Coustan criteria. The means of specific gravity-adjusted BPA concentrations measured during 1st and 2nd trimester were 2.12 and 2.11 $\mu\text{g/L}$, respectively, with a correlation coefficient of 0.26. Second trimester BPA concentrations were positively associated with blood glucose (P , trend=0.03). Specifically, women with BPA concentrations in the highest quartile had an adjusted mean glucose level of 119 (112, 126) mg/dL compared to women in the lowest quartile, whose adjusted mean glucose level was 108 (102, 114) mg/dL. No significant associations were observed between 1st trimester BPA concentrations and blood glucose levels. **Conclusion:** BPA concentrations in the 2nd trimester were positively associated with 2nd trimester glucose levels among women from a fertility clinic.

DIETARY FOLATE INTAKE AND FECUNDABILITY: A DANISH PROSPECTIVE COHORT STUDY

Heidi Theresa Cueto, Anders H. Riis, Elizabeth E. Hatch, Lauren A. Wise, Kenneth J. Rothman, Henrik T. Sørensen, Ellen M. Mikkelsen

Introduction: Folate, an antioxidant micronutrient primarily present in liver, green leafy vegetables, and beans is essential in cell growth and may play an important role in many aspects of female reproduction, including ovulatory function. However, little is known about potential beneficial effects of dietary folate on fecundability, the per cycle probability of conception. **Methods:** We evaluated the relation between dietary folate intake and fecundability in a prospective cohort study “Snart Forældre” (soon parents) of 1,161 Danish pregnancy planners enrolled between 2012 and 2015. Female participants completed a validated web-based food frequency questionnaire ten days after study enrollment. Dietary folate intake (in quartiles of <250, 250-349, 350-449, and ≥ 450 $\mu\text{g/day}$) was calculated based on reported frequencies and standard recipes for mixed foods. Bi-monthly follow-up questionnaires collected information on covariates, including dietary supplement use, last menstrual period, and pregnancy status during a 12-month follow-up period. Fecundability ratios (FRs) and 95% confidence intervals (CIs) were estimated using a proportional probabilities regression model adjusted for potential confounders. **Results:** Mean and median energy-adjusted dietary folate intakes were 383.0 $\mu\text{g/day}$ and 360.0 $\mu\text{g/day}$ (range: 135.7-945.5 $\mu\text{g/day}$). 410 women (35.3%) reached the recommended intake of ≥ 400 $\mu\text{g/day}$ solely from dietary sources. Preliminary analysis indicated a positive association between dietary folate intake and fecundability. The adjusted FRs were 1.04 (95% CI: 0.86-1.26), 1.12 (95% CI: 0.91-1.38), and 1.14 (95% CI: 0.90-1.64) for dietary folate intakes of 250-349, 350-449, and ≥ 450 $\mu\text{g/day}$, respectively, compared with folate intake of <250 $\mu\text{g/day}$. This association appeared stronger among folic acid supplement users, 350-449 vs. <250 $\mu\text{g/day}$: FR=1.33, 95% CI: 1.02-1.73. **Conclusion:** Overall, dietary folate intake was modestly associated with increased fecundability.

WITHIN- AND BETWEEN-SUBJECT VARIABILITY IN SEMEN PARAMETERS AMONG MEN FROM A FERTILITY CLINIC

Yu-Han Chiu, Regina Edifor, Feiby Laban Nassan, Audrey Gaskins, Paige Williams, Cigdem Tanrikut, Russ Hauser, Jorge Chavarro

Background: Semen parameters are clinically used as proxies of fertility and are known to have high within-man variability. It is unclear, however, whether a single sample could represent a man's long term average for research purposes. **Methods:** 329 men provided 768 semen samples at a fertility clinic (1 to 9 samples/subject) between 2005 and 2014 (median: 2010). Ejaculate volume, sperm concentration, total sperm count, motility and morphology were clinically assessed according to World Health Organization (WHO) standards. We used generalized linear mixed models to compare the parameters of each man's first sample with his long-term average parameters. We also calculated intraclass correlation coefficients (ICCs) for each parameter. Positive (PPV) and negative predictive values (NPV) were calculated by comparing the agreement in classification after applying the WHO lower reference limits to the first sample only and to each man's long-term average. **Results:** There were no significant differences in semen parameters between each man's first sample and his long term average. The mean difference between first sample parameters and long-term averages ranged from -0.01% (-0.40%, 0.39%) for morphology to 1.14% (-1.25%, 3.52%) for total motility. Between-person variability was consistently larger than within-person variability, as reflected in the ICCs, which ranged from 0.55 for morphology to 0.76 for sperm concentration. However, when semen parameters were dichotomized according to WHO reference limits, using a single sample resulted in low PPV (range: 44-78%) and the average of two semen samples was needed to achieve high PPV (range: 88-100%) and NPV (range: 96-100%). **Conclusions:** One semen sample may be sufficient in epidemiologic studies aimed at identifying average differences in semen quality between individuals. Studies where the goal is to estimate differences in the prevalence of below WHO reference limits may benefit from collecting two or more samples.

PERICONCEPTIONAL MATERNAL BISPHENOL-A AND FECUNDABILITY

Kyley Cox

Cox KJ, Stanford JB, Porucznik CA (University of Utah, Salt Lake City, UT) **Background:** Bisphenol-A (B) is an endocrine disrupting chemical with nearly ubiquitous exposure. Effects of BPA on human reproduction are controversial, but reproductive dysfunction has been observed in animal models. Our objective was to examine maternal urinary BPA concentration and fecundability. **Methods:** A prospective, pre-conception cohort of couples (women 18-35, men 18-40) without known infertility were recruited, and women observed cervical mucus to identify an estimated day of ovulation (EDO) and fertile window. Women collected first-morning urine samples beginning during the fertile window and continued until the onset of menses or EDO+18 days, and BPA was measured in each sample. Geometric means for each woman were calculated and categorized into tertiles. Cox proportional hazards models for discrete survival time were performed to assess women's urinary BPA tertile and fecundability, adjusted for age, household income, education level, BMI, and parity. Fecundability odds ratios (FOR) <1.0 indicate reduced fecundity and longer time to pregnancy (TTP), whereas FORs >1.0 indicate enhanced fecundity and shorter TTP. **Results:** Among 71 conception cycles, women collected mean 18.6 ± 6.3 urine samples per cycle. Tertile classifications were as follows: low ≤ 1.73 ng/mL, medium ≥ 1.74 -<2.70 ng/mL, high ≥ 2.70 ng/mL. Compared to women in the low BPA tertile, women in the medium BPA tertile were 0.993 (95% CI 0.463, 2.132) times as likely to conceive, and women in the high tertile were 0.906 (95% CI 0.436, 1.883) times as likely to conceive, but the differences were not statistically significant. **Conclusion:** In this sample of 71 conception cycles, there was a pattern of lower fecundability among women with moderate to high BPA exposure, but no statistically significant differences were observed.

DOES ENVIRONMENTAL CONCERN INFLUENCE WOMEN TO POSTPONE PREGNANCY? THE ENVIRONMENTAL WORRY SCALE AND THE EFFECT ON REPRODUCTIVE DECISION MAKING

Leah Zilversmit, Arti Shankar, Christopher Mundorf, Jeffrey Wickliffe, Emily Harville

Background: Previous studies indicate that environmental worry may lead to behavior change. We examined how women's environmental concerns were affected by Deepwater Horizon and if they were associated with postponing pregnancy. **Methods:** 1,526 women of reproductive age from oil spill affected areas were interviewed between 2012 and 2015. We used Hodapp et al's environmental worry scale and grouped questions into personal and general environmental concerns. We asked women if they had changed behavior due to the oil spill, including postponing pregnancy. We calculated bivariate associations between the environmental worry variables and oil spill exposure and demographic variables, then created log-Poisson models to calculate risk ratios for postponing pregnancy and environmental concern, adjusting for direct exposure to the oil spill. **Results:** There were 56 (5%) women who postponed pregnancy due to the oil spill. Environmental worry was higher among women who reported postponing pregnancy. After adjusting for direct exposure to the oil spill, there was an association between reported postponed pregnancy and general environmental worry (Risk Ratio [RR]=1.08, 95% Confidence Interval [CI] 0.99, 1.18) and personal worry (RR=1.09, 95% CI 1.01, 1.18). **Conclusions:** Women with higher levels of environmental worry were more likely to report postponed pregnancy due to the oil spill compared to those with lower levels of environmental worry. This could indicate that environmental concern caused women to delay pregnancy. Our study indicates that environmental concern is a possible predictor for family planning.

PHYSICAL ACTIVITY, BODY SIZE, AND MALE FECUNDITY IN A NORTH AMERICAN PRECONCEPTION COHORT STUDY

Lauren Wise

Some studies indicate that physical activity (PA) has a deleterious effect on semen quality. Bicycling, in particular, has been associated with lower semen quality, though the mechanisms of action may be different from that of PA in general. The literature on male obesity and fecundity is also mixed. We assessed the association between male PA, body size, and fecundability among couples participating in the Pregnancy Study Online (PRESTO), a North American web-based preconception cohort study. At baseline, men reported data on medical history, lifestyle, behavioral, and anthropometric factors (e.g., BMI and waist circumference), and type (e.g., running, bicycling, walking) and frequency (average hours/week) in the last year. Male and female data were linked, and pregnancy status was updated every 8 weeks for up to 12 months or until reported pregnancy. Fecundability ratios (FR) and 95% confidence intervals (CI) were estimated using proportional probabilities regression, controlling for female and male age, education, smoking, multivitamin use, sleep duration, intercourse frequency, and male and female BMI. Analyses were restricted to 647 couples (78%) who had been trying to conceive for ≤ 6 cycles at study entry. FRs for 1-2, 3-4, 5-6, and ≥ 7 vs. <1 hour(s)/week of vigorous were 0.98 (CI=0.78-1.24), 0.80 (CI=0.62-1.04), 0.94 (CI=0.70-1.25), and 0.82 (CI=0.61-1.11), respectively. The FR for ≥ 60 vs. <20 MET-hours/week of total was 0.82 (CI=0.63-1.07). The FRs for bicycling ≤ 1 , 2, and ≥ 3 vs. 0 hour(s)/week were 0.72 (CI=0.53-0.99), 0.81 (CI=0.63-1.05), and 0.75 (CI=0.49-1.15), respectively. Neither male BMI nor waist circumference was appreciably associated with fecundability. In sum, vigorous PA, total METs of PA, and bicycling tended to show inverse associations with male fecundity. There was, however, little evidence of a dose-response relation, and given the weak associations, the extent to which PA and bicycling influence fecundity remains unclear.

A RANDOMIZED TRIAL OF WEB-BASED FERTILITY-TRACKING SOFTWARE AND FECUNDABILITY

Lauren Wise, Elizabeth Hatch, Joseph Stanford, Craig McKinnon, Amelia Wesselink, Kenneth Rothman

FertilityFriend.com (FF) is a fertility-tracking software program that allows users to chart their menstrual cycles and record fertility signs, such as cervical fluid quality and ovulation predictor kit (OPK) use. We assessed whether randomization to FF use was associated with improved fecundity in the Pregnancy Online Study (PRESTO), a North American web-based preconception cohort study. At baseline, women completed a health history survey and were randomized with 50% probability to receive a premium FF membership. Women were followed every 8 weeks for up to 12 months or until reported pregnancy. The analysis was restricted to women who had been attempting to conceive for ≤ 6 cycles at study entry (N=1,444). Using an intent-to-treat analysis, we estimated fecundability ratios (FR) and 95% confidence intervals (CI) using proportional probabilities regression. Baseline characteristics were evenly distributed between the two randomization groups; 87% completed follow-up (became pregnant or reached other study endpoint). Pregnancy was reported during follow-up by 60% of the 737 women randomized to FF and 62% of the 707 women not randomized to FF. The FR comparing those randomized vs. not randomized to FF was 0.95 (95% CI=0.84-1.07) overall; it was 0.92 (CI=0.80-1.05), 0.89 (CI=0.67-1.18), and 1.57 (CI=0.97-2.54) for those trying <3 , 3-4, and 5-6 cycles at study entry, respectively. Of those randomized to FF, 54% actually used the software. Those trying for 5-6 cycles had higher actual use of FF (58%), higher OPK use (18%), and a faster median time to OPK use (1.5 weeks) than those trying for <3 cycles at study entry. Randomization to FF was not associated with fecundability overall, but it was associated with faster conception among women who had been trying to conceive for 5-6 cycles at study entry. Non-use of FF may have attenuated our results and differential loss-to-follow-up may have introduced a downward bias.

EXPOSURE TO BISPHENOL A AND MENSTRUAL CYCLE CHARACTERISTICS IN A PRECONCEPTION COHORT STUDY OF DANISH AND AMERICAN WOMEN

Amelia Wesselink, Shruthi Mahalingaiah, Lauren Wise, Kristina Thayer, Michael McClean, Ellen Mikkelsen, Elizabeth Hatch

Exposure to bisphenol A (BPA), an endocrine disrupting chemical, is widespread in the United States and Denmark. The extent to which BPA exposure is associated with menstrual cycle characteristics is unknown. Among 115 pregnancy planners enrolled in preconception cohort studies from Denmark (Snart Forældre) and the United States (Pregnancy Study Online, PRESTO), we evaluated preconception levels of urinary BPA in relation to baseline self-reported measures of menstrual cycle irregularity, cycle length (<27 , 27-29, ≥ 30 days), long bleed length (≥ 5 days in duration), and heavy bleed (≥ 21 ds or tampons per menses). Women with irregular cycles were excluded from analyses of bleed length and heaviness of bleed. For the 6% of samples that were below the limit of detection (LOD), we assigned the LOD divided by the square root of 2. Prevalence ratios (PR) and 95% confidence intervals (CI) for creatinine-adjusted urinary BPA (in tertiles) and each menstrual characteristic were estimated using log-binomial regression models, controlling for age, body mass index (kg/m²), and cohort. Median BPA was 0.69 ng/ml (interquartile range: 0.43-1.34). PRs and 95% CIs for 2nd and 3rd tertiles versus the 1st tertile of BPA levels were 0.67 (95% CI: 0.26-1.72) and 1.14 (95% CI: 0.49-2.66) for menstrual cycle irregularity; 0.79 (95% CI: 0.32-1.98) and 0.69 (95% CI: 0.23-2.06) for heavy bleed; 0.66 (95% CI: 0.20-2.18) and 0.27 (95% CI: 0.03-2.07) for short cycle length; and 1.16 (95% CI: 0.67-2.01) and 1.07 (95% CI: 0.59-1.92) for bleed length ≥ 5 days, respectively. In preliminary analyses, we found little evidence to support an association between BPA and menstrual cycle characteristics. Limitations of the study include the small sample size, cross-sectional assessment of exposure and outcome, and use of a single measure of BPA. Future analyses based on a larger sample will incorporate repeated measures of BPA and assess menstrual characteristics prospectively in time.

HORMONAL PROFILES OF MENSTRUAL PATTERNS DURING THE LUTEAL-FOLLICULAR TRANSITION.

Melanie Jacobson, Penelope Howards, James Kesner, Juliana Meadows, Jessica Spencer, Lyndsey Darrow, Metrecia Terrell, Michele Marcus

Menstrual function, a marker of women's reproductive health, is determined by a complex endocrine axis that controls the ovaries and endometrium. However, defining individual menstrual cycles requires identifying menses onset, which is complicated by irregular bleeding and spotting. The late luteal phase is characterized by declining progesterone and estrogen levels, but how these hormonal profiles may relate to menstrual bleeding patterns has not been studied. We examined creatinine-adjusted urinary estrone-3 glucuronide (E13G) and pregnanediol-3 glucuronide (Pd3G) levels in relation to bleeding patterns in 96 premenopausal women (ages 20-47) who kept daily menstrual diaries and collected first morning urine samples for at least 2 consecutive cycles or 1 luteal-follicular transition period (n=165 transitions). Menses onset was defined as the first of 2 consecutive days of bleeding in which ≥ 1 day was more intense than spotting. We used linear mixed models to estimate associations between luteal phase hormone levels and bleeding patterns. Transitions with ≥ 1 days of spotting prior to or at menses onset (spotting transitions) had shorter luteal phases (median=12 days; n=71) than non-spotting transitions (13 days; n=94). Spotting transitions had higher Pd3G levels late in the luteal phase, with larger differences at menses onset (37.4%, 95% confidence interval (CI): 17.7%, 60.4%) than 5 days before menses (9.3%, 95% CI: -6.5%, 27.6%). Spotting transitions were preceded by slower rates of Pd3G decline compared with non-spotting transitions, whereas E13G declines were more similar; on average, a one unit change in Pd3G and E13G per day was associated with a decreased risk of spotting during the transition (risk ratio (RR)=0.87, 95% CI: 0.73, 1.04 and RR=0.95, 95% CI: 0.88, 1.03, respectively). These results suggest that luteal phase Pd3G levels may be related to menstrual bleeding patterns. Conversely, bleeding patterns may provide insight into luteal phase Pd3G levels.

PRECONCEPTION WEIGHT CHANGE AND PREGNANCY LOSS AMONG FECUND WOMEN

Rose Radin, Sunni Mumford, Lindsey Sjaarda, Robert Silver, Neil Perkins, Laurie Leshner, Torie Plowden, Stefanie Hinkle, Chandra Swanson, Keewan Kim, Enrique Schisterman

Overweight women tend to have a higher risk of pregnancy loss, and maintained weight loss has been shown to reduce this risk. However, few data address how recent weight change may impact pregnancy loss among fecund women. We prospectively examined the risk of pregnancy loss associated with recent weight change and attempted weight loss among 785 women who became pregnant during a preconception trial of low-dose aspirin and live birth in the US, 2007-2011. Participants were healthy, 18-40 years old, and had a history of 1-2 pregnancy losses. A baseline questionnaire collected participant minimum and maximum weights, and attempt to lose weight, over the past 12 months. Study visits continued monthly for up to 6 menstrual cycles and through pregnancy. Using bodyweight measured approximately two weeks post-conception, we categorized participants according to a weight loss $\geq 5\%$ of their maximum weight, weight gain $\geq 5\%$ of their minimum weight, both, or neither. Log-binomial models estimated the risk ratio (RR) and 95% confidence interval (CI) of pregnancy loss, adjusted for maximum body mass index (BMI) in the past year, age, parity, number of prior losses, pregnancy loss in the past year, and the selection of pregnant women. There were 188 pregnancy losses (24%). Relative to a constant weight, the pregnancy loss RR for recent weight gain was 1.47 (95% CI: 1.01-2.16); and for recent weight loss was 1.02 (95% CI: 0.63-1.64). Relative to no recent weight-loss attempt, the pregnancy loss RR=1.06 (0.77-1.46) for attempted weight loss. Results were consistent after stratifying by maximum BMI ≥ 25 kg/m². In summary, recent weight gain $\geq 5\%$ was associated with a higher risk of pregnancy loss, while recent weight loss $\geq 5\%$ and attempted weight loss were not appreciably associated with risk. Further studies are needed to confirm these findings as they suggest a potentially modifiable risk factor for pregnancy loss.

FAT SOLUBLE MICRONUTRIENTS AND TIME TO PREGNANCY

Keewan Kim, Enrique F. Schisterman

Background: Maternal nutrition may impact fecundity. Yet, the association between fat-soluble micronutrients and time to pregnancy (TTP) has not been examined. We assessed the relationship between preconception fat soluble micronutrient levels and TTP among women with a history of 1-2 prior pregnancy losses. Methods: The EAGeR Trial was a multicenter, block-randomized, double-blind, placebo-controlled clinical trial that assessed the effect of preconception-initiated daily low dose aspirin on reproductive outcomes. Women attempting pregnancy, aged 18-40 years, with 1-2 previous pregnancy losses, and no history of infertility were included. Fat-soluble micronutrients, including zeaxanthin, cryptoxanthin, lycopene, α -carotene, β -carotene, α -tocopherol, and γ -tocopherol, were measured in serum from 1207 women at baseline. We used Cox proportional hazard regression models for discrete survival time, accounting for left truncation and right censoring, to calculate fecundability odds ratios (FOR) and 95% confidence intervals (CI). Models were adjusted for age, race, smoking, body mass index, exercise, income, parity, vitamin use, site, and total cholesterol. Results: A log unit ($\mu\text{g/dL}$) increase of α -carotene (FOR 1.19, 95% CI 1.02, 1.40) was associated with shorter TTP. For α -carotene, concentration above US average (≥ 2.92 $\mu\text{g/dL}$) was associated with shorter TTP (FOR 1.29, 95% CI 1.08, 1.54) compared to below US average. γ -tocopherol above US average (≥ 1.87 mg/dL) was associated with longer TTP (FOR 0.80, 95% CI 0.66, 0.97) relative to below US average, though a log unit increase of γ -tocopherol was not associated with TTP. Conclusions: We observed associations between certain fat soluble micronutrients, particularly α -carotene, and TTP among women with a history of prior pregnancy loss. The potential for these nutrients to influence fecundability deserves further exploration.

LOW-DOSE ASPIRIN AND SPORADIC ANOVULATION IN THE EAGER TRIAL

Rose Radin, Lindsey Sjaarda, Neil Perkins, Robert Silver, Zhen Chen, Laurie Leshner, Noya Galai, Jean Wactawski-Wende, Sunni Mumford, Enrique Schisterman

Background: Among women with a single recent pregnancy loss, daily preconception low-dose aspirin (LDA) has been associated with an increased live birth rate with no effect on pregnancy loss. The mechanism underlying this effect is unclear, but it may work through ovulatory function. Methods: We estimated the effect of LDA on the per-cycle risk of anovulation among 1,214 women randomized to daily preconception LDA or placebo in the EAGeR Trial, 2007-2011 (ClinicalTrials.gov, NCT00467363). Stratified analyses were performed within categories of eligibility criteria: original stratum (1 documented pregnancy loss at < 20 weeks gestation in the past 12 months; ≤ 1 live birth) and expanded stratum (1-2 documented pregnancy losses at any gestational age, at any time in the past; ≤ 2 live births). Participants used fertility monitors to measure daily urinary luteinizing hormone (LH) levels for 1-6 menstrual cycles while attempting pregnancy, with pregnancy tests administered monthly. A cycle was considered anovulatory in the absence of both an hCG-detected pregnancy and an LH surge as defined by algorithms identified from the literature. Log-binomial regression models were used to estimate risk ratios (RR) and 95% confidence intervals (CI) for the effect of LDA on anovulation, accounting for correlated data and number of cycles. Results: Among 4,305 cycles, LDA was not associated with anovulation (LDA: 7.9%, placebo: 7.3%; RR=1.13, 95% CI: 0.80, 1.60). Results were similar in analyses stratified by eligibility criteria. Conclusions: Daily LDA had no appreciable effect on anovulation among women with a history of 1-2 pregnancy losses, or among women with only a single recent loss. LDA may affect fertility via other pathways such as embryonic development, tubal transport of the gametes and embryo, and implantation. These mechanisms warrant further study.

PA041

PREGNANCY AND BIRTH OUTCOMES AT THE TIME OF THE GULF OIL SPILL: A VITAL STATISTICS ANALYSIS

Emily Harville

Background: Pregnant women are often vulnerable to the social and environmental disaster. We examined whether the Gulf oil spill (summer 2010) was related to pregnancy outcomes in Louisiana. **Methods:** Louisiana state vital statistics data were examined from 2008-2012. Parishes near the area of the oil spill were classified as “exposed”, while the rest of the state was classified as “unexposed”. Regions of those parishes especially close to the coast were classified as “highly exposed”. Births were also classified as occurring before, during (April 20, 2010 - July 15, 2010), or after the spill, and pregnancies were also classified as exposed in the 1st, 2nd, and 3rd trimesters. Outcomes examined included low birthweight, preterm birth, low Apgar score at 5 minutes, caesarean section, and lack of prenatal care. Multiple logistic regression was used to adjust for the race, age, marital status, education, smoking, multiple birth, and weight gain. Time-varying proportional hazards regression was used to examine effects on preterm birth. **Results:** Oil spill-affected regions were not at higher risk for perinatal complications. Risk of caesarean section and low Apgar score rose somewhat during and after the oil spill, but this rise was not greater in the affected parishes. **Conclusions:** With exposure analyzed at an ecologic level, little evidence is seen for strong effects of the Gulf oil spill on perinatal outcomes.

PA043

HOW DO LIMITS OF VIABILITY VARY INTERNATIONALLY? - A POPULATION BASED STUDY OF 12 EUROPEAN REGIONS.

Lucy Smith, Beatrice Blondell, Patrick Van Reempts, Elizabeth Draper, Bradley Manktelow, Henrique Barros, Marina Cuttini, Jennifer Zeitlin

Advances in resuscitation and care have now reached a stage where preterm babies who were once seen as non-viable now have significantly improved survival, suggesting a need for reconsideration of the limits of viability. We explore this in terms of births by gestation and birth weight across 12 geographic regions in Belgium, France, Italy, Portugal and the United Kingdom participating in the EPICE study. All live births and fetal deaths between 22+0 and 25+6 weeks gestation born in 2011-2012 excluding terminations of pregnancy were included. The main outcome measures were: percentage of births reported live; provision of antenatal steroids, surfactant and respiratory support; and survival (at discharge) and two major composite morbidities (neurologic and respiratory). At 22 weeks gestation the percentage of births reported as live born was consistently low irrespective of birth weight. Despite variation in intervention rates, survival to discharge was universally poor. At 23 weeks, patterns were similar to 22 week gestation births for babies below 500g. However, for births of 500g and over, countries varied in the percentage reported as live (33.3% to 69.6%; $P<0.0001$), levels of intervention and survival to discharge. Similar international variation in management was seen for babies born at 24 and 25 weeks gestation weighing under 500g, with the reported percentage of live births ranging from 10.7% to 57.1% ($P=0.010$). However despite variation in intervention levels, outcomes were extremely poor (4% survival). For 24 and 25 week births of 500g and over there was a consistently high levels of reported live births (74.4% to 80.2%; $P=0.656$), intervention and survival. In conclusion, wide international variation existed in the pragmatic definition of viability based on both gestational age and birth weight. Survival rates suggested that for babies of 23 weeks gestation and over, birth weight may be a better indicator of viability than gestation for decision-making.

PA042

FEASIBILITY OF LINKING LONG-TERM COHORT DATA TO OFFSPRING BIRTH RECORDS: THE BOGALUSA HEART STUDY

Emily Harville, Marni Jacobs, Tian Shu, Dorothy Breckner, Maeve Wallace

Background: Researchers in perinatal health, as well as other areas, may be interested in linking existing datasets to vital records data. We are unaware of other U.S.-based studies that have attempted to link vital records data for offspring information when the timing of the births was unknown. **Methods:** 5914 women who participated in the Bogalusa Heart Study (1973-2009), a long-running study of cardiovascular health in childhood, adolescence, and adulthood, were linked to vital statistics birth data from Louisiana, Mississippi, and Texas (1982-2010). Deterministic and probabilistic linkages based on social security number, race, maternal date of birth, first name, last name, and Soundex codes for name were conducted. Characteristics of the linked and unlinked women were compared using t-tests, chi-square tests, and multiple regression with adjustment for age and year of examinations. **Results:** The Louisiana linkage linked 4876 births for 2770 women; Mississippi linked 791 births to 487 women; Texas linked 223 births to 153 women, for a total of 6007 births to 3263 women. This represents a successful linkage of 55% of all women ever seen in the larger study, and an estimated 65% of all women expected to have given birth. Those linked had more study visits, were more likely to be black, and had statistically lower BMIs than unlinked participants. **Conclusions:** This study demonstrates the feasibility, to some degree, of linking unrelated study data to vital records data. The linked group had a somewhat more favorable health profile and was less mobile than the overall study population.

PA044

VITAMIN D DEFICIENCY IS ASSOCIATED WITH INCREASED RISK OF PRETERM BIRTH IN NON-CAUCASIAN WOMEN

Negar Tabatabaei, Josée Poirier, Catherine Herba, Nathalie Auger, Catherine Allard, William D. Fraser

Maternal vitamin D deficiency (plasma 25-hydroxy-vitamin D (25(OH)D) 75 nmol/L, maternal plasma 25(OH)D concentrations <50 nmol/L (odds ratio (OR) 4.51, 95% confidence interval (CI) 1.39, 14.57, $p=0.012$) and 50-75 nmol/L (OR 3.13, 95% CI 1.04, 9.40, $p=0.042$) were associated with increased risk of PTB in non-Caucasian pregnant women. These associations remained significant after adjustment for maternal age, pre-pregnancy body mass index, season of conception, parity and smoking history only at plasma 25(OH)D concentration 75 nmol/L (OR 4.14 95% CI 1.10, 15.51, $p=0.035$). However, maternal plasma 25(OH)D concentrations 75 nmol/L. These results suggest that maternal plasma 25(OH)D concentration <50 nmol/L at early gestation may be a risk factor for PTB in non-Caucasian women.

WHAT IS THE OPTIMAL GESTATIONAL AGE TO SCREEN FOR FETAL GROWTH RESTRICTION IN PATIENTS WITH LOW PREGNANCY ASSOCIATED PLASMA PROTEIN-A?

Michael Aziz

Objective: To determine the degree of association and the optimal gestational age (GA) at which to screen for fetal growth restriction (FGR) in patients with low pregnancy associated plasma protein-A (PAPP A). Additionally, we examined the association between the absolute PAPP A level and FGR. **Methods:** A retrospective cohort of 12,579 first trimester screenings (FTS) from 2013 to 2015 at a large maternal-fetal medicine practice were examined. The primary exposure was GA, and the primary outcome was FGR by abdominal circumference <5th percentile or estimated fetal weight <10th percentile. A secondary exposure of absolute PAPP A percentile was compared to FGR. Receiver-operator curves (ROC) were used to determine the degree of association and the point of optimal sensitivity and specificity. Patients with PAPP A <5th percentile and growth scans were included, and patients with other medical indications for screening growth scans, medication exposure, fetal/placental abnormalities, or missing data were excluded. **Results:** Of the 1,327 patients with low PAPP A, 754 patients with 1975 growth ultrasounds met criteria for analysis. Of these, 26 fetuses had FGR (1.31%). There was a slight association between GA and the development of FGR (AUC=0.62) at an optimal screening point of 36 weeks and 5 days (sensitivity = 0.35 and specificity = 0.66). Absolute PAPP A percentile was not associated with development of FGR (AUC=0.54). **Conclusions:** After removing patients with other risk factors, the rate of FGR in the population with PAPP A less than the 5th percentile was lower than that of the general obstetric population. If providers opt to screen patients with low PAPP-A for FGR they should do so in the 36th week of gestation.

PLACENTAL WEIGHT: A FORGOTTEN FACTOR IN FETAL GROWTH FOR INFANTS OF MOTHERS WITH TYPE 1 DIABETES (T1DM)

Katherine Bowers, Supal Mehta, Tetsuya Kawakita, Menachem Miodovnik, Jane Khoury

Background: Determine if placental weight was associated with abnormal fetal growth in women with T1DM. In addition, we evaluated the effect of glycemic control on this association. **Study Design:** Retrospective analysis of a cohort of women with T1DM, followed as part of a program project grant. Maternal glycemic control was determined monthly by total Glycohemoglobin A1 (HBA1); measured by column chromatography, mean 5.5% (sd 1.5%). Poor glycemic control was defined as HBA1 \geq 8.5%. Birth weight outcomes were defined as; large for gestational age (LGA: birthweight >90th%ile according to gestational age, race and sex) and Asymmetric LGA (aLGA: LGA and ponderal index=weight/length³ >90th%ile). Multivariable logistic regression was used for analysis. Stratified analyses (HBA1; <8.5% vs. \geq 8.5%), by trimester, were conducted to assess the role of glycemic control on the association between placental weight and infant birth weight outcomes. **Results:** Outcome was assessed for 302 pregnancies with placental weight available. The women were 25.6 (4.9) years at conception, and 12.6 (8.6) years at diagnosis of T1DM, 15% were black and 56% White Class D or higher. Placental weight was significantly positively associated with LGA and aLGA. For the 1st trimester only this association varied by glycemic control (p=0.01). Stratified analysis of HBA1 level in the 1st trimester showed; for women with HBA1 < 8.5% there was no significant association between placental weight and infant weight outcome, whereas for women with HBA1 \geq 8.5 there was a strong association; Odds Ratio (95%CI): 13 (3, 54) for LGA and 7 (1, 41) for aLGA with placental weight in 4th vs 1st quartile. **Conclusions:** There is significant positive association between placental weight and birthweight outcome in infants of women with T1DM; particularly evident in pregnancies with poor glycemic control during the 1st trimester, highlighting the importance of good glycemic control early in gestation for these women.

MATERNAL OBESITY AND PRETERM BIRTH AMONG WOMEN WITHOUT PRE-PREGNANCY CHRONIC DISEASES

Sung Soo Kim

Pre-pregnancy obesity may increase preterm birth risk but whether obesity itself increases risk absent related co-morbidities is unknown. We estimated the independent impact of maternal obesity on preterm birth among women without comorbidity, using data from a retrospective US cohort across 12 clinical centers. Singleton deliveries (43,200 nulliparas, 63,129 multiparas) with a maternal pre-pregnancy body mass index (BMI) \geq 18.5kg/m² were analyzed among women without chronic diseases. Pre-pregnancy BMI was classified as normal (18.5-24.9, reference); overweight (25-29.9); class I (30-34.9); or class II/III obese (\geq 35). Risk of preterm birth was examined by gestational age (<28 weeks; 28 to <32weeks; 32 to <37weeks), subtype (spontaneous; indicated; no recorded indications) and parity (nulliparas; multiparas). Poisson regression with robust error variance calculated relative risks (RR) and 95% confidence intervals (CI) adjusted for age, race/ethnicity, parity, insurance, smoking or alcohol use during pregnancy, and study site. Risk of spontaneous [1.27(0.94-1.71), 1.89(1.31-2.73), 2.01(1.33-3.04)] and indicated [1.94(1.19-3.15), 2.49(1.34-4.62), 2.46(1.12-4.99)] preterm birth increased with maternal obesity(overweight, class I, and II/III, respectively) for <28 gestational weeks at delivery as well as for 32 to <37weeks [1.20(1.02-1.41), 1.75(1.43-2.15), 1.89(1.49-2.39)] among nulliparas. Multiparas with excess weight were at decreased risk of spontaneous [0.90(0.83-0.98), 0.87(0.78-0.97), 0.79(0.69-0.90)] and at increased risk of indicated [1.26(1.01-1.46), 1.37(1.13-1.65), 1.69(1.39-2.05)] preterm birth at 32 to <37weeks. Pre-pregnancy obesity was associated with increased preterm birth risk, both spontaneous and indicated, among women without chronic disease.

TRENDS IN PRETERM DELIVERY IN THE UNITED STATES 2006-2012 REVISITED: MAGNITUDE OF DECLINE AND POSSIBLE EXPLANATIONS

Claire Margerison-Zilko, Nicole Talge, Claudia Holzman

Background: In the United States (US), rates of preterm delivery (PTD)—overall as well as spontaneous and medically indicated—have declined since 2005. Changes in obstetric practice and/or interventions (e.g., progesterone) may underlie these temporal trends. On the other hand, methodological issues may affect the validity of these estimates. Of particular concern is the fact that inconsistent uptake of the 2003 revised birth certificate across states affects the approach to estimating gestational age and may also correlate with maternal characteristics related to PTD. **Methods:** Using US vital statistics data, our analytic sample included singleton births to women in one of the 17 states using only the 2003 birth certificate from 2006-2012; we excluded births missing an obstetric estimate of gestation, gestational ages <24 or \geq 45 weeks, and implausible combinations of birth weight and gestational age (final n=10,558,769). Use of progesterone to prevent PTD in women with prior PTD may explain some of the decline in PTD. If so, we would expect to see larger PTD declines in women with parity=2 and a prior PTD compared to: 1) primiparous women; and 2) women with parity=2 and no prior PTD. **Results:** We found smaller declines in overall, indicated, and spontaneous PTD (11.2, 8.6, and 11.3%, respectively) than previously reported. After adjustment for maternal race/ethnicity, age, marital status, education, and smoking during pregnancy, the decrease in odds of PTD associated with each additional year (2006-2012) was slightly larger among women with parity = 2 and a prior PTD (OR=0.96;95%CI:0.95,0.97) compared to primiparous (OR=0.97;95%CI:0.97,0.97) and parity = 2 with no prior PTD (OR=0.98;95%CI:0.98,0.98). **Conclusions:** Our analysis of US PTD trends from 2006-2012 using the same states over time suggests more modest declines in PTD than previously reported. A modest portion of the decline in PTD may be due to increasing use of progesterone among women with a prior PTD.

INTERACTION BETWEEN HETEROGENEOUS ENVIRONMENTAL QUALITY DOMAINS (AIR, WATER, LAND, SOCIO-DEMOGRAPHIC AND BUILT ENVIRONMENT) ON PRETERM BIRTH.

Shannon Grabich

Environmental exposures are often measured individually, though many occur in tandem. To address aggregate exposures, a county-level Environmental Quality Index (EQI) representing five environmental domains (air, water, land, built and sociodemographic) was constructed. Recent studies showed associations between EQI and health effects, including preterm birth (PTB), using individual domains as well as overall EQI; however, the interaction between domains has yet to be investigated. We explored interactions between each domain pair and PTB using National Center for Health Statistics data (2000-2005; n=19,171,351). We stratified by rural urban continuum codes (RUCC) and used fixed slope, random intercept multilevel logistic models, adjusted for maternal age, education, marital status, and race, to assess how interactions between individual domains relate to PTB (<37 weeks gestation). We calculated prevalence odds ratios (POR (95% confidence intervals (95%CI))) comparing residence in a county with poor environmental domain interactions (5th quintiles) to the referent of those who resided in the best quintile for each domain (1st quintiles). Trend across quintiles and interaction p-value <0.05 determined significance. Significant interactions were found between the air and land domain across RUCC models. For example, in the most rural counties the POR comparing the highest (worst quality) to lowest EQI quintile for air was 1.54 (1.28-1.86); land 1.13 (0.91-1.40) and interaction (0.74 (0.57-0.95). In the most urban environments, interactions were consistent across many of the environmental domains including socioeconomic with built, water and air. Comparing highest to lowest EQI quintile for built was 0.74 (0.63-0.88); land 0.68 (0.56-0.84); interaction 1.38 (1.06-1.80). Our results suggest interactions exist between different environmental domains with PTB, which should be considered in future statistical analyses. This abstract does not necessarily reflect EPA policy.

PA051

INFLUENCE OF HOUSEHOLD AIR POLLUTION ON PERINATAL OUTCOMES IN BANGLADESH: ANALYSIS FROM BANGLADESH DEMOGRAPHIC AND HEALTH SURVEY, 2011

Monjura Nisha, Ashrafal Alam, Camille Raynes-Greenow

Background: Perinatal mortality is 50/1000 pregnancies /year in Bangladesh. It is even higher in rural areas, where ~99% households rely on polluting fuels for cooking. Although household air pollution (HAP) from cooking fuels has been linked with perinatal outcomes, the association is not properly investigated. Aim: To examine the association between type of cooking fuels and perinatal outcomes. Methods: We analysed the Bangladesh Demographic and Health Survey (BDHS), 2011 which included 17,842 women aged 12-49 years. The outcome variables were perinatal mortality and baby's birth size smaller than average. Our main exposure variable was type of cooking fuels (clean fuels versus polluting fuels). We employed bivariate analysis to ascertain the association between main exposure variable and the outcomes variables. Also, binary logistic regression was performed to adjust the association for potential confounders such as maternal age, maternal education, birth order, wealth index and place of residence. Results: Compared to the women who used clean fuels for cooking, women cooked with polluting fuels were about 2 times more likely to have perinatal deaths [Odds ratio (OR): 1.81, 95% CI: 1.09, 2.98, p=0.018]. Similarly, women cooking with polluting fuels had 1.29 times more likelihood to deliver babies with a small birth size [OR: 1.29, 95% CI: 1.05, 1.58, p=0.015]. In adjusted models, the effect of polluting fuels was no longer significant for both perinatal death [adjusted OR: 0.78, 95% CI: 0.26, 2.29, p=0.65] and small birth size [adjusted OR: 1.12, 95% CI: 0.84, 1.02, p=0.44]. Conclusion: Cooking with polluting fuels has been associated with adverse perinatal outcomes. Some inconsistencies may remain in BDHS data which may have resulted in an insignificant association of use of polluting fuels with adverse perinatal outcomes. There is a need to conduct a prospective study to thoroughly investigate the association between HAP and perinatal outcomes.

THE IMPACT OF HOUSEHOLD AIR POLLUTION ON PERINATAL MORTALITY; RESULTS FROM A LARGE EMBEDDED COHORT STUDY IN A RURAL SETTING IN BANGLADESH.

Camille Raynes-Greenow, Michael J Dibley, Shams El Aifreen, Ashrafal Alam, Kingsley Agho, Tanvir Huda, Sajia Islam, on behalf of the Shonjibon Trial Study Team

Background: Household air pollution is the 3rd biggest cause to global morbidity and mortality, and the greatest risk to health in South Asia. Most of the exposure is from traditional cookstove use. Where exposure to known pollutants occurs due to incomplete combustion of solid fuels such as coal and animal dung. The perinatal burden due to household air pollution has been excluded from all global reports and is not clearly defined as there is a dearth of well-conducted prospective studies. Method: A cohort study to describe the perinatal burden was embedded in a cluster RCT of iron/folic acid supplementation in pregnant women in Bangladesh. Trial follow-up is now complete and data cleaning is 95% done. All known household air pollution exposure variables, antenatal risk factors and obstetric outcomes were collected. Relative risks (RR) with (95% confidence intervals) were calculated. Results: 35,554 pregnant women were recruited. Mean birthweight was ~2079g, mean gestation ~38weeks. We found a very high prevalence of HAP exposure, including almost universal use of traditional cookstoves (98.5%). There was an increased risk of neonatal mortality RR2.2 (95%CI 1.39, 3.05) with traditional stove use compared to any other stove types, and with single stove compared to more than 1 stove RR1.2 (1.07, 1.41). Indoor cooking compared to outdoor cooking appeared to be protective but was not significant RR0.73 (95%CI 0.46, 1.64). Further analysis including the interaction with iron/folic acid will be done once the data cleaning is finalized. Conclusions: Preliminary data show an increased risk of neonatal mortality with HAP. The relative protection of iron/folic acid supplementation has not yet been investigated. Despite massive international efforts to scale up the use of improved cookstoves to reduce exposure to household air pollution, the very high prevalence of traditional cooking suggests that there are major barriers to scale up in this region.

PA052

IMPACT OF MATERNAL FOOD SECURITY STATUS ON BIRTH SIZE OF INFANTS IN BANGLADESH

Morseda Chowdhury, Camille Raynes-Greenow, Michael Dibley, Ashrafal Alam

Low birthweight (LBW) affects 36-55% of all infants in Bangladesh. These infants are 20 times more likely to die than their normal weight counterparts and account for 60% to 80% of all neonatal deaths. There is strong evidence that poor maternal nutrition during pregnancy leads to low birthweight. The Bangladesh demographic and health survey (BDHS, 2011) collected data on birth size as a proxy to birth weight in a context where 71% births occur at home and are not weighed. We conducted secondary data analysis. All live born children (and their mothers) with birth size data (born within last 3 years of data collection) were eligible. We categorized the birth size (primary outcome) variables into 'small' ('smaller than average' and 'small'), and 'average/large' ('average', 'larger than average', and 'very large'). Food security status of women was categorized as 'food secure', 'mild insecurity', 'moderate insecurity' and 'severe insecurity' based on the BDHS cut off points. Logistic regression was performed to estimate the effects of maternal food security on birth size, controlling for residence, parents' education, economic status, number of children, birth order, indoor air pollution, sex of the child and other factors. Statistical significance was accepted at a probability level of 5%. Analysis was conducted in STATA adjusting for clustering effects. Out of 8,748 children, 17.6% were reported as born small. Among mothers, 65.2% was food secured and 24.7%, 8.5% and 1.7% were categorized as mild, moderate and severely food insecure respectively. The logistic regression showed that maternal food security significantly protected newborns from being small, compared to mild insecurity [OR=1.34 (95% CI: 1.15 to 1.55), p .00], moderate insecurity [OR=1.4 (95% CI: 1.15 to 1.79), p .00] and severe insecurity [OR=1.6 (95%, CI: 1.08 to 2.49), p.02]. Maternal food security status has a positive relation with birth size of infants after adjusting for socio-demographic, environmental and other relevant factors. Suggesting that investment in maternal food security will have a positive impact on infants' birth size.

ASSOCIATION BETWEEN PM2.5 AND PM2.5 CONSTITUENTS AND PRETERM BIRTH IN CALIFORNIA, 2000-2006

Ru Basu, Dharshani Pearson, Brian Malig, Rachel Broadwin, Kimberly Berger

Particulate matter (PM) has been associated with an increased risk of preterm birth (PTB) in numerous studies. However, very few studies have investigated the relationship between individual constituents of fine PM (PM2.5) and PTB, which can be informative for identifying sources of the most hazardous constituents and helping with regulatory efforts. With birth data provided by the Vital Statistics Division of the California Department of Public Health and air pollution data supplied by the US Environmental Protection Agency, we examined the association between the trimester-specific and full gestational prenatal exposure of PM2.5, individual constituents of PM2.5 and PTB. Data from 2000-2006 were examined in a retrospective cohort study with 255,286 California births. In logistic regression models adjusting for maternal demographic and other factors, we observed significantly increased risk of PTB with full gestation increase exposures of aluminum (Al), bromine (Br), ammonium (NH4), nitrate (NO3), organic carbon, zinc, silicon and overall PM2.5. For example, the percent change in odds of PTB associated with an interquartile range increase in NH4 was 8.6% (95% confidence interval : 6.0, 11.3); for NO3, 10.6% (8.1, 13.2); for Br, 8.5% (5.8, 11.2); and for Al, 4.8% (2.7, 7.0). Notably, for some of these constituents, the percent increase in odds of birth at 32 to 34 gestational weeks was double that of overall PTB. Alternatively, some constituents were significantly negatively associated with PTB, including chlorine (-9.4%; -11.1, -7.6), sodium (-12.1%; -13.7, -10.5), sodium ion (-13.3%; -15.3, -11.4), and vanadium (-7.0%; -9.8, -4.2). The estimates remained relatively unchanged after controlling for short and long-term apparent temperature. Reduction in traffic pollution, which is a main source of the NO3 and NH4 constituents and where the greatest detrimental effects were observed, may help attenuate risk of PTB in California.

ASSOCIATION BETWEEN VITAMIN D RECEPTOR GENETIC VARIATIONS AND PRETERM BIRTH

Shu Qin Wei

Association between vitamin D receptor genetic variations and preterm birth Bi WG, Wei SQ, Nuyt AM, Leduc L, Audibert F, Luo ZC, Julien P, Fraser WD. Department of Obstetrics and Gynecology, CHU Ste-Justine, University of Montreal Email: shu.qin.wei@umontreal.ca Objective: Preterm birth remains a significant health concern. Inflammation may play a role for preterm birth. Vitamin D is a known immune system immune/inflammatory mediators modulator and is associated with preterm birth. Vitamin D's effects are exerted via the vitamin D receptor (VDR) and there is VDR genetic variation in the population. However, it is unclear whether VDR gene single nucleotide polymorphisms (SNPs) has impact on preterm birth. The objective of this study was to evaluate the role of VDR gene polymorphism in preterm birth susceptibility. Methods: This was a prospective cohort. Vitamin D receptor gene [A I (rs7975232), BsmI (rs1544410), Cdx2 (rs11568820), FokI (rs2228570), TaqI (rs731236) and Tru91 (rs757343)] SNPs were genotyped using the Sequenom UNIT MassARRAY iPLEX Platform. 25-hydroxyvitamin D [25(OH)D] concentrations were measured at 12-18 weeks of gestation using chemiluminescence immunoassay. Multi-variable logistic regression analyses were performed to investigate the influence of genetic polymorphisms on the risk of preterm birth. Results: Maternal vitamin D receptor genes BsmI and TaqI polymorphisms were associated with vitamin D status in pregnancy. BsmI AA and TaqI CC genotypes were associated with an increased risk of preterm birth (aOR 2.36, 95% CI 1.26-4.43; aOR 2.29, 95%CI 1.19-4.40). There were statistical evidence of interaction between vitamin D receptor gene BsmI and TaqI polymorphisms and 25(OH)D levels for preterm birth. Conclusion: Our findings show a significant association between vitamin D receptor gene BsmI and TaqI polymorphisms and preterm birth in women with low vitamin D status during pregnancy.

ASSOCIATION BETWEEN AIR POLLUTION AND STILLBIRTH IN CALIFORNIA, 1999-2009

Ru Basu, Varada Sarovar, Brian Malig, Shelley Green

While air pollution and adverse birth outcomes have been examined extensively, very few studies have focused on stillbirth specifically. Using data in California from 1999 to 2009, we explored the relationship between stillbirth and prenatal exposures within 10 km to fine particles (PM2.5), nitrogen dioxide (NO2), sulfur dioxide (SO2), carbon monoxide (CO) and ozone (O3). Long-term relationships were assessed using logistic regression models, and the odds of stillbirth associated with mean pollutant exposure during various prenatal periods were reported. For the short-term analysis, a time-stratified case-crossover design was used to examine lags of up to one week of exposure, conveyed as the percent change in stillbirth. Maternal and other factors and temperature were adjusted for in both analyses. In the long-term analysis, we found that PM2.5 (odds ratio (OR) = 1.06; 95% confidence interval (CI): 0.99, 1.13 per 10-µg/m3 increase) and NO2 (1.08; 1.03, 1.13 per 10 ppb) during the entire pregnancy and O3 during the third trimester (1.03; 1.01, 1.05 per 10 ppb) were significantly associated with stillbirth. In models simultaneously examining two pollutants, stable associations were found for NO2 and O3. In the short-term analysis, we found a significant association for O3 (lag 4) in the unadjusted models during the warm season and whole year. An association was observed for SO2 in both adjusted and unadjusted models during the whole year (lag 4) and in the cold season (lag 5 and lag 2-5). When the monitor distance was limited to 5 km, an association was observed for NO2 for lags 4 and 5 during the warm season. No significant associations were observed for PM2.5 during the full year, although during the cold season PM2.5 exposure elevated the risk (lag 4). Our findings support the growing literature for both long- and short-term associations between air pollution and stillbirths, but more research is needed to confirm the potential causal relationship.

OXIDIZED LDL LEVELS ARE NEGATIVELY ASSOCIATED WITH BETA CELL FUNCTION IN NEWBORNS

Zhongcheng Luo

OBJECTIVE: Oxidized low-density lipoprotein (OxLDL) is proatherogenic and proinflammatory, and associated with insulin resistance in adults. The developing fetus is likely more susceptible to the deleterious effects of OxLDL. It is not known whether OxLDL may affect metabolic health in human fetuses/newborns. The present study sought to explore this question. RESEARCH DESIGN AND METHODS: In a singleton pregnancy cohort (n=248), we assessed OxLDL concentration and OxLDL/total LDL ratio in relation to beta cell function indices (insulin/glucose ratio, proinsulin/insulin ratio), quantitative insulin sensitivity check index (QUICKI), leptin and adiponectin concentrations in cord blood. RESULTS: OxLDL/LDL ratios were strongly correlated in cord and maternal plasma (r=0.47, p<0.001), and were substantially higher in cord plasma (1278.0±141.2 vs. 591.4±29.2 U/mmol, p<0.001). Cord plasma OxLDL concentration was negatively correlated with insulin/glucose ratio (r=-0.24, p<0.001), and positively correlated with proinsulin/insulin ratio (r=0.20, p<0.001) and QUICKI (r=0.16, p<0.01), but not correlated to leptin or adiponectin concentration. Adjusting for maternal and delivery characteristics, each log unit increase in cord plasma OxLDL concentration was associated with a 10.5% (95% CI: 5.5%-15.8%) decrease in cord plasma insulin/glucose ratio, a 3.1% (0.9%-5.2%) increase in QUICKI and a 7.8% (5.5%-15.8%) increase in proinsulin/insulin ratio, respectively. Similar associations were observed for cord plasma OxLDL/LDL ratio. CONCLUSIONS: Higher OxLDL concentrations were associated with lower beta cell function with a possibly compensatory increase in insulin sensitivity to maintain glucose homeostasis in fetuses/newborns. The present study is the first to demonstrate that OxLDL may have developmental toxicity to metabolic health in humans.

DO INTERNATIONAL VARIATIONS IN THE PRETERM BIRTH RATE REFLECT OVERALL DIFFERENCES IN THE GESTATIONAL AGE DISTRIBUTION?

Marie Delnord, Laust Mortensen, Ashna Hindori-Mohangoo, Béatrice Blondel, Mika Gissler, Jennifer L. Richards, Paromita Deb-Rinker, Naho Morisaki, Ann-Marie Nybo Andersen, Michael S. Kramer

Objective: Wide variations exist in preterm birth (PTB) rates and trends across high income countries. We investigated whether these differences reflect more global shifts in the gestational age (GA) distribution. **Methods:** We used aggregate population-based routine data on the GA distribution of singleton live births from 27 European countries in the Euro-Peristat project, the United States, Canada and Japan for the years 2000, 2004, 2008 and 2010. Data were available by mode of onset (spontaneous versus provider-initiated) for 11 countries in 2000, 14 in 2008 and 16 in 2010. We calculated rates of moderate and late PTB (32-36 weeks) and early term births (37-38 weeks GA) overall and by mode of onset as well as differences in the rates between years. We calculated mean GA at term. We studied associations using Pearson's correlation; these were adjusted for clustering within countries for time series analyses. **Results:** The median rate of moderate PTB was 4.4% [range from 3.6% to 7.4%] in 2000 and 4.9% [range from 3.5% to 7.0%] in 2010. The median early term rate was 18.2% [range from 12.4% to 27.5%] in 2000 and 22.1% [range 15.6% to 39.8%] in 2010. Mean GA ranged from 38.8 to 39.7 weeks in 2010. PTB rates were positively correlated with early term births in all years (Pearson's r ranging from 0.60 to 0.72, $p < .001$), and negatively associated with mean GA (r from -0.59 to -0.71, $p < .001$). Changes over time in the proportion of preterm births were strongly correlated with changes in the proportions of early term births (Pearson's cluster-adjusted coefficient=0.67, $p < .001$). Cross-sectional and time series results were similar for spontaneous and provider indicated births. **Conclusion:** Our results suggest that factors affecting the PTB rate also affect early term births and the GA distribution for both spontaneous and provider initiated deliveries warranting the consideration of population-based approaches to PTB prevention.

HEALTHY DIET IN PREGNANCY AND RISK OF LARGE FOR GESTATIONAL AGE INFANTS

Sneha Sridhar, Monique Hedderson, Fei Xu, LaToyia McGough, Melissa Harrison, Mihee Redman, Assiamira Ferrara

Large for gestational age (LGA) infants are more likely to become obese later in life. Obesity and excess gestational weight gain are both associated with an increased likelihood of having a large for gestational age infant. However, whether maternal diet quality during pregnancy influences excess fetal growth independently of these known risk factors is unclear. The aim of this prospective cohort study of 1,510 women (59% minorities) at Kaiser Permanente Northern California was to evaluate the association between early pregnancy diet (<23 gestational weeks) and LGA (> 90th percentile for gestational age and race based on the entire Kaiser Northern California population). Diet quality was assessed via food frequency questionnaire using the Healthy Eating Index (HEI) 2010 (J Acad Nutr Diet. 2013; 113(4) 569-80), where a greater total score indicates a healthier diet. Logistic regression was used; appropriate size for gestational age was the referent. After adjusting for maternal age, race/ethnicity, pregravid body mass index, parity, gestational diabetes, total daily energy intake, physical activity, income, and gestational weight gain, women whose HEI was in the highest quartile had significantly lower odds of having an LGA infant (Odds Ratio: 95% Confidence Interval): 0.50 (0.27 – 0.93) compared to those in the lowest quartile. The 2nd and 3rd quartiles were not associated with LGA (0.62 (0.34-1.11) and 0.93 (0.54-1.60), respectively). Our findings suggest that a better diet quality during early pregnancy may reduce risk of LGA. Interventions aimed at improving diet quality among pregnant women may be warranted to improve infant size at birth, which in turn may help reduce the infant's risk of obesity in the future.

THE PREVALENCE OF ADVERSE BIRTH OUTCOMES AMONG PREMENOPAUSAL BREAST CANCER SURVIVORS

Kristin Black, Diane Rowley, Hazel Nichols

With concurrent trends in delayed childbearing & improved breast cancer (BC) survival, there's a greater possibility that young BC patients may desire to have children after their treatment. The impact of BC treatment on reproductive health needs to be examined. Black women (compared to white) are more likely to deliver a preterm (PTB) or low birthweight (LBW) infant & be diagnosed with BC before age 40. This study aimed to determine if BC survivors (ages 18-45 at diagnosis) in North Carolina (NC) who delivered a live birth after their diagnosis have a greater prevalence of delivering a PTB or LBW infant than women in NC who weren't diagnosed with BC. NC cancer registry & birth record data were linked to examine the birth outcomes of BC survivors. Prevalence ratios (PR) & 95% confidence intervals (CI) of PTB & LBW were calculated using log binomial regression. Among 1,912,269 eligible live births from 1990-2009, 535 infants were born to BC survivors diagnosed during the same 20-year period. The BC survivors' mean age at diagnosis is 31.8 years & at infant delivery is 34.6. The study population is 72.3% non-Hispanic white ($n=1,383,302$) & 27.7% non-Hispanic black ($n=528,967$). About 10.8% ($n=206,134$) of the live births were PTB & 8.8% ($n=168,508$) were LBW. Controlling for race/ethnicity as a modifier & adjusting by mother's age at infant delivery, education, marital status, parity, smoking, & chemotherapy status, the PTB PR for infants born to BC survivors compared to white non-survivors is 1.33 (0.93-1.91) for blacks & 1.43 (1.04-1.97) for whites; & the LBW PR is 1.98 (1.34-2.91) for blacks & 1.12 (0.74-1.69) for whites. Regardless of race, young BC survivors have a greater risk of delivering a PTB or LBW infant than the general population. Yet, it seems that black survivors have a greater prevalence of LBW and white survivors have a slightly greater prevalence of PTB. These women may benefit from targeted preconception health services prior to and after BC treatment.

ASSOCIATION OF NEIGHBORHOOD CONTEXT WITH OFF-SPRING RISK OF PRETERM BIRTH AND LOW BIRTHWEIGHT: A SYSTEMATIC REVIEW AND META-ANALYSIS OF POPULATION-BASED STUDIES

Collette Ncube, Daniel Enquobahrie, Steven Albert, Jessica Burke

Findings from studies investigating associations of residential environment with poor birth outcomes have been inconsistent. In a systematic review and meta-analysis, we examined associations of neighborhood disadvantage with preterm birth (PTB) and low birthweight (LBW), and explored differences in relationships among racial groups. Two reviewers searched English language articles in electronic databases of published literature. We used random effects logistic regression to calculate odds ratios (and 95% confidence intervals) relating neighborhood disadvantage with PTB and LBW. Neighborhood disadvantage, most disadvantaged versus least disadvantaged neighborhoods, was defined by researchers of included studies, and comprised of poverty, deprivation, racial residential segregation or racial composition, and crime. We identified 1,314 citations in the systematic review. The meta-analyses included 7 PTB and 14 LBW cross-sectional studies conducted in the United States (U.S.). Overall, we found 27% [95%CI: 1.16, 1.39] and 11% [95%CI: 1.07, 1.14] higher risk for PTB and LBW among the most disadvantaged compared with least disadvantaged neighborhoods. No statistically significant association was found in meta-analyses of studies that adjusted for race. In race-stratified meta-analyses models, we found 48% [95%CI: 1.25, 1.75] and 61% [95%CI: 1.30, 2.00] higher odds of PTB and LBW among non-Hispanic white mothers living in most disadvantaged neighborhoods compared with those living in least disadvantaged neighborhoods. Similar, but less strong, associations were observed for PTB (15% [95%CI: 1.09, 1.21]) and LBW (17% [95%CI: 1.10, 1.25]) among non-Hispanic black mothers. Neighborhood disadvantage is associated with PTB and LBW, however, associations may differ by race. Future studies evaluating causal mechanisms underlying the associations, and racial/ethnic differences in associations, are warranted.

RACIAL DISPARITIES IN THE ASSOCIATION BETWEEN MATERNAL DEPRESSION AND PRETERM BIRTH RISK

Collette Ncube, Daniel Enquobahrie, Amelia Gavin

Objective: We investigated the associations between antenatal depression and preterm birth [PTB (< 37 completed weeks)]; particularly, exploring whether these associations differed by mother's race. **Methods:** Women receiving prenatal care at a university medical center obstetric clinic from January 2004 through March 2010, and delivering at the University's hospital were the source population for this study. Participants included 2,376 women delivering live-born singleton infants – Caucasian (N = 1,668), Asian (N = 293), Black (N = 223), and Hispanic (N = 192). At approximately 16 weeks gestation, respondents were screened for probable major/minor depression via the patient Health Questionnaire-9, and self-reported anti-depressant medication use. Medical records were used to determine infants' gestational age at birth, PTB status. Using race-stratified multivariable logistic regression models we adjusted for psychosocial factors (i.e. anxiety and domestic violence) and sociodemographic factors (i.e. age, marital status, education, smoking). **Results:** Caucasian mothers using anti-depressants during pregnancy had a 2.52-fold (95% CI: 1.44 – 4.43) increased risk of PTB, adjusting for major/minor depression and other covariates. Anti-depressant use was not associated with PTB among the other racial/ethnic groups – Black (OR = 3.92; 95% CI: 0.45 – 33.89), Asian (OR = 1.63; 95% CI: 0.11 – 24.17), and Hispanic (OR = 1.92; 95% CI: 0.10 – 36.91). Minor depression was not associated with PTB among any of the racial/ethnic groups in multivariable models. Asian mothers with probable major depression during pregnancy were more likely to have PTB infants (OR = 7.10; 95% CI: 1.30 – 38.77), adjusting for anti-depressant use and other covariates. However, major depression was not associated with PTB among the other racial/ethnic groups – White (OR = 0.63; 95% CI: 0.22 – 1.78), Black (OR = 1.31; 95% CI: 0.22 – 7.79), and Hispanic (OR = 0.36; 95% CI: 0.03 – 5.13). **Conclusion:** Caucasian mothers using anti-depressants during pregnancy are more likely to have preterm infants. This is consistent with other research published in this area; however this association is not significant for other racial groups. These findings suggest the importance studying racial disparities.

PA063

THE REPORTING OF STABILIZED AND RISK-ADJUSTED RATES OF STILLBIRTH AND NEONATAL DEATH BY PLACE OF DELIVERY: MBRRACE-UK

Bradley Manktelow, Lucy Smith, Elizabeth Draper, David Field, Jennifer Kurinczuk

Background: The routine collection, analysis and reporting of perinatal death is vital in order to facilitate improvements in obstetric and neonatal care. Information on all stillbirths and neonatal deaths in the United Kingdom (UK) is collected by MBRRACE-UK, enabling the calculation of stabilized & adjusted stillbirth, neonatal and extended perinatal mortality rates for the first time for organizations providing maternity services (NHS Trusts and Health Boards) in the UK. **Methods:** In order to compare organizations with similar patient risk profiles, the 162 organizations providing maternity services were divided into 5 'comparator groups' based on the availability of Neonatal Intensive Care and neonatal surgery and the number of births annually. A mixed effects logistic regression model was developed comprising fixed terms for the comparator groups and for baby and mother characteristics (gestational age, socio-economic status, mother's age, ethnicity, sex of baby, multiple birth), and a random term for the organizations. Standardized mortality rates were estimated for each organization as the ratio of predicted to expected outcomes, which were then multiplied by their comparator group average rates to obtain stabilized & adjusted rates. **Results:** In 2013 there were 780211 births, with 3173 stillbirths and 1334 neonatal deaths. The ranges of stabilized & adjusted rates for the providers were: 3.14 to 5.73 for stillbirths; 1.01 to 3.58 for neonatal death; 4.17 to 9.54 for extended perinatal deaths. **Conclusions:** This methodology provides robust information to support the delivery of high quality care. The reported mortality rate rates for each organization were stabilized to the average rate for similar organizations both reducing the effect of random variation and allowing more meaningful comparisons to be made. This information is vital to monitoring changes over time and to local, national and international comparisons.

BIRTH ORDER AND INFANT MORTALITY DUE TO EXTERNAL CAUSES IN THE UNITED STATES, 2000–2010

Katherine Ahrens, Marie Thoma, Margaret Warner, Lauren Rossen, Alan Simon

Research suggests higher birth orders may be at greater risk for childhood injury. The objective of our analysis was to evaluate the risk of infant death during the first year of life due to external causes, such as unintentional injury and homicide, by birth order. We used US national birth cohort linked birth-infant death data (2000-2010) and excluded twins and higher order multiples. Approximately 41%, 32%, 16%, 7%, and 5% of live births were first, second, third, fourth, and fifth and higher birth orders; 1450 infant deaths due to external causes occurred each year. Compared with first born (2.7 per 10,000 live births), higher birth orders were at higher risk of infant mortality due to external causes (second, 3.0; third, 3.5; fourth, 4.2; fifth or higher, 6.4). After adjustment for maternal age, marital status, race/ethnicity, and education in a logistic regression model, the corresponding odds ratios were: second, 1.84 (95%: 1.77, 1.92); third, 2.43 (95%: 2.32, 2.56); fourth, 2.99 (95%: 2.80, 3.19); and fifth and higher birth order, 4.32 (95%: 4.02, 4.64) in comparison to first born. The proportion of deaths due to external causes that were unintentional injury generally increased with birth order: first, 68%; second, 72%; third, 75%; fourth, 77%; and fifth or higher, 74% (adjusted risk ratio for each increase in birth order= 1.13 [95% CI: 1.09, 1.17]). In conclusion, infants born at higher birth orders were at higher risk of infant mortality due to external causes during their first year of life, particularly for unintentional injury. Our findings suggest the importance of assessing risk of injury (both fatal and non-fatal) in higher birth orders across infancy and childhood on a national level as well as investigating underlying mechanisms.

PA064

PRENATAL MATERNAL BEREAVEMENT AND ALL-CAUSE MORTALITY IN OFFSPRING: A NATIONWIDE COHORT STUDY FROM DENMARK AND SWEDEN

Yongfu Yu, Sven Cnattingius, Erik Thorlund Parner, Jørn Olsen, Naiqing Zhao, Jiong Li

Background Increasing evidence indicates that early life events could induce persistent negative effects on individual's physiology and risk of disease. Stress reaction due to bereavement during pregnancy may affect fetal development and cause negative impacts on offspring health, whereas little is known about the long-term effects of prenatal stress on the risk of death in later life. We aimed to examine the association between exposure to maternal bereavement during pregnancy and mortality in offspring. **Methods** The population-based cohort study included all children born in Denmark from 1973 to 2004 (n=1,944,899), and Sweden from 1973 to 2006 (n=3,308,609). We categorized them as exposed to bereavement during prenatal life if their mothers lost an elder child, husband, sibling, or rent during the period from one year before conception to the child's birth. The outcome of interest was all-cause mortality. Log-Linear Poisson regression was used to estimate mortality rate ratios (RRs) with 95% confidence interval to assess the effect of prenatal stress on offspring mortality. **Results** Exposure to prenatal stress was associated with an 11% increased risk of all-cause mortality in offspring (RR: 1.11, 95% confidence interval [CI]: 1.04–1.19). The association was more marked in children born to a mother who lost an elder child or spouse (RR: 1.33, 95%CI: 1.18–1.49). The magnitude of association differed in different age groups of offspring. We also found that the second trimester may be the most sensitive period of exposure (RR: 1.21, 95%CI: 1.03–1.43). **Conclusion** Our results suggest that maternal bereavement before child birth may increase offspring mortality risk. Pregnant women exposed to stress may be in need of social care and support to minimize stress to improve offspring health.

AGREEMENT ON SUFFOCATION AS A CAUSE OF DEATH BETWEEN SURVEILLANCE DATA SOURCES FOR SUDDEN UNEXPECTED INFANT DEATHS (SUID)

Sharyn Parks Brown

Background. According to US-mortality data derived from death certificates (DC), accidental sleep-related suffocations have risen since 1990, with greatest increases after 1996. Diagnostic preference changes and improved death scene investigations are likely reasons. Variability in cause-of-death determination for suffocations results from a lack of standardized definitions and biologic autopsy markers for these often unwitnessed events. **Methods.** We compared SUIDs reported in 2011 by 7 SUID Case Registry states to US DC data for the same states. Data from the DCs with underlying cause-of-death codes R99 (unknown cause), R95 (sudden infant death syndrome), and W75 (accidental suffocation & strangulation in bed) were compared to overall SUID numbers from the Registry. Per the Registry classification system, explained suffocations were deaths with a complete case investigation, non-conflicting evidence of suffocation or asphyxiation, full external airway obstruction, and no other potentially fatal conditions that might explain the death. Registry-explained suffocations were compared to DC W75-coded deaths. **Results.** The Registry identified 435 SUIDs versus 442 SUIDs from DCs (98% agreement). The Registry identified 53 explained suffocations versus 98 W75s in DCs (54% agreement). Twelve percent of Registry SUIDs were categorized as explained suffocation versus 22% of DCs coded as W75. **Conclusions.** Agreement between the numbers of cases identified in the Registry and in DCs suggests the Registry is achieving population-based surveillance. DC files identified nearly double the number of suffocations as the Registry, suggesting that vital statistics death certification may use a lower evidence threshold to classify infant suffocation deaths than does the Registry's classification system. Standardized, comprehensive case investigations to improve knowledge of risk factors and other evidence used in determining suffocations and other SUID is still needed.

BIOMARKERS OF STRESS IN THE PERICONCEPTIONAL PERIOD AND THE RISK OF PREGNANCY LOSS

Courtney Lynch

A number of retrospective studies have reported an association between stress and pregnancy loss. We sought to replicate this finding using prospectively collected data. From 2005-2009, we enrolled 501 couples who were trying to get pregnant in two U.S. states. Couples were followed for up to 12 months as they tried to get pregnant and through pregnancy if it occurred. Participants completed journals while trying to get pregnant and women continued through pregnancy if it occurred. Enrolled women collected saliva the morning following enrollment and the morning following their first study observed menses to measure cortisol and alpha-amylase, biomarkers of stress. Women were advised to test for pregnancy on the day of expected menses. A pregnancy loss was defined as a negative pregnancy test following a positive pregnancy test, onset of menses, or clinical confirmation. The mean age of female participants was 30 years and most (83%) were non-Hispanic white. A total of 344 singleton pregnancies were reported during the study. There were 98 (28%) pregnancy losses, with most (52%) occurring prior to four post-conception weeks. Using Cox's proportional hazards model, we modeled time to loss (post-conception days) to estimate hazard ratios (HRs). After adjustment for maternal age, maternal income, female race, alcohol consumption during pregnancy, and caffeinated beverage consumption during pregnancy, we found no evidence of an association between salivary cortisol [Hazard Ratio (HR) for the highest tertile versus the lowest = 0.65; 95% confidence interval (CI) = (0.38, 1.09)] or alpha-amylase [HR for highest tertile versus the lowest = 0.87; 95% CI = (0.51, 1.51)] and pregnancy loss with the biomarkers modeled in tertiles or continuously. It is unclear whether these findings reflect the absence of an association between biomarkers of periconceptional stress and pregnancy loss or a lack of statistical power to detect what could be a small effect size.

TRADITIONAL RISK FACTORS UNDERLIE THE RACIAL DISPARITY IN TERM INFANT MORTALITY RATES: A POPULATION BASED STUDY

Mary Orr

Background: Notwithstanding the contribution of preterm (< 37wks) birth rates to the long standing racial disparity in infant mortality rates (< 365d, IMR), a limited literature shows that the IMR of African-American term infants still exceeds that of non-Latino White term infants. **Objective:** To determine the extent to which traditional individual-level maternal and infant risk factors underlie the racial disparity in IMR among term births. **Methods:** Stratified and multivariable binomial regression analyses were performed on 2003-2004 National Center for Health Statistics linked live birth-infant death cohort files for African-American (AA) and White term (37-42wks) infants. Maternal variables examined included age, education, parity, marital status, and adequacy of prenatal care. Infant weight for gestational age was also calculated. **Results:** The IMR of AA (N=3,213) term infants exceeded that of White (N=8,719) term infants: 4.11/1,000 vs. 2.37/1,000, respectively; RR = 1.7 (1.67-1.81). SIDS was the leading cause of death among AA infants. In contrast, congenital malformations were leading cause of death among White infants. AA infants had a greater percentage of mothers with high-risk characteristics than White infants (p<0.01). Although race-specific IMR decreased as individual risk status improved, the racial disparity persisted across each singular risk factor. Interestingly, the IMR of AA infants born to married, college graduated mothers who received adequate prenatal care equaled 1.1/1,000 compared to 1.0/1,000 for their White peers, RR =1.09 (0.64-1.85). Most striking, the adjusted RR of first year mortality AA (compared to White) term infants equaled 1.0 (0.9-1.0). **Conclusions:** The racial disparity disappears among the lowest risk subgroup of mother. This finding has public health relevance.

ALL-CAUSE AND CAUSE-SPECIFIC INFANT MORTALITY AMONG INDIGENOUS CANADIANS

Gabriel Shapiro, Amanda Sheppard, Tracey Bushnik, Michael Kramer, Jay Kaufman, Seungmi Yang

Background: Infant mortality is a strong indicator of perinatal health, reflecting health status, access to health care, and effectiveness of prenatal care in the population. However, there has been no systematic report of overall and cause-specific infant mortality among Canada's three Indigenous populations (First Nations, Métis, and Inuit) compared to non-Indigenous Canadians based on a nationally representative sample. **Methods:** Data were from the Canadian Birth-Census Cohorts, which include births between May 1994 and May 1996 and between May 2004 and May 2006. The cohorts comprise a 20% sample of Canadian households for each of the two time periods, plus 100% of households on Aboriginal reserves and remote communities. Cause of death was determined from ICD-9 and ICD-10 codes on infant death registrations. **Results:** The 2006 cohort included 13,506 First Nations births, 2,267 Métis births, 1,730 Inuit births, and 112,112 births to non-Indigenous mothers. Overall infant mortality rates were 9.1 per 1000 among First Nations, 10.5 per 1000 among Métis, and 12.1 per 1000 among Inuit, compared to 4.4 per 1000 for the non-Indigenous population. Infant mortality rates were higher in all groups in the 1996 cohort compared to the 2006 cohort. Major causes of infant death differed between the Indigenous and non-Indigenous groups and varied somewhat between the three Indigenous populations. The most striking difference in cause of death between Indigenous and non-Indigenous populations was due to Sudden Infant Death Syndrome (SIDS), which contributed more than 20% of deaths in each of the three Indigenous populations, compared to less than 8% in the non-Indigenous population. **Conclusions:** These data present the first cause-specific infant mortality rates on a national sample of Indigenous Canadians and highlight the need to reduce rates of SIDS in Indigenous populations.

EARLY PREGNANCY COFFEE CONSUMPTION AND RISK OF MISCARRIAGE

Kristen Hahn, Elizabeth Hatch, Kenneth Rothman, David Savitz, Amelia Wesselink, Ellen Mikkelsen, Lauren Wise

Objective: To clarify the reasons for decreased coffee consumption during early pregnancy and to determine the relation between early pregnancy coffee consumption and risk of miscarriage. **Methods:** In a North American cohort of pregnancy planners (Pregnancy Study Online-PRESTO), participants answered a questionnaire during early pregnancy (average gestational age 8.7 weeks, IQR: 6.6-10.9) and reported whether they had decreased their coffee consumption after conception. Women who had decreased their coffee consumption reported the reasons for the decrease (aversion due to taste, aversion due to nausea, concern for the baby, other). Coffee consumption in the previous 2 months was reported on the early pregnancy questionnaire. Miscarriages were reported on a late pregnancy questionnaire. Multivariable logistic regression models were used to calculate odds ratios (OR) and 95% confidence intervals (CI), controlling for maternal age and gestational weeks at completion of the early pregnancy questionnaire. **Results:** Of 1,005 women completing the early pregnancy questionnaire, 59 (6%) reported a miscarriage. Most of the women (56%) reported decreasing their coffee intake in early pregnancy; of these women, 69% decreased out of concern for their baby and 31% decreased due to aversion to coffee. Compared with women who did not drink coffee, multivariable ORs for drinking <1, 1, and ≥ 2 cups of coffee/day were 0.89 (CI: 0.45, 1.73), 1.64 (CI: 0.79, 3.43), and 2.94 (CI: 1.15, 7.53), respectively. When we excluded the 174 women who reported an aversion to coffee, the respective ORs were 1.07 (CI: 0.53, 2.14), 1.67 (CI: 0.79, 3.50), and 3.08 (CI: 1.20, 7.96). **Conclusion:** In this preliminary analysis, the majority of women who decreased coffee consumption during early pregnancy did so out of concern for their baby. After excluding those with an aversion to coffee in an attempt to curtail reverse causation, increasing coffee consumption in early pregnancy was associated with increased miscarriage risk.

CHANGES IN PRETERM INFANT MORTALITY RATE AMONG BLACK AND WHITE POPULATIONS FROM 1995 TO 2009 IN THE UNITED STATES

Prabhu Viswanathan, Martha Wingate, Waldemar Carlo

Purpose of Study: Racial disparities in preterm birth (PTB) rate have narrowed in the recent years. Contrary to this, racial disparity trends in infant mortality rate have widened. Our hypothesis is that less reduction in preterm mortality in Black infants in the recent years, when compared to Whites, have contributed to these differences. **Methods Used:** The birth cohort data from the National Center for Health Statistics Linked Birth/Infant Death Cohort Files were used to evaluate the gestational age-specific mortality from 1995 to 2009. Eligible: Infants born at 20 to 36 weeks gestation (total of nine subgroups in 2-week intervals) and greater than 500 grams. Multivariable logistic regression with relative odds ratio (RORs) and 95% confidence intervals (CI) were used to examine changes in disparities in PTBs. **Summary of Results:** There was higher proportion of Black infants at the lowest gestational age (≤ 28 weeks, 34% Black vs. 46.5% White; ≤ 37 weeks, 22.6% vs. 54.4%; when compared to all live births, 15.7% vs. 61.2%) Preterm birth rates have declined in the recent years in both the races in terms of absolute numbers (between years 2006-09, in ≤ 28 weeks, decrease in 3.5 Black vs. 1 White PTB per 10000 live births; ≤ 37 weeks, 33.7 Black vs. 26 White per 10000 live births) **Conclusions:** Black infants are at a higher risk of being born preterm when compared to White infants, and the risk increases significantly as the gestational age decreases. The survival advantage of PTB Black infants compared to Whites has declined over time and this may contribute to the lack of decline in racial disparities in the overall infant mortality rate.

MODIFIABLE LIFESTYLE RISK FACTORS FOR ECTOPIC PREGNANCY: A PROSPECTIVE COHORT STUDY

Audrey Gaskins, Stacey Missmer, Janet Rich-Edwards, Paige Williams, Irene Souter, Jorge Chavarro

Background: Several non-modifiable risk factors for ectopic pregnancy (EP) have been recognized but the role of modifiable factors remains unclear. To date, there has been no prospective cohort study of risk factors for EP. **Methods:** Our prospective cohort study included 41,440 pregnancies reported by 22,356 women in the Nurses' Health Study II (1990-2009). Lifestyle factors were self-reported in 1989 and updated every 2 years. Pregnancies were self-reported with case pregnancies ending in EP and comparison pregnancies ending in live birth, spontaneous abortion, induced abortion, or stillbirth. Multivariable log-binomial regression models with generalized estimating equations were used to estimate the adjusted relative risks (aRRs) and 95% confidence intervals. Population attributable risks (PARs) were used to estimate the proportion of EPs that could have been avoided had all women adhered to specific low-risk practices. **Results:** Incident EP was reported in 411 (1.0%) pregnancies. After adjustment, former and current smokers had 1.30 (95%CI 1.01-1.66) and 1.85 (95%CI 1.36-2.52) times the risk of EP than never smokers. Among former smokers, the risk of EP 10 years after quitting was similar to never smokers (aRR=0.99). Among current smokers, even light smoking (1-4 cigarettes/day) was associated with increased risk of EP (aRR=1.83). Women consuming ≥ 10 g/day of alcohol had 1.55 (95%CI 1.11-2.15) times the risk of EP than never consumers. The PARs for former and current smoking and alcohol intake ≥ 10 g/day were 5%, 6%, and 5% respectively (18% jointly). BMI, rotating night shift work, and multivitamin use were unrelated to EP. Similar to previous studies, in utero exposure to DES (aRR= 3.53), earlier use of oral contraceptives (aRR=2.27 for <16 y vs. never), IUD use (aRR=4.73) and history of infertility (aRR=3.23), tubal ligation (aRR=15.78), or prior EP (aRR=8.65) were associated with higher risk of EP. **Conclusions:** Around 18% of EPs in this cohort could have been avoided through smoking prevention and limiting alcohol intake prior to pregnancy.

LIFE COURSE-ADJUSTED ASSOCIATIONS BETWEEN INTRAUTERINE ENVIRONMENT AND DNA METHYLATION IN YOUNG ADULT WOMEN OF A JERUSALEM PERINATAL STUDY SUB-COHORT.

Jonathan Huang

Background: Intrauterine environment (IUE), including maternal gestational weight gain (GWG) and pre-pregnancy BMI (p MI), have been associated with offspring adult DNA methylation and cardiometabolic phenotype. Methylation, directly or as a proxy, may mediate the IUE-adult phenotype relationship, however time-dependent confounding by life course factors may produce spurious associations. **Methods:** Among 589 adult women (mean = 32 years) of the Jerusalem Perinatal Study Family Follow-Up, we quantified peripheral blood DNA methylation in five candidate genes drawn from literature (ABCA1, INS-IGF2, LEP, HSD11B2, and NR3C1) using EpiTYPER/ MassARRAY. We used multivariable linear regression and marginal structural models (MSM), estimated by inverse probability weighting and g-formula, to control for life course factors and estimate IUE – adult methylation associations. **Results:** Across various models and accounting for multiple tests, higher GWG was inversely related to ABCA1 methylation ($\beta = -1.1\%$ per quartile, [95% CI: -2.0, -0.3]), after adjustment for ancestry, parental confounders, and offspring's own adolescent weight, education, parity, and smoking. Mediation by the latter four life course factors appeared minimal: MSM-based estimates for total, natural, and controlled direct effects were similar. Multiple imputation for missing values did not alter associations. Exploratory analyses suggest the relationship may be driven by mothers with lowest p MI. ABCA1 methylation appeared to mediate a relationship between maternal GWG and beta-cell function (indirect effect on HOMA- $\beta = -0.6\%$, [95% CI: -1.0, -0.1]), though these measures were contemporaneous. **Conclusions:** Life course factors, including some found to be related to adult DNA methylation, did not appear to be important time-dependent confounders of our observed associations. This extends previous findings, however questions of functional relevance and the potential mediation by inflammation and cell type remain.

MATERNAL ADIPOSITY AND DAUGHTERS' AGE AT MENARCHE: THE AVON LONGITUDINAL STUDY OF PARENTS AND CHILDREN

Rebecca Lawn, Debbie Lawlor, Abigail Fraser

Background: Earlier menarcheal age is associated with premature death, cardiovascular disease, and other adverse health outcomes. Greater maternal body mass index (BMI) is associated with greater daughters' BMI which in turn is associated with earlier menarche. Reported associations of maternal adiposity with daughters' menarcheal age are inconsistent. **Methods:** We examined associations between maternal pre-pregnancy BMI and gestational weight gain (GWG), and daughters' menarcheal age in a general population pregnancy cohort of 3935 mother-daughter pairs. Total GWG was derived from the first and last obstetric weight measurements. Incremental GWG was estimated from a linear spline multilevel model relating weight to gestational age (10 measurements per woman (IQR: 8 to 11)). **Results:** Mean menarcheal age was 12.63 (standard deviation: 1.17) years. There was no evidence to suggest departure from a linear relationship between pre-pregnancy BMI, GWG and daughters' menarcheal age. Pre-pregnancy BMI (mean difference: -0.33 months, 95% confidence interval [CI] -0.45, -0.22 per 1 kg/m²) and GWG (-0.16 months, 95% CI -0.25, -0.06 per kg) were inversely associated with daughters' menarcheal age with adjustment for maternal age, parity, socio-economic status, smoking, and maternal menarcheal age. Associations somewhat attenuated when daughters' birthweight, breastfeeding duration and pre-pubertal BMI were adjusted for. When GWG was examined by period in pregnancy (0-18, 18-28, 28+ weeks), GWG in weeks 28+ had the largest association with daughters' menarcheal age (-3.66 95% CI -6.73, -0.60 per kg/week), though confidence intervals overlapped with estimates for GWG in weeks 0-18 and 18-28. **Conclusions:** Greater pre-pregnancy BMI and GWG are associated with earlier daughters' menarcheal age, even when accounting for mothers' own menarcheal age and other potential confounders. These associations may be partially mediated by birthweight, duration of breastfeeding and pre-pubertal BMI.

EVALUATION OF GESTATIONAL WEIGHT GAIN GUIDELINES AMONG WOMEN OF NON-AVERAGE HEIGHT, WASHINGTON STATE 2003-2013

Vivian Lyons

OBJECTIVE: To conduct a population-based study evaluating whether maternal height modifies the impact of gestational weight gain on maternal and infant outcomes. **METHODS:** We used a retrospective cohort study of gestational weight gain based on Washington State linked birth certificate and hospital discharge data from 2003-2013. We grouped women by pre-pregnancy BMI levels (under, normal, overweight and obese) and gestational weight gain categories based on the Institute of Medicine 2009 Gestational Weight Gain Guidelines: less than recommended, recommended and greater than recommended. Outcomes of interest included primary C-section, 3rd/4th degree laceration, a maternal morbidity composite, and an infant morbidity composite. We then grouped maternal height into tertiles (short, average and tall) to examine possible effect modification between gestational weight gain and adverse birth outcomes, using logistic regression to estimate odds ratios. **RESULTS:** We identified 164,882 maternal and infant pairs from the Washington State database. For each outcome, the risk for each subgroup within pre-pregnancy BMI strata was compared to risk among average height women, 5'2"-5'8", with recommended gestational weight gain. Short women had higher risk of C-section [ranging from OR=1.35 (95%CI: 1.13-1.56) to OR=2.22 (95%CI: 2.03-2.40)], regardless of GWG, BMI or race. Tall women with greater than recommended gestational weight gain were at lower risk for C-section, 3rd/4th degree lacerations, maternal or infant morbidity than women of average height. We observed an overall pattern of increasing risk of adverse outcomes among shorter women, women with excess weight gain and overweight pre-pregnancy BMI. **CONCLUSIONS:** Tall women had overall lower risks of C-section and infant morbidity. Short women had an overall higher risk of C-section. This suggests that in the future, recommendations for optimal gestational weight gain need to incorporate maternal stature.

MATERNAL EXPOSURE TO CHILDHOOD MALTREATMENT AND RISK OF STILLBIRTH

Alexa Freedman, Carol Hogue, Alison Cammack, Jeff Temple, Robert Silver, Donald Dudley, Barbara Stoll, Michael Varner, George Saade, Deborah Conway, Robert Goldenberg

Childhood maltreatment (CM) is associated with health complications and behaviors, which increase the risk for adverse pregnancy outcomes in adulthood. Non-Hispanic black women may have a higher prevalence of CM and they experience a disproportionate burden of stillbirth, with a rate two times that of non-Hispanic white women. We used data from the Stillbirth Collaborative Research Network's (SCRN) population based case-control study conducted from 2006-2008 in Rhode Island and parts of Massachusetts, Georgia, Texas and Utah, and the SCRN-Outcomes after Study Index Stillbirth (SCRN-OASIS) study conducted in 2009, to explore the association between reported CM and stillbirth by race/ethnicity. The SCRN-OASIS study measured CM using the Childhood Trauma Questionnaire (CTQ). Our analysis included 273 singleton stillbirths (> 20 weeks' gestation) and 510 healthy term singleton live births (excluding births <37 weeks gestation, neonatal intensive care unit admission, or death) with CTQ scores, weighted to account for oversampling and differential consent. Dichotomized summary CTQ score and five subscales (physical abuse, physical neglect, emotional abuse, emotional neglect, and sexual abuse) were analyzed using multivariable logistic regression. For emotional abuse, physical neglect, and sexual abuse, the associations differed in direction between non-Hispanic white women (adjusted odds ratios [aOR] >1.0 and non-Hispanic black women (aORs < 1.0), although there was substantial overlap in the confidence intervals. Among non-Hispanic white women, physical neglect had the greatest association with stillbirth (aOR: 1.87; 95% confidence interval [CI]: 1.05, 3.34). However, this association did not hold in non-Hispanic black women (aOR: 0.86; 95% CI: 0.30, 2.41). Future research should examine cultural differences in reporting of CM by race and ethnicity and how this may affect observed associations between CM and pregnancy outcomes, including stillbirth.

THE FURAN FATTY ACID METABOLITE CMPF IN EARLY PREGNANCY AND RISK OF GESTATIONAL DIABETES MELLITUS

Chunfang Qiu

Background: Recent studies indicate that the furan fatty acid metabolite 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid (CMPF) is elevated in the plasma of humans with gestational diabetes mellitus (GDM), and type 2 diabetes patients. However, sample sizes in previous studies were small and the temporal association of CMPF with incident GDM has not been explored. **Methods:** We conducted a nested case-control study (140 GDM cases and 140 euglycemic controls) to examine maternal early pregnancy serum CMPF concentrations and subsequent GDM risk. Serum CMPF was measured in early pregnancy (15.5±3.2 weeks gestation) using enzyme-linked immunoassay. Data were collected using interviewer-administered questionnaires, food frequency questionnaire (FFQ) and review of medical records. Logistic regression procedures were used to calculate odd ratios (ORs) and 95% confidence intervals (CI). Partial correlation coefficients for natural-logarithm CMPF with maternal fish consumption as well as polyunsaturated fatty acids (PUFA) were examined. **Results:** Median serum CMPF concentrations were 113.7 ng/ml among GDM cases and 99.5 ng/ml among controls (p-value=0.126). Overall, women in the highest quartile for CMPF had 1.94-fold increased risk of GDM (95% CI: 1.16-3.24) compared to other women. Adjustment for confounders including age, race, family history of diabetes and pre-pregnancy body mass index slightly attenuated the associations (OR=1.73, 95%CI: 0.99-3.02). Serum CMPF is moderately correlated with dietary arachidonic acid (r=0.17, p-value=0.05) in GDM cases. However, serum CMPF was not correlated with fish or PUFAs intake. **Conclusion:** There is a potential association of early pregnancy CMPF with subsequent GDM risk. Future replication and mechanistic studies of observed association are warranted.

GESTATIONAL WEIGHT GAIN AND RISK OF GESTATIONAL DIABETES MELLITUS IN HISPANIC WOMEN

Megan Harvey, Barry Braun, Karen Ertel, Glenn Markenson, Penelope Pekow, Lisa Chasan-Taber

Findings for the association between gestational weight gain (GWG) and risk of gestational diabetes mellitus (GDM) have been conflicting and often biased due to the inclusion of weight gain after the diagnosis of GDM. Hispanic women are more likely than other subgroups to exceed the Institute of Medicine (IOM) guidelines for GWG and are at higher risk of developing GDM, yet have been underrepresented in previous studies. Therefore, we examined this association among 1,250 pregnant Hispanic participants in Proyecto Buena Salud, a prospective cohort study conducted in Massachusetts from 2006 to 2011. Information on GWG, GDM and abnormal glucose tolerance (AGT) was abstracted from medical records and confirmed by the study obstetrician. A total of 49.8% of women exceeded IOM guidelines for GWG up to the time of GDM screen, 14.3% had AGT and 4.6% were diagnosed with GDM. Increasing education (Odds Ratio (OR) = 2.1, 95% Confidence Interval (CI) 1.1-4.1 for post high school vs. less than high school; $p_{trend} < .001$), marital status (OR=2.3, 95% CI 1.1-4.7 for married vs. single), generation in the United States (OR=2.4, 95% CI 1.3-4.3 for 1st vs. 2nd generation; $p_{trend} < .001$), age (OR=9.7, 95% CI 4.2-22.4 for >30 vs. 16-19 years; $p_{trend} < .001$), and pre-pregnancy body mass index (BMI) (OR=1.1, 95% CI 1.05-1.13 for each one unit increase in BMI; $p_{trend} < .001$) were positively associated with GDM. After adjusting for pre-pregnancy BMI, age, and obstetric history, women who exceeded IOM guidelines for GWG were not at increased risk for AGT (OR=0.95, 95% CI 0.57-1.58) or for GDM (OR=0.85, 95% CI 0.38-1.91), as compared to women who gained within IOM guidelines. Each one-pound increase in GWG in the first trimester was also not significantly associated with AGT (OR=1.00, 95% CI 0.98-1.03) or GDM (OR=1.01, 95% CI 0.97-1.05). Parity and pre-pregnancy BMI did not modify observed findings. In summary, in this population of Hispanic women, GWG was not significantly associated with GDM.

TRIGGERS OF PREECLAMPSIA: A CASE CROSSOVER STUDY

Jane Ford, Kathrin Schemann, Rob Herbert, Jillian Patterson, Jonathan Morris, Christine Roberts

Background: Risk factors for preeclampsia are well established; the triggers associated with gestational age of onset are not. The aim of this study was to establish whether a recent infection or other triggers were associated with preeclampsia onset. Methods: We used a case-crossover design with the case window being 1-7 days preceding a preeclampsia diagnosis; the control window was 8-14 days prior to diagnosis. Women with singleton pregnancies of ≥ 20 weeks gestation, diagnosed with preeclampsia were eligible for inclusion. Triggers (recent infection and others) were investigated via questionnaire and associated diagnoses through medical review. Preeclampsia was defined as hypertension ($\geq 140/90$) and proteinuria (protein/creatinine ratio ≥ 30). Infections were self-identified with symptoms lasting more than 24 hours. Conditional logistic regression was used to analyse discordant pairs; unadjusted odds ratios (ORs) are reported. Results: Among 284 women recruited, 25 (8.7%) women had a new infection in the case window and 21 (7.3%) in the control window. There was no statistically significant association between onset of infection in the case vs control window (OR 1.24, CI 0.65-2.34). Consumption of caffeine (OR 0.51, CI 0.33-0.77), spicy food (0.49, CI 0.30-0.81) and alcohol (0.26, CI 0.10-0.71) were inversely associated with preeclampsia onset. Conclusion: Onset of new infection in the 7 days prior does not appear to be associated with timing of preeclampsia onset. Decreased consumption of caffeine, spicy food and alcohol may be prodromal markers. Changes in such behaviour may be an early marker to initiate further clinical investigation.

GENETIC VARIATIONS RELATED TO MATERNAL WHOLE BLOOD MITOCHONDRIAL DNA COPY NUMBER : A GENOME-WIDE AND CANDIDATE GENE STUDY

Tsegaselassie Workalemahu

Background: Accumulating evidence suggests that mitochondrial dysfunction underlies adverse pregnancy complications. While some candidate gene studies have reported associations of mitochondrial DNA (mtDNA) copy number, a biomarker of mitochondrial function, with variations in nuclear DNA, no prior study investigated genome-wide nuclear DNA variation and mtDNA copy number associations. We conducted a genome-wide association study (GWAS) and a candidate gene (genes participating in mitochondrial biogenesis and oxidative phosphorylation) association study of maternal mtDNA copy number. Methods: Analyses were performed among participants (N=471) of a placental abruption case-control study conducted in Lima, Peru. Maternal peripheral blood was collected during labor and delivery admission. Genotyping for single nucleotide polymorphisms (SNPs) was conducted using the Illumina Cardio-Metabo Chip platform. Whole blood mtDNA copy number was measured using qRT-PCR techniques. A total of 119,629 SNPs were evaluated in the GWAS study while 161 SNPs (in 32 genes) were evaluated in the candidate association study. Linear regression models were used to calculate beta estimates and related nominal p-values. Results: Identified associations were not statistically significant at the genome-wide level (p-value $< 5.00 \times 10^{-8}$). The top hit in our genome-wide analysis was chr19:51063065 in FOXA3 (empirical p-value = 2.20×10^{-6}). A total of 134 SNPs had p-values < 0.001 . These included rs17111633 in CNNM1 (p-value = 6.32×10^{-6}) and chr19:51083059 in MYOP (p-value = 3.23×10^{-5}). In the candidate association study, several SNPs in PRKG, PRKCA, SP1, and THRB were associated with mtDNA copy number (p-values < 0.05). Conclusion: Variations in nuclear DNA are potentially associated with mtDNA copy number. Future larger studies are warranted to replicate findings and identify functions of identified genes in relation to mitochondrial function.

SHOULD PREGNANT WOMEN BE ADVISED TO TAKE CALCIUM SUPPLEMENTS DURING PREGNANCY?

Luc Smits

Background Pre-eclampsia (PE) is defined as de-novo hypertension after 20 weeks' gestation plus proteinuria or other maternal organ dysfunction. Affecting 3-5% of all pregnancies, it is a major cause of maternal and neonatal mortality and morbidity. Calcium supplementation (1-2 g/day) during pregnancy has been shown to decrease the incidence of PE by 55%, and even stronger protective effects have been observed in subgroups. Despite its documented preventive effect, relative cheapness, and safety, pregnant women are not routinely advised by caregivers to use calcium supplements, either in Netherlands or elsewhere. Objective To estimate potential effects on population health and care expenses of advising Dutch pregnant women to use calcium supplements (1000 mg/day) during pregnancy. Methods Three scenarios were considered in a theoretical Dutch pregnant population and compared to current care. The three scenarios were: advising calcium supplements to (1) all women, (2) women with high PE risk, and (3) women with low calcium intake. Input parameters for the model were: Size of risk groups, Relative risk calcium vs. no calcium use, Incidence of pre-eclampsia, Cost of calcium, Current use of calcium, Cost of pre-eclampsia, Uptake of calcium use in new situation. Data sources were: Published literature, national registries and governmental reports, expert opinion. Results With recommending calcium supplementation to all vs current care, reduction in incidence of PE was 25% and net financial gain was 7.7 M€ per annum. With recommending calcium to high-risk women and women with low calcium intake, reductions were 8.5% and 13%, respectively, and 3.4 M€ and 4.7 M€ per annum. Discussion Our results provide support for advising calcium supplementation during pregnancy to all pregnant women. The analytical model can be used for the evaluation of the potential impact of other promising interventions in various populations and various outcomes.

GESTATIONAL WEIGHT GAIN PATTERNS IN RELATION TO SHORT-TERM BIRTH OUTCOMES

Sarah Pugh, Sungduk Kim, Paul Albert, Stefanie Hinkle, Roger Newman, Deborah Wing, William Grobman, Katherine Grantz

Gestational weight gain (GWG) is a simple clinical measure used throughout pregnancy to monitor maternal and fetal nutritional status. However, there is limited evidence on the pattern of GWG and how it relates to birth outcomes. Our objective was to describe patterns of GWG and examine their association with birthweight outcomes. We used a prospective cohort of 2,802 singleton pregnancies recruited from 12 US prenatal centers between 2009-2013. Prenatal weights were measured at study visits and abstracted from medical charts. Infant birthweights <2500g and ≥4000g were defined as low birthweight (LBW) and macrosomia, respectively. Small-for-gestational age (SGA) and large-for-gestational age (LGA) were calculated using race-specific fetal growth standards. Semi parametric, group-based trajectory models were used to estimate weight gain trajectories. Poisson regression with a robust error variance was used to calculate the relative risk of birth outcomes by the probability of trajectory membership. There were 2,795 women contributing 43,287 observations with a median (IQR) of 17 (15-19) visits. Four distinct trajectories were identified with total GWG ranging from 3.6 kg to 24.0 kg and 2nd/3rd trimester rates of gain from 0.08 to 0.76 kg/week. Compared with the moderate gain group, the two highest gaining trajectories were associated with a 1.5- to 2.3-fold increased risk of LGA and a nearly 2.0-fold increased risk of macrosomia while the lowest gaining group was associated with a 1.6-fold increased risk of SGA. There was no difference in the risk of low BW by trajectory. When stratified by pre-pregnancy BMI, results trended in the same direction with one additional finding. Compared with the moderate gain group, only normal weight women with a low GWG trajectory had a 2.3-fold increased risk of low BW. Our findings support an association between GWG patterns and the risk of birth outcomes. Identifying an early high pattern of weight gain could serve as an important target to modify the risk of LGA and macrosomia.

PATTERNS OF PSYCHOSTIMULANT USE FROM 2000-2010 IN PUBLICLY-INSURED PREGNANT WOMEN

Jacqueline Cohen, Yoonyoung Park, Krista Huybrechts, Brian Bateman, Sonia Hernandez-Diaz

Background: The diagnosis of attention deficit hyperactivity disorder (ADHD) in adults, children, and teens has increased in recent years. However, there is limited information on the patterns of use of stimulants in pregnancy and the safety of these medications in pregnancy is understudied. **Objective:** To describe the distribution and determinants of psychostimulant use in pregnancy. **Methods:** We conducted a descriptive study using a cohort of publicly-insured women linked to their live born infants, nested in the Medicaid Analytic eXtract (MAX) database. We assessed the patterns of use overall and by trimester of the following medications: amphetamine/dextroamphetamine, methylphenidate, clonidine, atomoxetine, guanfacine, and pemoline. **Results:** Among 1,524,128 linked deliveries, 8,143 women (0.5%) filled a prescription for a stimulant in pregnancy. Use of amphetamine/dexamphetamine was most common (53%) followed by methylphenidate (24%), clonidine (19%), and atomoxetine (7%). Stimulant use was associated with an ADHD diagnosis in 48% of exposed, and 26% of women with an ADHD diagnosis used a stimulant during pregnancy. The prevalence of use during pregnancy more than tripled over time: from 0.3% of pregnancies in 2000 to 1% in 2010. The proportion of pregnant women exposed sharply declined throughout pregnancy (prevalence of exposure: 0.5% in 1st trimester, 0.2% in 2nd trimester, and 0.1% in 3rd trimester). Few women initiated stimulants during pregnancy. Women who used stimulants in pregnancy were younger on average and more likely to be Caucasian than those who did not: 36% of the exposed vs 24% of the unexposed were <20 years and 72% exposed vs 40% were White. **Conclusions:** Use of stimulants in pregnancy increased between 2000 and 2010. The majority of women using stimulants at the start of pregnancy have discontinued by the second trimester. Additional information on the safety of these medications in pregnancy is urgently needed in light of these trends.

MATERNAL LIPIDS AND TIME TO PREGNANCY

Sarah Pugh, Enrique Schisterman, Neil Perkins, Sunmi Mumford, Lindsey Sjaarda, Richard Browne, Robert Silver, Jean Wactawski-Wende, Noya Galai, Joseph Stanford, Brian Wilcox, Ann Lynch

Evidence suggests that abnormal maternal lipid concentrations may reduce human fecundity. The objective of this study was to assess maternal cholesterol, triglyceride, and lipoprotein cholesterol levels in relation to time to pregnancy (TTP). The EAGeR trial followed 1228 women attempting pregnancy for up to 6 menstrual cycles. Total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride levels were measured in preconception serum samples collected at baseline and categorized by clinical cut-points for analyses. TTP was the number of menstrual cycles to a positive hCG pregnancy- or clinically-confirmed by ultrasound. Cox proportional hazard models were used to estimate fecundability odds ratios (FOR) adjusting for maternal age, race, education, alcohol use, treatment assignment, free fatty acid concentrations, and total cholesterol (particle models only). The N(%) of women with total cholesterol ≥200 mg/dl, LDL-C ≥130 mg/dl, and triglycerides ≥150 mg/dl was 148(12.3%), 94(7.9%), 280(23.2%), respectively, and 606(50.7%) had HDL-C <50 mg/dl. The FOR for TTP was reduced for all abnormal lipid components before and after confounder adjustment, indicating a longer time to pregnancy. Total cholesterol ≥200 mg/dl was associated with a 30% increased TTP (FOR: 0.70, 95% CI:0.54, 0.92) for hCG-detected pregnancy and a 35% increased TTP (FOR: 0.65, 95% CI:0.49, 0.87) for ultrasound-confirmed pregnancy, compared with women with total cholesterol <200 mg/dl. A significant decrease in fecundity associated with clinically undesirable lipoprotein cholesterol levels ranged from 16% (HDL) to 35% (LDL) for hCG-detected pregnancy and from 16% (HDL) to 38% (LDL) for ultrasound-confirmed pregnancy. Our results suggest that unfavorable maternal preconception lipid levels are associated with reduced fecundity and a longer TTP. As lipid levels are modifiable they may offer an important target to improve female fecundability.

PSYCHOSTIMULANT USE IN PREGNANCY AND RISK OF PLACENTAL COMPLICATIONS AND PRETERM DELIVERY

Jacqueline Cohen, Sonia Hernandez-Diaz, Brian Bateman, Krista Huybrechts

Background: Despite increasing use, there are limited data on the safety of stimulant use in pregnancy. Based on prior evidence, it can be hypothesized that stimulants may adversely affect fetal growth and placental. **Objective:** To determine if stimulant use in pregnancy is associated with increased risks of ischemic placental disease (including preeclampsia, placental abruption, and growth restriction) or preterm birth. **Methods:** A cohort study including pregnant women and linked live born infants enrolled in Medicaid from 2000-2010. Women had continuous coverage from 3 months before pregnancy until 1 month after delivery. Pregnancies with offspring diagnosis of chromosomal or major structural abnormalities were excluded. Exposures of interest were use of amphetamine/dextroamphetamine (AMP), methylphenidate (MPH), and atomoxetine monotherapy in the first half of pregnancy. The reference group included women who did not fill a prescription for a stimulant during the three months prior or first half of pregnancy. Risk ratios (RRs) and 95% confidence intervals (CIs) were estimated using log-binomial regression with propensity score weighting to control for confounding. **Results:** Among 1,472,672 deliveries, 0.4% were exposed to stimulant monotherapy in the first 20 weeks of pregnancy. Compared to non-users, AMP was associated with an unadjusted increased risk of preeclampsia, placental abruption, and preterm delivery. MPH was associated with an unadjusted increased risk of preeclampsia and growth restriction. After adjustment, including the severity of the underlying indication, AMP remained associated with preeclampsia, RR=1.34 (95% CI 1.11-1.61) but none of the other crude associations remained. Atomoxetine was not associated with any of the outcomes studied. **Conclusions:** AMP use may be associated with a small increased risk of preeclampsia. Confounding explained most of the crude associations between stimulants and the placental complications examined.

MATERNAL HEALTHCARE UTILIZATION IN INDONESIA: ANALYSIS OF DEMOGRAPHIC AND HEALTH SURVEY 2012

Vitri Widyaningsih, Megan Eagle, Claudia Holzman

Despite the continuous and synergistic effort by public and private entities, maternal mortality in Indonesia remains high, with 200 deaths/100,000 live births reported in 2010. Maternal healthcare is an important factor to reduce maternal mortality and morbidity. This study evaluates maternal healthcare utilization in Indonesia and its determinants. Using Indonesian 2012 Demographic and Health Survey data, we analyze information from 15,121 women to assess the use of maternal health care (antenatal, delivery and postpartum), and evaluate the effect of age, education, wealth, living in rural and urban area and living in Java-Bali islands on maternal healthcare utilization. Antenatal care by a healthcare provider was received by 95.4% women, however only 80.8% of women had skilled birth attendance, and 86.2% had one postpartum care. Our models included 5 covariates: age, education, wealth, urban/rural, and living in Java-Bali/not. Women with at most primary school or no education had higher odds to receive no antenatal care, skilled birth attendance, and postpartum care compared to women with college level education (Adjusted Odds Ratio (aOR) 4.19, 3.97, 2.79; respectively, $p < 0.05$). Comparing women from the lowest wealth to those in the highest wealth category, poorer women had increased odds to receive no antenatal (aOR 10.92), assisted birth (aOR 8.35), and postpartum care (aOR 5.80). Women living in rural areas or outside of Java-Bali islands were less likely to utilize maternal healthcare. Disparities due to social economic status and geographic location affect maternal healthcare utilization in Indonesia. Intervention programs should focus on disadvantaged populations: people from low social economic status, living in rural areas or outside of Java-Bali islands. Future research to assess the association of healthcare utilization on maternal morbidity and mortality will provide recommendations for public health interventions.

THE OTHER HISPANIC PARADOX? MATERNAL OBESITY, NATIVITY, AND GESTATIONAL DIABETES AMONG LATINA WOMEN IN NEW YORK CITY, 2011-2013

Teresa Janevic, Elizabeth Howell, Jennifer Zeitlin, Amy Balbierz

Maternal obesity and foreign-born status are often associated with an increased risk of gestational diabetes, yet the interplay between these characteristics has not been well studied. Our objective was to examine interrelationships between maternal obesity and foreign-born status with gestational diabetes among Latina women in New York City. We used linked electronic birth certificate data for Latina women ($n=92,549$) from 2011-2013. Pre-pregnancy BMI was categorized into five categories for analysis as a covariate and two categories (Obese/Morbid obese vs. Underweight/Normal/Overweight) for analysis as a dependent variable. We calculated adjusted relative risks using covariate-adjusted log-binomial regression. Covariates included parity, age, education, prenatal care, BMI, and insurance status. Foreign-born Hispanic women were at lower risk of maternal obesity/morbid obesity (Adjusted risk ratio (aRR) = 0.59, 95%CI=0.58, 0.61) but at higher risk of gestational diabetes (aRR= 1.35, 95%CI=1.27, 1.44). The increased risk with foreign-born status was present within each BMI category, with aRRs for foreign-born status ranging from 1.22 among obese women (95%CI= 1.11, 1.37) to 1.59 (95%CI=1.40, 1.81) among normal weight women. Future research should test explanations for this "other" Hispanic paradox, including nutritional influences, country of origin factors, and selection processes, as well as life course cardiovascular disease trajectories of foreign-born and U.S.-born Latina women.

CUMULATIVE PHYSIOLOGIC DYSFUNCTION AND PREGNANCY

Kimberly McKee, Diana Fernandez, Susan Groth, Chris Seplaki, Susan Fisher

Objective: To prospectively characterize cumulative physiologic dysfunction in pregnancy as a measure of the biological effects of maternal chronic stress and to examine its associations with gestational age and birth weight. Methods: Women <28 weeks gestation were enrolled from OB clinics in Rochester, NY. Cumulative physiologic dysfunction parameters included total cholesterol, IL-6, high sensitivity-CRP, systolic and diastolic blood pressure, BMI at <14 weeks gestation, glucose tolerance, and urinary albumin collected in the third trimester. Linear regression was used to estimate the association between physiologic dysfunction and birth weight and gestational age, respectively ($N=111$). Results: Results: Cumulative physiologic dysfunction (CPD) scores ranged from 0-6, out of a total of 8 parameters (Mean 2.09; SD=1.42). Three-fourths of the participants had a CPD score of 3.0 or less. The mean birth weight was 3,397 grams (SD=522.89), and the mean gestational age was 39.64 weeks (SD=1.08). Cumulative physiologic dysfunction was not significantly associated with either birth weight or gestational age. Conclusion: Refinement of a CPD score for pregnancy is needed, taking into consideration both the component parameters and clinical and pre-clinical cut-points for risk scoring. The biological effects of chronic stress on adverse birth outcomes require further research.

THE ROLE OF FETAL GROWTH AS A MEDIATOR OF THE RELATIONSHIP BETWEEN MATERNAL EXPOSURES AND PERINATAL DEATH

Alexandra V. C. Seaward, Olga Basso, Jay S. Kaufman, Robert Platt

Intra-uterine growth restricted infants have a higher risk of adverse perinatal outcomes, although the role of fetal growth as a causal mediator is not fully understood. Studies on fetal growth often use small-for-gestational age (SGA) thresholds from birth-weight-for-gestational-age charts, which are biased at preterm gestational ages when predicting perinatal outcomes. To adjust for these limitations, other methods for classifying fetal growth have been proposed. The study objective was to investigate fetal growth as a mediator (measured by SGA thresholds) between maternal exposures and perinatal death, using singleton live births and fetal deaths ($n=10,357,248$) from 2007-2009 US Vital Statistics birth cohort linked birth/infant death and fetal death datasets. Exposures were maternal smoking during pregnancy (never vs. smoker) and maternal race (white, black, other). Perinatal death was defined as fetal death ≥ 22 weeks gestation and neonatal death (infant death <28 days of life). SGA was defined as live birth-based (standard) or non-customized ultrasound-based. Log-binomial regression models were used to estimate the total effect of maternal smoking or race on perinatal death and the direct effect by conditioning on SGA. Log-binomial marginal structural models with stabilized inverse probability weighting were used to estimate the controlled direct effect (CDE) (setting mediator to non-SGA). Direct effect adjusted risk ratios were similar between the standard mediation model and MSM model for both exposures. CDE estimates differed depending on the definition of SGA, standard vs. ultrasound: (maternal smoking) RR 1.22 [95% CI: 1.16-1.27] vs. RR 1.14 [95% CI: 1.09-1.19], and (black race) RR 1.94 [95% CI: 1.89-2.00] vs. RR 1.84 [95% CI: 1.79-1.89]. Results suggest that SGA partially mediates the effect of maternal smoking or race on perinatal death but live birth-based SGA may overestimate the CDE. Future analyses will address the impact of unmeasured confounding.

VALIDITY OF A WEB-BASED QUESTIONNAIRE TO ASSESS PERINATAL OUTCOME

Marleen van Gelder, Saskia Vorstenbosch, Lineke Derks, Bernke te Winkel, Eugene van Puijenbroek, Nel Roeleveld

Previous validation studies showed that maternal recall of perinatal outcomes, including infant birth weight and gestational age, is generally excellent when using interviews or paper-based questionnaires. However, knowledge on the validity of data on perinatal outcome collected with Web-based questionnaires is limited. For 1,124 women with an estimated date of delivery between February 2012 and February 2015 participating in the PRenancy and Infant DEvelopment (PRIDE) Study in the Netherlands, we compared data on pregnancy outcome, including mode of delivery, plurality, gestational age, birth weight and length, head circumference, birth defects, and infant sex from Web-based questionnaires with data from obstetrical records. For the continuous outcome variables, intraclass correlation coefficients (ICC) with 95% confidence intervals (CI) were calculated, while sensitivity and specificity were determined for categorical variables. We observed only very small differences between the two methods of data collection for gestational age (ICC 0.85; 95% CI 0.83-0.88), birth weight (ICC 0.98; 95% CI 0.98-0.98), birth length (ICC 0.89; 95% CI 0.86-0.92), and head circumference (ICC 0.85; 95% CI 0.73-0.95). Agreement between the Web-based questionnaire and obstetrical records was high as well, with sensitivity ranging between 0.90 (post-term birth) and 1.00 (multiple outcomes) and specificity between 0.95 (emergency caesarean section) and 1.00 (multiple outcomes). In conclusion, the validity of the Web-based questionnaire for perinatal outcomes was similar or higher compared to the traditional modes of data collection. Therefore, Web-based questionnaires should be considered as a complimentary or alternative method of data collection in reproductive and perinatal epidemiology.

LONG-TERM RECALL OF TIME TO PREGNANCY

Anne Marie Jukic, D. Robert McConaughy, Clarice Weinberg, Allen Wilcox, Donna Baird

Despite the widespread use of retrospectively-reported time to pregnancy to evaluate fertility either as an outcome or as a risk factor for chronic disease, only two small studies have directly compared prospective data with later recall. The North Carolina Early Pregnancy Study (1982-1986) collected prospective time-to-pregnancy data from the beginning of participants' pregnancy attempt. In 2010 (24-28 years later) women were sent a questionnaire including lifetime reproductive history that asked about all prior times to pregnancy. Of the 202 women with prospective time-to-pregnancy data, 76% provided recalled time to pregnancy. A lower proportion of women with times to pregnancy (≥ 3 cycles) provided a recalled time to pregnancy than women with times to pregnancy < 3 cycles. Also, high gravidity or parity were associated with a lower likelihood of providing a recalled time to pregnancy. Women with very short or very long times to pregnancy (1 cycle or ≥ 13 cycles) had good recall of time to pregnancy. Positive predictive values, PPVs, of 1 or ≥ 13 cycles were 73% and 68%, respectively, while PPVs for other categories of time to pregnancy ranged from 38% to 58%. The weighted kappa statistic for recalled versus prospective time to pregnancy was 0.72 (95% confidence interval: 0.65, 0.79). Recalled time to pregnancy showed good agreement with prospective time to pregnancy. Informative missingness must be considered when imputing recalled time to pregnancy. Associations observed in future studies can be corrected for misclassification.

USING WEB-BASED QUESTIONNAIRES TO ASSESS MEDICATION USE DURING PREGNANCY: A VALIDATION STUDY IN TWO PROSPECTIVE COHORT STUDIES

Nel Roeleveld, Marleen van Gelder, Saskia Vorstenbosch, Bernke te Winkel, Eugene van Puijenbroek

Collecting valid self-reported data on medication use during pregnancy is challenging: medication use is likely to be underreported when using paper-based questionnaires or interviews. The aim of this study was to validate two comparable Web-based questionnaires with indication-oriented questions to assess prescription and over-the-counter medication use during pregnancy. Participants in the PRenancy and Infant DEvelopment (PRIDE) Study (n=387) and the Pregnancy Drug Registry pREGnant (n=166) completed a six-week paper-based diary on medication use in gestational weeks 19-24 or 26-31. In week 34, they completed a Web-based questionnaire, which included questions on the exact name of the medication, time period and frequency of use, and quantity taken. To assess the degree of underreporting, the questionnaire's sensitivity (Se) with 95% confidence intervals (CI) was calculated with the medication diary as reference standard. Among the women who completed a diary, 65.7% used at least one medication in the six-week period. Sensitivity of the questionnaire was high for many medication groups, including topical corticosteroids (Se 0.89; 95% CI 0.74-1.00), levothyroxine (0.76; 0.56-0.97), antiepileptics (0.88; 0.75-1.00), antacids (0.77; 0.69-0.85), and ferrous fumarate (0.77; 0.54-1.00). Sensitivity was lower for medication for short-time use, with sensitivities of 0.50 (95% CI 0.22-0.78) for systemic antibiotics, 0.50 (0.38-0.62) for ear, eye, nose and throat pre-rations, 0.59 (0.52-0.67) for analgesics, and 0.56 (0.49-0.64) for acetaminophen specifically. No differences in sensitivity were observed between the PRIDE Study and pREGnant questionnaires. In conclusion, for a large number of medication groups, underreporting in a Web-based questionnaire is limited. For some medications, however, a substantial number of exposures will be missed with this method of data collection, but the degree of underreporting is much lower compared to paper-based questionnaires.

HEALTHY WORKER BIASES IN STUDIES OF OCCUPATIONAL EXPOSURES AND PREGNANCY OUTCOMES

Candice Johnson, Carissa Rocheleau, Christina Lawson, Barbara Grajewski, Penelope Howards

Background. The literature on healthy hire bias and healthy worker survivor bias has focused mainly on studies of chronic disease and mortality. The effects of these biases might differ in studies of pregnancy outcomes because of social and cultural reasons causing healthy women to leave the workforce to care for children or family (affecting healthy hire bias) and because of the relatively short risk period for adverse pregnancy outcomes (affecting healthy worker survivor bias). Methods. We used directed acyclic graphs (DAGs) to illustrate structures of healthy hire bias and healthy worker survivor bias in studies of occupational exposures and adverse pregnancy outcomes. We also examined structures of other healthy worker biases previously described in pregnancy studies: reproductively unhealthy worker effect (women with live births leave the workforce to care for children, women with non-live births return to work), insecure pregnancy effect (women with prior adverse pregnancy outcomes reduce or eliminate exposures in subsequent pregnancies), and desperation/privilege effect (choice of returning to work after pregnancy depends on financial situation). Results. Given our study design and exposure and outcome definitions, healthy hire bias, reproductively unhealthy worker effect, and desperation/privilege effect created open backdoor paths (confounding) between occupational exposure and outcome that can be closed by conditioning on measured confounders. Insecure pregnancy effect was most easily addressed by limiting the study to first pregnancies. Existence of healthy worker survivor bias depended on study design and definitions of exposure and outcome. Conclusions. The occurrence of healthy worker biases in studies of occupational exposures and pregnancy outcomes depends on characteristics of the study. Many of these biases have the structure of open backdoor paths and can be addressed analytically using standard techniques such as restriction or regression modeling.

VALIDATION OF MATERNAL RECALL OF EARLY PREGNANCY MEDICATION EXPOSURE USING PROSPECTIVE DIARY DATA

Alexandra Sundermann, Katherine Hartmann, Sarah Jones, Eric Torstenson, Digna Velez Edwards

Data about the accuracy of maternal recall for classifying early pregnancy medication exposure is meager. Nonetheless, we often use this approach in cohorts to evaluate the impact of pharmaceuticals on the developing fetus. We examined nonsteroidal anti-inflammatory drugs (NSAIDs) as an example of a drug type that is difficult to study due to intermittent and primarily over-the-counter use and underrepresentation in medical and pharmaceutical records. This validation study evaluated a subset of 256 women from the Right From The Start study (2000–2012), a prospective pregnancy cohort, who participated in daily medication diaries initiated prior to conception. Maternal recall of NSAID and selective serotonin reuptake inhibitor (SSRIs) use in early pregnancy was examined by comparing prospectively collected diary data (gold standard) to first trimester interview. SSRIs were evaluated in order to have a prescription medication comparator. Sensitivity, specificity, percent agreement, and kappa statistic were calculated to quantify recall validity. Sensitivity and specificity for recall of NSAID exposure were 81.6% and 63.3%, respectively (kappa statistic: 0.46), with 74.6% agreement for exposure classification. Sensitivity and specificity for recall of SSRI exposure were 73.3% and 99.2%, respectively (kappa statistic: 0.77), with 97.7% agreement. Our findings suggest the validity of maternal recall varies with medication type and prospective data collection should be prioritized when studying early pregnancy drug exposures.

PRE-PREGNANCY BODY MASS INDEX AND GESTATIONAL WEIGHT GAIN: HOW WELL DO DATA FROM THE PREGNANCY RISK ASSESSMENT MONITORING SYSTEM AND BIRTH CERTIFICATE AGREE WITH THE MEDICAL RECORD?

Nicholas Deputy, Andrea Sharma, Jennifer Bombard, Timothy Lash, Usha Ramakrishnan, Laura Schieve, Aryeh Stein, Michael Nyland-Funke

Prepregnancy body mass index (BMI) and gestational weight gain (GWG) are important determinants of maternal and infant health. The Pregnancy Risk Assessment Monitoring System (PRAMS) and 2003 revised birth certificate (BC) are valuable data sources to study BMI and GWG, but few studies have assessed data validity and how maternal characteristics influence validity. We compared anthropometric data used to calculate BMI or GWG from PRAMS (height, prepregnancy weight) and BC (height, prepregnancy weight, delivery weight) to medical record (MR) for 1,267 New York City and Vermont PRAMS respondents in 2009. We calculated mean difference (PRAMS or BC minus MR) and agreement (within ± 1 or ± 5 units) between sources, overall and by maternal characteristics. We categorized BMI and GWG per World Health Organization and Institute of Medicine guidelines, respectively; agreement in BMI and GWG categories by PRAMS or BC compared to MR was evaluated using kappa statistic (κ). Height from PRAMS or BC was within ± 1 inch of MR for 87% and 89% of records, respectively. Compared to MR, PRAMS underestimated prepregnancy weight by 0.6 pounds (lbs) (standard error (SE) 1.1) while BC overestimated by 1.1 lbs (SE 1.0); notably, BMI category influenced over/underestimation. Prepregnancy weight from PRAMS or BC was within ± 5 lbs of MR for 70% and 76% of records, respectively. Compared to MR, there was substantial agreement in BMI category by PRAMS ($\kappa=0.77$) and BC ($\kappa=0.79$). Delivery weight from BC was underestimated by 1.6 lbs (SE 0.9) and was influenced by BMI category; delivery weight was within ± 5 lbs of MR for 80% of records. For full-term, singleton deliveries, compared to MR, there was moderate agreement ($\kappa=0.53$) in GWG category by BC. Error in weight data and misclassification of BMI and GWG categories may introduce bias into studies using PRAMS and BC data; notably, error may differ by maternal characteristics. Studies should examine how misclassification influences associations of interest.

USING INSURANCE CLAIMS DATA TO IDENTIFY AND ESTIMATE CRITICAL PERIODS IN PREGNANCY

Elizabeth Ailes, Regina Simeone, Emily Petersen, April Dawson, Suzanne Gilboa

Health insurance claims are a rich data source to examine medication use in pregnancy. However, identifying, and estimating the duration of, pregnancies in such data are difficult. Our objective was to identify pregnant women, their pregnancy outcomes, and date of their last menstrual period (LMP), to ultimately use in analyses of medication use at critical periods in pregnancy. We analyzed Truven Health MarketScan® Commercial Claims and Encounters Databases from 2008–2013. We included women 15–44 years of age with > 11 months of enrollment per year on a health insurance plan that covered prescription drugs. From a literature search, we identified diagnosis and procedure codes indicating the end of a pregnancy. We identified all inpatient admissions and outpatient service claims with these codes. We developed an algorithm to assign: 1) pregnancy outcome (ectopic pregnancy, induced or spontaneous abortion, livebirth, or stillbirth), and 2) gestational age, to each inpatient or outpatient visit. We estimated the LMP as the admission (for inpatient visits) or service (for outpatient visits) date minus the gestational age. To identify pregnancies with any exposure in a given calendar year, we included pregnancies ending in the subsequent year, then restricted to pregnancies with an LMP or end date in a given year. To differentiate visits associated with separate pregnancies, we required > 2 months between one pregnancy's end and the LMP of the next pregnancy. From 2008–2012, our study sample included an average of 5.8 million women of reproductive age per year. We identified an average of 548,000 pregnancies per year (range: 447,459 in 2008 to 629,239 in 2011), of which 81% resulted in a livebirth. Most women with pregnancies had only one pregnancy in the year (96%; range: 1–4 pregnancies in one year). This work will inform future efforts to identify medication use during critical periods of pregnancy and preconception using health insurance claims data.

RACIAL DIFFERENCES IN SEASONAL PATTERNS OF VITAMIN D AMONG PREGNANT WOMEN IN DURHAM, NORTH CAROLINA

Devika Chawla, Jessie Buckley, Bernard Fuemmeler, Sara Benjamin Neelon, Susan Murphy, Cathrine Hoyos, Julie Daniels

Recent research suggests that insufficient vitamin D during pregnancy increases risk of adverse pregnancy outcomes. Black women have lower 25 (OH)D concentrations during their pregnancy compared to White and Hispanic women. Although strong seasonal patterns of vitamin D levels have been established, seasonality of vitamin D is often assumed to be similar across race. To test this assumption, we examined seasonal variability in plasma 25(OH)D concentrations at first prenatal visit among 520 pregnant women from 2009 to 2012 in the Newborn Epigenetic Study (NEST), a racially-diverse pregnancy cohort in Durham, North Carolina. We explored the seasonal pattern by comparing the difference in mean summer (June–August) and mean winter (December–February) 25(OH)D concentrations between Black, Hispanic, and White women using t-tests. Overall mean 25 (OH)D concentrations were significantly higher among White (51.1 nmol/L, $p<0.0001$) and Hispanic (41.8 nmol/L, $p<0.0001$) women compared to Black (mean = 33.4 nmol/L) women. The mean summer-winter differences were 12.7, 14.2, and 10.2 nmol/L for White, Hispanic, and Black women, respectively. These summer-winter differences in vitamin D levels were moderately greater for White ($t=1.41$, $p=0.080$) and significantly greater for Hispanic ($t=2.45$, $p=0.007$) women compared to Black women. Despite greater seasonal variability among White and Hispanic women, the lowest absolute mean 25(OH)D concentrations were observed among Black women during the winter months. Further work will characterize the seasonal pattern (e.g. amplitude, period, phase shift) of vitamin D by race and other covariates (prenatal vitamin use, vitamin D supplement use, maternal age, pre-pregnancy BMI). Since most etiologic vitamin D research uses a single-sample biomarker, this work will inform racial differences in exposure misclassification. Additionally, this work may assist clinicians in identifying high-risk populations for vitamin D deficiency during pregnancy.

PA097

SIBLING ANALYSES OF THE ASSOCIATION BETWEEN FEVER AND COMMON INFECTIONS IN PREGNANCY AND ACADEMIC PERFORMANCE IN THE OFFSPRING

Julie Dreier, Gabriele Berg-Beckhoff, Per Kragh Andersen, Anne-Marie Nybo Andersen

Background Impaired academic performance in children has been linked to prenatal exposure to fever and infections, but sufficient adjustment for important genetic-, environmental and social influences can be challenging. To reduce confounding we compared exposure discordant siblings in order to assess the impact of these prenatal exposures on academic performance in the child. **Methods** This study was based on pairs of siblings born during 1997-2003 within the Danish National Birth Cohort. Maternal exposure to fever and common infections was prospectively assessed in two pregnancy interviews. Assessments of academic performance (Rasch scores) from the Danish National Tests were retrieved through linkage with the child's civil registration number for the years 2010-2013. Pairs of siblings where 3rd grade mathematics assessments (n pairs=1222) and 4th grade linguistic performance (n pairs=2781) were available for both children, were included in the analyses. Paired t-tests were used to estimate mean (μ) differences in average test scores in exposure discordant siblings. **Results** Prenatal fever and infection exposure were reported in 27.8% and 60.1% of pregnancies in the overall cohort. The sibling comparisons revealed no differences in academic performance according to prenatal fever exposure in neither language assessments (-0.06, 95% confidence interval (CI): -0.13; 0.01) nor mathematic assessments (0.08, 95% -0.03; 0.19). Similar findings were observed for prenatal exposure to any infections (language: 0.04, 95% CI: -0.03; 0.11 and mathematics: 0.03, 95% CI: -0.07; 0.12). When specific infections, such as genitourinary infections, diarrhea and prolonged cough were considered separately the findings were essentially the same. **Conclusions** Academic performance was not affected by prenatal exposure to fever nor common infections when shared familial confounders were effectively adjusted for in analyses of exposure discordant siblings.

PA099

HERPES SIMPLEX VIRUS-2 SEROPREVALENCE AND ULTRASOUND DIAGNOSED UTERINE FIBROIDS IN A LARGE POPULATION OF YOUNG AFRICAN-AMERICAN WOMEN

Kristen Moore

For decades reproductive tract infections (RTI) have been hypothesized to play a role in uterine fibroid development. The few previous studies conducted used self-reported RTI history and had inconsistent findings. We investigated this hypothesis further using serology, a immunological measure of past exposure. We focused on herpes simplex virus type 2 (HSV-2) because prior published data have suggested a possible association, and serology for HSV-2 is much more sensitive than self-report. We used cross-sectional enrollment data from African- American women ages 23-34 who were screened for fibroids with a standardized ultrasound examination at their enrollment into a prospective study of fibroid incidence and growth (recruitment 2010-2012). Age- and multivariable-adjusted logistic regression were used to estimate odds ratios (ORs). Of 1,696 participants, 1,658 had blood drawn and HSV-2 serology results; 22% had fibroids. There was no significant association between HSV-2 seropositivity and fibroid presence (multivariable- adjusted OR: 0.94 95% confidence interval: 0.73, 1.20); nor were there any associations with size of largest fibroid, number of fibroids, or total fibroid volume. Our data provide no evidence for the influence of HSV-2 exposure on fibroid risk in young African-American women. Further study of other serologically measured RTIs is warranted.

PA098

RECALL OF EXPOSURES DURING EARLY PREGNANCY

Helen Chin, Donna Baird, D. Robert McConaughy, Anne Marie Jukic

Studies of exposures during pregnancy often rely on participant recall; but data on long-term recall are limited. We used data from the North Carolina Early Pregnancy Study (1982-86) to examine the consistency between prospectively collected and retrospectively reported exposures. Women who conceived reported their weekly intake of alcoholic (beer, wine, liquor) and caffeinated (coffee, tea, and soda) beverages, and their use of vitamins over the first 8 weeks of gestation (gold standard). Women were asked to recall these same exposures on a follow-up questionnaire 25 years later (2010-11). They were also asked to indicate how sure they were of their responses (4-level scale from unsure to quite sure). This analysis was limited to women whose pregnancies resulted in a live birth and who participated in the follow-up study (n=109). Of the 52 women who reported drinking coffee (the most frequent caffeinated drink) and 56 women who reported not drinking coffee at follow-up, the overall accuracy of recall was 70% (positive predictive value (PPV): 0.65, negative predictive value (NPV): 0.75). The overall accuracy of recall for drinking wine (the most frequent alcoholic drink) was 67% among the 24 women who reported drinking wine and the 84 women who reported abstaining at follow-up (PPV: 0.38, NPV: 0.75). Of the 85 women who reported taking vitamins and the 22 women who reported not taking vitamins at follow-up, the overall accuracy of recall was 65% (PPV: 0.73, NPV: 0.36). At follow-up, women who were more sure (codes 3 or 4 vs. codes 1 or 2) were not more accurate in their recall of coffee, wine, or vitamin use than women who were less sure of their responses. Long-term recall of early pregnancy exposures is difficult, even for actively engaged participants; self-perceived "sureness" is not predictive of accuracy.

PA100

DEMOGRAPHIC AND SCREENING CHARACTERISTICS OF GESTATIONAL CARRIERS AND TRADITIONAL SURROGATES IN THE UNITED STATES

Erika Fuchs, Abbey Berenson

Introduction: Guidelines for the use of gestational carriers (GC), intended to protect GC and the intended rent(s), were first published in 2012 by the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. Whether these screening recommendations are being implemented in practice and whether they are also being implemented for traditional surrogates (TS), despite a lack of guidelines for the use of TS, has not been reported. **Methods:** Women ≥ 18 years of age who delivered a baby after 2008 as a result of a GC or TS arrangement were invited to complete a brief online survey on health and screening behaviors related to their most recent GC or TS arrangement and their demographic characteristics. From November 2015-January 2016, the study was advertised in relevant online groups and through email listservs. Of 230 eligible respondents, 209 complete surveys were included in these analyses. Differences between GC and TS were examined using chi-squared and Fisher's exact tests and t-tests in Stata SE Version 14.1 with $\alpha=0.05$. **Results:** More respondents were GC (92%) than TS (8%). GC were older (33.2 vs. 29.6 years), less likely to be students (13.6% vs. 47.1%), and more likely to have private health insurance (89.5% vs. 70.6%) than TSs, but there were no differences on other demographic measures. There was no difference in number of previous births, but GC were less likely than TS to have had more than 3 previous cesarean sections (1.1% vs. 17.7%). GC were more likely than TS to have received a complete medical evaluation (96.9% vs. 70.6%), to have met with a mental health professional (92.6% vs. 70.6%), and to feel they had adequate information about risks (69.1% vs. 35.3%). **Discussion:** This study provides preliminary evidence that guidelines for GC are being implemented. Differences in characteristics between GC and TS warrant further investigation. Professional organizations may consider providing guidance on the use of TS.

U.S. TRENDS AND PREDICTORS OF LONGER LENGTH OF STAY OF POSTPARTUM HOSPITALIZATIONS, 1998-2013

Jonetta Johnson, Elena Kuklina

Background: U.S. rates of complications during delivery hospitalizations have increased during last two decades. Limited information is available on rates of hospitalizations during the postpartum period. The objectives of this study were to identify leading causes and describe trends for these hospitalizations and examine predictors of longer length of stay (LOS) during them. **Methods:** We used the 1998-2013 Nationwide Inpatient Sample and International Classification of Diseases, 9th Revision codes to identify 998,705 postpartum hospitalizations and their primary diagnosis. We estimated prevalence, rates per 10,000 delivery hospitalizations and trends overall and for the leading causes of postpartum hospitalizations. We used multinomial logistic regression to examine associations between the leading causes of postpartum hospitalizations and LOS (≥ 4 , 3 or 2 days versus 1 day). We used SUDAAN software to account for the complex sampling design and sample weights to provide population-based estimates. **Results:** From 1998-2013, overall postpartum hospitalizations increased 71%. For the 2012-13 period, the leading causes of postpartum hospitalizations were 19.9% for infection, 14.7% for hypertensive disorders and 5.2% for mental disorders. These estimates increased 51%, 93% and 73%, respectively, compared with the 1998-99 period. In models stratified by leading causes and adjusted for age, race, insurance type and hospital characteristics, postpartum hospitalizations for infections and mental disorders were more likely to have a LOS ≥ 4 and 3 days versus 1 day. Black compared with white women and women with Medicaid compared to those with private insurance were more likely to have a LOS ≥ 4 versus 1 day whereas women in the Midwest and West compared to women in the Northeast were less likely to have LOS ≥ 4 versus 1 day. **Conclusion:** Our findings show an increasing trend in postpartum hospitalizations and disparities in LOS by socio-demographic and geographic indicators.

MEDIATION ANALYSIS OF THE ASSOCIATION BETWEEN LABOR INDUCTION AND CESAREAN DELIVERY: FINDINGS FROM THE FIRST BABY STUDY

Kristen Kjerulff

Studies comparing women whose labor is induced to those who begin labor spontaneously report higher cesarean delivery rates among those who are induced, with generally around double the risk of cesarean delivery among women who are induced. What remains unclear is the extent to which this increased risk is attributable to maternal characteristics and indications for labor induction, or to labor-related factors that occur more commonly in association with or after labor induction. Using data from a prospective cohort study of 2,851 nulliparous women with singleton pregnancies attempting vaginal delivery, we evaluated whether increased risk of cesarean delivery after labor induction in comparison to spontaneous labor is explained primarily by maternal characteristics, indications for labor induction or labor-related factors. Multivariate logistic regression and mediation models were used in analyses. More than a third were induced (34.3%) and 24.8% delivered by cesarean. Induced women were more likely to deliver by cesarean (35.9%) than those in spontaneous labor (18.9%), (odds ratio (OR) = 2.35, 95% confidence interval (CI) 1.97-2.79, $p < .0001$) and more than half of those induced at 0 centimeters dilation (53.9%) delivered by cesarean. Adjustment for maternal characteristics and indications for labor induction reduced this OR to 1.74 (95% CI 1.42-2.14, $p < .0001$), and additional adjustment for labor-related factors reduced it to 1.08 (0.82-1.41). The increased risk of cesarean delivery after labor induction was mediated mainly by labor-related factors - including lower cervical dilation among induced women and higher rates of dysfunctional labor, dystocia, fetal intolerance of labor, use of epidural analgesia and maternal request of cesarean during labor. Nulliparous women who are induced are more likely to deliver by cesarean than those who begin labor spontaneously, primarily due to labor-related factors that are associated with or follow labor induction.

SOURCES OF INFLUENCE ON PREGNANT WOMEN'S PREFERRED MODE OF DELIVERY

Melissa Amyx, Xu Xiong, Luz Gibbons, Pierre Buekens

Background: Understanding influences on preferred delivery mode is vital for planning interventions to reduce cesarean section (CS) rates and for ensuring that women receive factual information. Our objective is to determine if sources of information (people or media) influencing a pregnant woman's preferred delivery mode or if knowledge of CS indications differ by hospital type or sources of influence. **Methods:** A secondary analysis of the Women's Preference for Delivery Mode in Argentina Study was conducted. Nulliparous women aged 18-35, >32 weeks gestation with live, singleton pregnancies were included, while women with an indication for CS, pre-existing disease/pregnancy complications, or use of assisted reproductive technology were excluded. Proportion of women indicating sources influencing preferred delivery mode was determined by hospital type (private [PV] vs public [P]). Knowledge of evidence-based absolute indications for CS was presented by sector and by influence level of sources, stratified by hospital type. **Results:** 382 (183 PV, 199 PB) pregnant women participated. PV women's delivery preferences were less influenced by people (mothers, mother-in-laws, other family, friends; $p < 0.05$); women were more likely to not have/use internet, TV/movies, prenatal classes, magazines, and books ($p < 0.05$). PV women had greater knowledge (20.8% excellent) compared to women (7.5%; $p < 0.0001$). PV women influenced by books very much/a lot were less likely to have poor knowledge (5.0%) compared to women influenced a little/not at all (16.3%) or who do not have/use (37.5%; $p < 0.05$); women influenced by the internet very much/a lot were less likely to have poor knowledge (18.4%) compared to women influenced little/not at all (26.9%) or who don't use (40.5%; $p < 0.05$). **Conclusion:** Compared to women, PV women's (of higher socioeconomic status) preferences are less influenced by people but more influenced by media; PV women are more knowledgeable of CS indications.

CESAREAN DELIVERY AT FIRST CHILDBIRTH AND SUBSEQUENT FERTILITY: A 36 MONTH PROSPECTIVE COHORT STUDY

Kristen Kjerulff

Over the past two decades studies conducted in countries around the world have reported lower fertility rates subsequent to cesarean delivery. However, none of the prior studies prospectively interviewed women to determine if this lower rate of subsequent fertility was voluntary or due to decreased likelihood of conceiving subsequent pregnancies and/or increased rate of pregnancy loss. In the First Baby Study (FBS), 3,006 women aged 18 to 36 were enrolled and delivered their first child at hospitals throughout Pennsylvania in 2009 to 2011. Participants were surveyed during their third trimester and then at 1, 6, 12, 18, 24, 30 and 36 months postpartum. Twenty percent of the participants dropped out of the study over the course of the 36 month follow-up period, leaving 2,423 women who completed the 36 month survey, constituting the study cohort. Among those whose first childbirth was vaginal, 43.8% had a subsequent live birth, and among those whose first delivery was cesarean 37.1% did ($p = .002$). The odds ratio (OR) for cesarean versus vaginal of not having a subsequent birth was 1.32 (95% confidence interval (CI): 1.11-1.59). After adjustment for maternal age, education, race/ethnicity, marital status, first birth pregnancy intendedness, pre-pregnancy body mass index, health insurance and pre-first childbirth fertility treatment, the OR was 1.28 (95% CI: 1.06-1.55). Women whose first delivery was by cesarean were equally likely to try to conceive a second child during the follow-up period (54.9%), as those whose first delivery was vaginal (55.2%) ($p = .93$), but were less likely to conceive while trying to conceive (cesarean = 80.9%, vaginal = 88.0%, $p < .0001$) and while not trying to conceive (cesarean = 28.2%, vaginal = 35.0%, $p < .0001$). There were no differences in pregnancy loss. In conclusion, first childbirth by cesarean section increases the risk that a woman will have difficulty conceiving a subsequent pregnancy, but not of pregnancy loss.

A COMPARISON OF FOUR METHODS TO ASSESS THE RELATION BETWEEN GESTATIONAL WEIGHT GAIN AND STILLBIRTH: FINDINGS FROM THE STILLBIRTH COLLABORATIVE RESEARCH NETWORK

Cassandra Gibbs Pickens, Carol Hogue, Penny Howards, Michael Kramer

Gestational weight gain (GWG) may be a modifiable risk factor for stillbirth (fetal death ≥ 20 weeks gestation), but it is difficult to evaluate since it is highly correlated with gestational age at delivery (GA), a potential confounder. Several methods of accounting for GA have been proposed. We used these methods to examine the association of GWG with stillbirth, while considering prepregnancy body mass index (BMI). The Stillbirth Collaborative Research Network is a population-based case-control study that obtained data via medical record abstraction and maternal interview. After excluding those with preexisting diabetes, multiple gestations, GA < 20 weeks, BMI < 18.5 , or missing data, 426 stillbirths and 1459 live births remained. In logistic regression models, we examined the association of GWG with stillbirth using 4 variables: total GWG; net GWG (GWG—infant birthweight); GA-specific GWG z-score; and weekly rate of GWG in the 2nd/3rd trimesters ($[\text{GWG} - \text{estimated 1st-trimester GWG}] / [\text{GA} - 13 \text{ weeks}]$). For total GWG, net GWG, and GWG rate, we included linear and quadratic terms. For GWG z-score, we fit a restricted cubic spline with knots at the 5th, 50th, and 95th percentiles. All models were adjusted for prepregnancy BMI and confounders. Models with total and net GWG were also adjusted for GA. Results for total and net GWG were null (e.g., adjusted odds ratio [aOR] and 95% Confidence Interval [CI] for the 10th v. 50th percentile = 1.2 [0.9, 1.5] for total GWG and 1.1 [0.9, 1.4] for net GWG). However, low GWG z-score and low GWG rate had an increased odds of stillbirth (e.g., aOR [95% CI] for 10th v. 50th percentile = 1.5 [1.3, 1.7] for GWG z-score and 1.6 [1.4, 1.9] for GWG rate). Results differed slightly by BMI. Low GWG may be associated with increased stillbirth risk if GWG measures that account for GA (z-score, rate) better reflect the impact of GWG than measures that adjust for GA (total, net GWG). However, the source of the discrepancies requires further evaluation.

ENDOMETRIOSIS AND ADVERSE PREGNANCY OUTCOME: A DANISH COHORT STUDY

Maria Tølbøll Glavind, Tine Brink Henriksen, Axel Forman, Linn Håkonson Arendt

Background: Endometriosis is a chronic gynecological disease of the reproductive age, characterized by pelvic pain and infertility. Recent research has associated endometriosis with adverse pregnancy outcome, however this topic is still controversial, and results remain inconclusive. Thus, we aimed to investigate the association between endometriosis and the risk of pre-eclampsia, caesarean section, postpartum haemorrhage, preterm birth, and small for gestational age (SGA), in a large Danish birth cohort, while taking assisted reproductive treatment (ART) into account. **Materials and Methods:** We performed a population-based study using data from the Aarhus Birth Cohort (ABC) between 1989-2013, including 82,793 singleton pregnancies. We identified women with a diagnosis of endometriosis in the Danish National Patient Registry, and in the Danish National Pathology Registry and Data Bank. Further information was obtained by linkage to the Danish Medical Birth Registry, and the Danish ART-Registry. Data was analysed using logistic regression, with results presented as crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs). Potential confounders, was identified using directed acyclic graphs (DAGs), and missing data was addressed by use of multiple imputation. **Results:** During the study period 1,213 women from the ABC were diagnosed with endometriosis, and a total of 1719 singleton births was recorded among these women. Endometriosis was associated with an increased risk of preterm birth (aOR = 1.67 95% CI, 1.37-2.05). Compared with unaffected women, women with endometriosis also had an increased risk of pre-eclampsia (aOR = 1.37 95% CI, 1.06-1.77) and caesarean section (aOR = 1.83 95% CI, 1.60-2.09). ART did not explain these findings. No association was found between postpartum haemorrhage or SGA, and endometriosis. **Conclusions:** Women with endometriosis were at increased risk of preterm birth, pre-eclampsia and caesarean section, irrespective of use of ART.

TERM ELECTIVE INDUCTION OF LABOR VERSUS EXPECTANT MANAGEMENT TO REDUCE RISK OF CESAREAN SECTION AMONG OBESE WOMEN

Cassandra Gibbs Pickens, Carol Hogue

The optimal time and method of delivery for obese women (pregnancy body mass index [BMI] $\geq 30 \text{ kg/m}^2$) is unknown. Labor induction to prompt early delivery may prevent cesarean section (CS) and other complications that arise late in gestation, including fetal demise. We examined, at each week of pregnancy from 37 to 40 weeks gestation, whether elective induction of labor (eIOL; induction with none of the conditions that may justify delivery < 39 weeks, as defined by the Joint Commission) or expectant management (delivery by any method, including IOL, in later weeks) resulted in lower risks of CS among obese women. Linked vital records and hospital discharge data for all California deliveries from 2007-2011 yielded 231,586 pregnancies after excluding those with multiple gestations, non-vertex presentation, previous CS, gestational age (GA) < 37 or > 42 weeks, chronic disease, gestational diabetes, or fetal anomalies. With a se rate Robust Poisson regression model for each GA-specific comparison, we calculated conditional risk ratios (RRs) comparing eIOL in each week of gestation to expectant management, stratifying by parity and obesity class (1-3) and adjusting for maternal age, race/ethnicity, education, insurance, trimester of prenatal care initiation, and birth year. Elective IOL reduced the risk of CS by a factor of 0.5 to 0.8 compared to expectant management (e.g., adjusted RR [aRR] and 95% Confidence Interval [CI] for eIOL at 38 weeks vs. expectant management = 0.7 [0.7, 0.8] among class 1 obese nulliparas). Associations were stronger in multiparas than in nulliparas (e.g., among class 3 obese women, aRR [95% CI] for eIOL at 40 weeks vs. expectant management = 0.5 [0.4, 0.6] in multiparas and 0.7 [0.7, 0.8] in nulliparas). There were no clear trends by GA or BMI. Elective IOL between 37 and 40 weeks, compared to expectant management, decreases the risk of CS in obese women. Infant outcomes should be examined before a randomized controlled trial is recommended.

ANALYSIS OF BIRTHS AT HOME IN ENGLAND AND WALES BY TIME OF DAY AND DAY OF THE WEEK USING LINKED ADMINISTRATIVE DATA

Niru Dattani

Background Clinical policies from the 1970s onwards in England and Wales have aimed at intervening to increase the extent to which births occur during working hours on weekdays in the belief that this is safer for mothers and babies. In parallel with this, the proportion of births at home fell to under one per cent in the late 1980s before starting to rise again. This has led to questions about the timing of spontaneous birth and its relation to planning of services. **Methods** The timing of home and hospital births was compared as part of a larger series of data linkage studies in which birth data from civil registration in England and Wales were linked to data recorded when a National Health Service (NHS) Number, a unique identifier, is allocated to newborn babies. These data have been routinely linked and are available from 2005. Day of the week was derived from the baby's date of birth and home and hospital births were identified using place of birth recorded at civil registration. Time of birth was taken from the NHS Numbers for Babies dataset. Data about births from 2005 to 2012 were analysed in the secure facilities Virtual Micro-Data Laboratory (VML) at the Office for National Statistics. **Results** Numbers of births at home varied by time of day and numbers of births per hour were higher during the night, both for term and preterm babies. In contrast, births in hospital, which account for the majority of births in England and Wales, were concentrated onto weekdays. **Discussion** Further linkage currently underway to data about care at delivery will enable analysis of the contribution of obstetric intervention to the timing of births in hospital. Our analysis will also inform the National Health Service in the planning of the midwifery and obstetrics staffing levels by time of day.

NEONATAL AND MATERNAL OUTCOMES FOLLOWING MID-PELVIC OPERATIVE VAGINAL DELIVERY

Giulia Muraca, Yasser Sabr, Rollin Brant, Geoffrey Cundiff, KS Joseph

OBJECTIVE: To quantify differences in neonatal and maternal morbidity and mortality associated with midpelvic operative vaginal delivery (OVD), compared with cesarean delivery in labour. **METHODS:** All singleton, term deliveries in Canada (excluding Quebec) from 2003 to 2013 following midpelvic OVD or cesarean delivery in labour were included, with data obtained from the Canadian Institutes for Health Information. The primary outcomes included composite neonatal morbidity/ mortality (stillbirth, neonatal death, intubation, convulsions, severe birth trauma) and composite maternal morbidity/mortality (death, severe postpartum hemorrhage, sepsis, shock, cardiac complications, acute renal failure, obstetric embolism, evacuation of incisional hematoma). Logistic regression was used to obtain adjusted odds ratios (AOR) and 95% confidence intervals (CI). **RESULTS:** The study included 203,287 deliveries. The composite neonatal and maternal outcome rates were 1.3% and 1.4%, respectively. Among infants born following OVD for dystocia, neonatal outcome rates were increased with midpelvic forceps (AOR 2.81, 95% CI 2.26, 3.49), midpelvic vacuum (AOR 3.04, 95% CI 2.37, 3.90), and sequential instrument use (AOR 4.61, 95% CI 3.16, 6.72) when compared with cesarean delivery. When OVD was indicated for fetal distress, neonatal outcome rates following midpelvic forceps (AOR 1.31, 95% CI 1.15, 1.49) and sequential midpelvic OVD (AOR 2.26, 95% CI 1.79, 2.85) were increased compared with cesarean delivery. Maternal outcome rates were increased following midpelvic forceps (AOR 1.19, 95% CI 1.06, 1.32) and sequential OVD (AOR 1.27, 95% CI 1.01, 1.61) but decreased following midpelvic vacuum (AOR 0.63, 95% CI 0.55, 0.73) compared with cesarean delivery. **CONCLUSION:** In singleton, term deliveries, midpelvic OVD is associated with an increase in severe neonatal morbidity/mortality, while maternal morbidity/mortality is increased with midpelvic forceps use compared with cesarean delivery.

DIFFERENTIAL RATES OF UNPLANNED POST-PARTUM Hysterectomy BY INTENTIONS OF PREGNANCY AT CONCEPTION

Dongmei Li, Margaret Demment, Christopher Glantz, Martha Wojtowycz, James Shelton, Jamie Gifford, Scott Dexter, Timothy Dye

Background: Hysterectomy is a common procedure in reproductive-age women. Clinicians increasingly attempt alternative strategies for treatment of underlying conditions before attempting a hysterectomy, though how treatment varies by the woman's intentions of having been pregnant is unclear. **Methods:** Upstate NY's Perinatal Data System from the Albany, Syracuse, Rochester, and Buffalo regions (n = 696,498) from 2004 – 2014 was used to examine associations between intention of pregnancy (unwanted (UW) vs. intended (INT)), age, ethnicity, risks during pregnancy (smoking, gestational weight gain (GWG) less than recommendation), and unplanned hysterectomy (UH) post-partum. Adjusted associations between intention of pregnancy, demographics, pregnancy risk, and UH were examined using logistic regression (SAS v9.4). Pathway analysis using maximum likelihood estimation methods with Monte Carlo integration (Mplus version 7.3) tested associations between UW and UH. **Results:** 5.5% of women (n = 38,452) reported their pregnancy was UW. UW, older age, Hispanic ethnicity, smoking during pregnancy, and inadequate gestational weight gain were significantly related (>0.05) to having UH. Significant direct associations with UH were observed for unwanted pregnancy (aOR:1.48; 95% CI, 1.08 to 2.03), older age (aOR: 1.14; 1.12-1.16), smoking during pregnancy (aOR: 1.78; 1.42 -2.24), Hispanic ethnicity (aOR:1.51; 1.07-2.13), and inadequate GWG (aOR:1.53; 95% CI, 1.21 to 1.93). UW had an additional indirect effect on UH through significant effects on smoking during pregnancy (aOR:3.36; 3.29 -3.43) and inadequate GWG (aOR: 2.02; 1.97-2.06). **Conclusions:** After adjusting for confounders, UW was significantly related to UH. That said, given that the overall hysterectomy rate for UW more closely approximates national population-based rates, it may be that practitioners focus more aggressively on uterus-preserving procedures post-partum with INT compared with UW, reflected in an atypically low UH rate among INT.

TEMPORAL AND REGIONAL VARIATION IN OPERATIVE VAGINAL DELIVERY BY PELVIC STATION, CANADA, 2004-2013

Giulia Muraca, Yasser Sabr, Rollin Brant, Geoffrey Cundiff, KS Joseph

INTRODUCTION: Understanding the widespread decline in operative vaginal delivery (OVD) is hindered by a lack of information on pelvic station, as rates of severe neonatal and maternal morbidity vary by pelvic station. We sought to describe temporal and regional variation in the use of OVDs by pelvic station among full term singletons. **METHODS:** OVD rates were estimated using information from the Discharge Abstract Database of the Canadian Institute for Health Information between 2004 and 2013 (n=2,284,109). OVDs were stratified by pelvic station and rotation of the fetal head. Temporal trends were assessed using the Cochran-Armitage test for linear trend in proportions by year. Geographic variation was assessed by calculating the rate and 95% confidence interval (CI) of each mode of delivery by province for the period 2010-13. **RESULTS:** The OVD rate decreased from 14.6% in 2004 to 13.9% in 2013 (P<0.0001). Forceps deliveries decreased from 3.1% to 2.5%, primarily due to decreases in midpelvic forceps delivery (28.9% decrease, P<0.0001). Overall vacuum delivery rates decreased by 4.0% (P=0.006); however, vacuum deliveries increased at outlet and low pelvic stations (26.0% and 15.1% increase, respectively) and remained stable at midpelvic station. Rates of sequential instrument use decreased over the study period (P<0.0001). Failed OVD rates were high (3.4% of all deliveries) and increased by 17.6% (P<0.0001). OVD rates varied widely by province. **CONCLUSION:** Temporal trends in OVD rates varied by pelvic station, with outlet, low and failed OVDs increasing and midpelvic OVD decreasing significantly, chiefly due to a decline in midpelvic forceps use. Vacuum extraction is increasingly replacing forceps deliveries at outlet and low fetal stations, while caesarean deliveries are replacing forceps deliveries at midpelvic stations. Wide variations in OVD rates across provinces suggest differences in instrument preference and/or an evolution in standards of practice.

DIAGNOSTIC THRESHOLDS FOR GESTATIONAL DIABETES AND CHILDHOOD OVERWEIGHT AND OBESITY

Samantha Ehrlich

The International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommends lower diagnostic thresholds for gestational diabetes based on associations with delivering a large for gestational age neonate (Diabetes Care 2010;33:676-82). However, the thresholds at which risk of childhood obesity increases remains unclear. This cohort study, conducted among 45,872 mother-child pairs delivering at Kaiser Permanente Northern California in 1995-2004, used electronic health record data to estimate the associations of fasting, 1-hour and 2-hour glucose thresholds for gestational diabetes with childhood overweight/obesity and obesity at 5-7 years of age for four mutually exclusive groups: 1) glucose below an IADPSG threshold (reference); 2) glucose meeting an IADSGG threshold but below a Carpenter and Coustan (CC) threshold; 3) glucose meeting a CC threshold but below a National Diabetes Data Group (NDDG) threshold; and 4) glucose meeting a NDDG threshold. During this time period, only women meeting the full NDDG criteria received a gestational diabetes diagnosis and treatment. Childhood overweight/obesity and obesity at 5-7 years of age were determined by the Centers for Disease Control and Prevention growth standards (i.e., ≥85th and ≥95th percentiles for age and sex, respectively). Logistic regression models were adjusted for maternal age, race-ethnicity, parity, education, and body mass index. Childhood overweight/obesity [Odds Ratio= 1.26 (95% Confidence Interval 1.03, 1.55)] and obesity [OR= 1.28 (1.02, 1.60)] were only associated with meeting the NDDG threshold for the fasting time point; similar findings were obtained when women with gestational diabetes by the full NDDG criteria were excluded. These results suggest that programming for childhood overweight/obesity and obesity only occurs with pregnancy fasting glucose ≥105 mg/dl, as previously recommended by the NDDG.

BREASTMILK FEEDING AND INFANT BODY COMPOSITION

Katherine Bell, Carol Wagner, Henry Feldman, Mandy Brown Belfort

Background: The extent to which breastmilk is protective against later life obesity is controversial. Differences in infant body composition may reflect future obesity risk. Our aim was to assess associations of breastmilk feeding with body composition at 6-7 months of age in healthy infants. **Methods:** We performed a secondary analysis of data from a previous study of maternal vitamin D supplementation during lactation. Mothers reported breastfeeding via monthly feeding diaries. At 6-7 months of age, participating infants underwent body composition measurement using dual-energy X-ray absorptiometry and research staff measured infant weight and length. We estimated associations of breastfeeding (any vs none) with infant body composition (fat mass, lean mass, total mass, body fat percentage) and z-scores for weight, length, and body mass index (BMI, kg/m²), adjusting in linear regression for sex, gestational age, birth weight z-score, race/ethnicity, maternal BMI, maternal education level, and insurance type. **Results:** Of 276 infants included in the analysis, 214 (78%) were breastfed (median duration, 7 months). Formula fed infants had lower birth weights (3249g vs 3455g, $p<0.01$) and birth weight z-scores (-0.22 vs 0.16, $p<0.01$) than breastfed infants, but at 6-7 months weight and BMI z-scores were substantially higher in formula fed infants (weight z-score 0.32 higher, 95% confidence interval [CI]: 0.02, 0.62; and BMI z-score 0.50 higher, 95% CI: 0.16, 0.84). Length z-score did not appear different (0.11, 95% CI: -0.17, 0.39). At 6-7 months of age, formula fed infants had 699g more lean mass (95% CI: 521g, 878g) and 3.5% lower body fat percent (95% CI: -5.6%, -1.3%). **Conclusions:** As compared with breastmilk feeding, formula feeding was associated with higher BMI and weight z-scores at 6-7 months of age but lower body fat percent. These differences may have implications for future obesity risk.

PLACENTAL 11 β -HSD2 AND CORD PLASMA CORTISOL LEVELS, METABOLIC AND CARDIOVASCULAR HEALTH INDICES IN INFANTS

Lu Chen

Objective: Glucocorticoids may be involved in fetal "programming" of cardiometabolic risk. Placental 11 β -hydroxysteroid dehydrogenase 2 (11 β -HSD2) can convert cortisol to cortisone to avoid fetal exposure to high cortisol levels. It is not known whether placenta 11 β -HSD2 and circulating cortisol levels are related to cardiometabolic health parameters in early life. We sought to address this question in infants at 1-year of age, and evaluate the influence of gestational diabetic mellitus (GDM). **Methods:** This was a prospective cohort study of 26 GDM and 249 non-diabetic singleton pregnant women and their infants. Maternal blood samples (24-28 and 32-35 weeks of gestation), umbilical cord blood, placenta tissues and infant blood samples (fasting at 1-year) were collected. Placenta 11 β -HSD2, maternal and cord plasma cortisol concentrations were measured. Outcomes included glucose metabolic health biomarkers at birth and 1-year of age, skinfold thickness, blood pressure and carotid intima-media thickness at 1-year. **Results:** Cord blood cortisol concentrations were significantly lower in gestational diabetic vs. non-diabetic pregnancies, while placenta 11 β -HSD2 levels were similar. However, there were no significant differences in all observed metabolic and cardiovascular outcomes among infants between GDM and non-diabetic groups. Maternal and cord blood cortisol levels were positively correlated ($r=0.17$ to 0.25). Cord blood cortisol levels were negatively correlated with IGF-1 levels ($r=-0.14$) and beta function indices at birth ($r=-0.30$, $p<0.0001$), and negatively correlated to skinfold thickness at 1y. Placental 11 β -HSD2 levels were negatively correlated with cord blood cortisol levels ($r=-0.14$, $p=0.03$), positively correlated with insulin sensitivity ($r=0.16$, $p=0.04$), borderline significantly negatively correlated with systolic blood pressure ($r=-0.16$, $p=0.057$), but uncorrelated to carotid intima-media thickness in infants at 1-y. **Conclusions:** There is some evidence suggesting that placenta 11 β -HSD2 and circulating cortisol levels may affect insulin sensitivity and beta cell function in early life.

LOW APGAR SCORE AND LONG TERM MORBIDITIES: A POPULATION BASED COHORT STUDY WITH UP TO 18 YEARS OF FOLLOW-UP

Tamar Wainstock, Asnat Walfisch, Ruslan Sergienko, Eyal Sheiner

Introduction: Apgar score is used world wide to measure newborn viability and vitality, and is a predictor of short term infant morbidity and mortality. We aimed to evaluate the association between low 5 minutes Apgar score and long term morbidity. **Methods:** A population based retrospective cohort study was conducted, including 250,828 singletons born between the years 1999-2013. Follow-up time was 10.24(mean) \pm 5.9 years (0- 18 years, median ~10.4). Exposure status was defined by 5 minutes Apgar of <7 (exposed) or ≥ 7 (unexposed). The outcome variables were offspring's hospitalizations due to cardiology, respiratory, urinary, hematology, neurology or endocrinology morbidities. Binary logistic general estimating equations were used to evaluate the association between the exposure and outcomes, adjusting for suspected confounders, specifically preterm birth. **Results:** The incidence density ratios for all hospitalization causes were higher among the exposed group (for Cardiology 0.2/1000 vs. 0.9/1000 person years [py], Relative Risk [RR]=3.86, 95%CI 3.12-4.61; Urinary 0.7/1000 vs. 1.7/1000 py, RR=2.53, 95%CI 1.98-3.07; Respiratory 5.8/1000 vs. 11.8/1000 py, RR=2.04, 95%CI 1.83-2.25; Hematology 1/1000 vs. 2.7/1000 py, RR=2.67, 95%CI 2.24-3.1; Endocrinology 0.4/1000 vs. 0.9/1000 py, RR=2.05, 95%CI 1.30-2.79; and Neurology 1/1000 vs. 3/1000 py, RR=3.09, 95%CI 2.68-3.5). After adjusting for preterm birth, maternal age, hypertension, ethnicity and follow-up time, low Apgar remained a risk factor for cardiology, hematology and neurology related hospitalizations (Adjusted Odds Ratios: 2.82 [95%CI 1.35-5.83]; 1.65 [95%CI 1.07-2.56]; 1.93 [95%CI 1.26-2.96], respectively). **Conclusions:** Low 5 minutes Apgar score was associated with cardiology, hematology and neurology related long term morbidities. Adjustment for preterm birth did not affect this association. Our results suggest Apgar score can be used as a possible risk factor for selected long term morbidities.

CARDIOMETABOLIC INDICATORS AT 7 YEARS OF AGE: DOES IT MAKE A DIFFERENCE TO BE A MULTIPLE? GENERATION XXI (G21) BIRTH COHORT STUDY

Maria João Fonseca, Milton Severo, Henrique Barros

Multiples differ from singletons in several characteristics at birth that could influence outcomes later in life. As there is much controversy regarding such effects, we evaluated a large number of cardiometabolic indicators in Porto (Portugal) G21 birth cohort at 7 years follow-up. Anthropometric measurements, body composition (bioelectrical impedance), and fasting blood samples were obtained. Age- and sex-specific z-scores were calculated. We studied 5431 children from singleton pregnancies, 196 twins and 12 triplets (70% participation). Linear mixed-effects models were used to allow for correlation of continuous outcomes, and a random intercept per birth and/or within-birth correlation matrix was specified. Fixed regression coefficients and 95% confidence intervals (β : 95%CI) were computed. The intra-birth correlation ranged from 0.29 for diastolic blood pressure (DBP) and 0.85 for C-reactive protein (CRP). Multiples had significantly lower z-scores of weight (-0.43: -0.60; 0.25), height (-0.44: -0.61; 0.27), BMI (-0.46: -0.67; 0.25), Fat Mass Index (-0.32: -0.50; 0.14), waist circumference (-0.38: -0.55; 0.20), waist-to-height ratio (-0.16: -0.30; 0.02), systolic (-0.20: -0.36; 0.03) and DBP (-0.24: -0.41; 0.07), adjusted for maternal age, education and pre-pregnancy BMI. When birth weight and mode of delivery were included in the model, only SBP and DBP remained different. Glucose, insulin, HDL-cholesterol, triglyceride and CRP crude levels were similar in both groups. At age 7, multiples appeared to present better cardiometabolic indicators, and except for blood pressure, the differences were explained by a lower weight at birth, which seems to track to childhood.

MEASUREMENT OF PERSONAL CARE AND CONSUMER PRODUCT PHENOLS IN 6 TO 12 WEEK OLD INFANTS

Margaret Adgent, Virginia Stallings, Donna Baird

Triclosan, bisphenol A, benzophenone-3, 2,4- and 2,5-dichlorophenol (24-DCP and 25-DCP), and methyl- and propylparaben are chemicals commonly present in personal care and consumer products. Widespread exposure to these chemicals has been documented in children and adults. However, exposure in infants has not been well characterized. Health effects due to exposure are unclear, but may involve antimicrobial action or hormone disruption. We measured these 7 phenols in 353 urine samples from 200 U.S. infants at 6-8 (t1) and 12 weeks (t2) of age. For n=153 with paired samples, we assessed the within-subject correlation between t1 and t2. We also assessed correlations between chemicals, and used multiple linear regression to examine associations between urinary chemical concentrations (log_e(ng/mg creatinine)) and demographic and sample collection characteristics (feeding method, race, maternal age and education, time of day and season of collection). We detected all chemicals in >90% of samples, except triclosan, detected in 64%. Infant samples had substantially higher levels of methylparaben (geometric mean: 230ng/ml), compared to published levels in children (33–53ng/ml (Environ Health Perspect. 118(5) 2010 679-685)). Correlations between t1 and t2 were 0.46 (methylparaben), 0.39 (propylparaben) and >0.50 for all others. Parabens were highly correlated with each other ($r>0.60$), as were 24- and 25-DCP (byproducts of water chlorination, among other sources). Benzophenone-3, a sunscreen agent, was lower in black infants (vs. white), while 25-DCP and parabens were higher. Benzophenone-3 and DCPs were higher in the summer. Triclosan was higher in breast (vs formula) fed infants. Conclusion: Infants are exposed to phenolic chemicals found in personal care and consumer products; exposures are associated with race and season. Some are very high. More research is needed to understand the products and behaviors associated with exposures.

THE ASSOCIATION BETWEEN LIVER ENZYME VALUES AND RISK FOR TYPE 2 DIABETES MELLITUS AMONG HISpanic CHILDREN AGED 10-14.

Shane Fernando, Jenifer Gehlsen, Kimberly Fulda, W. Paul Bowman, Nusrath Habiba

Purpose: Type 2 Diabetes Mellitus (T2DM) continues to increase among children in the United States. Evidence points towards markers of liver health (Alanine Aminotransferase [ALT] and Gamma-Glutamyl Transferase [GGT]) as predictors of insulin resistance and T2DM risk in adults. However, few studies have investigated liver enzymes as an early identifier of increased T2DM risk in children. This study investigates whether increases in ALT and GGT are associated with being high risk for T2DM in Hispanic children aged 10-14. Methods: Data were obtained from 232 Hispanic children aged 10-14 in North Central Texas participating in a study examining risk for T2DM. Associations between ALT and GGT with risk for T2DM were assessed using logistic regression models for each gender, controlled for blood pressure, high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides (TG) and age. Results: Among 232 Hispanic children the mean age was 11.90±1.41, while 49.6% of subjects were female. Average ALT was 22.06±5.35 in boys and 15.69±10.66 in girls while average GGT was 17.14±7.75 in boys and 13.75±5.27 girls respectively. One point increase in ALT was significantly associated with a 3.8% (95% Confidence Interval [CI] 1.001-1.085) and 2.4% (95% CI 1.009-1.057) increased odds of being high risk for T2DM in girls and boys, respectively. One unit increases in GGT were significantly associated with a 7.0% (95% CI 1.01-1.162) and 18.5% (95% CI 1.077-1.304) increased odds of being high risk for T2DM in girls and boys, respectively. Conclusion: The study results suggest that ALT and GGT are significantly associated with being high risk for T2DM. Further longitudinal studies to confirm the use of liver enzymes as predictors of T2DM risk is warranted.

RELATIONSHIP BETWEEN QUALITY OF PARENT-CHILD RELATIONSHIP AND PERCENT BODY FAT

Jenifer Gehlsen, Shane Fernando, Kimberly Fulda, Nusrath Habiba

Purpose: parent-child relationship quality and attachment affect childhood obesity risk, but few studies have examined parent-child relationship and percent body fat (PBF). This study seeks to evaluate factors contributing to a positive parent-child relationship to determine which are associated with a decreased PBF in children. Methods: Data were obtained from 290 10-14 year olds in North Central Texas participating in a study examining risk for Type 2 Diabetes Mellitus (T2DM). Questions on parental quality of relationship were measured using three Likert scale questions, including "How would you describe your relationship to your child," "How well can you and your child share ideas or talk about things that really matter" and "How well do you feel you are coping with the day to day demands of parenthood". Associations were assessed using linear regression models with standardized betas controlled for parent gender, child's race 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 relationship with their child resulted in a decreased PBF ($S\beta$ -0.057, $p<0.3$), increased sharing of ideas resulted in decreased PBF ($S\beta$ -0.04, $p<0.05$) and improved ability to cope with parenthood decreased PBF ($S\beta$ -0.052, $p<0.3$). Conclusion: parent-child relationship quality was associated with a decrease in PBF after controlling for parent type, child's race and age. Interventions seeking to reduce PBF in children should potentially target parent-child relationship quality, paying particular attention to sharing of ideas and parenting coping.

THE USE OF ALTERNATIVE PEDIATRIC HEALTH CARE PROVIDERS BY U.S. WOMEN WHO BREASTFEED

Sarah Keim, Alexis Tchaconas, Andrew Adesman

Pediatricians, family physicians and nurse practitioners (traditional HCPs) provide most primary care for US children. In addition to or instead, families may choose alternative health care providers (AltHCPs) like naturopaths, chiropractors, and others. Depending on the specialty, AltHCPs may practice unlicensed, training programs vary in quality and accreditation, and care may not be comprehensive or evidence-based. Women who breastfeed for extended durations (>1 year) may be interested in pediatric AltHCPs because many strongly support breastfeeding. We distributed an online survey through La Leche League networks to US women who breastfed at least 1 child for >1 year. Of 57852 respondents, 57202 reported their oldest child had a traditional HCP during infancy; 650 reported using an AltHCP. The most common AltHCPs were naturopaths (366), chiropractors (231), homeopaths (32). Women who chose an AltHCP were more likely to be primiparous, have only some college education, and live in Mountain/Pacific states, but they did not differ by maternal age and race as compared to women who chose a traditional HCP. Log-binomial regression with adjustment for parity, education, and region was used. Women who chose an AltHCP were more likely to be comfortable/very comfortable discussing their decision to breastfeed more than a year with their child's HCP (adjRR=1.17, 95% CI: 1.15, 1.19) and were more likely to feel somewhat/very supported by them (adjRR=1.26; 1.24, 1.28). Women with an AltHCP were less likely to indicate family recommendations (adjRR=0.74; 0.62, 0.87), WIC (adjRR=0.77; 0.62, 0.95), and child refusal to take a bottle (adjRR=0.86; 0.74, 0.996) were somewhat/very important factors in their decision to breastfeed >1 year. Although most women chose traditional HCPs, women who chose AltHCPs suggested their providers played a more positive role in breastfeeding support. Future research should evaluate other aspects of the nature and quality of care by AltHCPs.

MATERNAL GESTATIONAL WEIGHT GAIN AND OFFSPRING'S WEIGHT AT 12 MONTHS OF AGE IN RURAL GUANGXI PROVINCE, CHINA: THE MEDIATING ROLE OF BIRTH WEIGHT

Olubunmi Orekoya, Jihong Liu, Sarah Rothenberg, Nansi Boghossian, Linda Hazlett

Little is known about the status of maternal gestational weight gain (GWG) and its association with offspring's weight in developing countries. In a prospective cohort (2014-2015) of 396 pregnant women and their offspring living in rural Guangxi province of China, a border town near Vietnam, we examined the association between GWG and offspring's weight-for-age (WA) Z scores at 12 months using multiple linear regression models. In our cohort, mean total GWG and mean gestational age (GA) at delivery was 11.7kg (± 1.5) and 39.1 weeks (± 1.2), respectively. Gaining inadequate weight during pregnancy (51%) was more prevalent than gaining excessive (19.2%) or adequate (29.8%) weight, based on the Institute of Medicine's guidelines for GWG. At 12 months after birth, 23.4% of infants were below the 10th WA percentile according to the World Health Organization growth standards. After adjusting for infant's sex and GA at birth, and mother's ethnicity, occupation, education, prepregnancy body mass index (BMI), and pregnancy complications, total GWG was positively associated with WA Z-scores at borderline significance ($\beta=0.02$; $p=0.054$). However, this association was no longer significant when birthweight-for-gestational age was added ($p=0.54$). We also found that mean WA Z-scores for infants born to farmers or Zhuang ethnicity were significantly lower when compared to non-farmers ($\beta=-0.21$; $p=0.04$) or Han and other ethnicities ($\beta=-0.28$; $p=0.04$), respectively, while offspring of mothers with gestational diabetes had a higher WA Z-scores ($\beta=0.89$; $p=0.02$). In conclusion, we found a borderline significant association between GWG and offspring's weight at 1 year, which is possibly mediated through infant's birth weight. Our results suggest that targeted nutrition programs should be designed to help pregnant women gain healthy weight during pregnancy and assist healthy growth of infants living in rural areas.

MATERNAL LIPIDS DURING PREGNANCY AND CHILD WEIGHT STATUS AT AGE 3

Chantel Martin, Catherine Vladutiu, Anna Maria Siega Riz

The intrauterine environment is critical in the development of child obesity. Evidence suggests an association between maternal glucose levels during pregnancy and child weight status, but little is known about maternal lipids. Previously, we found an association between maternal diet and triglyceride levels at mid-pregnancy. In this study, we examine the longitudinal associations between maternal lipid levels (total cholesterol, high density (HDL) and low density lipoprotein (LDL) cholesterol, and triglycerides) and child weight status at age 3 among 139 mother-child dyads enrolled in the Pregnancy, Infection, and Nutrition study. Measured height and weight at 3 years were used to calculate body mass index (BMI) z-score. Lipid levels from fasting blood samples were collected at two time points during pregnancy (<20 weeks and 24-29 weeks) and categorized into tertiles. Multiple linear regression models estimated the association between lipid levels and BMI z-score. At 24-29 weeks, higher maternal triglyceride levels were associated with increased BMI z-score after adjusting for pre-pregnancy BMI, gestational age at blood draw, smoking status during pregnancy, total weight gain at end of second trimester, and pregnancy-induced hypertension (Tertile 3 vs. Tertile 1: Beta=0.42, 95% confidence interval (CI): 0.03, 0.81). Further adjustment for childhood factors (birthweight z-score and exclusive breastfeeding) strengthened the association (Tertile 3 vs. Tertile 1: Beta=0.50, 95% CI 0.14, 0.86). In adjusted models, we also observed an association between higher maternal triglyceride levels and child BMI z-score at <20 weeks, but the estimate was not statistically significant (Tertile 3 vs. Tertile 1: Beta=0.33, 95% CI: -0.06, 0.73). These results suggest that child BMI may be influenced by maternal triglyceride levels during pregnancy. Further analyses are needed to elucidate the role of diet in the associations that we observed.

LONG-TERM IMPACT OF THE STRONG4LIFE MAINTENANCE OF CERTIFICATION PROGRAM ON PEDIATRICIAN WEIGHT-BASED COUNSELING

Patricia Cheung, Wendy Palmer, Jean Welsh, Gazmararian Julie

Objectives: To evaluate the impact of a six-month Maintenance of Certification (MOC) program (involving an in-person behavioral therapy training, online course, in-practice meetings, and monthly peer chart reviews) on pediatrician weight-based counseling. **Methods:** Pediatricians completing the MOC program in 2013-2014 were eligible for the study. During the MOC, peers of participating pediatricians assessed 15 randomly selected well-child visit charts each month, which provided data at baseline, 3-month, and 6-month follow-up. Office managers performed retrospective chart reviews for 12-month follow-up. Outcome data included pediatrician documentation of obesity prevention messaging (use of a Healthy Habits form or asking about fruit and vegetable consumption, sugar-sweetened beverages, eating out, physical activity, and screen time), physical exam measures (height, weight, body mass index percentile, blood pressure), and goal setting. Unadjusted and adjusted analyses, controlling for pediatrician demographics and hours of patient care, electronic medical record use, and practice size, were conducted using generalized estimating equations and hierarchical models. **Results:** One hundred pediatricians completed the MOC program. Preliminary results show that health messaging documentation increased from baseline (44%), to 3-month (93%) and 6-month follow-up (96%), and decreased slightly at 12-months (93%). Similarly, goal setting increased from baseline (16%), to 3-month (85%), and 6-month follow-up (87%), and decreased slightly at 12-months (78%). Physical exam measurement documentation was consistently high (99-100%). Additional analyses by individual behavior and adjusted for covariates will be presented. **Conclusions:** Improvements in weight-based documentation were sustained for six months after MOC completion. Further studies need to be conducted to elucidate the extent to which this improved weight-based counseling documentation reflects improved practice.

MEASUREMENT OF CARDIOMETABOLIC RISK IN EARLY CHILDHOOD

Laura Anderson, Jonathon Maguire, Gerald Lebovic, Patricia Parkin, Catherine Birken

Background: Emerging research suggests that cardiometabolic risk (CMR) in childhood may be an important mediator of the association between adverse early life exposures and adult disease risk. However, there is no consensus regarding the definition of CMR in early childhood. **Objectives:** To compare current definitions of CMR and evaluate the validity and reliability of a continuous CMR score in early childhood. **Methods:** Cross-sectional and longitudinal data were analyzed from the TARGeT Kids! cohort study. Healthy children were recruited and followed yearly at scheduled primary care pediatric and family medicine visits in Toronto, Canada (2008-2015). Blood, physical measures and questionnaires were available on 1418 children 3-6 years of age. Multiple definitions of CMR were compared and the criterion validity and reliability were evaluated using Pearson correlation coefficients. **Results:** One existing definition of CMR was the mean of age and sex standardized z-score measures of waist circumference, triglycerides, glucose, systolic blood pressure and the inverse of HDL cholesterol. This CMR z-score was significantly associated with child body mass index ($r=0.35$; $p<0.0001$). The mean CMR z-score was 0.33 (SD=0.55) in overweight and obese children and -0.05 (SD=0.5) in normal weight children. 2% of young children met an adapted definition of the metabolic syndrome and the continuous CMR z-score was significantly greater in these children. Moderate reliability was observed for the tracking of the CMR z-score over a mean follow-up of 16 months ($r=0.67$; $p<0.0001$). **Conclusions:** A continuous z-score measure of CMR is associated with known cardiovascular risk factors and may track throughout early childhood. Future studies are needed to develop a harmonized definition of CMR in early childhood and to evaluate if CMR in early childhood is associated with adult risk of heart disease and diabetes.

GROWTH TRAJECTORIES OF BODY MASS INDEX DURING THE FIRST YEAR OF LIFE AND THEIR POTENTIAL DETERMINING FACTORS

junxiu liu

Little is known about trajectories of body mass index (BMI) in the first year of life and the determinants of these trajectories. We used data from the Infant Feeding Practices Survey II with at least two BMI measurements (n=2320). We applied latent class growth analysis to identify distinct BMI trajectories using BMI values at birth, 3, 5, 7 and 12 months of age. Using multinomial logistic regression models, we examined the associations of the identified BMI trajectories with prenatal and early life risk factors. We found three trajectories of BMI during the first year of life, which were labeled as “low-stable” (81.6% of infants), “high-stable” (15.6%) and “rising” (2.8%) trajectories. Risk factors for infants being in the high-stable versus low-stable trajectory included being born to a Hispanic mother (adjusted odds ratio (AOR): 1.96, 95% CI: 1.20-3.21) and Non-Hispanic Black mother (3.22; 1.83-5.66), smoking during pregnancy (1.73; 1.12-2.70), and male child (1.35; 1.05-1.73). Risk factors for being in the rising versus low-stable trajectory included being born to a Non-Hispanic Black mother (3.20; 1.03-9.97). Full adherence to the guidelines of the American Academy of Pediatrics for both breastfeeding exclusivity and duration significantly reduced the risk of the infant being in the rising (0.28, 0.08-0.92) compared to the low-stable trajectory. In conclusion, this prospective longitudinal study suggests that distinct BMI trajectories are evident among children during the first year of life. Maternal factors such as being Non-Hispanic Black and smoking during pregnancy may increase the likelihood of being in a high-stable BMI trajectory. Improving adherence to breastfeeding guidelines may protect infants against being in the rising trajectory.

Poster Session B

DOES LOW DIET QUALITY MODIFY THE ASSOCIATION BETWEEN SELF-REPORTED DIABETES AND BIRTH DEFECTS?

Suzanne Gilboa

Pregestational diabetes (PGDM) is a strong risk factor for birth defects. Studies suggest high diet quality may be protective. We explored whether low diet quality modified the association between PGDM and birth defects by estimating their independent and joint effects and calculating the relative excess risk due to interaction (RERI). We hypothesized that the highest risk would be among women with PGDM and low diet quality. We analyzed 1997-2009 National Birth Defects Prevention Study (NBDPS) case-control data, for birth defect categories with at least 200 cases, including women with self-reported type 1 or 2 diabetes, and women reporting no diabetes (i.e. excluded women with gestational diabetes or unknown diabetes status). We used a previously-developed NBDPS diet quality index (DQI) based on food consumption in the year before pregnancy. Low diet quality was defined as a DQI below the 25th percentile based on the distribution among controls. Because of sparse sample size in the stratum of PGDM and low diet quality, crude odds ratios and RERIs were calculated. After exclusions, 39 groupings of birth defects (sample size range: 203 – 3,829 cases) and 9,087 controls were included. Ten groupings (anencephaly, anotia/microtia, 2nd or 3rd degree hypospadias, heterotaxia with a congenital heart defect, atrioventricular septal defect, hypoplastic left heart syndrome, right ventricular outflow tract obstruction defects [and its subgroups of pulmonary valve stenosis and pulmonary atresia], and muscular ventricular septal defect) had a significantly elevated point estimate for the joint effect of PGDM and low diet quality which was higher than the point estimate for PGDM alone. However, 15 other groupings had a significantly elevated point estimate for the joint effect which was lower than the estimate for PGDM alone. All RERI estimates were consistent with the null. These results do not provide sufficient evidence of an interaction between PGDM and low diet quality.

BREASTFEEDING AND MOTOR DEVELOPMENT AMONG TERM AND PRETERM INFANTS IN A U.S. COHORT

Kara A. Michels, Akghar Ghassabian, Sunni L. Mumford, Rajeshwari Sundaram, Erin M. Bell, Scott C. Bello, Edwina Yeung

Background: Although components of breast milk aid in development, the effect of breastfeeding as opposed to formula feeding on child cognitive development is debated. The relationship between breastfeeding and motor development is of interest because early motor skills can be an important predictor of later language and cognitive abilities. The influence of breastfeeding is of particular interest among preterm infants, given their higher risk for developmental delays. Methods: The Upstate KIDS study enrolled mothers delivering live births in upstate New York between 2008-2010. Mothers reported infant motor development at 4, 8, 12, 18, and 24 months postpartum; information on breastfeeding and formula feeding was reported at 4 months. Accelerated failure time models were used to compare times to standing or walking alone across infant feeding types while adjusting for maternal characteristics, fertility treatment, day care initiation, and infant plurality, gender, and baseline Ages and Stages Questionnaire pass status. Main models were stratified by preterm birth status. Sampling weights were used to account for study design. Results: The prevalence of exclusive breastfeeding among preterm infants (n=737) was lower than among term infants (n=3533; 13% versus 29%, respectively), but the prevalence of exclusive formula feeding was higher (68% versus 51%). Compared to exclusive formula feeding, exclusive breastfeeding was associated with faster time to walking (acceleration factor [AF] 0.96; 95%CI 0.94, 0.99) and standing (AF 0.92; 95%CI 0.88, 0.96) among term infants. An effect of accelerated walking among preterm infants was suggested, but not precise (AF 0.91; 95%CI 0.83, 1.01). Conclusions: We found times to achieve motor milestones were faster among exclusively breastfed term infants than those fed only formula. While our results provide support for current breastfeeding guidelines, they likely do not translate into a large clinical or public health impact.

ASSOCIATION OF MATERNAL STRESSORS AND SOCIAL SUPPORT WITH RISKS OF GASTROSCHISIS AND HYPOSPADIAS

Suzan Carmichael, Chen Ma, Sarah Tinker, Gary Shaw

Maternal psychosocial stress is a suggested risk factor for varied adverse pregnancy outcomes, but evidence specific to structural birth defects (excepting orofacial clefts) is limited. One recent small study in humans suggested an association of stress with gastroschisis, and experimental studies suggest an association with hypospadias. We examined the association of maternal stressful life events and social support with risks of gastroschisis and hypospadias, using data from the population-based case-control National Birth Defects Prevention Study. We examined maternal self-report of 7 life events (relationship difficulties, legal/financial problems, violence/crime, illness/injury, death of someone close, moving, changing jobs) and 3 sources of social support (emotional, financial, help with daily tasks) during 3 months before and 3 months after conception, among mothers of 593 gastroschisis cases, 1,142 male hypospadias cases, and 4,399 controls without major malformations (2,249 males). A stressful life events index equaled the sum of 'yes' responses to the 7 stress questions (higher is worse). Social support questions were also summed to form an index (higher is better). We used logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CI), adjusted for maternal race-ethnicity, age, parity, education, body mass index, smoking, drinking, and use of vitamin supplements. Results for gastroschisis varied for mothers who were <20 versus ≥20 years old and are provided separately. The OR for a 4-point increase in the stress index was 1.4 (95% CI 1.3-1.5) for gastroschisis among older mothers and 1.0 (0.9-1.1) among younger mothers, and 1.0 (95% CI 0.9-1.0) for hypospadias. The OR for a maximum score of 3 on the social support index (versus a score of 0) for the 3 respective groups was 0.6 (95% CI 0.4-1.0), 1.0 (0.4-2.8), and 0.6 (0.4-0.9). Given the lack of prior research on these outcomes and stress, results should be interpreted with caution.

MATERNAL ANTIHYPERTENSIVE MEDICATION USE AND RISK OF CONGENITAL HEART DEFECTS: UPDATED RESULTS FROM THE NATIONAL BIRTH DEFECTS PREVENTION STUDY, 1997-2011

Sarah Fisher, Alissa Van Zutphen, Angela Lin, Martha Werler, Paul Romitti, Charlotte Druschel, Marilyn Browne

Previous National Birth Defects Prevention Study (NBDPS) findings from 1997-2003 suggested that maternal antihypertensive medication use was associated with congenital heart defects (CHDs). We re-examined associations for 5 specific antihypertensive medication classes in relation to 11 specific CHD types with NBDPS data from 1997-2011. After excluding mothers who reported preexisting diabetes, a multiple birth, antihypertensive medication use for another indication, or unknown hypertension information, we compared self-reported maternal exposure data on 10,617 CHD cases and 11,137 non-malformed controls. We calculated adjusted odds ratios [95% confidence intervals] to estimate risk of specific CHDs associated with antihypertensive medication use during the month before conception through the third month of pregnancy. For CHD types with at least five exposed cases, we adjusted for maternal age, race/ethnicity, body mass index, first trimester cigarette smoking, and NBDPS site. Overall, 1,264 (11.9%) case mothers and 1,018 (9.1%) control mothers reported hypertension during pregnancy, and 164 (1.5%) case mothers and 102 (0.9%) control mothers reported early pregnancy antihypertensive medication use for hypertension. Compared to untreated hypertensive mothers, mothers who reported β-blocker use had increased risk of delivering an infant with pulmonary valve stenosis (2.1 [1.1-3.9]), perimembranous ventricular septal defects (4.1 [1.7-10.0]), and atrial septal defects (2.0 [1.1-3.5]). Renin-angiotensin system blockers were associated with perimembranous ventricular septal defects (6.9 [1.4-33.3]) and atrial septal defects (2.7 [1.0-7.2]). Odds ratios for the same CHDs were elevated but not statistically significant among mothers who used antiadrenergic agents, calcium channel blockers, and diuretics. Our results support and expand upon earlier NBDPS findings that β-blockers and renin-angiotensin system blockers may be associated with increased risk of specific CHDs.

MATERNAL THYROID DISEASE, THYROID MEDICATION USE AND BIRTH DEFECTS AMONG MOTHERS IN THE NATIONAL BIRTH DEFECTS PREVENTION STUDY

Meredith Howley, Sarah Fisher, Alissa Van Zutphen, Dorothy Waller, Suzan Carmichael, Marilyn Browne

Thyroid disorders are common among women of reproductive age. Hypothyroidism affects an estimated 2–3% of pregnancies, and hyperthyroidism affects an additional 0.1–1%. While animal and epidemiologic studies have found an increased risk of birth defects associated with thyroid disease, thyroid medication use during pregnancy (anti-thyroid medication in particular) may also be associated with birth defects. We used data from the National Birth Defects Prevention Study (NBDPS) to examine the risk of a range of birth defects associated with both maternal thyroid disease and thyroid medication use, among births from the most recent study years (2006–2011). The NBDPS collected information on pregnancy exposures, including disease status and medication use, via telephone interview. Maternal thyroid disease status was based on self-reported thyroid disease or thyroid medication use during pregnancy. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression for birth defects with 5 or more exposed cases, controlling for maternal age, race-ethnicity, and study center. In our preliminary analysis of 12,809 birth defect cases and 4,885 unaffected controls, 754 (5.9%) cases and 202 (4.1%) control mothers reported thyroid disease or thyroid medication use. Thyroid disease or thyroid medication use during pregnancy was associated with anencephaly (OR=1.86, 95% CI=1.14, 3.02), choanal atresia (2.38, 1.11–5.09), and esophageal atresia (1.66, 1.05–2.61). Further analyses of the association between both thyroid disease and medication use and the risk of specific birth defects are ongoing. We will compare the above results with risk estimates for infants born in earlier study years and discuss potential explanations for observed differences.

MATERNAL CARDIAC DISEASE IN PREGNANCY AND POSTPARTUM: A POPULATION BASED STUDY IN CANADA

Shiliang Liu

Maternal Cardiac Disease in Pregnancy and Postpartum: A population Based Study in Canada Shiliang Liu, Jocelyn Rouleau, Juan Andrés León (Public Health Agency of Canada, Ottawa, Canada) **Abstract** Objective To determine the prevalence of major maternal cardiac disease, the associated chronic conditions, and maternal outcome. **Methods** Data on all hospital deliveries and postpartum rehospitalisations in Canada (excluding Quebec) between 2003 and 2012 were obtained from the Canadian Institute for Health Information. We identified women with cardiac disease using ICD-10 codes O903, O994, I05-I08, I21, I22, I42, I43, I46 or I50. A cohort for sensitivity analysis was also identified using ICD-10 codes O903 or O994 AND any of the above I codes. Maternal in-hospital death and severe obstetric complications were selected as outcome measures. Population attributable risk (PAR%) was used to estimate the effects on the population. **Results** A total of 10 290 women were identified, yielding an overall rate of cardiac disease of 3.4 per 1000. The annual rates ranged between 3.1 and 3.6 per 1000 (p for trend >0.5). Chronic hypertension (adjusted odds ratio [aOR] 8.8; 95% Confidence intervals [CI] 7.6–10.4), anemia (aOR 3.7; 95% CI 3.4–4.0), alcohol/drug abuse (aOR 3.1; 95% CI 2.8–3.5) and obesity (aOR 2.1; 95% CI 1.8–2.4) were identified as major risk factors. R% for overall severe maternal morbidity, shock and ventilation increased, respectively, from 3.4, 4.6, and 9.5 to 4.3, 9.4 and 12.9 (all p<0.01) between 2003–2007 and 2008–2012. R% for maternal death (within one year) increased from 33.6% (95% CI 22.5–44.8) to 56.2% (95% CI 43.5–68.1). **Conclusions** We have showed an increased effect of maternal cardiac disease on severe obstetric complications, and maternal death, though the underlying cause has yet been explained.

RECENT TRENDS IN BIRTH PREVALENCE OF CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT (CAKUT) IN CANADA AND POTENTIAL REASONS FOR CHANGE.

Shiliang Liu

Recent trends in birth prevalence of congenital anomalies of the kidney and urinary tract (CAKUT) in Canada and potential reasons for change. Shiliang Liu, Jane Evans, Juan Andrés León, Julian Little, for the Canadian Perinatal Surveillance System (Public Health Agency of Canada). **Background:** CAKUT are common malformations with varied genetic and environmental causes. They are the primary cause of childhood end-stage kidney disease, and may lead to renal failure later in life. This study aimed to examine recent changes in the birth prevalence and epidemiology of CAKUT in Canada. **Methods:** Data on livebirths, stillbirths and identified terminations of pregnancy in Canada (excluding Quebec) between 2002 and 2013 were obtained from the Canadian Institute for Health Information. CAKUT cases were coded using ICD-10 CA and classified into various subtypes including renal agenesis, renal dysplasia, hydronephrosis or obstructive nephropathy and autosomal recessive polycystic kidney disease (ARPKD). **Results:** A total of 16 200 cases was identified, yielding an overall birth prevalence rate of 48.4 per 10,000 total births, with a male to female ratio of 2.2. Rates of renal agenesis, renal dysplasia and hydronephrosis respectively increased from 3.4, 1.7, 16.7 per 10,000 to 4.2, 3.5 and 22.6 per 10,000 (p value for trends all <0.001) between 2002 and 2013, while ARPKD declined from 1.88 to 0.41 per 10,000 (p<0.001). Obstructive nephropathy (36.6%), unilateral renal agenesis (6.0%) and multicystic dysplasia (5.1%) were the commonest malformations. Seventeen percent had associated anomalies, including chromosomal abnormalities (1.4%), nonchromosomal recognizable disorders (2.8%) and other patterns of multiple malformations (13.0%). **Conclusion:** Changes in utilization of prenatal screening, frequency of abnormal developmental processes, and coding practices are likely contributors to the changes observed in the birth prevalence of CAKUT. Further investigation is warranted, including the possible role of maternal factors in accounting for increases in renal agenesis and obstructive nephropathy.

BIRTH DEFECTS ASSESSMENT OF INFANTS BORN TO MICRO-ELECTRONICS AND MACHINE MANUFACTURING FACILITY WORKERS

Sharon Silver, Lynne Pinkerton, Carissa Rocheleau, James Deddens, Adrian Michalski, Alissa Van Zutphen

Background: Concerns about solvent releases from a microelectronics and business machine manufacturing facility in upstate New York led to this assessment of birth defects among infants born to facility employees. **Methods:** Children born 1983–2001 to male and female employees were enumerated and matched to New York State's Congenital Malformations Registry. Reported structural birth defects were compared to numbers expected based on state rates (excluding New York City), generating Standardized Prevalence Ratios (SPRs). Exposure assessors classified each employee as ever/never potentially exposed at the facility to metals, chlorinated hydrocarbons, and other hydrocarbons during windows critical to organogenesis (female workers) or spermatogenesis (male workers); among workers, adjusted Prevalence Ratios (aPRs) were generated to evaluate associations between potential exposures and specific birth defects. **Results:** Structural defects were at expectation for births to male workers [SPR=1.01, 95% confidence interval (CI) 0.77–1.29, n=60] and lower for births to female workers (SPR=0.84, 95% CI 0.50–1.33, n=18). Among full-term infants of male workers, the SPR for ventricular septal defects (VSDs) was 1.58 (95% CI 0.99–2.39, n=22); for infants of females, the SPR was 0.84 (95% CI 0.23–2.15, n<5). Within the cohort, potential paternal exposure to metals (primarily lead) was associated with a statistically significant increase in VSD risk (aPR=2.70, 95% CI= 1.09–6.67, n=7). For potential paternal exposure to chlorinated hydrocarbons, the aPR for VSDs was 1.55 (95% CI 0.52–4.65, n<5). **Conclusion:** While overall SPRs were near expectation, paternal exposure to metals appeared to be associated with increased risk for VSDs in infants. Take-home of occupational exposures, non-occupational exposures, and chance could not be ruled out as causes for this finding. Case numbers for many outcomes in this study were small, precluding full assessment of the role of occupational exposures.

ASSOCIATIONS BETWEEN CRANIOFACIAL BIRTH DEFECTS AND DISINFECTION BY-PRODUCT EXPOSURES IN MASSACHUSETTS, 2000-2004

John Kaufman, Michael Wright, Amanda Evans, Zorimar Rivera-Núñez, Michael Narotsky

Epidemiological studies suggest that women exposed to disinfection by-products (DBPs) in treated water have an increased risk of delivering babies with some birth defect types, though evidence for associations between craniofacial defects (CFDs) and specific DBPs is limited. We used a case-control design of birth defects in Massachusetts from 2000-2004 with complete trihalomethane (THM) and haloacetic acid (HAA) data. We randomly matched each case (n=371) to 10 controls based on week of conception. We used weight-averaged aggregate first trimester DBP exposures across all quarterly monitoring sample locations linked to individuals based on residence at birth. Adjusted odds ratios (aORs) were calculated for four CFDs in relation to 13 DBP exposures categorized based on distributions of the available data, including bromoform (TBM), chloroform (TCM), bromodichloromethane (BDCM), dibromochloromethane (DBCM), monochloroacetic acid (MCA), dichloroacetic acid (DCA), trichloroacetic acid (TCA), monobromoacetic acid (MBA), dibromoacetic acid (DBA), THM4 (sum of TBM, TCM, BDCM, DBCM), HAA5 (sum of MCA, DCA, TCA, MBA, DBA) and DBP9 (sum of THM4 and HAA5). We detected elevated aORs for cleft palate with DBP9 quintiles (aOR range: 2.05-6.36), the upper three THM4 quintiles (aOR range: 1.29-2.54), DCA quartiles (aOR range: 1.27-2.44), the upper BDCM tertile (aOR=1.32; 95%CI: 0.65, 2.71), the upper DBCM decile (aOR=1.30; 95%CI: 0.57, 2.99), and an exposure-response relationship with HAA5 quintiles (aOR range: 1.53-3.30). We detected elevated aORs for eye defects with THM4 quartiles (aOR range: 2.59-4.02), HAA5 tertiles (aOR range: 1.23-1.88), TCA quartiles (aOR range: 3.96-4.92), and TCM quartiles (aOR range: 2.03-6.18). No elevated aORs were detected for cleft lip or ear defects. Though our analyses were limited by small case numbers, this is the first study to examine HAAs with CFDs, and the third to examine brominated DBPs, thus adding some specificity to previous research.

MATERNAL LEVELS OF PERFLUOROALKYL AND POLYFLUOROALKYL SUBSTANCES DURING PREGNANCY AND EXECUTIVE FUNCTION IN THE OFFSPRING

Cathrine Carlsen Bach, Zeyan Liew, Niels Bjerregård Matthiesen, Tine Brink Henriksen, Ellen Aagaard Nohr, Bodil Hammer Bech, Beate Ritz, Jørn Olsen

Background: Perfluoroalkyl and polyfluoroalkyl substances (PFASs) are ubiquitous in the environment and accumulate in humans. PFASs are suspected to affect the neuropsychological function of children, but only few studies have investigated the association between intrauterine PFAS exposure and childhood executive function. Methods: We included 1356 children from the Danish National Birth Cohort born 1996-2003. The levels of 16 PFASs were measured in maternal plasma during pregnancy. At 5 years of age, the executive function of the children was assessed by the Behavior Rating Inventory of Executive Function (BRIEF). The test scores were standardized to a mean of 50 and a standard deviation of 10. We examined the associations between the levels of seven PFASs (quantified in at least 50 % of the samples) and BRIEF scores by multivariable linear regression adjusted for potential confounders, including the maternal intelligence quotient. Results: We found no clear associations between PFAS exposures and BRIEF scores rated by day-care employees. However, considering the rent ratings, perfluorooctanoate (PFOA) and four sulfonated PFASs, including perfluorooctane sulfonate (PFOS), were associated with an increase in executive function difficulties; the most extreme estimate was 3.0 (95 % confidence interval 0.7, 5.2) for PFOA, highest versus lowest quartile, but no clear dose-response relationships were identified. Conclusions: Intrauterine exposure to some PFASs was associated with executive function difficulties in childhood in a large sample of Danish children. Given the widespread nature of PFAS exposure, these findings may have public health implications and warrant further investigation.

PRENATAL EXPOSURE TO SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS) AND COGNITIVE FUNCTION IN CHILDHOOD

Hanan El Marroun, Tonya White, Vincent Jaddoe, Frank Verhulst, Bruno Stricker, Henning Tiemeier

Background: Selective Serotonin Reuptake Inhibitors (SSRIs) are considered safe and are frequently used during pregnancy. However, evidence about the potential long-term consequences of prenatal SSRI exposure on child neurodevelopment is sparse. Aim: To prospectively investigate whether intrauterine SSRI exposure is associated with childhood cognitive function as reported and observed in a population-based study. Method: 385 children prenatally exposed to maternal depressive symptoms (no SSRI exposure), 71 children prenatally exposed to SSRIs and 5,427 unexposed children were included. Child cognitive functioning was assessed with maternal report of the Behavior Rating Inventory of Executive Functioning – Preschool (BRIEF-P) at 4 years (n=4,020), a non-verbal intelligence quotient (IQ) assessment at 5 years (n=5,001) and a neuropsychological functioning battery was assessed at 7 years (n=1,194). Results: Prenatal exposure to SSRIs was not related to maternal reported executive function problems at 4 years of age, nor was it related with observed non-verbal IQ at age 5 and neuropsychological function at 7 years. Exposure to maternal depressive symptoms without SSRIs was related to maternal report of shifting problems (B=1.07; 95% Confidence Interval (CI):0.58-1.56) and emotional control problems (B=0.95; 95% CI:0.44-1.48) at 4 years of age. However, no associations between exposure to depressive symptoms and observed non-verbal IQ at 5 years or neuropsychological function at 7 years were found. Conclusions: In the current population-based study, prenatal SSRI exposure was not associated with childhood cognitive function (assessed by maternal report and observations). Prenatal exposure to depressive symptoms was associated with reported executive function, but not with observed cognitive outcomes. Further long-term drug safety studies are needed to derive evidence-based recommendations.

MATERNAL LEVELS OF PERFLUOROALKYL AND POLYFLUOROALKYL SUBSTANCES DURING PREGNANCY AND ATTENTION IN THE OFFSPRING

Cathrine Carlsen Bach, Zeyan Liew, Tine Brink Henriksen, Ellen Aagaard Nohr, Bodil Hammer Bech, Beate Ritz, Jørn Olsen

Background: Perfluoroalkyl and polyfluoroalkyl substances (PFASs) have been used in a wide range of products since the 1950s and are measurable in the blood of humans all over the world. A few studies have suggested that PFAS exposure may affect the neuropsychological function of children, but only few studies have estimated the association between in utero PFAS exposure and attention difficulties in childhood. Methods: We included 1425 children from the Danish National Birth Cohort, born 1996 - 2003. The levels of 16 PFASs were measured in maternal plasma obtained during pregnancy. At 5 years of age, the attention of the children was assessed by the Test of Everyday Attention for Children at Five (TEACh-5). We included seven PFAAs with quantifiable levels in at least 50 % of the samples and examined the associations between PFASs and TEACh-5 scores by multivariable linear regression adjusted for potential confounders, including the maternal intelligence quotient. Results: Most PFASs were not associated with impaired selective attention, however perfluorooctane sulfonamide (PFOSA) was associated with impaired selective attention [compared to the lowest quartile standardized mean differences (95 % confidence intervals) were -0.3 (-0.5, 0.0) for the second quartile, -0.4 (-0.6, -0.2) for the third quartile, and -0.5 (-0.7, -0.3) for the fourth quartile]. We found no clear associations between PFAS exposure and sustained attention. Conclusions: Intrauterine exposure to PFOSA was associated with an increase in selective attention difficulties in a large sample of Danish children. The exposure to six other PFAAs was not associated with either impaired selective or sustained attention.

PRENATAL ACETAMINOPHEN USE AND CHILD'S ATTENTION, EXECUTIVE AND MOTOR FUNCTION AT AGE 5

Zeyan Liew, Cathrine Bach, Beate Ritz, Jørn Olsen

Background: Recent research evidence suggested that in-utero exposure to acetaminophen, the most commonly used pain and fever medication in pregnancy, may have long-term neurodevelopmental consequences in the offspring. Here we aim to examine whether maternal use of acetaminophen affects children's attention, executive and motor function at age 5. **Methods:** We studied 1,491 mothers and children enrolled in the Danish National Birth Cohort (DNBC; 1996-2002). Acetaminophen use in pregnancy was prospectively recorded in three telephone interviews. Child attention and motor function was assessed at age 5 with the Test of Everyday Attention for Children at Five (TEACH-5) and the Movement Assessment Battery for Children (MABC) administered by trained psychologists. The Behavior Rating Inventory of Executive Function (BRIEF) was completed by parents and teachers to assess children's executive function. We employed multiple linear regression and logistic regression analysis adjusting for maternal IQ, indications of acetaminophen use, and other confounding factors. We used inverse-probability-weights (IPW) to account for sampling and non-participation in this DNBC sub-cohort. **Results:** First trimester use of acetaminophen was associated with poorer overall attention scores in children at age 5 (estimated mean difference -0.29; 95%CI -0.59, 0.01) compared to non-users as the reference group. Ever use of acetaminophen in pregnancy was associated with a 2-fold increase in the odds for rent-rated executive difficulties (the metacognition index) (OR=2.00; 95%CI 0.90, 4.44), but we did not find patterns for timing-specific exposure effects and no association for prenatal acetaminophen use and motor function scores in children. **Conclusions:** Maternal acetaminophen use during pregnancy was associated with poorer attention and executive functions in 5-year olds. Our findings add some evidence that acetaminophen exposure in utero may alter neurodevelopment in offspring.

RESILIENCE FACTORS FOR CHILD DEVELOPMENT: A COMMUNITY-BASED COHORT STUDY IN ALBERTA, CANADA

Erin Hetherington

Introduction: Children of mothers with mental health challenges are at increased risk of developmental delays. However, which protective factors have the potential to promote resilience and mitigate risk for developmental problems is not well understood. **Objective:** To identify protective factors for child development at two years of age among children of mothers with mental health risk. **Methods:** Data from the All Our Babies (AOB) longitudinal cohort study in Calgary, Canada was used. Maternal mental health risk was defined as having two or more of the following: history of abuse, previous mental health condition, or poor prenatal or current mental health. Global child development was measured using the Ages and Stages Questionnaire. Social-emotional and behavioural development was measured using two scales from the Brief Infant Toddler Social Emotional Assessment. Among families with maternal mental health risk, three logistic regression models were built for each area of child development (global, social-emotional and behavioural). Protective factors that were considered included maternal factors (e.g. social support, optimism), child factors (e.g. gestational age, sex) and family factors (e.g. marital status, relationship happiness). **Results:** Among children of mothers with maternal mental health risk (28%), protective factors for positive global child development included: renting elf efficacy (OR 5.05, CI: 1.97, 12.96), social support (OR 2.46, CI: 1.21, 5.03) and relationship happiness (OR: 2.22, CI: 1.00-4.89). These factors were also protective for social-emotional and behavioural development. Additional protective factors for behavioural development included use of a recreation facility in the community and mother's perceived ability to fulfill competing responsibilities. **Conclusion:** As these protective factors are modifiable, these results can inform community based strategies to optimize early childhood development among families at high risk of poor outcomes.

HYPERTENSIVE DISORDERS WITH PLACENTAL INSUFFICIENCY ASSOCIATED WITH INCREASED AUTISM AND INTELLECTUAL DISABILITY RISK

Paula Krakowiak, Daniel Tancredi, Guibo Xing, Cheryl Walker

BACKGROUND: Pregnancies complicated by hypertensive disorders have been linked to poor neurodevelopmental outcomes, such as autism and intellectual disability (ID). Hypertensive disorders can lead to inflammation, vascular damage, and restricted nutrient transfer at the placental level; these physiologic changes may result in aberrant neurodevelopment. Although we have previously investigated preeclampsia and placental insufficiency (PI) in relation to neurodevelopmental outcomes, we were unable to examine the finer categories of hypertensive disorders, including chronic hypertension only and hypertension with superimposed preeclampsia. **OBJECTIVE:** To determine whether the risk for autism or ID relative to the general population (GP) differed across specific categories of hypertensive disorders and whether the presence of PI changed these associations. **METHODS:** We used a large population-based cohort of California births from 1991 to 2008 with linked information on autism and ID diagnoses from the California Department of Developmental Services (DDS). Hypertensive disorders were identified by ICD-9-CM codes and grouped into chronic hypertension (HTN), preeclampsia (PE), and HTN with superimposed PE (HTN+PE), and evidence of PI included intrauterine growth restriction, oligohydramnios and/or small-for-gestational-age birthweight. We conducted log-binomial regression models with mutually exclusive categories of hypertensive disorders plus or minus PI as predictors of interest and neurodevelopmental disorders autism and ID as outcomes relative to GP. All models were adjusted for birth year, maternal age, race, delivery payer, and parity to estimate risk ratios (RR) and 95% confidence intervals (CI). **RESULTS:** Women with any type of hypertensive disorder had approximately a 20% increased risk for having a child with autism relative to GP. Although PI alone was only modestly associated with autism, the risk for autism increased in relation to these hypertensive disorders in the presence PI: 19% to 32% for HTN and 23% to 35% for PE. HTN+PE was associated with a 39% increased risk for ASD; however, HTN+PE in the presence of PI was not associated with ASD. Associations between hypertensive disorders and ID were more pronounced. Women with HTN+PE had a nearly 2-fold increased risk for having a child with ID; whereas women with PE or HTN only each had a 1.4-fold increased risk for ID. In contrast to autism, PI alone was associated with a nearly 3-fold increased risk for ID. Similar to autism, the presence PI with any hypertensive disorder elevated the risk for ID: 40% to 214% for HTN+PE; 40% to 214 for HTN, and 31% to 186% for PE. **CONCLUSIONS:** Risks for autism and especially for ID were increased in fetuses whose mothers had any form of hypertensive disorder during pregnancy, particularly when PI was present. Suboptimal placental limits oxygen and nutrient transfer creating oxidative stress, growth restriction and progressive hypoxemia. Although the exact causal mechanisms linking hypertensive disorders and adverse neurodevelopmental outcomes are unknown, improved pre-pregnancy health may help to reduce the likelihood of developing these conditions.

DEVELOPMENTAL RISK FACTORS FOR CHILDHOOD ASTHMA

Madeline Rice

Childhood lung function, including asthma, may have fetal origins. We therefore sought to evaluate developmental risk factors for childhood asthma in a cohort of children born to women enrolled during pregnancy, with either mild gestational diabetes mellitus or lesser degrees of glucose intolerance, and followed up 5-10 years after birth. At follow-up, children had their height and weight measured and parents were queried regarding their child's diet, home environment, and whether the child had been diagnosed or treated for asthma. Logistic regression model selection based on a k-fold cross-validation approach was used to select the best model for the cohort overall and for males and females separately and estimate odds ratios (OR) and 95% confidence intervals (CI). This analysis included 950 children who were followed up at a median age of 7 years. Overall, 13% reported childhood asthma (males 15%, females 11%, p=.07). The variables associated with childhood asthma varied between males and females. Spontaneous preterm birth (OR 5.9, CI 2.0-18.0), maternal marital se ration during the index pregnancy (OR 3.9, CI 1.4-10.5) and higher dairy consumption (OR 1.4 per unit increase in servings per day, CI 1.1-1.6) were associated with asthma in males, whereas childhood exposure to low socioeconomic status (OR 3.5, CI 1.6-7.7) and high child body mass index (OR 1.4 per unit increase z-score, CI 1.1-1.9) were associated with asthma in females. Maternal asthma and not breastfed were associated with asthma in both males and females, although more strongly associated in males (maternal asthma OR 4.2, CI 1.8-9.8 in males, OR 2.8, CI 1.1-6.8 in females; not breastfed OR 4.1, CI 2.3-7.5 in males, OR 2.2, CI 1.2-4.3 in females). In multivariable analysis, mode of delivery was not associated with childhood asthma. In conclusion, the intrauterine environment and early development plays a role in childhood asthma. Fetal programming of asthma was more apparent in the male children.

AUDITORY BRAINSTEM RESPONSES AND THEIR ASSOCIATION WITH AUTISM SPECTRUM DISORDER: A SYSTEMATIC REVIEW

Nicole Talge, Brooke Tudor, Julie Markant, Paul Kileny

Early identification of autism spectrum disorder (ASD) may facilitate enrollment in and responsiveness to interventions. At present, behavior does not differentiate ASD risk prior to 12 months of age, but biomarkers may inform risk before behavioral symptoms emerge. To this end, auditory brainstem responses (ABRs) may be worth consideration due to their measurement (non-invasiveness; high reliability) and conceptual (well-characterized neural generators) features. We performed a systematic review of studies investigating links between ABRs and ASD. ABRs are electrophysiological responses consisting of 5 waves (I-V) from which latencies and amplitudes are derived, values that reflect the degree of dendritic branching, myelination, and synchrony of firing within the central auditory pathway. Common ABR parameters include absolute latencies (I, III, V), inter-peak latencies (I-III; III-V; I-V), and amplitudes. When possible, we calculated ear- and component-specific estimates of effect size (Cohen's d), adjusting for study-specific sample sizes (12 to 166 participants) and the number of studies contributing to the effects (4 to 16 studies). ABRs and ASD have been evaluated almost entirely with cross-sectional designs and in relation to latencies. Despite the large age range represented (2-40 years), participants with ASD exhibited longer latencies for all components relative to typically developing participants, with the largest pooled effects associated with binaural averages ($d=0.8-1.0$) and Wave V latencies ($d=0.5-1.0$). When effect sizes could not be calculated (8 studies), 63% reported significant findings on at least 1 latency measure. ABRs and ASD may be associated. However, studies rarely control for middle ear dysfunction or screen for hearing loss, and it is unclear whether ABR findings precede ASD diagnosis. Future work addressing these issues will inform the viability of the ABR as a prognostic and/or etiologic biomarker for ASD.

THE POPULATION IMPACT OF SEVERE NEONATAL MORBIDITY AND ACUTE HEALTH ON DEVELOPMENT AMONG CHILDREN BORN AT TERM: A RECORD-LINKAGE COHORT STUDY

Jason Bentley, Francisco Schneuer, Samantha Lain, Natasha Nassar

Background: To investigate the impact of severe neonatal morbidity (SNM) and hospitalization during early childhood on the development of cognitive, motor, behavioral, emotional and social skills by school age. Methods: Record-linkage cohort study of all singleton live births in New South Wales, Australia, ≥ 37 weeks gestation without major congenital conditions and with a child development assessment in 2009 or 2012. Development was assessed in five main domains (physical health and well-being, language and cognitive skills, social competence, emotional maturity, and communication skills and general knowledge). Children with a score < 10 th percentile nationally were considered developmentally vulnerable (DV) in that domain. Generalized estimating equations were used to estimate the crude and adjusted associations for SNM and number of hospital admissions with being DV. Results: Among the 138,215 children in the cohort, 2.1% had SNM and 40.8% had at least one admission to hospital. DV ranged from 5.1% (language and cognitive skills) to 8.4% (social competence), and was higher among children with SNM (6.3% to 11.0%) and increased with an increasing number of hospital admissions (1 admission: 5.6% to 9.0%; 2 admissions: 6.0% to 9.2%; ≥ 3 admissions: 6.8% to 11.0%). SNM was associated with being DV, and adjusted odds ratios (aOR) ranged from 1.14 (95% Confidence Interval [CI]: 1.00, 1.29) for communication skills to 1.24 (95% CI: 1.09, 1.41) for emotional maturity. Compared to children with no admissions, those admitted three or more times had aORs between 1.18 (95% CI: 1.09-1.28) for emotional maturity and 1.41 (95% CI: 1.32, 1.51) for physical health and well-being. Conclusions: SNM and admission to hospital in childhood are associated with poor development by school age. Strategies to reduce SNM and hospital admissions in childhood and additional monitoring of these children may improve outcomes.

BEHAVIORAL DEVELOPMENT FOLLOWING EARLY LIFE ORGANOCHLORINE EXPOSURE

Aske Hess Rosenquist

Background: The organochlorine compounds Polychlorinated Biphenyls (PCBs) and Dichlorodiphenyldichloroethylene (DDE) are ubiquitous environmental contaminants. Studies have linked the contaminants with altered neurodevelopment and child development, but the results are inconsistent and there is limited evidence on the aspect of social behavior. Objective: To investigate the association between early life organochlorine exposure and adverse social behavior in children between 5 and 9 years of age. Methods: Data was obtained from the INUENDO birth cohort consisting of mother-child pairs from Greenland and Ukraine ($n = 1,018$). We examined maternal serum concentrations of 2,2',4,4',5,5'-hexachlorobiphenyl (CB-153) and 1,1-dichloro-2,2-bis(p-chlorophenyl)-ethylene (p,p'-DDE), biomarkers for PCBs and DDE. Postnatal cumulative exposure within the first 12 months of delivery was estimated using a verified toxicokinetic model. Behavioral development of the children at follow-up was assessed by their parents using the Strength and Difficulties Questionnaire. Exposures were divided into tertiles and logistic regression was used to analyze the association between the exposures and behavioral development. Results: For the prenatal exposure the pooled adjusted odds ratio (95 % confidence interval) comparing the 3rd tertile to 1st tertile for adverse behavior were 0.93 (0.35 ; 2.52) for CB-153 and 1.23 (0.55 ; 2.75) for p,p'-DDE. The postnatal results were slightly different, but no clear association was observed between tertiles of neither prenatal nor postnatal exposure to CB-153 or p,p'-DDE in relation to behavioral changes. Also results stratified on countries did not indicate clear association between PCB or DDE exposure and adverse social behavior. Conclusion: This follow-up study of Greenlandic and Ukrainian populations showed no clear association between early life exposure to PCBs or DDE and adverse behavioral development of children at 5 to 9 years of age.

CORRELATION OF PREMENSTRUAL SYNDROME AND PREMENSTRUAL DYSPHORIC DISORDER WITH EATING DISORDERS IN A NATIONAL SAMPLE

Carrie Nobles, Luana Marques

Objective: Bulimia nervosa (BN) and binge eating disorder (BED) effect 1.5% and 3.5% of women, respectively, and are associated with significant impairment in occupational and social functioning, decreased quality of life and increased risk of chronic health conditions. Premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD) are comprised of cyclical psychological symptoms, including disturbances in mood and affect, as well as physiological symptoms, including bloating and changes in appetite, which may serve as triggers for binge eating and/or purging. Little past research has evaluated the independent association of PMS and PMDD with eating disorders. Methods: participants were drawn from the nationally-representative Collaborative Psychiatric Epidemiological Surveys, conducted from 2001-2003. Weighted multivariable logistic regression modeled the association between lifetime PMS and PMDD and lifetime odds of eating disorders. Results: Among 8,694 women participating in CPES, 133 (1.0%) had BN and 185 (1.8%) BED. Additionally, 3,489 (42.4%) had PMS and 366 (4.2%) PMDD. After adjustment for age, race/ethnicity, income, education, age at menarche, birth control use and comorbid mental health conditions (major depressive disorder, dysthymia, bipolar disorder, social phobia and substance use disorder), PMDD was associated with a greater than 5-fold odds of BN (OR 5.5, 95% CI 2.2, 19.2) and PMS with a 2-fold greater odds of BN (OR 2.3, 95% CI 1.1, 4.9). Additionally, in weighted linear regression, women with PMDD reported a longer duration of BN symptoms, although these results were attenuated after adjustment (mean difference 5.8 years, 95% CI -1.2, 12.7). PMDD and PMS were not significantly associated with BED in multivariable models. Conclusions: Women with PMS and PMDD have a higher odds of BN, independent of comorbid mental health conditions. Future research should investigate whether PMS and PMDD affect the onset and duration of eating disorders.

THE ADVERSE REPRODUCTIVE HEALTH CONSEQUENCES OF LIMITED REPRODUCTIVE RIGHTS

Maeve Wallace, Katherine Theall

Reproductive rights – the ability to decide whether and when to have children – shape women's socioeconomic and health trajectories across the life course. The objective of this study was to examine reproductive rights in association with infant mortality (IM; <1 year of age), preterm birth (PTB; <37 weeks) and low birth weight (LBW; <2,500g) across states in the US. Live birth and linked birth and infant death records in the US in 2012 were grouped by state. A reproductive rights composite score was assigned to records from each state based on the following indicators for the year prior to birth (2011): mandatory sex education; expanded Medicaid eligibility for family planning; mandatory rental consent/notification policies for minors seeking abortion; mandatory abortion waiting periods; public funding for abortion; percentage of women in counties with abortion providers; pro-choice government; and insurance mandates for infertility treatment coverage. Scores were ranked by quartile with the highest quartile reflecting states with strongest reproductive rights. IM was compared across state quartile ranks. Multi-level models estimated the risk of PTB and LBW associated with reproductive rights score controlling for maternal race, age, education, insurance and state-level poverty rates. IM increased across every quartile of rights score from a mean low of 5.1 per 1,000 in states with the strongest rights to 6.7 per 1,000 in states where rights were weakest. Rates of LBW and PTB were lowest in states with the highest quartile scores (7% and 10% respectively, compared to 8-8.5% and 11.5-12.6% in lower quartiles). After adjustments, women who lived in states with lower scores were 17-22% more likely to deliver preterm and 9-24% more likely to have a LBW infant compared to women in states with the strongest rights. State-level reproductive health policies appear to influence rates of IM and adverse birth outcomes among women residents.

FACTORS ASSOCIATED WITH POSTPARTUM USE OF LONG-ACTING REVERSIBLE CONTRACEPTIVES: RESULTS FROM THE PREGNANCY RISK ASSESSMENT MONITORING SYSTEM (PRAMS), NINE STATES, 2009-2011

Titilope Oduyebo

Objectives: Contraception use among postpartum women is important to prevent unintended pregnancies which can adversely affect maternal and infant health. Long-acting reversible contraceptives (LARCs; intrauterine devices and implants) are highly effective, yet few US women use them. We sought to examine factors associated with LARC use among postpartum women. **Methods:** We analyzed 2009-2011 data from the Pregnancy Risk Assessment Monitoring System, a population-based survey among women with recent live births. We included data from nine states (AR, CO, MI, NE, OH, OR, RI, TN, UT). We estimated prevalence of LARC use among non-pregnant women (n=36,070). Among women using reversible contraception (n=25,707), we used multivariable logistic regression to examine associations between maternal characteristics and LARC use. **Results:** The overall prevalence of postpartum LARC use was 17%, and state-specific estimates ranged from 12% in Ohio to 25% in Utah. Factors associated with postpartum LARC use included: public insurance (adjusted odds ratio [AOR] = 1.47; 95% confidence interval [CI] = 1.29-1.66) or no insurance (AOR = 0.55; 95% CI = 0.31-0.97) versus private insurance at delivery; age ≤24 years (AOR = 1.65; 95% CI = 1.46-1.86), or >35 years (AOR = 0.80; 95% CI = 0.66-0.97) versus 25-34 years; and black, non-Hispanic race/ethnicity (AOR = 0.72; 95% CI = 0.61-0.85) versus white, non-Hispanic race/ethnicity. **Conclusions:** LARC use by postpartum women varies by factors, including state of residence, insurance status, age, and race/ethnicity. Strategies to increase LARC use may include facilitating consumer awareness, provider education and promoting access through insurance coverage, and public health initiatives.

INCREASING 25-HYDROXYVITAMIN D (25(OH)D) DECREASES THE OCCURRENCE OF LONG MENSTRUAL CYCLES

Anne Marie Jukic, Anne Steiner

In rodents, vitamin D deficiency has been associated with both dramatic reductions in fertility and prolonged menstrual cycles. Treatment with vitamin D improves menstrual cyclicity in women with polycystic ovarian syndrome. Two studies of self-reported menstrual cycle length reported that 25(OH)D is related to menstrual cycle length or regularity. No studies have prospectively examined vitamin D and menstrual cycle length in women with no known fertility problems. We used data from a prospective cohort study of time to pregnancy, Time to Conceive, to examine the associations of vitamin D with menstrual cycle length. Women ages 30-44 enrolled in Time to Conceive early in their attempt to become pregnant. At baseline, women provided a blood sample that was spotted, dried, and stored frozen. Women kept daily diaries that included menstrual bleeding, for up to four months. 25(OH)D was measured at baseline using liquid chromatography tandem mass spectrometry. We analyzed the association between log-transformed menstrual cycle length and log-transformed 25(OH)D using linear mixed models that adjusted for age, race, body mass index, recent hormonal birth control use, and cycle-specific changes in vitamin use. There were 373 women in our sample who contributed a total of 1278 menstrual cycles. The mean 25(OH)D was 35 ng/ml and 30% of women were below 30 ng/ml, the Endocrine Society cutpoint for sufficiency. A one-unit increase in the natural log of 25(OH)D was associated with a 5% decrease in menstrual cycle length (95% Confidence interval (CI): 0.5%, 10%, p=0.03). Increasing 25(OH)D was associated with a reduced odds of long (>35 days) menstrual cycles (For a 1-unit increase in the natural log of 25(OH)D, odds ratio(CI): 0.32 (0.14, 0.75), p=0.01). Increasing 25(OH)D was not associated with the occurrence of short (<21 days) menstrual cycles (p=0.92). In a population of naturally-cycling women increasing 25(OH)D was associated with normalization of menstrual cycle length.

SMOKING AND ASSOCIATED TREATMENT AND CLINICAL OUTCOMES AMONG WOMEN UNDERGOING ASSISTED REPRODUCTIVE TECHNOLOGIES

Karilynn Rockhill, Van Tong, Dmitry Kissin, Sheree Boulet, Yujia Zhang, Denise Jamieson, Lucinda England

Smoking causes infertility, conception delays, and ectopic pregnancy. Using the National ART Surveillance System, we assessed the percentage of assisted reproductive technology (ART) cycles for which women self-reported smoking in the 3 months prior to treatment and evaluated associations between smoking and selected outcomes. We analyzed data on fresh and frozen ART cycles performed during 2009-2013 in all 50 states and Puerto Rico (n=718,239). We compared demographic characteristics, prior infertility diagnoses, and treatment procedures by smoking status among all cycles using chi-square tests. Multivariable logistic regression adjusting for confounders was used to assess independent associations between smoking and the following: cycle cancellations among all fresh and frozen cycles, treatment outcomes (implantation, ectopic pregnancy, and intrauterine pregnancy) among cycles with ≥1 fresh embryo transferred, and pregnancy outcomes (miscarriage, stillbirth, and live birth) among intrauterine pregnancies. Analyses accounted for clustering of cycles by state, clinic, and woman. Overall, in 1.9% of all ART cycles (n=13,303) the woman indicated smoking in the 3 months prior to treatment. Compared with nonsmoking cycles, a higher percentage of smoking cycles were among women who were less than 34 years, multi-gravida, multiparous, and had previous diagnoses of tubal factor, male factor, and unexplained infertility. Smoking cycles were more likely to be cancelled prior to fresh oocyte retrieval or frozen embryo transfer than nonsmoking cycles (adjusted odds ratio: 1.17; 95% confidence interval: 1.07-1.27); no significant associations were found between smoking and treatment or pregnancy outcomes. A low proportion but substantial number of ART cycles indicated smoking in the 3 months prior to treatment. Smoking increased the odds of cycle cancellation. Providers should continue to encourage women to enter ART treatments tobacco free.

BREASTFEEDING HISTORY AND RISK OF ENDOMETRIOSIS IN THE NURSES' HEALTH STUDY II

Leslie V Farland, A. Heather Eliassen, Rulla M. Tamimi, Donna Spiegelman, Stacey A Missmer

Background: Endometriosis is a chronic gynecologic condition with few known modifiable risk factors and a suspected hormonal etiology. Breastfeeding has been shown to mitigate risk of other chronic diseases that are hypothesized to be influenced by circulating hormones. We investigated the association between breastfeeding and incidence of endometriosis in the Nurses' Health Study II. **Methods:** From 1989 until 2011, 67,610 parous women were followed, among whom 3,741 laparoscopically confirmed endometriosis cases were diagnosed. Women reported duration of total breastfeeding, exclusive breastfeeding, and amenorrhea for each pregnancy. Cox proportional hazard models, adjusted a priori for potential confounding factors were used to calculate relative risks (RR) and 95% confidence intervals (CI) of endometriosis. **Results:** History of total and exclusive breastfeeding duration were significantly associated with decreased risk of endometriosis. For every three additional months of total breastfeeding per pregnancy, women experienced an 8% lower risk of endometriosis (RR:0.92, CI:0.90-0.94; P-trend<0.0001) and a 14% lower risk for every three additional months of exclusive breastfeeding (RR: 0.86, CI: 0.82-0.90; P-trend<0.0001). Parous women who never breastfed were at 1.6-fold higher risk of endometriosis compared to women who breastfed for > 36 months (RR:1.64, CI: 1.38-1.97). The magnitude of the effect of breastfeeding appeared strongest among women who gave birth within the last 5 years (P-value, interaction: 0.04), however the protective association was consistently significant across all groups of women. **Conclusion:** We found that among parous women, breastfeeding was inversely associated with risk of endometriosis. Given the chronic and incurable nature of endometriosis, breastfeeding should be further investigated as an important modifiable behavior to mitigate risk.

ASSOCIATIONS BETWEEN DIETARY MINERALS AND REPRODUCTIVE FUNCTION IN PREMENOPAUSAL WOMEN

Keewan Kim, Jean Wactawski-Wende, Kara A. Michels, Torie C. Plowden, Ellen N. Chaljub, Sunni L. Mumford

Background: Although minerals are linked to a broad spectrum of reproductive outcomes, it is unknown whether intake of minerals via food influences hormone levels and ovulation. We investigated associations between dietary minerals and sugar and reproductive hormones and anovulation in healthy women. **Methods:** Hormones were measured up to 8 times per menstrual cycle for up to 2 cycles from 259 regularly menstruating women in the BioCycle Study. Intakes of calcium (Ca), phosphorus (P), magnesium (Mg), iron (Fe), zinc (Zn), copper (Cu), manganese (Mn), selenium (Se), sodium (Na), potassium (K), and sugar were assessed via 24-hour dietary recalls up to 4 times per cycle. Dietary minerals and sugar were dichotomized based on the recommended dietary allowance (RDA) or US average intakes. We used weighted linear mixed models to evaluate the associations between intake of minerals and sugar and hormones. Generalized linear models were used to determine risk of anovulation. Models were adjusted for age, body mass index, race, physical activity, and total energy, protein, and fiber intakes. **Results:** We found a positive association between Ca intake and progesterone. Na intake \geq RDA was inversely associated with follicle-stimulating hormone and luteinizing hormone, positively associated with progesterone, and was protective against anovulation (relative risk [RR] 0.37, 95% confidence interval [CI] 0.14, 0.99). A positive association between Mn intake \geq RDA and testosterone was suggested, as was a decreased risk of anovulation (RR 0.49, 95% CI 0.24, 1.00), compared to intake < RDA. Mg intake \geq RDA was positively associated with testosterone, whereas inverse associations were detected with K and sugar intakes \geq US average. **Conclusions:** Dietary minerals and sugar may influence hormones and ovulatory function in healthy women. However, serum mineral levels may contribute differently to reproductive function.

PERCEIVED STRESS AND TIME TO PREGNANCY

Jihye Park, Karen Schliep, Joseph Stanford

Background: The effect of perceived stress on human fecundability is not well studied, with most research relying on cross-sectional or retrospectively collected data. **Methods:** We conducted a secondary data analysis of Study of Time to Pregnancy in Normal Fertility (NCT00161395). Women ages 18–35, in a relationship of proven fertility who desired to conceive were block-randomized to receive intervention (fertility monitoring instruction) or control (advice to have intercourse 2–3 times per week). All women completed a daily diary recording bleeding, intercourse, alcohol, tobacco, coffee, tea, soda, medication, illness, and perceived stress (scale 1 to 10). They were also asked about pregnancy intention at the beginning of each cycle. Participants were followed for up to 7 cycles. Cox proportional hazards regression with discrete time was used to examine the impact of time-varying perceived stress (averaged across each cycle) on Fecundability Odds Ratio (FOR), accounting for right censoring. **Results:** Among the 121 women who completed ≥ 1 cycle, 99 (82%) conceived. We found no association between perceived stress and pregnancy (FOR: 1.06, 95% CI: 0.92, 1.22) after adjusting for woman's age, parity, education. With the additional adjustment for daily exposures, intervention group, and cycle intention, perceived stress was marginally associated with higher fecundability (FOR: 1.17; 95% CI: 0.99, 1.37). **Conclusion:** Further research is needed to tease apart the interplay between perceived stress, responses to stress, stress biomarkers, and reproductive health.

COMPARING BIOMARKERS OF OVARIAN RESERVE IN A POPULATION-BASED COHORT: ANTI-MÜLLERIAN HORMONE AND ANTRAL FOLLICLE COUNT

Penelope Howards, Amy Fothergill, Melanie Jacobson, Ann Mertens, Jessica Spencer

Anti-Mullerian hormone (AMH) and antral follicle count (AFC) are markers of ovarian reserve that have been used in fertility clinics to evaluate the reproductive potential of patients, and with more women delaying pregnancy, there is an interest in their value as predictors of ovarian aging in the general population. However, the correlation between these markers has primarily been evaluated in a clinical setting. We examined their correlation in a cohort of women (n=366) originally recruited to represent the general population in a study of fertility in female cancer survivors. Eligibility criteria for these women included being aged 22 to 45 years old and never having been diagnosed with cancer. They also had to have a uterus and at least one ovary for the clinic visit. A detailed interview collected information on demographics and reproductive history, serum was collected to measure AMH (Ansh labs assays), and total AFC was measured by transvaginal ultrasound. The overall Spearman correlation coefficient for AMH and AFC was 0.80. The correlation was stronger for women ages 40-47 ($r=0.79$) than for younger age groups (35-39: $r=0.63$, 22-34: $r=0.70$). The correlation for African American women was similar ($r=0.77$) to that of white women ($r=0.81$). The correlation was stronger for women using hormonal contraception ($r=0.87$) than for women not using hormonal contraception ($r=0.77$) and was weakest for women with polycystic ovaries ($r=0.47$). The correlation decreased slightly across increasing BMI groups (underweight and normal: $r=0.83$, overweight: $r=0.81$, obese: $r=0.77$). AMH and AFC appear to be strongly correlated in reproductive-aged women recruited from the general population with modest variation depending on their characteristics. Collecting blood is easier than performing transvaginal ultrasounds; given the strong correlation between AMH and AFC, measuring AMH alone may be the most practical measure of ovarian reserve for population-based studies.

PARENTAL CHARACTERISTICS CAN EXPLAIN WHY JAPANESE INFANTS ARE THE SMALLEST IN THE UNITED STATES

Naho Morisaki, Emily Oken, Ichiro Kawachi, Takeo Fujiwara

BACKGROUND: In the United States, Asian infants are generally born smaller in size compared to white infants, and Japanese infants are the smallest among all distinctively reported races in national natality files. **OBJECTIVE:** To elucidate whether the apparent large birthweight differences between non-Hispanic white and Japanese infants can be explained by known parental characteristics. **STUDY DESIGN:** Using US natality data, we evaluated 4,147,535 singleton term live births of infants born to parents of non-Hispanic white or Japanese race in the United States from 2009–2012. Couples were categorized by parental race (white parents, n=4,131,822; Japanese father/white mother, n=2,380; white father/Japanese mother, n=7,501; Japanese parents n=5,832). We used multivariate regression to sequentially adjust for parental characteristics to determine differences in birthweight between races. **RESULTS:** Infants born to two Japanese parents were 315 (95% confidence interval [CI]: 303, 326) grams smaller than infants born to two white parents. Social risk factors for lower birthweight (maternal education, marital status, smoking status, initiation of antenatal care) and differences in maternal age and parity only minimally explained any difference. After additionally adjusting for paternal race, maternal height, body mass index and gestational weight gain, the average birthweight difference was substantially attenuated to 29 (95% CI: 10, 49) grams. **CONCLUSION:** Birthweight differences between Japanese and non-Hispanic white infants could be explained by differences in parental characteristics. In addition to Japanese women being shorter and thinner than white women, lower gestational weight gain, primarily from self-restriction, is a contributing factor to lower birth weight among Japanese infants. Fetal growth potential may be very similar across different racial groups when parent sizes are similar and societal and medical needs are met.

HEALTHY LIFESTYLE DURING EARLY PREGNANCY AND RISK OF GESTATIONAL DIABETES MELLITUS

Sylvia E Badon, Daniel A Enquobahrie, Paige D Wartko, Raymond S Miller, Chunfang Qiu, Bizu Gelaye, Michelle A Williams

Background: Previous studies have found associations between healthy lifestyle before pregnancy and reduced risk of gestational diabetes mellitus (GDM); however, the association of healthy lifestyle during early pregnancy with GDM has not been examined. **Methods:** Study participants (N=3,005) were identified from the Omega study, a prospective pregnancy cohort in Washington State. Reported diet, physical activity, smoking, and stress during pregnancy (5–25 weeks gestation) were dichotomized into healthy/unhealthy using Alternate Healthy Eating Index-2010 (AHEI) score, minutes/week of leisure time physical activity (LT), smoking history, and perceived stress scale (PSS), respectively, and combined into a lifestyle score (0–4). GDM diagnosis was abstracted from medical records. Regression models adjusted for age, race, and parity were used to determine relative risk of GDM related to healthy lifestyle. **Results:** Overall, 20% of participants had healthy diet (AHEI score ≥ 62), 66% were physically active (≥ 150 min/wk of LTPA), 95% were non-smokers, and 55% had low stress (PSS ≤ 3). Individually, healthy diet, physical activity, and low stress were associated with 12–25% lower risk of GDM; however estimates were not statistically significant. Not smoking was associated with 45% reduced risk of GDM (95% CI: 0.30, 0.99). Each additional healthy lifestyle component was associated with 21% lower risk of GDM (95% CI: 0.65, 0.96). Women with 4 healthy lifestyle components had 77% lower risk of GDM (95% CI: 0.07, 0.75) compared to women with no healthy lifestyle components. Adjustment for pre-pregnancy BMI slightly attenuated associations (RR=0.83; 95% CI: 0.68, 1.01). **Conclusion:** Healthy lifestyle during early pregnancy, consisting of healthy diet, physical activity, low stress, and not smoking, is associated with reduced risk of GDM. Public health messaging and interventions promoting multiple aspects of healthy lifestyle during pregnancy should be considered for prevention of GDM.

MATERNAL HEALTHY LIFESTYLE DURING EARLY PREGNANCY AND OFFSPRING BIRTHWEIGHT – OFFSPRING SEX-SPECIFIC ASSOCIATIONS

Sylvia E Badon, Raymond S Miller, Michelle A Williams, Daniel A Enquobahrie

Background: Individual maternal lifestyle components during pregnancy have been associated with offspring birthweight (BW); however, associations of combined lifestyle components with offspring BW and potential differences by offspring sex have not been examined. **Methods:** participants (N=2,924) were identified from the Omega study, a pregnancy cohort study in Washington State. Reported lifestyle components, diet, smoking, stress, and physical activity, during early pregnancy (5–25 weeks gestation) were dichotomized into healthy/unhealthy using Alternate Healthy Eating Index-2010 (score ≥ 62), current smoking, perceived stress scale (score ≤ 3), and leisure time physical activity (LT) duration (≥ 150 minutes/week), respectively. Diet, smoking, and stress were combined into a lifestyle score (0–3). Because of an expected inverse association with BW, LTPA was not included in the score. Offspring BW was abstracted from medical records. Regression models were used to determine mean differences in BW related to lifestyle score and LTPA overall and stratified by offspring sex. **Results:** Overall, 20% of participants had healthy diet, 95% were non-smokers, 55% had low stress levels, and 66% were physically active. Lifestyle score and LTPA were not associated with BW overall ($\beta=9$; 95% CI: -13, 31 and $\beta=-8$; 95% CI: -41, 24, respectively) but associations differed by offspring sex (interaction P=0.10 and 0.05, respectively). Among males, maternal lifestyle score was marginally associated with 22g greater BW (95% CI: -9, 53). This association was not observed among females ($\beta=-6$; 95% CI: -38, 25). LTPA was marginally associated with lower BW among females ($\beta=-36$; 95% CI: -81, 10) but not males ($\beta=18$; 95% CI: -27, 64). **Conclusion:** Maternal healthy lifestyle consisting of healthy diet, non-smoking, and low stress during early pregnancy is associated with greater BW among male, but not female, offspring. Future studies to replicate findings and assess potential mechanisms are warranted.

TRAJECTORIES OF PRENATAL WEIGHT GAIN AMONG LOW BIRTHWEIGHT AND PRETERM BIRTH INFANTS: A MULTI-LEVEL ANALYSIS

Kohta Suzuki, Rei Tsukahara, Zentaro Yamagata

Some guidelines have been established to control maternal weight gain during pregnancy in Japan. Although prenatal weight gain may be associated with fetal growth, the difference of the weight gain trajectories of low birthweight (LBW) and preterm birth (PTB) infants compared with those of normal birthweight and term infants have not been clarified. Thus, this study aimed to describe prenatal weight gain trajectories for LBW and PTB infants. From three hospitals in Yamanashi Prefecture, prenatal check-up data from 932 women were collected. Mean number of check-ups during pregnancy was 11.2. Of these women, 454 (48.7%) were primipara. Mean maternal age at delivery was 31.0 years. Weight gain during pregnancy was defined as the difference between pre-pregnancy maternal weight and weight at the last check-up before delivery. Mean weight gain during pregnancy was 10.1 kg. Multilevel analysis (random intercepts and slopes model) was conducted to determine the estimates of slopes in each gestational period for LBW, PTB, and normal birthweight infants. As a result, significant interaction between gestational duration and LBW on prenatal weight gain was observed. The prenatal weight gain trajectory among women who gave birth to LBW infants was lower after the first trimester. Moreover, maternal weight constantly increased during the second and third trimesters. On the other hand, the trajectory of women who gave birth to PTB infants was mostly similar to that of women who gave birth to term infants. In conclusion, this is the first study to describe prenatal weight gain trajectories among LBW and PTB infants using multilevel analysis. The trajectory of prenatal weight gain among LBW infants was different from that of normal birthweight infants. These results may contribute to the ability to predict perinatal outcomes like LBW by prenatal weight gain. A further study to clarify the effect of prenatal weight gain on birthweight needs to be conducted.

EFFECT OF MATERNAL SMOKING DURING PREGNANCY ON CHILDHOOD GROWTH BY QUARTILE OF BIRTH WEIGHT USING MULTILEVEL ANALYSIS

Kohta Suzuki, Miri Sato, Sonoko Mizorogi, Ryoji Shinohara, Zentaro Yamagata

Maternal smoking during pregnancy is associated with childhood obesity; however, whether maternal smoking affects childhood growth according to birth weight has not been examined. Thus, this study aimed to examine the effect of maternal smoking on childhood growth stratified by quartile of birth weight using multilevel analysis. The study participants were 1,956 women and their single-born babies, born between April 1, 1991, and March 31, 2003, who had complete data for birth weight, maternal body mass index (BMI) before pregnancy, and smoking status during pregnancy. Maternal smoking status during pregnancy was collected using a questionnaire at their pregnancy registration. Childhood growth was estimated by BMI z-score, established by the World Health Organization. Birth weight and anthropometric data were collected from 1,950 (at birth, 99.7%), 1,643 (at age 3 years, 84.0%), 1,517 (at age 5 years, 77.6%), 1,487 (at age 7–8 years, 76.0%), and 1,491 (at age 9–10 years, 76.2%) children. Quartile of birth weight was determined by sex and parity (first vs. second or higher). Multilevel analysis, including both individual and age as different level variables, by each quartile of birth weight was used to describe the trajectories of BMI z-scores for statistical analyses. In every quartile group, although children born to smoking mothers were leaner at birth, their BMI z-score increased rapidly by age 3; after age 3, these children were larger than children born to non-smoking mothers. Significant interactions between maternal smoking during pregnancy and each age of children were seen in children in the third- and fourth-quartiles of birth weight. Particularly in the children in the third-quartile, the difference of trajectories between children of smoking and non-smoking mothers was larger than the other groups. In conclusion, the effect of maternal smoking during pregnancy on childhood growth seemed more apparent among children in the third quartile of birth weight.

BIRTHWEIGHT CENTILES FOR BABIES BORN IN THE UK: IS IT TIME FOR AN UPDATE?

Sarah Seaton, Lucy Smith, Martin Perkins, David Field, Elizabeth Draper, Jennifer Kurinczuk, Pauline Hyman-Taylor, Bradley Manktelow

Birthweight for gestational age provides an indicator of pre- and postnatal health as well as survival in the first year. Thresholds are used to identify babies needing additional monitoring or investigation. Current UK birthweight centiles were introduced in 1995 and updated methodologically in 2009 (now known as the WHO charts). These centiles are based on 9443 births using data which are now up to 30 years old. These births were mainly in East Anglia with under-sampling of certain gestational ages, particularly 32–36 weeks. We investigated the performance of these charts using data for England and Wales (approx. 696,000 births) and, as appropriate, develop new charts. Data were obtained from singletons born at 24–42 weeks gestation from 1 Feb 2013 to 31 Dec 2013 in England and Wales from the NHS Numbers for Babies dataset. Babies alive at the start of care in labour were included, and exclusions were made for unrecorded, undefined or implausible birthweight or sex. Our analyses showed that the WHO charts generally performed well given the age of the data and sample size. However, poor performance was seen at 32–36 weeks where data was lacking and at 35 weeks at <2nd centile are managed as at risk of hypoglycaemia. Our analysis suggests approximately 3000 additional babies may need monitoring. Our new charts, which will be available via an online system, will allow babies to be allocated more accurately to the appropriate care pathway.

“THEY’LL BE HOME BY THEIR DUE DATE”: AN APPLICATION OF MULTISTATE MODELLING FOR NEONATAL LENGTH OF STAY

Sarah Seaton, Lisa Barker, Elizabeth Draper, Keith Abrams, Bradley Manktelow

In the UK, 1 in 10 babies need specialist neonatal care after birth. For those born very preterm who survive, this care may last several months. Neonatal care is broadly defined as intensive (e.g. ventilation); high dependency (e.g. drug infusion) or special care (e.g. phototherapy). A preterm baby is likely to need a combination of these levels of care. Historically, there has been little research into the prediction of length of stay in neonatal care, and the research which does exist has never considered the levels of care received. Additionally, most work has excluded babies that die during their time in neonatal care, who contribute workload to the health service during the time they are alive and therefore should be included in estimates. Conventional statistical approaches are unable to capture the complexity of the nature of neonatal care. Multistate modelling can be utilised to allow prediction of time until any one of a number of events occur (i.e. death or discharge). However, prior to these events it can also include “intermediate steps” such as the different levels of care received by the baby. Approximately 21,100 singleton babies were born at 24–31 weeks gestation and discharged from a neonatal unit in England between 2011 and 2014. These babies required over 1,200,000 days of specialist neonatal care. Using this data, multistate modelling methods were used to describe the probability of receiving each level of neonatal care, or of being discharged home or dying. Unadjusted analyses and analyses adjusted for gestational age will be presented graphically. On the first day of life, 82% of babies were receiving intensive care; 13.3% were receiving high dependency and 4.7% were receiving special care. For healthcare systems increasingly focussed on costs, it is important to consider everything that happens during the care pathway, and not just overall length of stay. These methods provide important estimates for planning services and counselling parents.

RISK FACTORS FOR MORTALITY IN INDIVIDUALS WITH CONGENITAL HEART DISEASE IN THE NORTH OF ENGLAND

Kate Best, Judith Rankin

BACKGROUND: Few studies have reported long-term survival estimates associated with congenital heart disease (CHD), or risk factors associated with mortality. This information is important for health and social service planning. **METHODS:** Cases of CHD born between 1985–2003 in Northern England and notified to the Northern Congenital Abnormality Survey (NorCAS) were included in this study. The NorCAS data was linked to death registrations in 2008. Kaplan-Meier estimates were calculated and multivariable Cox regression was performed to assess risk factors for mortality. **RESULTS:** There were 5,070 cases of CHD notified to the NorCAS, of which 85.2% survived to age 20. The risk of mortality decreased by 7% for every year’s increase in year of delivery (Hazard ratio (HR)=0.93, 95% confidence interval (CI): 0.91–0.94; $p<0.001$). Compared to term cases, very preterm cases and moderately preterm cases were at increased risk of mortality (HR=6.29, 95% CI: 4.68–8.41 and HR=1.83, 95% CI: 1.51–2.23, both $p<0.001$). Compared to cases of average birthweight, cases of low birthweight were at increased risk of mortality (HR= 1.28, 95% CI: 1.08–1.51; $p=0.004$) and cases of high birthweight were at decreased risk of mortality (HR=0.73, 95% CI: 0.57–0.94; $p=0.016$). Compared to isolated cases, cases with structural extra-cardiac anomalies and cases with chromosomal anomalies were at increased risk of mortality (HR=2.66, 95% CI: 2.11–3.37 and HR=2.98, 95% CI: 2.48–3.57, both $p<0.001$). Cases that were prenatally diagnosed were at increased risk of mortality (HR=2.80, 95% CI: 2.48–3.57; $p<0.001$). There were no significant associations between mortality and plurality, deprivation, sex or maternal age at delivery. **CONCLUSIONS:** Twenty year survival for individuals with CHD was 85.2%. Less recent year of delivery, lower gestational age, low birthweight, the presence of ECAs and prenatal diagnosis increased the risk of mortality. Prenatal diagnosis is likely to act as a proxy for disease severity.

THE IMPACT OF EXTREME MATERNAL OBESITY ON GESTATIONAL AGE AT DELIVERY; A NATIONAL STUDY OF BIRTHS IN ENGLAND

Kate Best, Emma Slack, Judith Rankin, Nicola Heslehurst

Background Many studies have examined the association between maternal BMI and gestational age at delivery, but few have investigated the association with maternal extreme obesity (BMI ≥ 50 kg/m²). **Methods** We included women who delivered live births in 16 UK maternity units between 1990-2007. Multinomial logistic regression was used to estimate odds ratios (ORs) of extreme preterm birth (PTB) (20-27 weeks), very PTB (28-31 weeks), moderately PTB (32-36 weeks), early term (37-38 weeks), late term (41 weeks) and post-term birth (≥ 42 weeks), compared to full term birth (39-40 weeks), according to maternal BMI (underweight (<18.5 kg/m²), recommended (18.5-24.9 kg/m²), overweight (25-29.9 kg/m²), moderately obese (30-34.9 kg/m²), severely obese (35-39.9 kg/m²), morbidly obese (40-49.9 kg/m²) and extremely obese). Missing data were imputed using multiple imputation. **Results** Of 477777 women, 2.7% were underweight, 46.0% were recommended weight, 21.5% were overweight, 8.1% were moderately obese, 2.9% were severely obese, 1.2% were morbidly obese and 0.1% were extremely obese. The odds of extreme PTB, very PTB, moderately PTB and post-term birth were increased in all categories of obesity, but the effect sizes were highest in extremely obese women. Compared to recommended weight women, extremely obese women were at 2.7 times the odds of extreme PTB (95% confidence interval (CI): 1.2-6.2; $p=0.002$), 1.7 times the odds of very PTB (95%CI: 0.7-4.1; $p=0.246$), 2.2 times the odds of moderately PTB (95%CI: 1.6-3.0; $p<0.001$), 1.8 times the odds of early term birth (95%CI: 1.4-2.3; $p<0.001$), 1.3 times the odds of late term birth (95%CI: 1.0-1.6; $p=0.080$) and 2.3 times the odds of post-term birth (95%CI: 1.6-3.1; $p<0.001$). **Conclusion** While all obese women were at increased risk of PTB and post-term birth, extremely obese women were at the greatest risk. Notably, extremely obese women were 2.7 times more likely to have an extreme PTB, which has the greatest risk to both mother and baby.

PB039

ETHNIC DIFFERENCES IN BIRTH WEIGHT IN SURINAME: RESULTS FROM THE 'S LANDS HOSPITAL PARAMARIBO

Ashna Hindori-Mohangoo, Chequita Heye, Olivier Ramkhelawan

Background: Studies on Surinamese migrants living in the Netherlands revealed ethnic differences in birth weight between Surinamese and native-Dutch newborns. Surinamese-Creole and Surinamese-Hindustani newborns had higher rates of low birth weight compared with Dutch newborns. This study explored ethnic differences in birth weight in Suriname. **Methods:** Data on 4522 live term singleton births from the 's Lands Hospital in Paramaribo were analyzed (February 2011 - December 2012). Mean birth weight \pm standard deviation was compared between different maternal ethnic groups, including Creole, Hindustani, Indigenous, Javanese, Maroon and else (Caucasian, Chinese, mixed and others). Linear regression models were used to assess independent associations between maternal ethnicity and birth weight adjusting for maternal age (<25 years vs. ≥ 25 years), parity (0 vs. 1 vs. ≥ 2 previous pregnancies), health insurance (social vs. other) and prenatal care (yes vs. no). **Results:** Mean birth weight was 3168 ± 455 grams (range 3001- 3238) and differed significantly between maternal ethnic groups ($p<0.001$). Hindustani babies had significantly lower mean birth weights (3001 grams; 95% confidence interval 2971-3030 grams) compared with other ethnic groups. Mean birth weight was also lower among younger mothers, with a first delivery, with a social health insurance and without prenatal care. Multivariate analyses revealed that Hindustani babies had significantly lower birth weights than Indigenous babies (-231grams; 95% confidence interval -298 to -164). **Conclusions:** Birth weight differs by maternal ethnic groups in Suriname. Although further research is needed to assess whether these differences are constitutional or pathological, Hindustani mothers are important target groups for preventive interventions to improve perinatal and infant outcomes in Suriname.

PREGNANCY OUTCOMES AMONG WOMEN WITH CONGENITAL HEART DEFECTS IN A LARGE PRIVATE INSURANCE CLAIMS DATABASE

Regina Simeone

Advances in treatment are allowing women with congenital heart defects (CHDs) to live to reproductive age and beyond. Pregnant women experience increases in blood volume, cardiac output and ventricular mass that can cause obstetric and fetal complications in women with CHDs. We used 2008-2013 Truven Health MarketScan® Commercial Claims and Encounters data to estimate the prevalence of selected pregnancy outcomes among pregnant women with CHDs compared to pregnant women without CHDs. We included women aged 15-44 years enrolled for at least 11 months in a private insurance plan. We used diagnosis and procedure codes to identify pregnancies and estimate gestational week at pregnancy end. Women were defined as having a CHD if they had a CHD diagnosis code in an inpatient claim or ≥ 2 CHD diagnoses in outpatient claims, separated by ≥ 30 days. We excluded women with isolated patent ductus arteriosus. Preliminary results indicate that from 2008 to 2013 there were 11,536 pregnancies among 9,345 women with CHDs, and 2,083,826 pregnancies among 1,786,067 women without CHDs. Among pregnancies in women with CHDs, compared to those without, respectively, larger percentages ended in live birth (81.0% and 74.8%) and stillbirth (0.9% and 0.5%), while smaller percentages ended in spontaneous (13.2% and 17.2%) and induced abortion (2.9% and 5.0%) and ectopic pregnancy (1.8% and 2.1%) ($p<0.001$ for all). After adjusting for maternal age and limiting to pregnancies ending in live birth, pregnancies in women with CHDs were more likely to be born early preterm (< 34 weeks gestation) (prevalence ratio (PR) 6.5; 95% confidence interval (CI) 5.6-7.5), late preterm (34-36 weeks gestation) (PR 1.7; 95% CI 1.6-1.7), and delivered by cesarean section (PR 1.3; 95% CI 1.2-1.3). While the majority of pregnancies to women with CHDs end in live birth, these pregnancies might be at increased risk of adverse pregnancy outcomes.

PB040

FOLIC ACID KNOWLEDGE AMONG PREGNANT WOMEN IN THE SINT VINCENTIUS HOSPITAL: THE PERISUR-PROJECT

Ashna Hindori-Mohangoo, Rajnie Mehilal, Lynn Leermakers, Maureen Lichtveld, Symone Detmar, Manodj Hindori

Background: Adequate folic acid intake during the periconceptional period can prevent development of congenital anomalies, including neural tube defects and congenital heart defects. The aim of this study was to investigate the degree of knowledge regarding the protective effects of folic acid in pregnant women seeking care at the Sint Vincentius Hospital in Paramaribo, Suriname. The findings of the study will inform the selection of the target audiences and tailor the content for future health education intervention. **Methods:** During January and August 2013, a total of 603 pregnant women were requested to voluntarily complete a validated questionnaire on folic acid knowledge, periconceptional use, information sources and social demographic characteristics. Verbal informed consent was obtained from all participants. Information on folic acid knowledge was based on answers to the following question: "Have you ever heard or read about folic acid?" **Results:** Data on 591 eligible respondents were analyzed (response rate 98%). From all respondents, 75% had knowledge about folic acid and 12.5% used folic acid during the periconceptional period. The general practitioner was the most common information source of folic acid (63.3%), followed by the internet (25.1%) and the gynecologist (18.1%). Most notable was that only 2.7% of respondents were informed by a midwife. Women without knowledge of folic acid were significantly more often younger than 25 years [OR 1.7], non-insured [OR 3.1] and their level of comprehension of the Dutch language was not good [OR 4.4]. They more often had a Chinese [OR 3.4] or Javanese [OR 1.9] ethnicity and were more often lower educated, OR 7.6 and 3.1 for women with a primary and secondary educational level, respectively. Multivariate analyses revealed that the educational level and the level of comprehension of the Dutch language were independently associated with the knowledge of folic acid. **Conclusions:** Periconceptional intake of folic acid was low in the Sint Vincentius Hospital. Lower educated women and women with a poor Dutch comprehension are important target groups for health education campaigns. Since prenatal care in the Sint Vincetius Hospital is done by gynecologists and not by midwives, gynecologists should be involved in health education interventions.

AMBIENT TEMPERATURE AND EARLY DELIVERY

Sandie Ha

Ambient temperature is associated with mortality and morbidity, but it is unclear whether extremes of temperature increase preterm birth risk. We linked 223,375 singleton deliveries ≥ 23 gestational weeks from 12 US sites to local temperature. Exposure to hot (>90 th percentile) or cold (<10 th percentile) using site-specific temperature distributions were defined for 3-months preconception, every 7 weeks during the first 2 trimesters, 6 weeks before delivery, and whole pregnancy. Births were categorized into 4 groups: early preterm (EPTB, <32 weeks), late preterm (PTB, 32-36 weeks), early term (ETB, 37-38 weeks), and full term (≥ 39 weeks). Poisson regression with generalized estimating equations calculated the relative risk (RR) and (95% confidence interval) for early deliveries associated with hot/cold exposures compared to full term after adjustment for month of conception, humidity, site, infant sex, maternal demographics, parity, insurance, pre-pregnancy body mass index, pregnancy complications, and smoking or drinking in pregnancy. Acute ambient temperature effects were estimated separately for warm season (May-Sept) and cold season (Oct-April) in a case-crossover analysis using conditional logistic regression. Compared to the mild temperature group (10-90th percentile), those exposed to hot or cold during weeks 1-7 had higher risk of EPTB [RRhot: 1.11(1.01-1.21); RRcold: 1.20(1.11-1.30)], PTB [RRhot: 1.05(0.99-1.14); RRcold: 1.09(1.04-1.15)], and ETB [RRhot: 1.04(1.02-1.07); RRcold: 1.03(1.00-1.05)]. Similar findings were observed for hot exposures during weeks 15-21. In the warm season case-crossover, each $^{\circ}\text{C}$ increase in temperature during the previous week was associated with a significant 4-5% increase in the risk of EPTB, PTB, and ETB. During the cold season, each $^{\circ}\text{C}$ increase was associated with 1-2% decrease in risk. Extreme ambient temperature relative to the usual environment may have early and acute impact on the risk of early delivery.

ASSOCIATION BETWEEN INFLUENZA IMMUNIZATION DURING PREGNANCY AND PERINATAL OUTCOMES.

Darios Getahun, Michael Fassett, Morgan Peltier, Vicki Chiu, Deborah Wing, Steven Jacobsen

Introduction: Influenza vaccination during pregnancy is known to prevent severe influenza illness and preterm birth. We assessed the association between influenza vaccine and pregnancy outcomes by the time of vaccination and maternal race/ethnicity. **Methods:** We conducted a retrospective cohort study of singleton pregnancies delivered at ≥ 20 weeks in all Kaiser Permanente Southern California (KPSC) hospitals between 2008-2014. The exposures and outcomes of interest were ascertained from clinical diagnosis codes from KPSC electronic health records and Kaiser Immunization Tracking System (KITS). We limited the analysis to women who were pregnant during the influenza season ($n=225,049$). Adjusted odds ratios (OR) and 95% confidence intervals (CI) were used to estimate the magnitude of associations between immunization status during pregnancy and adverse perinatal outcomes. **Results:** Of the 225,049 women in these analyses, 47% were vaccinated during their pregnancy. Women who were vaccinated during their pregnancy were at lesser risk of influenza disease (OR 0.59, 95% CI 0.53-0.66), preterm birth (OR 0.82, 95% CI 0.79-0.84), preterm rupture of membranes (OR 0.8, 95% CI 0.76-0.85), placental abruption (OR 0.87, 95% CI 0.8-0.95), neonatal intensive care unit admission (OR 0.84, 95% CI 0.82-0.87), still birth (OR 0.69, 95% CI 0.56-0.85). We observed a weak association between influenza vaccination and intrauterine growth restriction (OR 1.07, 95% CI 1.02-1.12) and no association with preeclampsia (OR 1.01, 95% CI 0.98-1.05). **Conclusions:** Our results suggest that influenza vaccine during pregnancy is associated with significantly lower risk of adverse perinatal outcomes. Counseling pregnant women about vaccination may be beneficial to lower risk of adverse perinatal outcomes.

MATERNAL CIRCULATING PLGF LEVELS IN RELATION TO FETAL INSULIN SENSITIVITY AND BETA-CELL FUNCTION INDICES IN INFANTS BORN SMALL-FOR-GESTATIONAL-AGE

Hua He

Objective: Low maternal circulating placenta growth factor (PlGF) levels are predictive of poor fetal growth or small-for-gestational-age (SGA). SGA infants are more likely to develop type 2 diabetes in adulthood. It is unknown whether maternal PlGF is associated with insulin sensitivity and β -cell function in early life. The present study sought to address this question. **Methods:** This was a nested case-control study in a prospective pregnancy cohort ($n=2366$) in Quebec, including 162 SGA (birth weight <10 th percentile) and 162 appropriate-for-gestational-age (AGA) (25th-75th percentiles) singleton non-malformations infants matched by ethnicity, smoking status and gestational age. The primary outcomes were cord blood biomarkers of insulin sensitivity (QUICKI) and β -cell function (insulin/glucose ratio, proinsulin/insulin ratio). Other outcomes include insulin and insulin-like growth factor-1 (IGF-1) concentrations. **Results:** Maternal plasma PlGF concentrations were substantially lower in SGA versus AGA infants (median, 444.08 vs. 825.60 pg/ml, $P<0.0001$), so were cord plasma proinsulin (median, 8.98 vs. 12.38 pmol/L, $P=0.0009$) concentrations and insulin/glucose ratios (median, 0.04 vs. 0.06, $P=0.0381$). Overall, maternal plasma PlGF concentrations were positively correlated to cord plasma insulin/glucose ratios ($r=0.13$, $P=0.0443$), insulin ($r=0.14$, $P=0.0288$) and IGF-1 ($r=0.29$, $P<0.0001$) concentrations, and negatively correlated to QUICKI ($r=-0.13$, $P=0.0459$). SGA newborns with low maternal PlGF (<25 th percentile of maternal circulating PlGF concentrations in AGA infants) had lower insulin/glucose ratios than AGA newborns ($P=0.0257$). Adjusting for maternal and infant characteristics, each log unit increase in maternal plasma PLGF was associated with a 0.19 log unit increase in cord plasma IGF-1 ($P=0.0019$) and a 0.13 log unit decrease in proinsulin/insulin ratio ($p=0.0470$), respectively. In SGA newborns, each log unit increase in maternal plasma PlGF was associated with a 0.21 log unit decrease in cord plasma proinsulin/insulin ratio ($p=0.0451$). **Conclusions:** Low maternal circulating PlGF may indicate low β -cell function in SGA newborns. Whether this may be related to long-term postnatal metabolic health remains to be clarified.

GESTATIONAL WEIGHT GAIN AND THE BLACK-WHITE DISPARITY IN PRETERM BIRTH

Stephanie Leonard, Lucia Petito, Olof Stephansson, Yvonne Cheng, Jennifer Hutcheon, Lisa Bodnar, Barbara Abrams

Disparities in preterm birth rates between non-Hispanic black and white women in the United States are poorly understood. We investigated the association between gestational weight gain (GWG) and preterm birth and assessed differences in this relationship between white and black births in the 2011-2014 U.S. Birth Data Files ($n=7,402,008$). Our sample included live-born singletons without congenital anomalies. We calculated weight gain-for-gestational age z-scores, which account for gestational age and prepregnancy body mass index category, and categorized GWG z-scores as low (<-1), reference (-1 to $+1$), and high ($>+1$) and preterm birth as early (<32 wk) and late (≥ 32 and <37 wk). We used multivariate logistic regression models to estimate the associations between GWG category and preterm birth. We tested for multiplicative interaction between GWG and race in the models with likelihood ratio tests. To test for additive interaction, we used Wald tests after running equivalent multivariate linear-binomial models. Overall, high and low GWG were associated with early preterm birth. However, associations were stronger in blacks (multiplicative interaction $P<0.0001$). For example, high GWG (compared to white women with reference GWG) was associated with adjusted odds of 4.56 (95% confidence interval (CI): 4.43, 4.70) for black and 1.61 (95% CI: 1.57, 1.66) for white mothers. The corresponding predicted marginal rate of early preterm birth per 1,000 live births associated with high GWG was 31 in blacks and 11 in whites. High and low GWG were also associated with late preterm birth, with a weak multiplicative interaction between race and GWG. However, there was a stronger additive interaction ($P<0.0001$), indicating that the association between GWG and late preterm birth did not differ by race. Results from these recent national data suggest a complex relationship between GWG and early and late preterm in black and white women that deserves further study.

PREGNANCY COMPLICATIONS IN WOMEN EXPOSED AS FETUSES TO MATERNAL PRE-EXISTING CHRONIC DISEASES

Tuija Mannisto, Mika Gissler, Eero Kajantie, Hannele Laivuori, Johan Eriksson, Risto Kaaja, Anneli Pouta, Marja Vaarasmaki

Maternal chronic diseases increase the risk of pregnancy complications. Whether women who as fetuses had been exposed to maternal chronic diseases have higher risk of pregnancy complications is unknown. The FinnGeDi study included data on all births in Finland in 2009 (N=60,790) from the Medical Birth Registry (MBR). Women born in 1987 or later who had a pregnancy resulting in a birth in 2009 had available data on their fetal exposures from the MBR (N=4,461). A woman was considered to have been exposed to maternal chronic diseases as a fetus if her mother had pre-existing diabetes, hypertension, thyroid disease, asthma, heart disease, gastrointestinal disease or renal disease while expecting her. The odds ratios (ORs) and 95% confidence intervals (CIs) of pregnancy complications were estimated using logistic regression, adjusted for covariates. Overall, 77 women (1.7%) had been exposed to maternal chronic diseases in utero. There were no significant differences in the prevalence of women requiring artificial reproductive treatment between exposed or non-exposed women. Also, no difference in the prevalence of pregnancy complications such as gestational hypertension or preeclampsia, preterm birth, placenta previa, placental abruption, or neonate requiring intensive care treatment was observed between exposed or non-exposed women. However, women with fetal exposure to maternal chronic diseases had higher odds of gestational diabetes (OR 2.30, 95% CI 1.16-4.57) than non-exposed women. Specifically, the odds were higher in women with fetal exposure to maternal diabetes or hypertension. In conclusion, among women who as fetuses were exposed to pre-existing maternal chronic diseases, particularly to diabetes and hypertension, had increased odds of gestational diabetes. The findings may be due to familial predisposition to metabolic disturbances or due to fetal programming caused by the maternal condition.

STRESSORS AND MISCARRIAGE: MULTIPLE DOMAINS IN LIFE-COURSE PERSPECTIVE

Yu Li, Claire Margerison-Zilko, Kelly L. Strutz, Claudia Holzman

Prior studies have provided evidence linking stressors before pregnancy and miscarriage, but few of these have used a life-course perspective or considered stressors in multiple domains. Our study examined multiple domains of stressors across the life-course from childhood through adulthood and pregnancy. Data came from women with at least one previous pregnancy in the Pregnancy Outcomes and Community Health (POUCH, 1998-2004) study (n=2,112). Stressors were assessed via questionnaire; domains examined were abuse/witnessing violence, loss of someone close, economic hardship, legal and substance abuse. Each domain was coded as during childhood only, adulthood only, both childhood and adulthood, or neither. We used logistic regression models to estimate the associations between stressors and miscarriage, using the proportion of miscarriages per # of previous pregnancies as outcome. We also examined effect modification between race/ethnicity and stressors. All models were adjusted for maternal age, race/ethnicity, education, and marital status. Among African American (AA) women miscarriage was associated with abuse (Odds Ratio(OR): 1.28, 95% CI 1.03,1.58) and legal (OR: 2.68, 95%CI 1.74,4.12) stressors occurring in both childhood and adulthood and with substance use during childhood only (OR: 1.33, 95%CI 1.02,1.72). No significant associations were observed for white/other women. Life stressors in multiple domains—some dating back to childhood and carried through to adulthood—appear related to miscarriage, but only among AA women. Future studies might explore life stressors and specific causes of miscarriage, with a goal of risk stratification and prevention.

FETAL EXPOSURE TO MATERNAL HYPERTENSIVE DISORDERS OF PREGNANCY IS ASSOCIATED WITH ADOLESCENT OFFSPRING CARDIAC STRUCTURE BUT NOT FUNCTION

Simon Timpka, Corrie Macdonald-Wallis, Nishi Chaturvedi, Paul W. Franks, Debbie A. Lawlor, Abigail Fraser

Background: Exposure to maternal preeclampsia in utero is associated with congenital heart defects, higher blood pressure (BP) in childhood and adulthood, and increased risk of stroke later in life. We aimed to investigate whether maternal HDP (hypertensive disorders of pregnancy: preeclampsia, gestational hypertension, and essential hypertension) are associated with offspring cardiac structure and function in adolescence. Methods: Offspring included in the Avon Longitudinal Study of parents and Children (ALS C), a prospective pregnancy cohort, underwent echocardiography (mean age 17.7 years, SD 0.3, N=1,592). We used linear regression to examine whether maternal HDP were associated with cardiac structure and systolic/diastolic function in adolescence. Results in main model were adjusted for maternal age, pre-pregnancy BMI, parity, glycosuria/diabetes, education, and smoking during pregnancy. Results: Exposure to maternal preeclampsia (0.025; 95% confidence interval, 0.0080 to 0.043), gestational hypertension (0.010; 0.0018 to 0.017), and essential hypertension (0.021; 0.0039 to 0.038) were all associated with greater offspring relative wall thickness. Preeclampsia was also associated with a smaller left ventricular end diastolic volume in offspring (-9.0 ml, -15.0 to -3.1). We found no associations between exposures and several measures of offspring systolic/diastolic cardiac function. Conclusion: Maternal HDP are associated with aspects of adolescent offspring cardiac structure but not cardiac function. Exposure to maternal hypertension in utero was associated with greater mean relative wall thickness whereas preeclampsia was also associated with reduced mean left ventricular end diastolic volume. Additional follow-up of this cohort will clarify whether these structural differences result in poorer health outcomes.

ANTIBIOTIC EXPOSURE IN INFANCY AND RISK OF CHILDHOOD OVERWEIGHT AND OBESITY: A SYSTEMATIC REVIEW AND META-ANALYSIS

Avanthi Ajjarapu, Linda Snetselaar, Vanessa Curtis, Wei Bao

Previous studies examining the association between early-life exposure to antibiotics and development of childhood overweight and obesity have yielded conflicting results. We aimed to systematically review available evidence and quantitatively summarize the associations of antibiotic use in infancy with childhood overweight and obesity through meta-analysis. We conducted a systematic literature search using PubMed and EMBASE databases through November 20, 2015. Studies were eligible for inclusion if they examined antibiotic exposure in infancy (less than 2 years of age) and obesity/overweight status (based on Body Mass Index (BMI) or BMI-z scores) at childhood. Adjusted odds ratios (ORs) and corresponding 95% confidence intervals (CIs) from individual studies were pooled using a random-effects model. We identified 490 potentially relevant studies from initial search. Of these, 5 studies were included for systematic review and meta-analysis. We found a significant and positive association between antibiotic exposure in infancy and childhood overweight and obesity (pooled OR: 1.13; 95% CI: 1.03-1.25). More specifically, an association between early life antibiotic exposure and childhood obesity (pooled OR: 1.05; 95% CI: 1.01-1.09) and childhood overweight (pooled OR: 1.23; 95% CI: 1.04-1.44) were observed. In addition, there was evidence suggesting that male gender, antibiotic exposure at less than 6 months, broad-spectrum antibiotic use, and greater frequency of antibiotic exposure were associated with a greater risk for childhood overweight and obesity. In conclusion, findings from this systematic review and meta-analysis indicated that antibiotic exposure in infancy was associated with a greater risk of overweight and obesity in childhood. Due to the limited evidence available, our findings warrant confirmation in future studies.

PB049

FAT INTAKE IN PREGNANCY AND OFFSPRING INSULIN RESISTANCE-EFFECT MODIFICATION BY GESTATIONAL DIABETES MELLITUS

Ekaterina Maslova

Background: Offspring of women with gestational diabetes mellitus (GDM) are at risk for insulin resistance. The role of fatty acids in programming offspring metabolic health have been demonstrated in animal studies. Evidence among humans remains scarce; even less is understood among high-risk populations of GDM offspring. **Objective:** To examine the association of fat intake in pregnancy with offspring markers of insulin resistance. **Methods:** We used data from the Diabetes and Women's Health Study that included 606 women with a GDM index pregnancy and 628 control women nested in the Danish National Birth Cohort. Fat intake was quantified using a food frequency questionnaire in gestational week 25 and was subdivided into saturated fat (SFA), monounsaturated fat (MUFA), and polyunsaturated fat (PUFA). At age 9-16 years, the offspring underwent a clinical examination which included a fasting blood sample. Primary outcomes included fasting plasma insulin and HOMA-IR. Secondary, body composition was evaluated using a DXA scan (subset of 650). Multivariable analyses were conducted applying a 1:1 substitution of carbohydrates for fat. **Results:** Mean(SD) fat intake was 81(17)g/day and 79(15)g/day among GDM and control women, respectively. No association were observed for total fat and SFA intake with any of the considered outcomes. Substitution of 100 kcal of maternal carbohydrates for MUFA was associated with 41% (95%CI: 3%,92%) increase in HOMA-IR and 37% (95%CI: 4%,80%) increase in fasting plasma insulin among GDM offspring. Also among GDM offspring, PUFA was related to a 38% (95%CI: 6%,59%) decrease in HOMA-IR and a 35% (95%CI: 6%,55%) decrease in fasting insulin when replacing 100 kcal of carbohydrates. Adjusting for total body fat % strengthened the results for PUFA only. We found no associations with any of the body composition measures. None of the relations for the control dyads reached statistical significance. **Conclusions:** MUFA intake in pregnancy was associated with adverse markers of insulin resistance in the 9-16 year old GDM offspring, while the opposite was observed for PUFA intake. Quality of fat, rather than total fat, intake may be a more important determinant of insulin resistance among offspring exposed to GDM.

PB051

DAUGHTERS OF MOTHERS WHO SMOKE: IN UTERO TOBACCO EXPOSURE AND SUBSEQUENT PRENATAL SMOKING IN FEMALE OFFSPRING

Collette Ncube, Beth Mueller

Objective: Prenatal exposure to tobacco is associated with adverse health outcomes for the mother and child, and has been associated with an increased risk of tobacco smoking and nicotine dependence in offspring. The objective of this study was to examine the risk of prenatal smoking among females who were themselves exposed to tobacco smoke in utero. **Methods:** Using a population-based cohort study design we linked birth record data of mothers and daughters delivering 1984-1996 and 1996-2013, respectively in Washington State. The exposure was mothers' prenatal smoking (any versus no smoking at any time during pregnancy), and the outcome was daughters' prenatal smoking (any versus no smoking at any time during pregnancy). Using multivariable log-binomial regression we obtained adjusted relative risk (RR) estimates and 95% confidence intervals (CI) of the association between mothers' and daughters' prenatal smoking. **Results:** Daughters exposed to tobacco smoke in utero were almost twice as likely to smoke during their pregnancy, compared to unexposed daughters (RR = 1.77; 95% CI: 1.72, 1.83, adjusted for the year the daughter delivered, her marital status and educational attainment, and the mothers' race/ethnicity). Increased risks were observed in all racial, income, and age groups examined. **Conclusions:** Female children exposed to tobacco constituents in utero have increased risk of smoking later on during their own pregnancy, emphasizing the importance of exposures during the prenatal period. The mechanisms leading to prenatal smoking are multifactorial and likely include behavioral, genetic, epigenetic and environmental factors. An understanding of this risk factor for prenatal smoking may guide healthcare providers and target smoking cessation interventions to at-risk children.

PB050

THE ROLE OF MATERNAL ADVERSE CHILDHOOD EXPERIENCES AND RACE IN INTERGENERATIONAL HIGH-RISK SMOKING BEHAVIORS

Veronica Pear

Adverse childhood experiences (ACE) are associated with increased risk of smoking in children and adults, and have recently been associated with both prenatal smoking and next-generation child smoking. We assessed three exposure-outcome associations: (1) maternal ACE and prenatal smoking; (2) maternal ACE and early initiation of smoking in children; and (3) prenatal smoking and early initiation of smoking in children, modified by maternal ACE. We also tested these associations for effect modification by maternal race/ethnicity. Our study sample consisted of 4,775 mother-child dyads from the National Longitudinal Survey of Youth 1979 and its partner study, the NLSY79 Children and Young Adults survey. We analyzed three ACE exposures (physical abuse, household alcohol abuse, and household mental illness), prenatal smoking status, and age of smoking initiation in their children. Adjusted risk ratios (aRR) were estimated using log-linear regression models that accounted for the complex survey design. Multiplicative interaction was assessed by Wald tests. We found that history of physical abuse was associated with prenatal smoking in all races/ethnicities (aRR, 1.41; 95% Confidence Interval (CI), 1.17-1.70) and household mental illness was a risk factor for smoking only in black mothers (aRR, 1.59; 95% CI, 1.02-2.47). Childhood physical abuse was associated with offspring smoking (aRR, 1.19; 95% CI, 1.06-1.34), as was household alcohol abuse (aRR, 1.18; 95% CI, 1.07-1.29). Maternal ACE modified an association between prenatal smoking and child smoking in Hispanics (aRR with ACE, 1.39; 95% CI, 0.80-2.40; aRR without ACE, 0.85; 95% CI, 0.65-1.10), but not in other race/ethnicities (global p-value for interaction, 0.18). These findings from a national sample suggest that early life adversity is associated with high-risk smoking behaviors in women and their children.

PB052

RACIAL DISPARITIES IN THE TRANSGENERATIONAL TRANSMISSION OF LOW BIRTHWEIGHT RISK

Collette Ncube, Daniel Enquobahrie, Jessica Burke, Steven Albert

Background: Low birthweight (LBW) is associated with life course health and disease. Recent evidence supports familial aggregation of LBW risk; however, significant gaps remain in understanding of potential intergenerational transmission of LBW risk. We examined the association of mothers' LBW status with infant LBW risk, and whether the association differed by mothers' race. **Methods:** participants were 6,633 non-Hispanic (NH) white and NH black infants (born 2009-2011) and their mothers (born 1979-1998) in Allegheny County, Pennsylvania. Birth records were used to determine birth weight and race. We created categorical variables of LBW status (< 2500 grams), and LBW subgroups - moderate LBW (1,500-2,499 grams) and very LBW (<1,500 grams). Hierarchical Generalized Linear Modeling for binomial and multinomial logistic regression were used to calculate Odds Ratios (OR) and 95% confidence intervals (CI). Stratified analyses, and an interaction between maternal LBW and race, were conducted to assess effect modification by mothers' race. **Results:** Maternal LBW was associated with 1.53 (95% CI: 1.15 – 2.02) and 1.75 (95% CI: 1.29 – 2.37) fold increases in risk of infant LBW and moderate LBW, respectively, but not very LBW (OR = 86; 95% CI: 0.44 – 1.70). The interaction between maternal LBW and mothers' race was marginally significant (P = 0.07). In stratified analyses, associations were observed among NH blacks, and not among NH whites. **Conclusion:** Maternal LBW is associated with increased risk of infant LBW, particularly MLBW, and the association is stronger for NH black mothers.

POSTPARTUM MATERNAL MORTALITY AND CESAREAN DELIVERY: A POPULATION-BASED STUDY IN BRAZIL

Ana Paula Esteves-Pereira, Catherine Deneux-Tharaux, Marie-Hélène Bouvier-Colle, Maria do Carmo Leal

Objective: Cesarean delivery rates continue to increase worldwide and reached 57% in Brazil in 2013. It is unlikely that such a rapid change in obstetrical risk happened to justify such an increase, yet instead, it suggests an enlargement of the range of cesarean indications to non-medical purposes. Although the safety of this surgery has improved in the last decades, this trend is a concern because it carries potential risks to women's health and may be a modifiable risk factor of maternal mortality. This paper aims to investigate the risk of postpartum maternal death directly associated with cesarean delivery in comparison to vaginal delivery in Brazil. **Methods:** This was a population-based case-control study performed in eight Brazilian states. To control for indication bias, deaths due to antenatal morbidity were excluded. We included 73 cases of postpartum maternal deaths from 2009-2012. Controls were selected from the "Birth in Brazil Study", a 2011 nationwide survey including 9221 postpartum women. We examined the association of cesarean section and postpartum maternal death by multivariate logistic regression, adjusting for confounders. **Results:** After controlling for indication bias and confounders, the risk of postpartum maternal death was almost three-fold higher with cesarean than vaginal delivery - adjusted odds ratio (adjOR) of 2.9 and 95% confidence interval (CI) of 1.6-5.1. This was mainly due to deaths from postpartum hemorrhage (adjOR 3.04 95% CI 1.4 - 6.6) and the combination of deaths from pulmonary embolism, amniotic fluid embolism and complications of anesthesia (adjOR 10.9 95% CI 2.2 - 55.3). **Conclusion:** Cesarean delivery is an independent risk factor of postpartum maternal death, in a context where most cesareans are performed before the onset of labor. Clinicians and patients should consider this fact in balancing the benefits and risks of the procedure.

DIFFERENCES IN SYSTEMIC MATERNAL IMMUNE BIOMARKERS BY FETAL SEX

Brandie Taylor

Objective: Small studies suggest that fetal sex alters maternal inflammation possibly explaining associations between male fetal sex and pregnancy complications. We examined fetal sex and maternal immune biomarkers in 250 first and 392 second trimester serum samples. **Methods:** Data was obtained from a previous nested case-control study of maternal immune markers and preeclampsia within the Collaborative Perinatal Project (CPP). Associations between RANTES, interleukin (IL)-6, IL4, IL5, IL12, IL10, IL8, IL1-beta, interferon (IFN)-gamma, tumor necrosis factor (TNF)-beta, transforming growth factor (TGF)-beta and fetal sex were examined. Assay data that falls below the limit of detection (non-detects) can lead to bias with traditional methods. We used a modified version of cox regression developed by Dinse et al. to handle data with non-detects. Hazard ratios (HR) and 95% confidence intervals (CI) adjusted for maternal age, race, body mass index and smoking are reported. Analysis among uncomplicated pregnancies only did not alter the results. Neither did adjusting for pregnancy complications. **Results:** Male fetal sex was associated with IFN-gamma (HRadj 2.0, 95% CI 1.2-3.2) in the first trimester. In the second trimester, male fetal sex was associated with IL1-beta (HRadj 0.7, 95% CI 0.5-0.9), IL5 (HRadj 0.7, 95% CI 0.6-0.9), TNF-beta (HRadj 0.6, 95% CI 0.4-0.9), IL4r (HRadj 0.8, 95% CI 0.6-0.9), and IL10 (HRadj 0.8, 0.6-1.0). **Conclusions:** Male fetal sex was associated with an increased rate of a first trimester pro-inflammatory cytokine and decreased rates of second trimester pro-inflammatory (TNF-beta and IL1-beta), anti-inflammatory (IL4r) and regulatory cytokines (IL5 and IL10). Reduction in maternal regulatory/anti-inflammatory markers by male fetal sex is consistent with a previous study. Immune biomarker levels and function vary across gestation. Thus, fetal sex may impact the maternal immune milieu but this may be more robust as gestation progresses.

MATERNAL MORTALITY IN OBESE WOMEN: A NATIONAL STUDY IN FRANCE

Ana Paula Esteves-Pereira, Monica Saucedo, Marie-Hélène Bouvier-Colle, Catherine Deneux-Tharaux

Objective: Following the trend in the general population, the prevalence of obesity is increasing among pregnant women worldwide. Previous studies have reported a higher incidence of pregnancy complications in obese women. However, whether this leads to an increased risk of severe maternal outcomes, and through what mechanisms, has been poorly assessed. Our objective was to test and quantify the association between obesity and maternal death, and to explore its explanatory mechanisms, globally and by main cause of death. **Study design:** Population-based case-control study using national data. Cases were 148 maternal deaths selected from the French National Confidential Enquiry into Maternal Deaths for 2007-2009. Controls were 13,377 women from the 2010 French National Perinatal Survey, a national representative sample of parturients. Associations between obesity (BMI ≥ 30 kg/m²) and maternal death were studied through multivariable logistic regression, with covariates included by successive steps corresponding to our explanatory hypotheses. **Results:** The proportion of obesity was 20.9% in cases and 9.9% in controls, crude OR 2.4 (95% CI 1.6-3.6). Among cases, the primary cause of death was cardiovascular diseases in obese women (32%) and hemorrhage in non-obese women (17%). Obesity was associated with a higher risk of maternal mortality independently from education level, nationality, age, parity, previous cesarean, adjOR 1.6 (95%CI 1.0-2.4). This excess risk was mainly due to deaths from cardiovascular diseases, adjOR 4.4 (95%CI 1.9-10.4) and from amniotic fluid embolism, adjOR 3.1 (95%CI 1.1-8.9). **Conclusion:** Obesity is an independent risk factor for maternal mortality, mainly cardiovascular and amniotic fluid embolism deaths. These results emphasize the need for optimal screening, diagnosis, and management of cardiovascular diseases in obese women before and during pregnancy.

PREGNANCY-ASSOCIATED MORTALITY AFTER BIRTH, SPONTANEOUS ABORTION, OR INDUCED ABORTION IN FINLAND, 2001-2012

Mika Gissler, Elina Karalis, Anna-Maija Tapper, Veli-Matti Ulander

OBJECTIVE: We compared mortality rates for women who were pregnant or within 1 year of pregnancy termination with all other women of reproductive age. Pregnancies were categorized into pregnancies ending in births, induced abortions, and spontaneous abortions. **STUDY DESIGN:** This is a population-based, retrospective cohort study from Finland for years 2001-2012. Information on all deaths of women aged 15 to 49 years (n=10,402) was received from the Cause-of-Death Register and linked to the Medical Birth Register (n=693,331 births), the Register on Induced Abortions (n=127,897 induced abortions), and the Hospital Discharge Register (n=121,716 spontaneous abortions) to identify pregnancy-associated deaths (n=268, 2.6%). **RESULTS:** The age-adjusted mortality rate for women during pregnancy and within 1 year of pregnancy termination was 28.4 deaths per 100,000 pregnancies, which was significantly lower than the mortality rate among non-pregnant women, 46.0 per 100,000 person-years (risk ratio 0.59, 95% CI 0.52-0.67, p<0.001). The mortality was higher after a spontaneous (33.7/100,000, p=0.009) or induced abortion (74.6/100,000, p<0.001) than after a birth (21.3/100,000). The mortality rate was decreased for all medical causes for pregnant women (13.6/100,000, p<0.001) and for all pregnancy types - births (11.4/100,000, p<0.001), spontaneous abortions (13.4/100,000, p=0.022), and induced abortions (20.5/100,000, p=0.040) - compared to non-pregnant women (26.6/100,000). For deaths from injuries and accidents, the mortality rate was lower after a birth (8.1/100,000, p<0.001), but increased after a spontaneous (22.8/100,000, p=0.039) or induced abortion (49.5/100,000 p<0.001) compared to for non-pregnant women (14.8/100,000). **CONCLUSION:** Our study supports the healthy pregnant woman effect for all pregnancies, including those not ending in births. The increased rate of deaths due to injuries and accidents among women with recent spontaneous or induced abortion requires attention.

PSYCHOSOCIAL STRESS DURING EARLY PREGNANCY IS ASSOCIATED WITH INCREASED RISK OF BACTERIAL VAGINOSIS IN NON-CAUCASIAN WOMEN

Negar Tabatabaie

There is a gap of knowledge on the associations between acute psychosocial stressors during pregnancy (PSP) and bacterial vaginosis (BV). Also, non-Caucasian women may be at higher risk of BV during pregnancy. Therefore, we measured the association of acute stressors including pregnancy-related anxiety, perceived stress (PS) and depression symptoms (using the Center for Epidemiologic Studies Depression Scale; CESD-10) with the risk of BV in early pregnancy (8-14 wk of gestation) in 441 women from the 3D longitudinal cohort study, considering the moderating role of ethnicity. Self-report questionnaires were used to measure the acute stressors. Bacterial vaginosis was diagnosed based on Nugent score by gram staining of the vaginal smear and was categorized as follows: no bacterial vaginosis (NBV, score: 0-3), intermediate bacterial vaginosis (IBV, score: 4-6) and bacterial vaginosis (BV, score ≥ 7). Associations between maternal PSP and BV status were investigated using ordinal logistic regression. Maternal pregnancy-related anxiety (odds ratio (OR): 1.24, 95% confidence interval (CI) (1.02, 1.50), $p=0.03$), PS (OR: 1.32, 95% CI (1.07, 1.61), $p=0.01$) and depressive symptoms (OR: 1.11, 95% CI (1.01, 1.23), $p=0.04$) were associated with increased risk of BV in non-Caucasian women ($n=119$) after controlling for maternal age, pre-pregnancy BMI, marital status, past and current history of smoking and of presence of sexually transmitted infections. In contrast, maternal pregnancy-related anxiety (OR: 0.95, 95% CI (0.86, 1.05), $p=0.32$), PS (OR: 0.96, 95% CI (0.86, 1.08), $p=0.50$) and depressive symptoms (OR: 1.02, 95% CI (0.95, 1.09), $p=0.58$) were not associated with risk for BV in Caucasian women ($n=322$). This study suggests that maternal PSP is associated with a small but significant increased risk of BV in non-Caucasian women in early pregnancy. Further studies should examine associations between acute PSP and vaginal infection by ethnicity in communities under high stress.

INCREASING COMPLEXITY OF DIABETES IN PREGNANCY AND IMPLICATIONS FOR MATERNAL AND NEONATAL MORBIDITY AND MORTALITY

Amy Metcalfe, Yasser Sabr, Jennifer Hutcheon, Lois Donovan, Janet Lyons, Jason Burrows, KS Joseph

Diabetes in pregnancy increases the risk of adverse maternal and neonatal outcomes. However, the association between maternal comorbidity (e.g. hypertension, thyroid disorders) in diabetic pregnancies and maternal and infant health is not well understood. This study aimed to describe temporal trends in the prevalence of comorbidity in pregnancies with Type 1 (T1DM), Type 2 (T2DM) and gestational (GDM) diabetes and its association with maternal and infant outcomes. National hospitalization data (Canada except Quebec) from 2004-2013 were obtained on singleton pregnancies in women with diabetes who delivered at ≥ 36 weeks of gestation ($n=115,435$). Non-parametric tests for trend were used to examine temporal patterns in the prevalence of comorbidity and chi square tests were used to examine the association between comorbidity and severe maternal (e.g. embolism, uterine rupture, death) and neonatal (e.g. asphyxia, birth injuries, death) outcomes. Overall, 22.6% of T1DM, 29.0% of T2DM and 13.8% of GDM pregnancies had one or more comorbidity. A significant increase was observed in the prevalence of comorbidity in T2DM ($p=0.01$) and GDM ($p<0.001$) pregnancies over time, while the prevalence of comorbidity in T1DM pregnancies remained stable ($p=0.98$). The presence of comorbidity was not associated with severe maternal ($p=0.77$) or neonatal ($p=0.67$) outcomes in women with T1DM. While no difference was observed in maternal outcomes ($p=0.79$) for women with T2DM with comorbidity, their infants were more likely to experience an adverse event (17.6% vs 14.9%, $p=0.004$). Women with GDM and a comorbidity were less likely to experience a severe maternal event (3.1% vs 3.5%, $p=0.004$); however, their infants were more likely to suffer from a severe neonatal outcome (12.0% vs 9.7%, $p<0.001$). In the past decade, both T2DM and GDM have increased in complexity due to the presence of comorbid conditions. Comorbidity in women with T2DM and GDM is associated with worse neonatal outcomes.

INCREASING RATES OF COMORBIDITIES IN PREGNANCY: TEMPORAL TRENDS IN THE UNITED STATES FROM 1992 TO 2012

Amy Metcalfe, James Wick, Paul Ronksley

The presence of pre-existing or pregnancy-induced disease during pregnancy can alter obstetric management and place the mother and fetus at increased risk of adverse outcomes. Recently, an obstetric comorbidity index has been developed to predict the risk of serious adverse events, based on the presence of pre-existing conditions (e.g. diabetes), pregnancy-induced conditions (e.g. pre-eclampsia) and advanced maternal age. Annual data on women hospitalized for delivery between 1992 and 2012 were obtained from the National Inpatient Sample and the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality, representing a 20% sample of hospital discharges from across the United States. Chi square tests for trend were used to examine temporal patterns in the proportion of pregnancies affected by comorbidities across the 20-year period and were stratified by maternal race. In 1992, 34.3% of pregnancies had a comorbidity score of ≥ 1 ; this significantly increased to 44.1% by 2012 ($p<0.001$). While significant increases were observed for all races, the relative rate of change was lowest for Whites (26.1% increase) and highest for Asian/Pacific Islanders (49.1% increase). Increasing rates of pre-existing and pregnancy-induced disorders were observed in all races. In 1992, 6.3% and 16.3% of pregnancies involved at least one pre-existing condition or pregnancy-induced condition respectively; this increased to 10.6% and 25.3% in 2012 ($p<0.001$). While the greatest relative increase in the prevalence of pre-existing conditions was observed in Asian/Pacific Islanders, this group had the lowest absolute rate of pre-existing conditions overall. The rate of both pre-existing comorbidities and pregnancy-induced disease is increasing in pregnant women in the United States and varies substantially by race. These trends provide valuable insight into the increasing medical complexity of pregnancy in the United States.

ARE YOU WHAT YOUR MOTHER ATE: MATERNAL SUGAR-SWEETENED BEVERAGES INTAKE IN PREGNANCY AND OFF-SPRING GROWTH AND OBESITY THROUGH AGE 7 YEARS?

Yeyi Zhu

Sugar-sweetened beverages (SSB), the leading source of dietary added sugars, have been related to impaired glucose homeostasis and obesity. Epidemiologic data on the intergenerational impact of SSB intake on offspring cardiometabolic outcomes are sparse. We prospectively investigated maternal SSB intake in pregnancy in relation to child growth and risk of obesity through age 7 y among high-risk children born to gestational diabetes (GDM) pregnancies. A total of 918 mother-singleton child dyads from the Danish National Birth Cohort were included. Diet in pregnancy was assessed by a food frequency questionnaire. Offspring body mass index z-scores (BMIZ) by WHO references were calculated using weight and length/height measured at birth, 5 mo, 12 mo, and 7 y. Overweight/obesity (OW/OB) was defined by WHO cutoffs. Linear and Poisson regression with robust standard errors were used, adjusting for non-dietary/dietary factors such as prepregnancy BMI, total energy, and intakes of meat, grain and sweets. Maternal SSB intake in pregnancy was significantly and positively associated with offspring BMIZ (adjusted β per 1 cup increase/day = 0.08, 95% CI: 0.02, 0.14) and risk of OW/OB at 7 y [adjusted relative risk (aRR) comparing the highest (Q4) vs. lowest quartile (Q1) = 1.59, 95% CI: 1.01, 2.48, P for trend = 0.011]. The association was more pronounced among children who consumed more SSB in childhood. Specifically, among offspring who consumed SSB \geq once/week at 7 y, aRR (95% CI) for OW/OB comparing maternal Q4 vs. Q1 was 1.76 (1.02, 3.04), whereas the corresponding aRR was 1.10 (0.50, 2.41) for children who consumed SSB $<$ once/week. No significant associations were observed between pregnancy SSB intake and offspring growth in infancy. In conclusion, intrauterine exposure to high intake of SSB was significantly and positively related to BMIZ and risk of OW/OB at 7 y among children of women with GDM. The associations might be modified by offspring SSB consumption in childhood.

AMBIENT AIR POLLUTION AND RISK OF GESTATIONAL HYPERTENSION

Yeyi Zhu

Air pollution exposure has been linked to increased blood pressure and hypertensive disorders in the general population, but data on gestational hypertension (GH) are limited. We investigated criteria air pollutants and air toxics preconception, during early gestation and weekly up to gestational week 20 in relation to GH risk in a nationwide US cohort (Consortium on Safe Labor, 2002–2008). We compared 6,074 GH cases to 199,980 normotensive singleton pregnancies identified by medical records. Air pollution exposures were estimated by modified Community Multiscale Air Quality models. Poisson regression with generalized estimating equations estimated relative risks by interquartile range (IQR) for air pollutants and high exposure (≥ 75 th percentile) for air toxics, after adjustment for study site and major demographic and perinatal risk factors. For each IQR increase, GH risk was significantly increased 18% for sulfur dioxide (SO₂) and 5% for particulate matter ≤ 10 μ m (PM₁₀) during the three months preconception; and 11% for nitrogen oxides (NO_x), 22% for SO₂, 5% for PM₁₀, and 8% for particulate matter ≤ 2.5 μ m (PM_{2.5}) during the first trimester. Elemental carbon and dust particles were also positively associated with a significant 6–7% higher risk of GH in the first trimester. With regard to polycyclic aromatic hydrocarbons, high exposures to benzo[a]-pyrene, ideno[1,2,3-cd]pyrene, and naphthalene during both preconception and the first trimester were significantly associated with an 8–20% higher GH risk. Among volatile organic compounds, o-xylene and toluene were consistently associated with a significant 17–23% higher risk across all the exposure windows studied. Overall, positive associations between air pollutants and GH risk were observed, which were more pronounced during the first trimester for criteria air pollutants and during the three months preconception for air toxics, suggesting early exposures may be important for GH risk.

SEVERE MATERNAL MORBIDITY RATES AND RELATED HOSPITAL QUALITY MEASURES IN MARYLAND.

Lawrence Reid

Background: Maryland's rate of severe maternal morbidity (SMM) is significantly higher than published national and state composite rates. The maternal mortality rate in Maryland from 2009–13 was seven percent higher than the national rate and had increased nearly 40% since 2004–08. This study examines the risk factors, hospital quality measures and social determinants associated with SMM in Maryland from 2005–14. Methods: Delivery hospitalizations, including medical risk factors, demographic characteristics and selected hospital quality measures, were obtained from the Maryland Health Services Cost Review Commission. Other hospital quality measures came from the Centers for Medicare & Medicaid Services and Maryland Vital Statistics. Zip code data on households and education were obtained from US Census. Based on previously published algorithms, we examined SMM deliveries adjusted for length of stay, transfer status and mortality using ICD-9 diagnoses and DRG codes. Hierarchical generalized estimated equations modeled factors associated with SMM. Results: Among 655,259 delivery hospitalizations from 2005–2014, 11,817 had a SMM diagnosis. In 2014, there were 18.5 SMM deliveries for every 1,000 delivery hospitalizations, an increase of 24% from 2005 primarily due to a 52% increase in blood transfusions (BT). Black NH mothers adjusted odds ratio (AOR) for SMM= 1.4 (95% CI: 1.4–1.5) compared to White NH mothers. Mothers <20 had AOR for SMM= 1.2 (95% CI: 1.1–1.3) compared to mothers 20–24. Women with chronic hypertension and heart disease had higher AORs for SMM. Hospitals with a greater percentage of low risk cesarean births, Medicaid insured, Black NH deliveries, fewer vaginal births after cesarean, or lower patient experience ratings had higher AORs of SMM. Results similar when BT was excluded. Conclusion: The current study suggests a need to understand the link between several hospital quality measures and SMM in order to improve maternal health.

A LONGITUDINAL STUDY OF PLASMA CONCENTRATIONS OF BRANCHED-CHAIN AND AROMATIC AMINO ACIDS AND RISK OF GESTATIONAL DIABETES

Cuilin Zhang, Yeyi Zhu, Paul Albert, Jagteshwar Grewal, Stefanie Hinkle, Shristi Rawal, Mike Tsai

Emerging evidence suggests that branched-chain amino acids (BCAA: including leucine, isoleucine, valine) and aromatic amino acids (AAA: phenylalanine, tyrosine) and some other amino acid (AA) degradation products may play a critical role in glucose metabolism and the etiology of type 2 diabetes in non-pregnant individuals. Their role in the development of gestational diabetes (GDM) is unclear. Furthermore, data on longitudinal trajectories of levels of these AA across pregnancy are lacking. We aimed to prospectively address the data gaps in a case-control study of 107 GDM and 214 non-GDM women (matched on age, race/ethnicity, and gestational age at blood collection) in a multi-racial cohort, the NICHD Fetal Growth Studies-Singletons. GDM diagnosis was based on medical record review. AA profile was measured by liquid chromatography using plasma collected at gestational weeks (GW) 8–13, 16–22, 24–29, and 34–37. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) of GDM related to AA (in quartiles) were estimated using conditional logistic regression after adjusting for age, pre-pregnancy body mass index, and other GDM risk factors. Levels of BCAA decreased slightly across different trimesters of pregnancy. BCAA and AAA levels in the 1st trimester (GW 8–13) did not differ significantly between women who were subsequently diagnosed with GDM and those who were not. In the 2nd trimester (GW 16–22), levels of one BCAA and both AAA became significantly higher among GDM cases than controls and strongly associated with GDM risk even after the adjustment of other risk factors; aOR (95% CI) comparing the highest vs. lowest quartile was 3.59 (1.44, 8.94) for isoleucine, 3.67 (1.54, 8.76) for tyrosine, and 2.54 (1.03, 6.26) for phenylalanine (all Ps for linear trend across quartiles <0.001). In conclusion, branched-chain and aromatic amino acids may be implicated in the pathogenesis of GDM and their roles in the 1st trimester may differ from the 2nd trimester.

FACTORS ASSOCIATED WITH ELEVATED C-REACTIVE PROTEIN IN THREE COHORTS OF REPRODUCTIVE AGE WOMEN

Chandra Swanson, Enrique Schisterman, Rose Radin, Sunni Mumford, Neil Perkins, Aijun Ye, Torie Plowden, Noya Galai, Robert Silver, Jean Wactawski-Wende, Lindsey Sjaarda

Inflammation has been associated with an increased risk of adverse reproductive outcomes, though factors linked to high inflammation are not well understood and may differ across sub-populations. Thus, our objective was to describe characteristics of women with elevated inflammation in three distinct cohorts of reproductive-age women. Thus, we examined high-sensitivity C-reactive protein (hsCRP) data from the BioCycle Study (N=259), the Effects of Aspirin in Gestation and Reproduction Trial (EAGeR) (N=1228), and the National Health and Nutrition Examination Survey (NHANES) (N=1435). Within each study, we categorized participants as low (<2 mg/L) or high (≥ 2 mg/L) hsCRP, after excluding acutely elevated hsCRP (>10 mg/L). T-tests and χ^2 tests compared characteristics between low and high hsCRP groups. The geometric mean (95% CI) hsCRP was 0.91 mg/L (0.8, 1.1) for BioCycle, 1.4 mg/L (1.3, 1.5) for EAGeR, and 1.5 mg/L (1.3, 1.7) for NHANES. Though some factors varied across populations, women with high hsCRP were consistently more likely to have higher body mass index ($P<0.001$), greater waist circumference ($P<0.001$), and higher total cholesterol ($P\leq 0.01$), low-density lipoprotein ($P\leq 0.02$), and triglyceride levels ($P<0.01$) in all three cohorts evaluated. Factors such as higher systolic and diastolic blood pressure, higher pulse rate, decreased high-density lipoprotein levels, low sleep duration, increased age, increased glucose, parity, lower income, lower education, less physical activity, smoking, and unmarried status were more common in the high hsCRP group in some studies, but not all. Thus, factors related to elevated hsCRP may differ based on the population studied. Differences may be due to inclusion criteria and prior health status. Better understanding this variation may improve approaches for study design, analysis, and interpretation when evaluating the effects of chronic inflammation on fertility and pregnancy.

PREVENTING UNINTENDED PREGNANCY: GENDER-DIFFERENCES IN CONTRACEPTION USE AMONG URBAN YOUNG ADULTS

Allison Casola, Deborah Nelson, Freda Patterson

Background: Inconsistent and ineffective contraception use is high among sexually active adolescents and is related to 85% of unintended pregnancies (UP). Given this high rate, it is imperative to identify key factors associated with contraception non-use so that high-risk sub-groups for UP can be characterized. **Methods:** Cross-sectional data, of 9th-12th grade students completing the 2015 Youth Risk Behavior Survey (YRBS) in the Philadelphia School District, were analyzed. Multivariate regression models were used to examine mental health, sexual activity, substance use and neighborhood violence indicators on reported non-use of contraception, among sexually active youth. Contraception was defined as the use of condoms, birth control pills, implants, vaginal ring, patch, or shot, during the last time having sex. **Results:** participants were mostly female (54%), Black (44%) and aged 15-16 years (54%). One third (34%; n=215) of respondents reported no contraception use, and this rate was significantly higher in females than males (39% vs 29% respectively; $p < .01$). Independent of gender, students who reported being electronically bullied online (aOR=2.728, 95%CI 1.338-5.559), having four or more lifetime sexual partners (aOR=1.754, 95%CI 1.116-2.759), using drugs or alcohol before sex (aOR=2.094, 95%CI 1.166-3.761) and not feeling safe in their neighborhood (aOR=1.587, 95%CI 1.016-2.478) were significantly more likely to report no contraception use. In gender-stratified models, having four or more lifetime sexual partners and using drugs/alcohol before sex were associated with no contraception use in females, but not males. **Discussion:** These data, from a representative sample of urban youth, suggest that electronic bullying, high sexual activity, substance use during sex and community safety may be factors contributing to UP. Results from this study could be used to inform targeted outreach efforts to decrease UP in urban youth.

ANTIDEPRESSANT MEDICATION DURING PREGNANCY AND EPIGENETIC CHANGES IN UMBILICAL CORD BLOOD: A SYSTEMATIC REVIEW.

Anne-Cathrine Viuff, Lars Henning Pedersen, Kasper Jacobsen Kyng, Nicklas Heine Staunstrup, Anders Børglum, Tine Brink Henriksen

Introduction: Epigenetic mechanisms are important for the regulation of gene expression and differentiation in the fetus and the newborn child. Maternal depression and antidepressant use may lead to epigenetic changes with life-long impact on child health. The aim of this review is to investigate whether there is an association between exposure to maternal antidepressants during pregnancy and epigenetic changes in the newborn. **Material and methods:** Systematic literature searches were performed in MEDLINE and EMBASE. We included original studies on pregnant women and their children with a history of maternal depressed mood, use of antidepressant medication, and measurements of epigenetic changes in umbilical cord blood. Citations and references from the included articles were investigated to locate further relevant articles. The completeness of reporting as well as the risk of bias and confounding was assessed. **Results:** Six studies were included. They all investigated methylation changes. Genome-wide methylation changes were examined in 184 children and methylation status in specific genes was examined in 96 children exposed to antidepressant medication. Three of the studies found an association between use of antidepressant medication during pregnancy and methylation status at various CpG sites measured in cord blood of the newborn. One of these studies found an association in African-Americans, but not Caucasians. The remaining three studies only found associations between maternal mood and epigenetic changes in umbilical cord blood. **Conclusion:** The included studies have not established a clear association between use of antidepressant medication during pregnancy and epigenetic changes in the cord blood. Future studies with larger sample sizes and good validity of exposures are warranted in order to adjust for level of maternal depression, other maternal illness, maternal use of other types of medication and maternal ethnicity.

EPIGENETIC CHANGES IN NEWBORNS EXPOSED TO ANTIDEPRESSANT MEDICATION DURING PREGNANCY - A GENOME WIDE APPROACH

Anne-Cathrine Viuff, Tine Brink Henriksen, Lars Henning Pedersen, Kasper Kyng

Background Depression is a very common disease among pregnant women. In Denmark some 5% of all pregnant women are treated with antidepressants. The short term adverse effects on the newborn children are well described. Long term adverse outcomes, however, are suspected, but not well characterized. Epigenetic changes could be one of the key mechanisms through which exposure to maternal depression, anxiety or antidepressant medication may have long-term health consequences for the child. The epigenetic pattern is important for the translation of DNA to proteins and the process is influenced by external factors, e.g. antidepressant medication. **Methods** In this study we use a whole genome approach: Methylated DNA immunoprecipitation sequencing (MeDIP-sequencing) to establish the methylation patterns in cord blood from new born children exposed to antidepressant medication during pregnancy compared to those exposed to non-medicated depression and a group of children exposed to neither. Data on the births and the blood samples are from the Aarhus Birth Cohort and Biobank. This technique has to our knowledge not yet been used to investigate this issue. 100 blood samples from children exposed to antidepressant medication, 30 samples from children exposed to non-medicated depression and 50 control samples are being sequenced. **Results** Epigenetic results pending. **Perspectives** High quality epidemiological data and evaluation of epigenetic pathways provide unique ways to potentially link maternal exposure to monoaminergic drugs to adverse outcomes such as neonatal adaptations symptoms and later adverse neurodevelopmental outcomes. In the future these methods could also be used in evaluating the effects of other types of medication given to women during pregnancy and lactation.

ANTENATAL EXPOSURE TO SELECTIVE SEROTONIN REUPTAKE INHIBITORS AND AUTISM: A SYSTEMATIC REVIEW AND META-ANALYSIS

Hilary Brown, Neesha Hussain-Shamsy, Yona Lunskey, Cindy-Lee Dennis, Simone Vigod

The serotonin hypothesis of autism suggests that fetal exposure to high levels of serotonin could lead to the autism phenotype. However, previous studies have been unable to disentangle the role of antenatal selective serotonin reuptake inhibitor (SSRI) exposure from that of maternal mental illness (MMI). This systematic review and meta-analysis examined the relationship between antenatal SSRI exposure and child autism, with specific attention to MMI as a potential confounding factor. We searched Medline, EMBASE, PsycINFO, and CINAHL from database inception to May 21, 2015. We included published, peer-reviewed articles written in English. Two reviewers used standardized instruments for data extraction and quality assessment. We generated unadjusted and adjusted pooled estimates for studies of the same design for SSRI exposure during pregnancy (any and first trimester). Sub-analyses were conducted among studies with analyses that a) adjusted for MMI; and b) restricted to MMI. We included four case-control studies (pooled) and one retrospective cohort study (reported separately). The adjusted pooled odds ratios (aPOR) were 1.4, 95% CI 1.0-2.0 (any) and 1.7, 95% CI 1.1-2.6 (first trimester). In MMI-adjusted analyses, only first trimester exposure remained statistically significant (aPOR 1.8, 95% CI 1.1-3.1). In MMI-restricted analyses, neither exposure period was statistically significant. In the cohort study, MMI-adjusted relative risks, aRR, were 1.2, 95% CI 0.9-1.6 (any) and 1.4, 95% CI 0.99-1.9 (first trimester). The MMI-restricted aRR was 0.6, 95% CI 0.2-1.3 (any). The association between antenatal SSRI exposure in the first trimester and child autism risk cannot be completely explained by MMI or other factors. Future studies with adequate sample size and robust measurement of MMI both prior to, and during pregnancy, will help clarify its impact on autism risk in children exposed antenatally to SSRIs.

NEONATAL OUTCOMES OF INFANTS BORN TO WOMEN WITH INTELLECTUAL AND DEVELOPMENTAL DISABILITIES: A POPULATION-BASED STUDY

Hilary Brown, Virginie Cobigo, Yona Lunskey, Simone Vigod

Children born to women with intellectual and developmental disabilities (IDD) are at increased risk for developmental delay and poor physical health. However, minimal attention has been paid to indicators of neonatal health; intervening during this period may be even more important for prevention of negative outcomes. Our objective was to determine whether infants born to women with IDD are at increased risk, compared to infants born to women without IDD, for adverse neonatal outcomes. We conducted a population-based 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 were complications for which infants born to women with IDD were hypothesized to be at increased risk: preterm birth, small for gestational age, and large for gestational age. We also examined several secondary outcomes. We used multivariable modified Poisson regression to assess risk, adjusted for confounders (maternal age, parity, baseline maternal social and health characteristics, infant sex). Compared to infants born to women without IDD, infants born to women with IDD were at increased risk for preterm birth (10.9% vs. 6.3%; adjusted relative risk [aRR] 1.63, 95% confidence interval [CI] 1.47-1.80) and small for gestational age (17.5% vs. 12.1%; aRR 1.35, 95% CI 1.25-1.45) but not large for gestational age (8.2% vs. 8.4%; aRR 0.99, 95% CI 0.88-1.11). They were at increased risk for all secondary outcomes: stillbirth, neonatal mortality, and neonatal morbidity. This is the largest study to date to examine neonatal outcomes of infants born to women with IDD; our findings suggest the need to mobilize accessible supports to optimize the health of these infants.

PB071

HEALTH AND WELLBEING OF MOTHERS IN THE UNITED STATES, 2007-2012

Catherine Vladutiu, Katherine Ahrens, Sarah Verbiest, M. Kathryn Menard, Alison Stuebe

Pregnancy and child-rearing can impact chronic disease trajectories and health in later life. We examined women's health and wellbeing by parity and time since last live birth among a nationally representative sample of non-pregnant U.S. women, ages 20-44 years, in the National Health and Nutrition Examination Survey (NHANES) from 2007 to 2012. Health and wellbeing was assessed using physical measures (waist circumference, body mass index, blood pressure), laboratory measures (folate, cholesterol, hemoglobin A1C, chlamydial infection, heavy metals – lead, cadmium, and mercury) self-reported health status (depressive symptoms, general health, anxiety), behaviors (sleep, diet, smoking, drug use, physical activity), and conditions (anemia, asthma, chronic medical conditions). All analyses accounted for the multistage, complex sampling design. There were 2,975 women who met the eligibility criteria. Women reported their last live birth within 12 months (6.7%), >12 months and <3 years (10.0%), or ≥3 years (45.5%) prior to study participation; 37.8% were nulliparous. All mothers, regardless of time since last live birth, had a higher prevalence of high waist circumference (55.5%-66.8% vs. 47.0%), low HDL cholesterol (38.9%-45.9% vs. 25.5%), fair or poor general health (14.5%-18.1% vs. 9.2%), and higher blood cadmium levels (0.34-0.37 µg/L vs. 0.29 µg/L) as compared with nulliparous women, after adjustment for age. Mothers also had lower blood mercury levels (0.67-0.70 µg/L vs. 1.00 µg/L) and a lower prevalence of anxious days (54.1%-65.2% vs. 73.3%). No statistically significant differences were observed for blood pressure, hemoglobin A1C, blood lead levels, or chronic medical conditions, by each category of time since last live birth compared with nulliparous women. A better understanding of the long-term effects of pregnancy and child-rearing on chronic disease risk is needed to develop effective strategies for improving the health trajectories of mothers.

HOMICIDE AND SUICIDE DURING PREGNANCY IN NORTH CAROLINA: USING THE NORTH CAROLINA VIOLENT DEATH REPORTING SYSTEM TO IMPROVE CASE ASCERTAINMENT

Catherine Vladutiu, Anna Austin, Kathleen Jones-Vessey, Tammy Norwood, Scott Proescholdbell, M. Kathryn Menard

Maternal mortality surveillance systems have been implemented to improve reporting of pregnancy-related deaths in the U.S., but the ability of these traditional systems to capture violent deaths is unknown. We examined whether ascertainment of pregnancy-associated homicides and suicides could be improved by using an enhanced case ascertainment process that linked data from the North Carolina Violent Death Reporting System (NC-VDRS) to North Carolina's traditional maternal mortality surveillance files for women ages 10 to 55 years. We also examined the characteristics of these violent deaths. Between 2005 and 2011, 29 suicides and 55 homicides were identified among pregnant and postpartum women through enhanced case ascertainment as compared to 20 and 34, respectively, from traditional case ascertainment. The addition of the NC-VDRS to existing maternal mortality files increased the identification of pregnancy-associated violent deaths by 55.6%, resulting in increased mortality rates for suicide (from 2.3 to 3.3 deaths per 100,000 live births) and homicide (from 3.9 to 6.2 deaths per 100,000 live births). Among all cases identified through enhanced ascertainment, more than half of suicide victims (55.2%) had a current mental health diagnosis and nearly two-thirds of homicides (65.5%) were related to intimate partner violence. Linking traditional maternal mortality files to the NC-VDRS provided a notable improvement in ascertainment of pregnancy-associated violent deaths in North Carolina. This linkage also provided detailed information on the characteristics of these deaths which is not available through traditional case ascertainment and can inform whether violent deaths may be causally related to pregnancy. The inclusion of additional data sources in existing maternal mortality surveillance systems is needed to provide a better estimate of the burden of maternal mortality.

PB072

DEPRESSION, ANXIETY, AND ANTIDEPRESSANT TREATMENT: ASSOCIATION WITH IN-VITRO FERTILIZATION CYCLE OUTCOME

Carolyn E Cesta, Alexander Viktorin, Henrik Olsson, Viktoria Johansson, Arvid Sjolander, Christina Bergh, Alkistis Skalkidou, K.G. Nygren, Anastasia N Iliadou

Background Women experiencing infertility have high rates of symptoms of depression and anxiety. The aim of this study is to investigate associations between depression, anxiety, and treatment with antidepressants (AD) and in-vitro fertilization (IVF) cycle outcome in a Swedish nationwide register-based cohort study. Methods A total of 23,557 nulliparous women undergoing their first IVF cycle registered in the Swedish Quality IVF Register between January 2007 and December 2013 were included. Diagnoses of depression or anxiety and dispensations of AD prescriptions prior to the start of the cycle were extracted from the Swedish National Patient Register and the Prescribed Drug Register, respectively. Associations between exposures and IVF cycle outcome were evaluated using logistic regression to produce adjusted odds ratios (AORs) and 95% confidence intervals (CI). Results In total, 4.4% of the women had either AD or a diagnosis of depression or anxiety before their first IVF cycle. Compared to the reference group of women with no diagnoses or AD, the risk of failure to conceive and the failure to result in live birth was predominately increased for women exposed to AD other than selective serotonin reuptake inhibitors (AOR 2.45 95% CI 1.25-4.83; AOR 3.76 1.48-9.54) and for women with depression or anxiety with no AD (AOR 1.73 95% CI 1.23-2.44; AOR 1.66 95% CI 1.13-2.45). There was no increased risk for miscarriage within any of the exposure groups. Conclusions Treatment with AD prior to starting an IVF cycle is associated with a negative outcome. However, so is the presence of depressive illness or anxiety disorder without AD treatment, implying that the underlying disorder is important for the observed association. Whether the association between depression or AD medication and IVF outcome is attributable to the underlying diagnosis or confounded by lifestyle factors remain to be determined.

CORTISOL, SELF-REPORTED STRESS, AND IVF OUTCOMES IN A PROSPECTIVE COHORT OF WOMEN AND MEN UNDERGOING FERTILITY TREATMENT

Carolyn E Cesta, Henrik Olsson, Anastasia Nyman Iliadou

Introduction The investigation into whether stress affects the ability to become pregnant through assisted reproductive techniques is ongoing and has yet to produce definitive results or evidence towards a potential mechanism. However, few studies combine multiple measure of psychological and physiological stress with detailed biological data from the ART procedure. **Methods** Participants were recruited from September 2011 to December 2013 at 4 fertility clinics as part of the prospective Uppsala-Stockholm Assisted Reproductive technique (UppStART) study cohort. Baseline cortisol was measured in morning and evening saliva samples collected prior to the start of treatment. Self-reported stress was measured via response to the Perceived Stress Scale (PSS) and the Fertility Problem Stress Scale from the Copenhagen Multi-Centre Psychosocial Infertility research questionnaire. IVF cycle outcome data were collected from medical journals at the participating clinics. **Results** In total, 486 women and 431 men participated in the study and 158 first cycles with an embryo transfer resulted in pregnancy (42%). All individuals scored high on the Fertility Problem Stress scale. Preliminary results from logistic regression modeling do not show an association between any measure of stress (PSS or cortisol) and pregnancy. However, in a subset of 100 women, morning and evening cortisol showed a trend towards an association with the number of mature oocytes collected. Further analysis will include all data for oocytes, embryo number and quality, and sperm quality data for all participants. **Conclusions** Findings from this study will contribute to the much-needed knowledge of the influence of stress on the IVF cycle and its potential mechanism.

SERUM BRAIN-DERIVED NEUROTROPHIC FACTOR CONCENTRATIONS IN PREGNANT WOMEN WITH ANTEPARTUM POST-TRAUMATIC STRESS DISORDER WITH AND WITHOUT DEPRESSION

Na Yang, Bizu Gelaye, Qiuyue Zhong, Marta B. Rondon, Sixto E. Sanchez, Michelle A. Williams

Objective: There is accumulating evidence for the role of brain-derived neurotrophic factor (BDNF) in the pathophysiology of depression. The role of BDNF in the pathophysiology of post-traumatic stress disorder (PTSD) remains controversial; and no study has assessed BDNF concentrations among pregnant women with PTSD. We examined early-pregnancy BDNF concentrations among women with PTSD with and without depression. **Methods:** A total of 2,928 women attending prenatal care clinics in Lima, Peru, were recruited. Antepartum PTSD and depression were evaluated using PTSD checklist-civilian version (PCL-C) and patient Health Questionnaire-9 (PHQ-9) scales. BDNF concentrations were measured in 944 participants using a competitive ELISA. Logistic regression procedures were used to estimate odds ratios (OR) and 95% confidence intervals (95% CI). **Results:** Antepartum PTSD (37.4%) and depression (27.6%) were prevalent in this cohort of low-income pregnant Peruvian women. Approximately 19.9% of participants had comorbid PTSD-depression. Mean serum BDNF concentrations were lower among women with comorbid PTSD-depression as compared with women without either condition (mean \pm SD: 20.8 \pm 5.7 vs. 21.9 \pm 6.5 ng/mL, $P=0.06$). Compared to the referent group (those without PTSD and depression), women with comorbid PTSD-depression were 1.7-fold (95%CI: 1.08-2.66) more likely to have low (< 18.8ng/mL) BDNF concentrations. We observed no evidence of reduced BDNF concentrations among women with PTSD alone. **Conclusion:** BDNF concentrations in early pregnancy were only minimally and non-significantly reduced among women with antepartum PTSD. Reductions in BDNF concentrations were most pronounced among women with comorbid PTSD-depression.

SUICIDAL BEHAVIOR-RELATED HOSPITALIZATIONS AMONG PREGNANT WOMEN IN THE UNITED STATES, 2006 – 2012

Qiu-Yue Zhong

Background: Suicide is one of the leading causes of maternal mortality in many countries, but little is known about the epidemiology of suicide and suicidal behavior among pregnant women in the United States. We sought to examine trends and provide nationally representative estimates for suicidal ideation and suicide and self-inflicted injury (suicidal behavior) among pregnant women from 2006 to 2012 in the United States. **Methods:** Using the National (Nationwide) Inpatient Sample, pregnancy- and delivery-related hospitalizations were identified for women aged 12-55 years. Suicidal behavior and depression were identified by the International Classification of Diseases, Ninth Revision, Clinical Modification codes. Annual estimates and trends were determined using discharge and hospital weights. **Results:** The prevalence of suicidal ideation more than doubled from 2006 to 2012 (47.5 to 115.0 per 100,000 pregnancy- and delivery-related hospitalizations), whereas the prevalence of suicide and self-inflicted injury remained stable. Nearly 10% of suicidal behavior occurred in the 12-18-year group, showing the highest prevalence per 100,000 pregnancy- and delivery-related hospitalizations (158.8 in 2006 and 308.7 in 2012) over the study period. For suicidal ideation, blacks had higher prevalence than whites; women in the lowest income quartile had the highest prevalence. Although suicidal behavior was more prevalent among hospitalizations with depression diagnoses, more than 30% of hospitalizations had suicidal behavior without depression diagnoses. **Conclusions:** Our findings highlight the increasing burden and racial differences in suicidal ideation among US pregnant women. Targeted suicide prevention efforts are needed for high-risk pregnant women including teens, blacks, and low-income women.

PLASMA ADIPONECTIN AND DEPRESSIVE SYMPTOMS DURING PREGNANCY AND POSTPARTUM: RESULTS FROM A PROSPECTIVE COHORT.

Fernanda Rebelo, Dayana Farias, Claudio Struchiner, Gilberto Kac

Background: A protective effect of adiponectin on depression has been described in the literature but this association has not yet been investigated during the perinatal period. **Objective:** To evaluate the association of plasma adiponectin and symptoms of depression in women from early pregnancy to 30-45 days postpartum. **Methods:** Prospective cohort with four waves of follow-up: 5-13th; 22-26th; 30-36th gestational weeks; and 30-45 days postpartum. Study subjects were women 20 to 40 years old, free of chronic non-communicable or infectious diseases, bearing a singleton pregnancy and not making use of antidepressants. Depressive symptoms were measured using the Edinburgh Postnatal Depression Scale (EPDS; cutoff ≥ 11). Plasma adiponectin concentrations were measured by enzyme linked immunosorbent assay. Statistical analyses included linear mixed effects regressions to model the association between these time-dependent variables. **Results:** The prevalence of depressive symptoms was 35.5%, 22.8%, 21.8% and 16.9% in the 1st, 2nd, 3rd trimesters and postpartum, respectively. Values of adiponectin remained stable over pregnancy, with an increase at the postpartum. Women who remained non-depressed through all study periods tended to have higher values of adiponectin throughout pregnancy and postpartum, compared to those who had at least one depressive episode, but this difference was not statistically significant ($\beta = -0.14$; $p = 0.071$). Plasma adiponectin showed an inverse, but not significant association with EPDS scores in the multiple model ($\beta = -0.07$; $p = 0.320$). **Conclusion:** We found a high prevalence of depressive symptoms at early pregnancy. Plasma adiponectin seems to have an inverse relation with depressive symptoms during the perinatal period, but the association did not achieve statistical significance and our findings are inconclusive.

EFFECTS OF OCCUPATIONAL EXPOSURE TO ENDOCRINE DISRUPTORS AND WORK-RELATED STRESS ON PREGNANCY OUTCOME

Nel Roeleveld, Maya Schulpen, Marleen van Gelder

Over the past decades, the labor participation rate among women of reproductive age in Europe has gradually increased and with it the chances of being exposed to chemical, physical, and psychosocial factors that may negatively influence pregnancy. Therefore, we investigated the effects of maternal occupational exposure to endocrine disruptors and work-related stress during pregnancy on birth weight and gestational age. The study was conducted among women participating in the PRegnancy and Infant DEvelopment (PRIDE) Study. Based on job titles and descriptions, a job exposure matrix was used to assess the probabilities of exposure to endocrine disruptors. In addition, the level of work-related stress was measured in gestational week 17 by a validated version of the Job Content Questionnaire. Birth weight, low birth weight, gestational age, and preterm birth were the main outcome measures. For confounding adjusted effect estimates were calculated using linear and logistic regression analyses. In total, 1369 women who had a singleton pregnancy resulting in a live birth between January 1st 2012 and May 1st 2015 were included. Infant birth weights were reduced by 200 to 300 grams after maternal exposure to ethylene glycol ethers (EGEs), alkylphenolic compounds, and metals, in particular mercury. In contrast, exposure to EGEs and alkylphenolic compounds seemed to prolong gestation by 5 days. High total job demands and high job strain increased the risk of delivering a low birth weight infant (OR 3.1, 95%CI 0.9-11.3 and OR 3.3, 95%CI 0.9-12.1, respectively). Moderate/high job control was associated with a reduced risk of preterm birth (OR 0.5, 95%CI 0.3-1.1). This study indicated that employment during pregnancy may adversely affect infant birth weight via occupational exposure to endocrine disruptors or work-related stress, whereas prenatal exposure to endocrine disruptors and increased job control may benefit gestational age and reduce the risk of preterm birth.

ASSOCIATION OF ANTEPARTUM SUICIDAL IDEATION DURING THE THIRD TRIMESTER INFANT BIRTH WEIGHT AND WITH GESTATIONAL AGE AT DELIVERY

Bizu Gelaye, Fernanda Rebelo, Gloria Larrabure, Chunfang Qiu, Miguel Angel Luque Fernandez, Percy Pacora, Sixto Sanchez, Michelle Williams

Background: Antepartum suicidal behaviors including suicidal ideation and attempts are the leading causes of injury and maternal death worldwide. Although suicidal ideation is considered a symptom of depressive disorder, a substantial proportion of women with suicidal ideation do not meet clinical thresholds for depression. Objective: We evaluated the relationship of antepartum suicidal ideation with infant birth weight (BW) and gestational age at delivery (GA). Methods: A cohort of 1,183 Peruvian women were interviewed at 24-28 weeks of gestation. Antepartum suicidal ideation and depression were assessed using the patient Health Questionnaire 9 (PHQ-9). GA and BW were obtained from medical records. Multivariable linear and logistic regression procedures were used to estimate adjusted measures of association (β coefficients and odds ratios) and 95% confidence intervals (CI). Results: The prevalence of antepartum suicidal ideation was 8.7%. Women with suicidal ideation were more likely to have infants with lower BW (3267 \pm 511 vs. 3417 \pm 492g; $p=0.005$) compared with women without suicidal ideation. Antepartum suicidal ideation was independently and negatively associated with infant birth weight ($\beta=-94.2g$, $P=0.037$) after adjusting for confounders including depression. No statistically significant association was noted between suicidal ideation and mean GA. However, women who endorsed suicidal ideation were 3.48-times as likely to deliver a small-for-gestational age (SGA) newborn (95%CI: 1.59-8.74). Conclusion: Antepartum suicidal ideation, even after adjusting for depression, was associated with reductions in infant BW and increased SGA risk. If corroborated, antenatal care should be tailored to screen and provide additional mental health services and care to at risk patients.

MATERNAL DEPRESSION AND USE OF ANTIDEPRESSANTS DURING PREGNANCY INCREASE THE RISK OF ADVERSE PREGNANCY OUTCOMES: AN IPD META-ANALYSIS

Nel Roeleveld, Richelle Vlenterie, Monica Pop-Purceanu, Marleen van Gelder

Recent systematic reviews and meta-analyses examining the adverse effects of maternal depression and the use of antidepressants during pregnancy show inconclusive results. As a result, prospective parents, prenatal care providers, general practitioners, and psychiatrists cannot make evidence-based decisions on treatment possibilities. Therefore, we performed an individual patient data (IPD) meta-analysis on the associations between non-pharmacologically managed maternal depression or antidepressant use during pregnancy and the occurrence of preterm birth, low birth weight, small for gestational age (SGA), and poor Apgar scores. A systematic literature search was conducted until February 2015. For eligible publications ($n=201$), the methodological quality was independently assessed with the Newcastle-Ottawa Scale by two reviewers. All authors that could be traced were invited to share their original data. These individual patient data were used in a 1-stage random-effect meta-analyses based on logistic regression models. So far, data from 125,095 individual patients have been collected out of 22 studies. The preliminary analyses showed adjusted odds ratios for self-reported symptoms of depression ranging from 1.24 (1.06-1.45) for preterm birth and 1.36 (1.19-1.55) for low birth weight to 1.82 (1.38-2.40) for poor Apgar scores at 5 minutes. Adjusted odds ratios for antidepressant use during pregnancy ranged from 1.02 (0.68-1.53) for SGA and 1.43 (1.01-2.04) for low birth weight to 2.07 (1.58-2.72) for preterm birth. So for all pregnancy outcomes studied, associations were observed with self-reported symptoms of depression and antidepressant use, except for SGA and antidepressant use. This IPD meta-analysis overcomes the inconclusive results of other systematic reviews and meta-analyses and provides evidence-based information on the potential adverse effects of maternal depression and use of antidepressants during pregnancy on several pregnancy outcomes.

ASSOCIATION OF MIGRAINE HEADACHES WITH SUICIDAL IDEATION AMONG PREGNANT WOMEN IN LIMA, PERU

Lauren Friedman, Bizu Gelaye, Marta Rondon, Sixto Sanchez, B. Lee Peterlin, Michelle Williams

Background: Migraine and depressive disorders are highly prevalent and often comorbid conditions among reproductive aged women. Suicidal behaviors, including ideation and attempts, are considered symptoms of major depressive disorder, although they can occur with or without accompanying depression. Suicide is now a leading cause of maternal death globally, but there is limited evidence on the comorbidity between migraines and suicidal ideation, and no previous study has examined this association during pregnancy. Objective: To examine the association between migraine and suicidal ideation among a cohort of pregnant women. Methods: A cross-sectional study ($N=3372$) was conducted among women attending prenatal care clinics in Lima, Peru. Depression and suicidal ideation were assessed using the patient Health Questionnaire-9 (PHQ-9) scale. Migraine classification (including migraine and probable migraine) was based on International Classification of Headache Disorders (ICHD)-III beta criteria. Multivariate logistic regression analyses were performed to estimate odd ratios (OR) and 95% confidence intervals (95% CI). Results: The prevalence of suicidal ideation in this cohort was 16.0%. Suicidal ideation was more common among migraineurs compared with probable or non-migraineurs (25.6% vs. 22.1% vs. 12.3%, $p<0.001$). After adjusting for confounders, including depression, those with migraine or probable migraine had an increased odds of suicidal ideation (OR=1.71; 95%CI: 1.4-2.1), as compared with non-migraineurs. Women with migraine and depression comorbidity had 3.5-fold increased odds of suicidal ideation (95%CI: 2.67-4.64) compared with those who had neither condition. Conclusion: Migraines are associated with increased odds of suicidal ideation in pregnant women even when controlling for depression. If confirmed, there may be merits to screening patients for highly comorbid pain and mood disorders, including suicidal behavior, during pregnancy.

PB081

PREVALENCE OF STRESSFUL LIFE EVENTS DURING PREGNANCY AND ITS ASSOCIATION WITH POSTPARTUM DEPRESSIVE SYMPTOMS AMONG GEORGIA WOMEN

Florence Kanu

Experiencing stressful life events (SLEs) has negative consequences for both mother and infant. Several epidemiological studies have suggested a link between experiencing SLEs before and during pregnancy and higher reports of postpartum depressive symptoms (PDS). The purpose of our study was to examine the prevalence of SLEs and their association with self-reported PDS. Data from Georgia's Pregnancy Risk Assessment Monitoring System (PRAMS) were obtained from 2004-2011. Principal component analysis with varimax rotation was conducted to empirically assess variance among the 14 SLEs. Chi-square tests and weighted logistic regression models were conducted for cumulative number of stressors and by stress domain to predict PDS reporting. Race-specific models were also performed. Odds Ratios (OR) and 95% Confidence Intervals (CIs) were calculated. Fifteen percent of respondents reported experiencing PDS. All stress domains significantly predicted an increased odds of reporting PDS, with the strongest relationship observed between traumatic stress and PDS (OR: 2.16; 95% CI: 1.67-2.79). In the cumulative stress model, increased odds of reporting PDS was observed with increasing numbers of cumulative stressors. Each racial and ethnic group had an increased risk of reporting PDS due to experiencing traumatic stress, with the highest likelihood among Hispanic mothers (OR: 2.54; 95% CI: 1.34, 4.80). SLEs were significantly associated with reporting PDS among pregnant women in Georgia. Findings suggest the need for stress reduction interventions as one way to decrease experiences of PDS.

PB083

EFFECTS OF DEPRESSION ON LATER ONSET OF INTERNET ADDICTION IN PUBERTY: A COMMUNITY-BASED COHORT STUDY

Miri Sato, Kohta Suzuki, Sonoko Mizorogi, Zentaro Yamagata

Internet addiction (IA) has become a serious health problem in industrialized countries, especially among adolescents. Several studies have examined the associations between Internet usage, mental health, and IA. Although most of these studies treated mental health as a comorbidity of IA, it is still unclear whether depressive symptoms precede the onset of IA. This study aimed to examine the effects of depressive symptoms on later onset of IA. Study participants were 1045 students (5th-7th grades, age 10-12 years) who participated in an on-going community-based birth cohort study in a rural area of Japan. At baseline, the presence of depressive symptoms was assessed using the Birmleson Depression Self-Rating Scale for Children as a study factor. Two years later, IA was assessed using the Young Internet Addiction Test. Participants were identified as average Internet users, or users with moderate or severe addiction. In the analyses, we excluded children who used the Internet for more than 2 hours a day at baseline, because these children might already have IA. Finally, baseline participants were 858 and 781 participants were followed up (follow-up rate: 91%). Adjusting for age, sex, duration of Internet use, bedtime and weight status, because these factors were considered as confounders, multiple logistic regression analyses were conducted to examine the associations between depressive status and IA. As a result, depressive symptoms were found in 6.0% at baseline and 2 years later, 14.8% were defined as having some degree of IA. Depressive symptoms were significantly associated with later onset of IA (odds ratio, 2.4; 95% confidence interval, 1.1-5.2). In conclusion, it was suggested that having depressive symptoms was one of risk factors on later onset of IA.

PB082

TRAJECTORIES OF PERINATAL DEPRESSIVE AND ANXIETY SYMPTOMS IN A COMMUNITY COHORT

Hamideh Bayrampour

Objective: The evidence on the trajectories of perinatal depression is mostly based on studies composed of women at high-risk for poor mental health. Research on maternal anxiety trajectories is also scarce. Using a large community cohort, All Our Babies study, in Alberta, Canada, we examined trajectories of perinatal depressive and anxiety symptoms and compared characteristics of women across trajectories. **Methods:** Anxiety and depressive symptoms were measured at the 2nd and 3rd trimesters and at 4th and 12th months postpartum, among 1,445 women recruited from May 2008 to December 2010. Semi parametric group-based mixed modeling was performed to identify the optimal trajectory shape, number of groups, and proportion of the sample belonging to each trajectory. Model fit was evaluated using the Bayesian Information Criterion. Multinomial logistic regression analysis was conducted to compare characteristics across the trajectories. **Results:** Five distinct trajectory groups with constant and variable patterns were identified for both depressive and anxiety symptoms: "Minimal", "Mild", "Antepartum", "Postpartum", and "Chronic". Common risk factors of depression and anxiety across groups with elevated symptoms were history of mental health issues (OR varied from 1.83 to 7.64), history of abuse/neglect (OR varied from 1.67 to 8.97), and low social support (OR varied from 1.64 to 11.37). The magnitude of the influence of the psychosocial risk factors were greater in the "Chronic" group compared to others, suggesting a dose-related relationship. **Conclusion:** Heterogeneity of anxiety and depressive symptoms highlights the importance of multiple mental health assessments during the perinatal period. The patterns and intensity of postpartum depression differed between community and high-risk samples, underlining the significance of defining suitable cut-offs. Research to examine the impact of these trajectories on child outcomes is needed.

PB084

ANTENATAL AND POSTPARTUM DEPRESSION AND GESTATIONAL DIABETES RISK: UNTANGLING THE BIDIRECTIONAL RELATION IN A MULTI-RACIAL PROSPECTIVE LONGITUDINAL COHORT

Stefanie Hinkle, Germaine Louis, Paul Albert, Shristi Rawal, Yeyi Zhu, Cuilin Zhang

Depression has been linked to diabetes among non-pregnant individuals; however, which comes first and whether this applies to gestational diabetes (GDM) is less understood. We aimed to utilize a prospective, cohort with longitudinal depression assessment to assess its association during early pregnancy and GDM risk and the association between GDM and postpartum depression (PPD) risk. We used data from pregnant women without psychiatric disorders, diabetes or other chronic conditions before pregnancy in the NICHD Fetal Growth Studies- Singleton Cohort (2009-2013; n=2466). Depression was assessed in the 1st (8-13 weeks) and 2nd (16-22 weeks) trimesters and 6 weeks postpartum using a validated scale. GDM was diagnosed by medical record review (n=105). PPD was defined as a score ≥ 10 or anti-depression medicine use after delivery among a sub-sample with postpartum follow-up (n=198). Relative risks (RR) [95% confidence intervals (CI)] were estimated using log-Poisson regression adjusting for sociodemographic, pre-pregnancy body mass index and other GDM risk factors. PPD models adjusted for 1st trimester depression. GDM risk based on depression scores in each trimester alone, was elevated but not significant [highest vs. lowest quartile in the 1st and 2nd trimester was 1.65 (95% CI 0.81, 3.45) and 1.67 (95% CI 0.82, 3.44), respectively]; however, GDM risk increased with increasing depression in non-obese women (P-trend=0.04 for both trimesters), but not in obese women. Women in the highest vs. lowest quartile in both trimesters had a 4-fold (95% CI 0.94, 10.21) elevated GDM risk. Women with GDM had a 5-fold (95% CI 1.24, 17.05) increased PPD risk. The bidirectional relationship between depression and glucose intolerance phenotypes is present during the perinatal period. Depression early in pregnancy was associated with GDM risk and the risk was strongest in women with high depressive symptoms in both trimesters and in non-obese women. GDM was strongly associated with PPD.

CRITERIA AIR POLLUTANTS AND DEPRESSION AMONG US PREGNANT WOMEN

Anna Pollack, Kelsey Rivers, Shamika Ranasinghe, Tuija Männistö, Danping Liu, Pauline Mendola

One in five women are affected by depression, especially during reproductive years. Criteria air pollutant exposure is associated a range of health effects. However, depression and air pollution among pregnant women has not been examined. We evaluated the association between average criteria air pollutant exposure during pregnancy in relation to depression diagnosis. In a retrospective cohort of 203,989 women with 223,502 pregnancies, 7,648 women had depression noted in their delivery admission medical record or discharge summary. Criteria air pollutants were estimated with a modified Community Multiscale Air Quality model. Using the Consortium on Safe Labor data, average exposures to ozone (O₃), nitrogen oxides (NO_x), sulfur dioxide (SO₂), carbon monoxide (CO), and particulate matter (PM_{2.5}, PM₁₀) across the whole pregnancy were measured both as continuous variables and categorized in quartiles. Generalized estimating equations modeled exposure to average air pollutant levels across pregnancy with the risk of depression and were adjusted for age, race, study region, insurance, parity, pre-pregnancy BMI, smoking, and alcohol. O₃ and SO₂ were associated with an increased risk of depression (4th q vs. 1st q: odds ratio (OR): 1.58 (95% CI: 1.47, 1.70), 1.37 (1.24, 1.51), respectively). Each 10 unit increase in PM₁₀ was associated with increased risk of depression OR: 1.28 (1.16, 1.41) and PM_{2.5} and NO_x were at the borderline OR: 1.20 (0.97, 1.48) and 1.03 (0.99, 1.07). CO was associated with a decreased risk of depression OR: 0.91 (0.89, 0.93). In sensitivity analyses, NO_x and SO₂ were associated with an increased risk of any mental health diagnosis, OR: 1.004 (1.002, 1.005) and OR: 1.16 (1.03, 1.30). Other continuous criteria pollutants were not associated with mental health disorders. These findings in a large cohort of pregnant women suggest that select criteria air pollutants may be associated with depression in pregnant women.

EFFECT OF MATERNAL CITIZENSHIP ON THE ASSOCIATION BETWEEN HEIGHT AND RISK OF PRETERM BIRTH: POPULATION BASED STUDY IN BELGIUM

Virginie Van Leeuw, Wei-Hong Zhang, Charlotte Leroy, Yvon Englert

Objectives: Preterm birth is one of leading causes of neonatal morbidity and mortality. Maternal shorter height has been associated with increased risk for preterm birth (PTB). However, the effect of women's citizenship on this association has been rarely studied. The present study investigate the association between maternal height and the risk for PTB within maternal citizenship groups. **Methods** This is a population based study including all single live births from 2009 through 2013 in two Belgian regions, using the linked data of birth registry and hospital discharged data. Citizenship at birth is used for maternal nationality and categorized as: Belgium; Europe and Russia; sub-Saharan Africa; Maghreb; Central Asia and Southwest Asia. Maternal height was classed into 4 categories based on the 25th, 50th and 75th (with the 75th serving as reference). The relationships between maternal height and risk of PTB (< 37 weeks) were examined using the logistic regression models adjusting for potential confounding factors across different nationality. **Findings** Among 251 886 single live births included in the analysis, 7.2 % were PTB < 37 weeks. The average of maternal height varied among different nationality which ranged from 159 to 165 cm. Except for sub-Saharan Africa and Southwest Asia, the short status categories were associated with increased PTB risk across nationality groups, after adjusting the confounding factors (maternal age, parity, education, cohabiting status, employment status, BMI, diabetes, hypertension and pregnancy resulting from IVF). The inverse association between maternal height and PTB were found in all nationality groups. **Interpretation** The average maternal height varied across nationalities. Maternal shorter height is associated with an increased risk for PTB regardless of mother's country origin.

ASSESSING THE JOINT EFFECTS OF UN-MEDICATED MATERNAL DEPRESSIVE SYMPTOMS AND ALCOHOL CONSUMPTION IN PREGNANCY AND INFANT NEURODEVELOPMENTAL OUTCOMES.

Gretchen Bandoli

Background- Prenatal alcohol exposure (PAE) is an established risk factor for neurodevelopmental deficits in the offspring. Investigations into the neurodevelopmental effects of un-medicated maternal depression are inconsistent. We hypothesized that un-medicated maternal depressive symptoms would independently and jointly with PAE predict neurodevelopmental outcomes in infant offspring. **Methods-** We studied 344 participants from a randomized clinical trial of multivitamin supplements in pregnant women in Ukraine. Women were recruited based upon peri-conceptional alcohol use and followed up to 12 months postpartum. Maternal depressive symptoms were assessed using the Beck Depression Scale. Infant neurodevelopment was assessed with the Bayley Scales for Infant Development II Mental Development Index (MDI) and Psychomotor Development Index (PDI) at 6 and 12 months postpartum. Generalized linear regression models were constructed to assess the independent and joint effects of maternal depressive symptoms and PAE in models adjusted for sociodemographic and pregnancy characteristics. **Results-** PAE was independently associated with deficits in neurodevelopmental outcomes at 6 and 12 months, however, level of maternal depressive symptoms was not. We found marginal evidence of synergism of depressive symptoms and PAE, with larger deficits in those with both exposures observed for the PDI-6 months (p=0.06) and MDI-12 months (p=0.08). Additionally, there was a suggestion of sexual dimorphism; females had much stronger deficits from the joint effects of the exposures than males (p for interaction 0.05). While this interaction was not statistically significant at 12 months, the trend persisted. **Conclusion-** Infants exposed to both PAE and maternal depression may be at an increased risk of neurodevelopmental deficits. Health care providers should be aware of this possible synergism in their efforts to mitigate the neurodevelopmental effects of these co-occurring exposures.

ADVERSE BIRTH OUTCOMES AMONG SMALL- AND LARGE-FOR-GESTATIONAL AGE INFANTS BORN IN NORWAY TO WOMEN OF MIGRANT ORIGIN

Ingvil Krarup Sørbye

Background: Small-for-gestational age (SGA) and large-for-gestational age (LGA) infants are at heightened risk of poor outcomes; however less is known of the influence of maternal origin. Using nation-wide data, we examined variations in SGA/LGA and associated outcomes according to the mother's country of origin. **Methods:** We applied national fetal growth standards to 58115 live births in Norway between 2000-09 to mothers of migrant origin (21 countries). We calculated proportions of SGA/LGA (birth weight <10th and >90th centile) and associated risk of adverse maternal (emergency caesarean delivery (CD), 3-4th degree perineal tear) and adverse infant outcome (Apgar score <7 at 5 minutes, transfer to neonatal intensive care unit (NICU)). As reference we used data from 422930 births among women of Norwegian origin. **Results:** Proportions of SGA infants were highest in women of Pakistani origin (22.4%), followed by Indian (21.1%) and Sri Lankese origin (18.1%). Compared to the reference, the SGA risk was higher in 17 out of 21 minority groups, and highest in the Pakistani group (adjusted odds ratio (aOR) 3.9; 95% adjusted confidence interval =3.7-4.2). In all minority groups, LGA was less common compared to the reference. SGA infants had a lower risk of NICU transfer in all minority groups compared to the reference. However, SGA infants born to Somali, Indian and Ethiopian women had a doubled risk of low Apgar score (aORs 2.1-2.3). In 8 out of 21 minority groups, births to LGA infants had a 1.7-3.4 times increased risk of emergency CD, but no increased risk of perineal tears, compared to the reference. **Conclusions:** SGA infants born to women of migrant origin were less likely to be transferred to NICU, whereas low Apgar score, emergency CS and 3-4th degree perineal tear were not consistently associated to SGA/LGA across country groups. Classifying infants as SGA/LGA by national growth standards does not uniformly predict poor outcomes in minority populations living in Norway.

ARE ALL IMMIGRANT MOTHERS REALLY AT RISK OF LOW BIRTH WEIGHT AND PERINATAL MORTALITY? THE CRUCIAL ROLE OF SOCIO-ECONOMIC STATUS.

Judith Racape, Claudia Schoenborn, Mouctar Sow, Sophie Alexander, Myriam De Spiegelaere

Background Increasing studies show that immigrants have different perinatal health outcomes compared to native women. Nevertheless, we lack a systematic examination of the combined effects of immigrant status and socioeconomic factors on perinatal outcomes. Our objectives were to analyse national Belgian data to determine 1) whether socioeconomic status (SES) modifies the association between maternal nationality and perinatal outcomes (low birth weight and perinatal mortality); 2) the effect of adopting the Belgian nationality on the association between maternal foreign nationality and perinatal outcomes. **Methods** Data are related to all singleton births between 1998 and 2010 whose mothers were living in Belgium. Perinatal mortality and low birth weight (LBW) were estimated by SES (maternal education and parental employment status) and by maternal nationality (at her own birth and at her child's birth). We used logistic regression to estimate the odds ratios for the associations between nationality and perinatal outcomes after adjusting for and stratifying by SES. **Results** The present study includes all singleton births in Belgium between 1998 and 2010 (n= 1,363,621). Compared to Belgians, we observed an increased risk of perinatal mortality in all migrant groups (p<0.0001), despite lower rates of LBW in some nationalities. Immigrant mothers with the Belgian nationality had similar rates of perinatal mortality to women of Belgian origin and maintained their protection against LBW (p<0.0001). After adjustment, the excess risk of perinatal mortality among immigrant groups was mostly explained by maternal education; whereas for sub-Saharan African mothers, mortality was mainly affected by parental employment status. After stratification by SES, we have uncovered a significant protective effect of immigration against LBW and perinatal mortality for women with low SES but not for high SES. **Conclusions** Our results show a protective effect of migration against perinatal mortality and LBW among low SES. Hence, this study underlines the crucial role of the socioeconomic status to analyze the association between migration and perinatal health outcomes. Further studies are needed to analyse more finely the impact of socio-economic characteristics on perinatal outcomes.

PB091

RISK OF SEVERE MATERNAL MORBIDITY ASSOCIATED WITH IN VITRO FERTILIZATION

Catherine Deneux-Tharaux, Laurence Pelage, Camille le Ray, Pietro Santulli, Marie-helene Bouvier-Colle

OBJECTIVE: In contrast with adverse outcomes in the baby, the risk of maternal complications in IVF pregnancies is poorly documented; in addition, the involvement of multiple pregnancy in this potential risk, as well as the effect of oocyte's origin, is not clear. Our objective was to investigate the association between IVF and severe maternal morbidity (SMM), differentiating IVF with autologous oocyte (IVF-AO) and IVF with oocyte donation (IVF-OD). **STUDY DESIGN:** Population-based cohort-nested case-control study. Data source was the EPIMOMS study conducted in 6 French regions in 2013 (N=182300 deliveries). Cases were 2541 women with SMM (multicriteria definition). Controls were 3651 randomly selected women who delivered without SMM. Associations between IVF and SMM were analyzed with multivariate logistic regression, considering all-cause SMM, and the main causes of SMM (hypertensive disorders and obstetric hemorrhage). **RESULTS:** The risk of all-cause SMM was significantly higher in women whose pregnancy was obtained through IVF-AO than in women who conceived spontaneously (crude OR=2.3 95%CI[1.7-3.1]). This association became non-significant after adjustment for multiple pregnancy (adjOR=1.4[0.9-1.9]). IVF-AO was an independent risk factor for severe obstetric hemorrhage, although the strength of the association decreased after adjustment for multiple pregnancy and abnormal placentation. IVF-OD was strongly associated with SMM, and associations remained significant after adjustment for all considered covariables. **CONCLUSION:** The risk of SMM is higher in pregnancies obtained through IVF than in spontaneous pregnancies. However, the strength and nature of the association vary according to oocyte's origin. The SMM risk associated with IVF-AO is mainly explained by multiple pregnancy and should incite to limit multiple embryo transfer. With IVF-OD, the increase in SMM risk is more marked and not explained by multiple pregnancy; further studies focused on IVF-OD are needed.

UNDERSTANDING THE RISK OF SEVERE MATERNAL MORBIDITY IN MIGRANT WOMEN: A FRENCH POPULATION-BASED STUDY

Catherine Deneux-Tharaux, Zeldia Stewart, Elie Azria, Marie-hélène Bouvier-Colle

Objective: Previous studies suggest that the risk of severe maternal complications is increased in migrant women, but the explanatory mechanisms involved are poorly understood. Our objective was to assess the association between country of birth and severe maternal morbidity (SMM) and explore explanatory factors in France, a country where healthcare organization is based on a principle of universal access to care. **Study design:** Population-based cohort-nested case-control study. Data source was the EPIMOMS study conducted in 6 French regions in 2013, source population of 182300 deliveries. Cases were 2541 women with SMM (multicriteria definition). Controls were 3651 randomly selected women who delivered without SMM. Association between country of birth and SMM was studied through multivariable logistic regression, with covariates included by successive steps corresponding to our explanatory hypotheses. **Results:** Women born in sub-Saharan Africa were at higher risk of SMM than native women (crude OR=2.2 95%CI[1.8-2.7]). This risk remained higher after controlling for preexisting socio-demographic, medical and obstetrical characteristics and pregnancy characteristics (adjusted OR=1.9 95%CI[1.5-2.5]). This excess risk was found for each of the main components of SMM -hypertensive disorder, infection and hemorrhage-, not modified by adjustment for other characteristics except for the adequacy of prenatal care, which diminished the risk of severe hypertensive disorder and sepsis. The risk in women from other countries of birth was not different from native women. **Conclusion:** In France, women from sub-Saharan Africa are at higher risk of SMM. This excess risk seems independent from their preexisting characteristics but is reduced by adequate prenatal care. Additional studies are needed to elucidate the obstacles to optimal prenatal care in these women, and to explore complementary explanatory hypotheses, such as a differential care provided once a maternal complication occurs.

PB092

NEONATAL AND CHILD MORTALITY IN ONTARIO, CANADA IS ASSOCIATED WITH MATERNAL COUNTRY OF BIRTH

Ariel Pulver, Susitha Wanigaratne, Marcelo Urquia

BACKGROUND: Infant and child mortality rates vary substantially worldwide, but it is unclear whether these patterns persist among neonates and young children born to immigrant mothers in receiving countries. **OBJECTIVE:** To identify disparities in under-five mortality by maternal birthplace. **METHODS:** A retrospective cohort study of all infants born in Ontario, Canada from 1994 to 2013, using linked population-based administrative health and official immigration databases (n=2,510,142). We used logistic regression to estimate odds ratios (OR), with 95% confidence intervals (CI) for the association between maternal region of birth and under-five mortality, further dissected into neonatal, post-neonatal and 1 to 5 year mortality. **RESULTS:** 21.7% (n = 543,555) of all live births in the study period were to immigrant mothers. Under-five mortality rate was highest among children born to Caribbean mothers (7.6 per 1000 live births), followed by those born to mothers from Sub-Saharan (SS) Africa (6.7 per 1000 live births) and lowest among infants born to Eastern-European and East Asia-Pacific mothers (3.3 and 3.4 per 1000 live births respectively), while the rate among non-immigrants was 4.5 per 1000 live births. These disparities were more pronounced in the neonatal period. Compared to non-immigrant mothers, odds of neonatal mortality were 1.7 times higher for SS-African mothers (95%CI: 1.5, 2.0) and 2.1 times higher for Caribbean mothers (95% CI: 1.9, 2.4). Adjustment for sociodemographic characteristics did not substantially alter results. No significant associations for SS-African and Caribbean groups existed with post-neonatal and 1 to 5 year mortality. **CONCLUSIONS:** Children of SS-African and Caribbean women in Canada are at higher risk of mortality but this was driven by neonatal mortality. Associations between maternal morbidity and preterm birth among these groups may explain the observed associations.

MATERNAL AND PERINATAL HEALTH OF REFUGEES IN ONTARIO, CANADA

Susitha Wanigaratne

Background: Little is known about the health of refugee immigrant women who have migrated to high-income countries despite multiple and intersecting risk factors. **Objective:** To determine whether refugee women have greater risk of maternal and perinatal outcomes compared to non-refugee immigrants. **Methods:** We conducted a retrospective population-based study linking all hospital births in Ontario (2002-2013) to the Citizenship & Immigration Canada Permanent Resident database (2002-2012), which contains information on legal immigrants, including their refugee status and socio-demographic characteristics. Log-binomial regression, with a random effect for maternal country of birth, was used to examine the risk of adverse maternal and perinatal outcomes. The INTERGROWTH 21st Project international standard was used to identify small-for-gestational age <10th percentile (SGA) and large-for-gestational age >90th percentile (LGA) newborns. Risk Ratios (aRR) and 95% confidence intervals (CI) comparing refugees to non-refugee immigrants were adjusted for maternal age, socio-demographic and immigration characteristics. **Results:** Refugee women (n=22,300) had a higher aRR of gestational hypertension (1.13, 95% CI 1.03-1.24), preeclampsia (1.32, 95% CI 1.13-1.55) and c-section (1.05, 95% CI 1.00-1.10) compared to non-refugees (n=185,310). Singleton infants born to refugee mothers had a higher aRR of LGA (1.10, 95% CI 1.03-1.16) and preterm birth < 37 weeks (1.15, 95% CI 1.06-1.23) compared to infants of non-refugees. There was no difference in the risk of gestational diabetes, eclampsia, SGA, stillbirth, neonatal or perinatal mortality. **Conclusion:** Refugee women are at greater risk for some, but not all, adverse maternal and perinatal health outcomes compared to non-refugee women. Additional services may be needed to optimize the health of refugee immigrant women to Canada.

UNDERSTANDING THE REASONS FOR HIGH PERINATAL MORTALITY IN A LOW-INCOME FRENCH DISTRICT WITH A LARGE MIGRANT POPULATION

Jennifer Zeitlin, Priscille Sauvegrain, Aurélie Piedvache, Esther Guéry

Objective: Socially disadvantage is a risk factor for perinatal death, but how access to high quality health services contributes to these risks is not well understood. **Methods:** We investigated stillbirths and neonatal deaths in 2014 in Seine-Saint-Denis, a low-income district with high perinatal mortality rates (N=25037 births). This study included medical chart abstraction of clinical and sociodemographic characteristics, expert peer review of deaths and in-depth maternal interviews 2 to 4 weeks after delivery. Live births from the 2010 French National Perinatal Survey were used as a comparison population (N=429). **Results:** 227 infants (218 women) were included; 75 women were interviewed. In addition to known demographic factors (older age, primiparity), overweight and obese women had higher risks of perinatal death (adjusted odds ratios (aOR): 1.8 [95% IC: 1.1-3.0] and 2.2 [95% CI: 1.2-3.8], respectively) and constituted half of cases. 35% had a preexisting medical condition or a previous adverse obstetric outcome (vs. 15% for live births, aOR: 2.7 [95% CI: 1.5-4.8]). After adjusting for gestational week at delivery, there was no difference in the timing or number of prenatal visits between women with a death and a live birth. However, external experts judged that 75% of deaths were associated with sub-optimal care and that 33% were possibly or probably preventable. Poor care coordination and insufficient care given pregnancy complications were most frequent sub-optimal factors. Possibly preventable deaths were more common for women with gestational diabetes or hypertension (42% vs 28% without these complications, $p<.05$). In interviews, half of women reported difficulties accessing care. **Conclusion:** Commonly-used indices of prenatal care adequacy (number of visits, date at first visit) are not sufficient for assessing prenatal care in disadvantaged populations requiring access to specialists and management of chronic and emergent pregnancy complications.

PERINATAL HEALTH OUTCOMES FOR EAST AFRICAN IMMIGRANT POPULATIONS ARE UNEXPLAINED BY CLINICAL OR SOCIO-DEMOGRAPHIC RISK FACTORS: A POPULATION BASED STUDY IN VICTORIA, AUSTRALIA

Fetene B Belihu, Mary-Ann Davey, Rhonda Small

Background: Sub-Saharan African immigrant women are often treated as a single group in epidemiological studies of immigrant birth outcomes, potentially masking variations between countries. **Methods:** Cross-sectional population-based study of singleton births to women born in one of four East African countries (453 Eritreans, 1094 Ethiopians, 1,861 Somali and 1,404 Sudanese) relative to 427,755 Australian-born women was conducted using the Victorian Perinatal Data Collection in Australia. Pearson's chi-square test and logistic regression analyses were performed to estimate risk of perinatal mortality and selected adverse perinatal health outcomes for East African immigrants with adjustment for clinical and socio-demographic risk factors. **Results:** Compared with Australian-born women, East African immigrants as a group had elevated odds of perinatal mortality, (adjusted odds ratio [ORadj] 1.83, 95%CI 1.47, 2.28), small for gestational age births (ORadj 1.59 95%CI 1.46, 1.74), very low birthweight (ORadj 1.33, 95%CI 1.11, 1.58) and very preterm birth (ORadj 1.55, 95%CI 1.27, 1.90). Odds of preterm birth (ORadj 0.86 95%CI 0.76, 0.98) and macrosomia (ORadj 0.65 95%CI 0.51, 0.83) were lower. Individual country of birth analyses showed a more differentiated picture. Eritrean and Sudanese women fared worse on most outcomes, but Ethiopian women differed from Australian-born women only in relation to higher odds of very preterm birth and Somali women alone had significantly lower odds of preterm birth. **Conclusions:** Overall, East African countries of birth were associated with increased perinatal death and some adverse perinatal outcomes independent of clinical and socio-demographic risk factors, suggesting the need for strategies to enhance surveillance and health care delivery for these women. Analysis by individual country of birth groups has shown women from Eritrea and Sudan particularly are at increased risk, reinforcing the significance of antenatal identification of maternal country of birth.

MIGRANT FRIENDLY MATERNITY CARE IN A WESTERN URBAN CENTRE

Anita Gagnon, Lisa Merry, Jessica Safarian, Ayesha Baig, Rezi Amiri

Background and Purpose: Migrant-sensitive care provision has been identified as a priority in the World Health Assembly Resolution, "Health of Migrants". Little research has been done on the extent to which migrant-sensitive ('friendly') maternity care (MFMC) is currently being provided, factors that support or inhibit provision of such care, and whether specific components of MFMC may be more important than others. We sought to determine to what extent recommended components of MFMC are being provided to recently-arrived international migrant women giving birth in an urban Canadian city. **Methodology:** We conducted a mixed quantitative-qualitative study of 2636 women recently giving birth, speaking any language, in Canada <8 years, and from non-Western countries. The Migrant-Friendly Maternity Care Questionnaire was administered, and women's medical records were reviewed. **Results:** Women from over 97 countries, speaking any of 79 languages reported on their perceptions of how the health system responded to their needs including communication facilitation, promotion of social support, treatment of pre-pregnancy illnesses, early access to prenatal care, and responsiveness to preferences for care, among other indicators of MFMC. Most women reported positive experiences of maternity care; however, there remain critical issues to be addressed. Eleven percent of women did not receive timely prenatal care, over 10% did not always understand information provided by a health care provider, more than 90% reported not being asked about their preferences for care, and 8% reported never having someone who could speak their language. **Conclusions and Discussion:** Empirical data on MFMC, contextual factors supportive of that care, and associated reproductive health outcomes offer baseline data for programming and to permit benchmarking nationally and internationally.

PB097

REPRODUCTIVE HEALTH RESEARCH OF WOMEN MIGRANTS TO WESTERN COUNTRIES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Anita Gagnon, Kara Redden

Background: Influxes of migrant women of childbearing age to Western receiving countries have made their reproductive health a key priority for many governments. We therefore sought to determine if migrant women in Western countries have poorer reproductive health outcomes than non-migrants. **Methods:** We conducted a systematic review of literature identified from Medline, Embase, PsycInfo, Global Health, Social Work Abstracts, CINAHL, Web of Science and ProQuest Dissertations and Theses from 2010 to 2014 including studies of migrant women related to any sphere of reproductive health. Studies were assessed for quality, analysed descriptively and meta-analysed when possible. **Findings:** We identified 228 publications (~12,000,000 migrants), 51 of which were rated as fair or good; even fewer could be meta-analysed. Of the 51 studies, the most commonly reported outcomes were pregnancy-related. Other important elements of migrant women's reproductive health continue to be neglected – such as menopause (0%), sexual health behaviors (1%), STIs & HIV (1%), and infection during pregnancy (1%). The studies revealed heterogeneity in exposure definition, suggesting an ongoing need to use internationally standardized migration indicators. Literature on migrant women and their reproductive health outcomes is extensive, but the heterogeneity of outcomes poses challenges when determining effect size of outcomes of migrant women compared with women born in Western countries. **Conclusions:** Reproductive health outcomes differ by migrant subgroups. Research on non-pregnancy-related reproductive health outcomes is warranted to provide better care to migrant women with those issues. More work is needed to ensure researchers collect data from migrant women similarly – both in terms of migration-related variables and reproductive health outcomes.

PB099

MECHANISMS LINKING SUBJECTIVE REPORTS OF NEIGHBORHOOD DANGER AND SAFETY AND PRETERM DELIVERY AMONG AFRICAN AMERICAN WOMEN.

Shawnita Sealy-Jefferson

Perceptions of neighborhood danger and safety have been shown to predict preterm delivery (PTD) rates among African American women with less than a college education, however the mechanism underlying this association is unknown. Data from the Life-course Influences on Fetal Environments (LIFE) Study (2009-2011) of African American women residing in the Detroit-metropolitan area were used to examine potential mediation of the association between perceived danger and safety and PTD (defined as birth before 37 completed weeks of gestation), by depressive symptomatology, among women with ≤ 12 years of education ($n=365$). A validated scale was used to measure women's perceptions of their neighborhood danger and safety (higher=better). Depressive symptomatology was assessed with the Center for Epidemiologic Studies Depression Scale (CES-D). Preterm delivery occurred in 16% ($n=64$) of the study sample. Statistical mediation was assessed using an unadjusted logistic regression-based path analysis for estimating direct and indirect effects, and their associated bootstrap 95% confidence intervals. In the total effect model, perceptions of neighborhood danger and safety were inversely associated with PTD rates ($p=0.02$), however, there was no direct effect of perceived danger and safety on PTD rates ($p=0.08$). The indirect effect of perceived danger and safety on PTD, through CES-D was significant ($p=0.03$). The results of this study suggest that the association between perceptions of neighborhood danger and safety and PTD among African American women with ≤ 12 years of education operates, at least partially, through depressive symptomatology.

PB098

DIFFERENCES IN BIRTH WEIGHT BY MATERNAL AND PATERNAL NATIVITY IN CANADA

Tarannum Behlim

BACKGROUND: Several studies in various countries have compared perinatal outcomes by parental nativity. However, most are focused on maternal nativity, neglecting the father's. **OBJECTIVE:** To estimate differences in birth weight by both maternal and paternal nativity, accounting for ethnic origin. **METHODS:** This is an observational study using 121,212 singleton, live births between May 2004 and May 2006 to mothers residing in Canada based on the 2006 Census-Birth cohort. We compared sex- and gestational age-standardized birth weight z-score by nativity status of both parents. Parental nativity status was classified into four groups: i)both parents Canadian-born, ii)mother Canadian-born and father foreign-born, iii)mother foreign-born and father Canadian-born, and iv)both parents foreign-born. We used linear regression to estimate the mean differences after adjusting for parity, maternal education, parental age, and ethnicity. **RESULTS:** Preliminary results showed that, compared with boys of two Canadian-born parents, those with two foreign-born parents had a smaller adjusted birth weight for gestational age z-score [0.04 (95% CI: -0.07,-0.003) standard deviations (SD) points]. When only one parent was foreign-born, the difference was -0.02 (95% CI:-0.06,0.015) SD points for the mother and -0.01 (95% CI:-0.05,0.03) SD points for the father. The corresponding figures for girls were -0.06 (95% CI:-0.09,-0.02), -0.07 (95% CI:-0.11,-0.03), and -0.04 (95% CI:-0.08,-0.01), respectively. **CONCLUSION:** We saw a graded association between parental nativity status and birth weight for gestational age in both sexes. Our results highlight the importance of paternal nativity status in addition to the maternal nativity status for birth outcomes. We will further examine whether duration of residency in Canada by each parent plays a role in birth these weight differences.

PB100

NEIGHBORHOOD DISADVANTAGE AND PRETERM DELIVERY AMONG URBAN AFRICAN AMERICAN WOMEN.

Shawnita Sealy-Jefferson

The literature on whether neighborhood disadvantage impacts preterm delivery (PTD) is mixed. Using data collected from the Life-course Influences on Fetal Environments Study (2009-2011; $n=1,387$) comprised of postpartum African American women residing in the Detroit-metropolitan area, we examined the aforementioned relationship. Preterm delivery was defined as birth before 37 completed weeks of gestation. Study participant addresses were geocoded and spatially linked to 5-year block-group summary estimates (2007-2011) from the American Community Survey. An index of neighborhood disadvantage (which was rescaled by its interquartile range, to aid in interpretation) was derived from a principal components analysis of the following variables: % below poverty, % unemployed, % receiving public assistance income, % with college education, % African American, % female headed households, median income, and median value of owned homes. Given the absence of significant neighborhood-level variation in PTD rates in this cohort, we estimated prevalence ratios (PR) and 95% confidence intervals (CI) with log binomial regression models. In bivariate and adjusted models (controlling for age, education, income and marital status), we found no significant associations between administratively defined neighborhood disadvantage and PTD rates among African American women (adjusted PR: 1.03, 95% CI: 0.87, 1.23). Given the persistent racial disparity in PTD rates, more research seeking to identify novel risk and preventive factors for this adverse birth outcome is warranted, especially among African American women.

IMPACT OF MATERNAL SOCIAL DEPRIVATION ON MATERNAL AND PERINATAL SEVERE ADVERSE OUTCOMES: THE PRECARE COHORT STUDY

Elie Azria, Candice Estellat, Toni Alfaiate, Thomas Schmitz, Jean-François Oury, Laurent Mandelbrot, Dominique Luton, Philippe Ravaud

Objective Socioeconomic factors can have important effects on maternal and perinatal health. Our objective is to determine in a setting of universal access to prenatal health care services to which extent maternal social deprivation is associated with increased risk of severe maternal and perinatal adverse outcomes. **Study design** PreCARE study is a French urban prospective multicenter cohort study in which between September 2010 and October 2011 all pregnant women registered to deliver or delivered in one of the participating maternity unit and their newborns were recruited and followed. The analysis was restricted to the women with singleton pregnancies delivered after 22 weeks of gestation. Deprivation was defined by the presence of at least one of the following conditions: social isolation, insecure housing, unemployment, absence of basic health insurance (social security), undocumented migrants, and recent immigration. Outcomes studied included severe maternal morbidity, maternal and perinatal death, severe neonatal morbidity. Logistic regressions models were used for each outcomes to adjust for potential confounders and estimate Odds Ratios (OR). **Results** Among the 9312 women recruited in the PreCARE cohort study, the rate of mothers in a situation of social deprivation was 37.2%. After adjustment for potential confounders, maternal social deprivation was significantly associated with an increased risk of severe preeclampsia, eclampsia, thromboembolic complications, severe maternal sepsis and birthweight below the 5th centile. Overall, social deprivation was associated with increased risks of severe maternal (adjusted OR 1.30 [1.01-1.69]) and perinatal (adjusted OR 1.17 [1.00-1.37]) adverse outcomes. **Conclusion** This large prospective cohort study designed to address the issues of social inequalities in maternal and perinatal health showed in a setting of universal access to prenatal health care services the association between maternal social deprivation and increased risk of severe maternal and perinatal morbidity.

RESIDENTIAL MOBILITY PATTERNS AND CHANGES IN NEIGHBORHOOD QUALITY AMONG WOMEN MOVING BETWEEN PREGNANCIES IN THE PROVINCE OF ONTARIO, CANADA (2000-2011)

Ayaz Hyder, Hla-Hla Thein, Marcelo Urquia

Introduction: Research on residential mobility patterns among pregnant women is limited to moves during pregnancy yet preconceptional exposures have been associated with adverse birth outcomes. We explored residential mobility patterns among pregnant women during the interpregnancy interval and changes in neighborhood quality. **Methods:** We linked mother-child records from Ontario, Canada with best-known annual data on census tract of residence to determine which mothers moved in between two pregnancies (N=62,708). Census tracts were linked to neighborhood-level characteristics using census data. **Results:** Majority of mothers (34,278 or 55%) moved 1-2 times and average age at first move was 26.17 years (interquartile range: 22-30). A curvilinear relationship was observed between number of residential moves and proportion of births that were preterm birth or low birth weight. Post-move neighborhoods were of significantly higher quality along all characteristics except education, residential stability and median house value. **Discussion:** Our exploratory findings suggest that benefits of moving to higher quality neighborhoods may be offset by short interpregnancy interval and high number of moves during the preconceptional period.

IMPACT OF MATERNAL DEPRIVATION ON PRENATAL CARE UTILIZATION: THE PRECARE COHORT STUDY

Clémentine Gonthier, Candice Estellat, Toni Alfaiate, Thomas Schmitz, Jean-François Oury, Laurent Mandelbrot, Dominique Luton, Philippe Ravaud, Elie Azria

Objective Maternal social deprivation is associated with an increased risk of maternal and perinatal adverse outcomes. It is likely that inadequate prenatal care utilization (PCU) is an important intermediate factors. The health care system in France provides essential health services to all women irrespective of socioeconomic status. The aim of this study is to assess the impact of maternal deprivation on PCU in this setting of universal access to prenatal health care services. **Study design** PreCARE study is a French prospective multicenter cohort study in which all pregnant women delivered between September 2010 and October 2011 and their newborns were included. The present analysis was restricted to patients with singleton pregnancies delivered after 22 weeks of gestation. Deprivation was defined by 6 socioeconomic dimensions: social isolation, insecure housing, unemployment, absence of basic health insurance (social security), undocumented migrants, and recent immigration. An index of social deprivation validated on the 2010 French National Perinatal Survey was used. Poor attendance to prenatal care was defined using a PCU index based on national guidelines. Logistic regressions were used to estimate Odds Ratios (OR). **Results** Nine thousand three hundred and twelve women were included. Poor attenders represented 23.3% of the study population. Each of the 6 deprivation dimensions were significantly associated with an excess of risk of inadequate PCU. After adjustment on the potential confounders, recent immigration (aOR 2.3 [1.9-2.9]), unemployment (aOR 1.6 [1.3-1.8]), and insecure housing (aOR 1.3 [1.1-1.5]) remained associated with this risk. Furthermore a social gradient in terms of risk of inadequate PCU was observable. Women from Sub-Saharan Africa, less than 20 years old or having an unwanted pregnancy were particularly vulnerable. **Conclusion** Despite a system ensuring universal access to prenatal care services, social deprivation is independently associated with an increased risk of inadequate prenatal care.

MATERNAL AND PERINATAL MORBIDITY AMONG WOMEN IN RURAL VERSUS URBAN AREAS: A RESIDENCE-BASED APPROACH.

Sarka Lisonkova, Matthew Haslam, Leanne Dahlgren, Innée Chen, Anne Synnes, Kenneth Lim

OBJECTIVE: We examined the association between rural residence and severe maternal morbidity and perinatal outcomes. **METHODS:** A population-based retrospective cohort study, including all births to women residing in British Columbia, Canada, 2005-2010. We compared maternal mortality/severe morbidity (e.g., eclampsia) and adverse perinatal outcomes (e.g., perinatal death) between mothers residing in areas with moderate to no metropolitan influence (rural) and those living in metropolitan areas or areas with a strong metropolitan influence (urban). We used logistic regression to obtain adjusted odds ratios (AOR) and 95% confidence intervals (CI). **RESULTS:** Severe maternal morbidity was significantly higher among mothers residing in rural vs. urban areas (AOR=1.22, CI: 1.09-1.36). In particular, rural mothers had significantly higher rates of eclampsia (AOR=2.45, CI: 1.59-3.77), obstetric embolism (AOR=2.23, CI: 1.18-4.20), and uterine rupture/dehiscence (AOR=1.85, CI: 1.34-2.54). Perinatal mortality did not differ between rural and urban mothers, however, rural mothers had higher rates of severe neonatal morbidity (AOR=1.14, CI: 1.02-1.29), preterm birth (AOR=1.06, CI: 1.01-1.11), Apgar score <7 at 5 minutes (AOR=1.24, CI: 1.13-1.31), and large-for-gestational-age (AOR=1.14, CI: 1.10-1.19); and lower rates of small-for-gestational-age infant (AOR=0.90, CI: 0.85-0.95), and NICU admission (AOR=0.36, CI: 0.33-0.38). **INTERPRETATION:** Compared with urban mothers, rural women had elevated rates of severe maternal morbidity, including eclampsia, obstetric embolism, and uterine dehiscence/rupture. Rural infants had higher rate of severe neonatal morbidity, while the rate of NICU admission was lower compared with urban infants. Rural maternity care providers need to be aware of potentially life-threatening maternal and infant complications requiring advanced obstetric and neonatal care.

NEIGHBORHOOD ETHNIC DENSITY AND CHILDREN'S SOCIO-EMOTIONAL DEVELOPMENT IN THE EARLY CHILDHOOD LONGITUDINAL STUDY-BIRTH COHORT

Jennifer Richards, Michael Kramer

Aspects of residential segregation may be detrimental to women's and children's health, but some evidence suggests that conditional on material deprivation related to segregation, residence in co-ethnic enclaves is health-protective for perinatal and maternal mental health outcomes. We address the gap in evidence for the association between ethnic density and early childhood socioemotional health using data from the Early Childhood Longitudinal Study-Birth Cohort. Our study population included 4,850 singletons born in 2001 whose mothers were non-Hispanic white ($n=2,050$), non-Hispanic black ($n=800$), Hispanic ($n=1,000$), Asian ($n=800$), or American Indian/Alaskan Native ($n=200$). Using children's 9-month Zip Code Tabulation Area (ZCTA), ethnic density was defined as the proportion of ZCTA residents who were of their own racial/ethnic group and categorized in 4 groups (0-4.99%, 5-29.99%, 30-49.99%, 50% and above). Our primary outcome was children's mean total difficulties score at kindergarten age, comprising parent-reported items on emotional, conduct, hyperactivity, and peer problems. Survey-weighted linear regression models stratified by race/ethnicity were used to estimate the relationship between ethnic density and mean total difficulties scores, adjusting for individual-level covariates (household income and size; highest household employment level; maternal nativity, education and age at birth; maternal depression; child's age and sex; primary language spoken at home, family structure) as well as area-level deprivation. Results were suggestive of elevated total difficulties scores among American Indian/Alaskan Native and non-Hispanic white children residing in areas with lower ethnic density, compared with living in areas with 50% or above of respondents' own racial/ethnic group. There was no observed association between ethnic density and mean total difficulties score among non-Hispanic black, Hispanic, or Asian children.

IS NEIGHBORHOOD DISADVANTAGE OR AFFLUENCE ASSOCIATED WITH BREASTFEEDING PRACTICES? EVIDENCE FROM NEW JERSEY.

Jennifer Yourkavitch, Jennifer Kane, Gandarvaka Miles

Breastfeeding practices in the U.S. are suboptimal on average, despite evidence of numerous immediate and lifelong benefits for mothers and infants. Neighborhood disadvantage is negatively associated with several reproductive health outcomes. Prior research on its association with breastfeeding yielded mixed results, possibly due to suboptimal analyses, but fostered hypotheses about the role of neighborhood affluence as a distinct influence. Neighborhood disadvantage and affluence could influence a mother's breastfeeding practices through individual, social, and structural mechanisms. We linked birth certificates for healthy singletons whose mothers had complete data and resided in urban areas of New Jersey in 2006 ($n=53,064$) to census tract data ($n=1651$), and created indices for neighborhood disadvantage and affluence using factor analysis. We examined associations of these indices with breastfeeding at hospital discharge using multilevel log-binomial models. Neighborhood disadvantage was negatively associated with exclusive breastfeeding (Risk ratio (RR) 0.50, 95% confidence interval (CI): 0.47-0.53) and any breastfeeding (RR 0.71, 95% CI: 0.68-0.74). Models adjusted for confounding from age, marital status, parity, race-ethnicity, education, foreign-born status, working in the previous year, father's information reported, and type of health insurance attenuated all effects but maintained the direction of association for exclusive (RR 0.77, 95% CI: 0.74-0.82) and any (RR 0.90, 95% CI: 0.86-0.93) breastfeeding. Conversely, neighborhood affluence was positively associated with exclusive (RR 1.73, 95% CI: 1.66-1.81; adjusted RR 1.21, 95% CI: 1.16-1.27) and any breastfeeding (RR 1.44, 95% CI: 1.39-1.50; adjusted RR 1.20, 95% CI: 1.16-1.25). Future research on these associations should include hospital practices that support or discourage breastfeeding, spatial autocorrelation, and specific mechanisms in order to support appropriate interventions.

PERINATAL HEALTH OUTCOMES ARE ASSOCIATED WITH BOTH NEIGHBORHOOD SOCIOECONOMIC DISADVANTAGE AND NEIGHBORHOOD AFFLUENCE

Jennifer Buher Kane, Gandarvaka Gray, Jennifer Yourkavitch, Katherine King

Poor maternal social environments pose significant risk to perinatal health. Past studies of neighborhood environments have only examined the effects of deprivation/disadvantage on birth outcomes, despite a growing literature revealing the potential for neighborhood affluence to have a distinct influence on health outcomes. Using geocoded New Jersey birth certificate records from 1996 to 2006 ($N=871,633$) linked with US Census tract-level data, this study examined the associations between both neighborhood socioeconomic disadvantage (NSD) and neighborhood affluence (NA), and perinatal health indicators. We constructed multilevel linear (birthweight, BW) and logistic (intrauterine growth restriction, IUGR; low birthweight, LBW; preterm birth, PTB) regression models for all births and stratified by maternal race-ethnicity (White, Black, Hispanic, Asian). All models adjusted for individual-level covariates (maternal age, education, employment, insurance, nativity, marital status, parity; if father was identified on birth record; infant sex; and birth year). Three key findings emerged: 1) there is a statistically significant association between both NSD and NA, and perinatal outcomes (e.g., among Black women, a 1 standard deviation (SD) increase in NA was associated with a 9% decrease in the odds of LBW (95% confidence interval (CI): .87-.94); a 1 SD increase in NSD was associated with a 6% increase in the odds of PTB (95% CI: 1.04-1.09); 2) NSD and NA tend to explain higher amounts of neighborhood-level variance among Black women (range=12-43%) relative to women of other race/ethnicities (range=0-24%); 3) NA explains a higher proportion of neighborhood-level variance than NSD; this holds in the case of BW, LBW, IUGR, and PTB (e.g., among Asian women, NA explains 20% of the neighborhood-level variance in BW; NSD explains 12%). These findings suggest neighborhood affluence may add new knowledge pertaining to the fundamental social determinants of perinatal health.

CHANGE IN NEIGHBORHOOD DEPRIVATION AND PERINATAL HEALTH

Gandarvaka Miles, Jennifer Yourkavitch, Jennifer Buher Kane

The maternal neighborhood environment is believed to influence the health of her developing offspring through multiple social, behavioral, and biological mechanisms. However, few studies have investigated how change in the maternal environment between births impacts subsequent pregnancies. This study examined the association between change in neighborhood deprivation and the difference in sex-specific birth weight-for-gestational age (BWGA) z-scores between siblings born to 266,980 New Jersey mothers from 1996-2006. A neighborhood deprivation score (ranging from -3.5 to +10.9) was derived from Census data linked to geocoded maternal addresses reported on the birth certificate. Fixed effects linear regression was used to account for time-invariant maternal characteristics. Models were stratified by mother's between-birth mobility status: stayers (mothers residing in the same census tract at the time of both births, $N=150,329$) and movers (mothers who changed census tracts between births, $N=116,651$). The average between-birth change in neighborhood deprivation was greater among movers compared to stayers (+0.27 vs. -0.04). As expected, a between-birth increase in neighborhood deprivation was associated with a decrease in BWGA z-score among movers (-0.005 ± 0.002) when adjusting for time-varying maternal age and infant birth year. Among stayers, however, an increase in neighborhood deprivation was associated with an increase in BWGA z-score (0.028 ± 0.011). Estimates were attenuated after further adjustment for maternal characteristics (education, marital status, insurance type, parity), pregnancy behaviors (smoking, early prenatal care), and acknowledgment of paternity. These findings suggest changes in the level of maternal exposure to neighborhood deprivation between births may influence the health of future offspring. Further investigation of this association will examine the potentially modifying effects of baseline level of neighborhood deprivation.

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THE ASSOCIATION BETWEEN PATCHING ADHERENCE AND VISUAL ACUITY AT AGE 4½ IN THE INFANT APHAKIA TREATMENT STUDY

Carolyn Drews-Botsch, Marianne Celano, Eugenie Hartmann, Scott Lambert

INTRODUCTION: We examine the relationship between patching and visual acuity at age 4 ½ years in the Infant Aphakia Treatment Study. **METHODS:** 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 4½. 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. **RESULTS:** Hours of patching at each time point was correlated with patching at all other time points. Few (n=5) caregivers reported averaging more than 3 hours of patching in years 3-5 if they had not done so in the first 2 years. 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. **DISCUSSION:** We affirm the importance of patching to visual acuity in children after unilateral cataract extraction in infancy. **CONCLUSION:** 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.

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NEONATAL SEPSIS IN ARAB STATES IN THE GULF REGION: TWO-YEAR PROSPECTIVE STUDY

Abdullah Al-Ta'iar, Majeda Hammoud

Objective: Investigate the incidence and the pattern of causative organisms of culture proven Early-Onset Sepsis (EOS) and Late-Onset Sepsis (LOS) in Arab states in the gulf region. **Methods:** Five neonatal care units participated in this two-year prospective study in Kuwait, United Arab Emirates and Saudi Arabia. Data were collected prospectively using standardized data collection form. EOS was defined as the growth of a single potentially pathogenic organism from blood or cerebrospinal fluid in infants within 48 hours of birth with clinical and laboratory findings consistent with infection. Similarly, LOS was defined among the infants beyond 48 hours. **Results:** During the study period 67474 live births occurred among whom 102 EOS and 785 LOS occurred. The overall incidence of EOS was 1.5(95%CI:1.2-1.8) per 1000 live births and ranged from 2.64 per 1000 live births in Kuwait to 0.40 per 1000 live births in King Abdulaziz Hospital in Saudi Arabia. The incidence of LOS was 11.6(95CI: 10.8-12.5) per 1000 live births and ranged from 13.5 per 1000 live births in Kuwait to 5.2 per 1000 live births in Tawam hospital in United Arab Emirates. The most common causative organism for EOS was Group B Streptococcus GBS (60.0%) followed by E.coli (13%); while Coagulase-negative staphylococci (34.6%) followed by Klebsiella spp. (22.8%) were the main causative organisms for LOS. Case-fatality was 13.0% and 20.6% among EOS and LOS, respectively. **Conclusion:** The incidence and the pattern of causative organism of EOS in Arab states in the gulf region resembles that in developed countries. More than half of EOS were due to GBS which highlight the importance of intrapartum antibiotic prophylaxis. On the other hand, the incidence of LOS is higher than that reported from developed countries and resembles that in low-income countries. The later requires institutional policies and more efforts to reduce healthcare associated infection.

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IS AGE OF MENARCHE RELATED TO DIGIT RATIO OR BREASTFEEDING DURING CHILDHOOD?

Abdullah Al-Ta'iar

Background: Early age of menarche has been linked to various adverse health outcomes such as, obesity, type 2 diabetes and breast cancer. Many factors are thought to be linked to early age of menarche, one of which is breastfeeding, but this remains under intense debate. **Objectives:** To estimate the age of menarche among high school girls in Kuwait and to explore the association between age of menarche and breastfeeding or digit ratio. **Methods:** A cross-sectional study was conducted on 810 randomly selected female high school students from all governorates in Kuwait. Data on age of menarche was collected using self-administered questionnaire by the students; while the data on breastfeeding was collected by self-administered questionnaire sent to their mothers. To calculate digit ratio (2D:4D), finger lengths were measured using a digital caliper. Weight and height of female students were measured using digital scale and stadiometer. Multiple linear regression was used to investigate the association between age of menarche and breastfeeding or digit ratio. **Results:** Out of the 810 students selected, 50(6.2%) were absent or refused to participate, and out of the 761 mothers to whom the questionnaire was sent, 433(56.9%) responded. The mean (SD) age of menarche was 12.32(1.21) years (95%CI: 12.23-12.41). There was no significant association between age at menarche and breastfeeding in the first four months of life before and after adjusting for potential confounders. There was no significant association between age at menarche and digit ratio in either hand before and after adjusting for potential confounders. **Conclusion:** The estimated age at menarche among contemporary girls in Kuwait is similar to that in industrialized countries. Trends in age at menarche should be monitored because of their public health implications; and cohort studies are recommended to investigate if breastfeeding has a spinoff benefit in terms of delaying sexual maturity.

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TRAFFIC-RELATED AIR POLLUTION AND CHILDHOOD ACUTE LEUKEMIA IN OKLAHOMA

Amanda Janitz, Janis Campbell, Sheryl Magzamen, Anne Pate, Julie Stoner, Jennifer Peck

Background: While many studies have evaluated the association between acute childhood leukemia and environmental factors, knowledge is limited. Ambient air pollution has been classified as a Group 1 carcinogen, but studies have not established whether traffic-related air pollution is associated with leukemia. The goal of our study was to determine if children with acute leukemia had higher odds of exposure to traffic-related air pollution at birth compared to controls. **Methods:** We conducted a case-control study using the Oklahoma Central Cancer Registry to identify cases diagnosed between 1997 and 2012 (n=307). Controls were selected from birth certificates and matched to cases on week of birth (n=1,013). Using a novel satellite-based land-use regression model of nitrogen dioxide (NO2) and estimating road density, we evaluated the association between traffic-related air pollution and childhood leukemia using conditional logistic regression. **Results:** We observed an elevated, but non-significant, odds of exposure to the fourth quartile of NO2 (11.19-19.89 ppb) among the cases after adjustment for urbanization and maternal education. These estimates were stronger among children with acute myeloid leukemia (AML) than acute lymphoid leukemia, with an association among urban children with AML (4th quartile odds ratio: 5.25, 95% confidence interval: 1.09, 25.26). We observed no significant association with road density. **Conclusions:** Although we observed no association overall between NO2 or road density, this was the first study to observe an elevated odds of exposure to NO2 among children with AML compared to controls suggesting further exploration of traffic-related air pollution and AML.

INTERACTION EFFECT OF UNEXPECTED PREGNANCY AND YOUNGER MOTHERHOOD ON INFANT ABUSE: A RETROSPECTIVE COHORT STUDY IN JAPAN

Takeo Fujiwara

Background: Unexpected pregnancy can be a risk factor for infant abuse because young maternal age has been shown robust association with infant abuse in previous studies. However, few studies investigate whether unexpected pregnancy in conjunction with younger motherhood increases the risk of infant abuse. **Objective:** The aim of this study is to investigate interaction effect of unexpected pregnancy and younger motherhood on infant abuse. **Method:** Questionnaire inquiring on infant abuse, defined as shaking and smothering at least once during past month, was disseminated at 4-month-old health checkup at 11 municipalities in Aichi prefecture, Japan (valid response N=6,358). Then, the data collected at registration of pregnancy, including maternal age and feeling on her pregnancy were linked with the questionnaire response (linked N=6,056). Logistic regression was employed to see the association between 4 categorization (young motherhood (defined as less than 25 years old) or not and unexpected pregnancy or not) and infant abuse, adjusted for covariates (parity, gestational week at registration, whether returning to maternal house of origin to give birth, and depressive symptom). **Result:** At 4-month-old health checkup, 193 (3.2%) mothers reported infant abuse. In crude model, younger motherhood with unexpected pregnancy 2.87 (95% confidence interval (CI): 1.61-5.11) times more likely abuse their infants than older mother with expected pregnancy. Moreover, younger motherhood with expected pregnancy showed no higher risk on infant abuse than older mother with expected pregnancy. After adjusted for covariates, young motherhood with unexpected pregnancy remained to show significant association with infant abuse (odds ratio: 2.28, 95% CI: 1.26-4.12). **Conclusion:** Younger motherhood with unexpected pregnancy were high-risk for infant abuse. The current finding should be used to identify high-risk mothers on infant abuse.

PATERNAL AGE AND RISK OF CANCER IN CHILDHOOD

Stine Kjaer Urhoj, Ole Raaschou-Nielsen, Per Kragh Andersen, Laust Hvas Mortensen, Anne-Marie Nybo Andersen

Background Many childhood cancers are presumed to initiate in utero, and an increased number of de novo mutations in sperm with increasing age has been suggested as a mechanism. Our aim was to examine the association between paternal age at conception and specific types of childhood cancer using a cohort design. **Methods** We identified all children born alive in Denmark from 1978 through 2010 in the nationwide Danish Birth Register and linked to other nationwide registers. We estimated the relative rate of cancer with 95% confidence intervals (CI) according to paternal age. We included all main diagnostic groups and subgroups with more than 100 cases, using the International Classification of Childhood Cancer (3rd edition). The child's age was the underlying time. Paternal age was modeled as a linear term, in six categories, and by use of restricted cubic splines. We adjusted the analyses for maternal age, the child's year of birth, parental educational levels, parental ethnic origin, and maternal parity. **Results** Of the 2,006,312 children, 3649 had a cancer diagnosis before the age of 15 years. Leukemias constituted 30% (n=1110) of the cancer cases. The rate of leukemia was found to be 12% higher (95% CI: 3%-22%) for every 5 years increase in paternal age. This association was primarily due to a higher rate of acute lymphoid leukemia (ALL); compared with fathers aged 30-34 years, the adjusted hazard ratios of ALL in other age groups were as follows: <25, 0.81 (95% CI: 0.61-1.06); 25-29, 1.00 (95% CI: 0.84-1.19); 35-39, 1.05 (95% CI: 0.85-1.30); 40-44, 1.17 (95% CI: 0.84-1.63); 45+, 1.55 (95% CI: 1.02-2.35). The same pattern was found when paternal age was modeled using restricted cubic splines. Analyses of other cancer types did not show clear associations. (Results are preliminary). **Conclusions** The rate of acute lymphoid leukemia was found to be higher with higher paternal age, but advanced paternal age appears to play a minor role in the etiology of childhood cancer.

PARENTAL FERTILITY TREATMENT AND CHILDHOOD EPILEPSY - A NATIONWIDE COHORT STUDY OF 565,166 LIVE BIRTHS

Laura Ozer Kettner, Ulrik Schioler Kesmodel, Cecilia Høst Ramlau-Hansen, Bjørn Bay, Beate Ritz, Niels Bjerregaard Matthiesen, Tine Brink Henriksen

Background Fertility treatment includes hormonal stimulation of the woman and in vitro manipulation of gametes and embryos which ultimately may influence prenatal brain development. **Objective** To assess the association between fertility treatment and offspring epilepsy. **Methods** This nationwide cohort included all Danish pregnancies resulting in live-born singletons (1995-2003). Children conceived by fertility treatment and children developing epilepsy (until 2013) were identified from national Danish registries. The data were analyzed by Cox proportional hazards regression, adjusted for potential confounders. **Preliminary results** A total of 565,166 pregnancies were included, and 1.4% of the children developed epilepsy. Children conceived after ovulation induction or intrauterine insemination had a slightly higher overall risk of childhood epilepsy. The hazard ratio (HR) for two subtypes of epilepsy was 1.36 (95% CI 1.03 - 1.79) for idiopathic generalized epilepsy and 1.27 (95% CI: 0.97-1.66) for focal epilepsy. When separately assessing different hormones used in ovulation induction or intrauterine insemination, only Clomiphene Citrate was associated with an overall increased risk of childhood epilepsy. The result was consistent when applying a sibling design (HR=2.08; 95% CI: 1.06 - 4.10). Treatment with in vitro fertilization or intracytoplasmic sperm injection was not associated with an overall risk of childhood epilepsy. The type of procedure, the type of gametes used or the treatment indication did not affect the results. However, an increased risk of idiopathic generalized epilepsy was found (HR=1.43; 95% CI: 0.99- 2.05). **Conclusion** Children conceived by ovulation induction or intrauterine insemination with Clomiphene Citrate may be at increased risk of childhood epilepsy. Furthermore, children conceived by in vitro fertilization or intracytoplasmic sperm injection may be at increased risk of idiopathic generalized epilepsy.

FRACTURES IN 7-YEAR-OLD CHILDREN AS A RESULT OF AN INTERACTION BETWEEN BONE PROPERTIES AND PHYSICAL ACTIVITY: DIFFERENT FINDINGS FOR BOYS AND GIRLS

Ana Martins, Raquel Lucas, Teresa Monjardino, Fábio Araújo, Henrique Barros

Introduction: Fractures result from compromised bone quality, moderate to high energy trauma, or a combination of both. However, the interaction between bone physical properties and physical activity in producing fracture has been overlooked. **Objective:** To assess if fracture history is associated with bone physical properties at 7 years of age and if physical activity modifies this relation in both sexes. **Methods:** We used cross-sectional data collected from 2115 7-year-old children (52.1% male) of Generation XXI birth cohort (Porto, Portugal). Parents reported children's lifetime history of fracture. They also reported time spent in programmed sports and average time spent in active plays per week that were transformed into quartiles. Bone physical properties were determined by whole body dual-energy X-ray absorptiometry: lumbar spine (LS) and total body less head (TBLH) bone mineral content (BMC) and bone mineral density (BMD). Logistic regression was conducted to estimate odds ratios (OR), crude and adjusted for weight and height, with 95% confidence intervals (95% CI). Linear regression was used to calculate BMC and BMD means adjusted for height and weight. **Results:** Increased sports practice in boys (>240 min/week), but not in girls, was significantly associated with higher mean BMC (TBLH=611.4 vs. 598.8 g) and BMD (TBLH=0.632 vs. 0.621 g/cm²). No association was found between fracture and bone quality in boys. In girls, decreased BMC (OR TBLH= 0.12 (0.04-0.36)), OR LS= 0.40 (0.22-0.72) and BMD (OR TBLH= 0.21 (0.08-0.55)) were associated with fracture, but only in those who spent more time in active plays (>690 min/week). No such interaction was found in boys. **Conclusion:** Fractures in boys were likely to result from moderate or high energy trauma, independently of bone quality. In girls, fractures more likely resulted from the interaction of worse bone physical properties and increased activity levels.

SHAKEN BABY SYNDROME AND SOCIAL CAPITAL: A MULTI-LEVEL ANALYSIS OF CAREGIVERS OF INFANTS IN JAPAN

Aya Isumi

Background: Shaken baby syndrome (SBS) is the leading cause of death due to child abuse. Although previous studies have explored risk factors to prevent SBS, few studies have investigated the association of social capital with shaking towards infants. **Objective:** To assess the association between individual- and community-level social capital and shaking among caregivers of 3-4 month infants in Japan. **Methods:** A questionnaire was administered to parents who participated in a 4-month health checkup program in 45 municipalities of Aichi prefectures in 2012 (N=6,590). It asked frequency of shaking towards infants in the past month. Social capital was measured by 1) whether rents had someone who helped in times of trouble during their pregnancy, 2) numbers of persons to currently consult with about renting, and 3) whether they can consult with their partner, rents, relatives, friends in neighborhood, and friends not in neighborhood. Multilevel analysis was used to examine the association of individual- and community-level social capital and shaking. **Results:** Self-reported prevalence of shaking at least once in the past month was 3.9% (95% CI: 3.5%-4.4%). We found that rents having more than six persons to consult with were 42% less likely to shake their infants than those who had five or less individuals to consult with (OR: 0.58, 95% CI: 0.41– 0.83). Having friends to consult with in neighborhood was the most protective factor of shaking (OR: 0.69, 95% CI: 0.48– 0.99). These individual effects of social capital on shaking remained unchanged after considering community-level social capital. Community-level social capital was not found to be protective against shaking. **Conclusion:** Our preliminary findings suggest individual-level social capital, especially having more persons to consult with and having friends to consult with in neighborhood, is important to prevent SBS.

IMPACT OF CHILDCARE ARRANGEMENTS ON WEIGHT IN QUEBEC PRESCHOOL CHILDREN

Tanya Murphy

Background: Formation of healthy behavioural patterns relatively early in life may contribute to long-term healthy weight gain in childhood. Children from low socioeconomic backgrounds are particularly at risk for obesity. In 1997, Quebec (Canada) phased-in a low-cost, regulated childcare program making quality-controlled childcare more accessible to children from low income families, which presented a good opportunity to study the impact of preschool childcare arrangements on children's growth. **Objective:** Estimate differences in weight by childcare arrangement in early childhood. **Methods:** A representative birth cohort (1997-8) of infants from Quebec, Canada, were followed annually (n=2,045). Childcare was categorized as 1) regulated centre-based, 2) regulated family-based, 3) unregulated non- rental care, and 4) parental care. The difference in weight-for-height by type of childcare was estimated for children from ages 2 to 5 years old using hierarchical linear models to account for repeated measures per child. Potential confounders were balanced across exposure groups using propensity-score based methods. **Results:** Preliminary analyses for the first year (2.5 years old) estimate the average weight-for-height in boys attending regulated childcare is 0.5 kg (95% CI: 0.2–0.8 kg) greater than boys under predominantly rental care. Weight in girls did not differ by childcare arrangement; weight-for-height in regulated childcare was 0.1 kg lower (95% CI: -0.5–0.2 kg) compared to those under parental care. **Discussion:** While little overall difference in weight gain in the preschool years seems attributable to childcare arrangements, boys and girls may react differently to non- rental care. The inclusion of children from low socioeconomic families in all levels of childcare is an important strength of this study. Propensity score estimation for sub-groups—in particular two- and lone- rent families—and repeated measures will be discussed.

GREATER MORTALITY RISK AMONG BORDER HISPANIC TODDLERS DURING THE LAST DECADE

Jill McDonald, Lindsey Brantley

Introduction: Earlier work indicated that mortality in children ages 1-4 years in the 44 US-Mexico border counties was similar to US mortality and was lower in Hispanics than non-Hispanic whites (NHW). Early childhood mortality among border Hispanics (BH) has never been compared with that of US Hispanics (USH), however, and not with border NHW rates since 2004. **Objectives:** To compare BH mortality rates in children ages 1-4 years with USH rates and border NHW rates in recent years. **Methods:** We used 2000-2014 National Vital Statistics System data to examine Hispanic population deaths/100,000 in the 1-4 age group in US-Mexico border counties and in the US overall. We compared these rates to NHW rates by time period, urban status and cause of death. **Results:** During 2000-2014, deaths in border counties accounted for 9.1% of the 14,156 USH deaths in children 1-4 years. BH rates exceeded USH rates during 2005-2009 (BH:30.6, 95% CI=27.9-33.4; USH:26.4, 95%CI=25.7-27.1) and 2010-2014 (BH:25.1, 95% CI=22.6-27.6; USH:21.5, 95%CI=20.9-22.1). During 2010-2014, USH rates were lower (21.5, 95%95%CI=20.9-22.1) than US NHW rates (24.0, 95%95%CI=23.5-24.5), whereas BH rates were non-significantly higher (25.1, 95%CI=22.6-27.6) than border NHW rates (20.7, 95%CI=16.8-24.6). No excess was seen in large metro counties. BH exceeded USH rates for congenital anomalies (BH:4.1, 95%CI=3.5-4.7; USH:3.2, 95%CI=3.1-3.4) and cancer (BH:3.2, 95%CI=2.7-3.8; USH:2.5, 95%CI=2.4-2.68) and were borderline excessive for transport injury (BH:4.6, 95%CI=4.0-5.3; USH:4.0, 95%CI=3.8-4.1). **Conclusions:** Since 2005, early childhood mortality has been greater in BH than USH. The fact that the excess extends to multiple causes of death and is not seen in the most urban areas suggests that social determinants contribute to the disparity. Information on incidence of congenital anomalies, cancer and injury would help determine whether this disparity can be reduced by primary or secondary prevention.

DRIVER LICENSING AND MOTOR VEHICLE CRASH RATES AMONG ADOLESCENTS WITH VISION IMPAIRMENT

Julia M. Baker, Carolyn Drews-Botsch, Melissa R. Pfeiffer, Allison E. Curry

Motor vehicle crashes are the leading cause of death for adolescents. Vision impairment can further compromise driver safety, but research on the association between visual impairment and crash risk has paid little attention to whether an individual has good visual acuity in both eyes and the impact of unilateral vision impairment on teen driving. Impairments of binocularity may affect teen driving by impacting peripheral vision, depth perception and/or the ability to scan the environment for hazards. We examined rates of driver licensing (minimum age in NJ is 17) and, among licensed drivers, 1- and 2-year motor vehicle crash risk among adolescents with unilateral vision impairment and amblyopia compared with normal-sighted counter parts. Electronic health records for 61,379 NJ residents who were patients of The Children's Hospital of Philadelphia's (CHOP) healthcare network, were born 1987-1995, and had a visit within 4 years of driving-eligible age were individually linked to NJ's statewide driver licensing and crash databases through June 2012. Subjects were classified based on ICD-9-CM diagnostic codes either at a CHOP visit or on the list of known chronic conditions. Those with unilateral vision impairment (N=62) were less likely than those without impairment to be licensed by their 18th birthday (40% vs. 66%, p<.001). Among licensed drivers, data suggest that those with unilateral vision impairment had higher crash risks 1-year (28% vs 16%, risk ratio (RR)=1.8, 95% confidence interval (CI): 0.9-3.3) and 2-years (36% vs 23%, RR=1.6, 95% CI: 0.9-2.7) post-licensure. Those with a history of amblyopia (N=392) also had lower rates of licensure by age 18 (47% vs 66%, p<.001), but no evidence of elevated crash risk (14% vs 16% at 1 year; 21% vs 23% at 2 years). These preliminary data suggest that unilateral vision impairment and amblyopia may impact teen driving by reducing the number of teens licensed but that history of amblyopia does not increase crash risk.

PROMPTLY ASSESS TRENDS IN BIRTH PREVALENCE OF CEREBRAL PALSY UP TO AGE 4 IN SOUTH CAROLINA USING ADMINISTRATIVE SOURCES INCLUDING MEDICAID DATA, 1996 TO 2009

Qing Li, Stephen Kinsman, Rita Ryan, Dorothea Jenkins, Melbourne Hovell

Objective: To assess promptly trends in the birth prevalence of cerebral palsy (CP) in the full spectrum and its variations across subgroups using multiple administrative data sources, including Medicaid data. **Methods:** A population-based historical prospective cohort study. Among 755,433 live births from 1996 to 2009 in South Carolina (SC), we identified 2,080 patients (44% died) up to age 4 from Medicaid (1,952 cases) and Hospital Discharge (768 cases) with ICD-9 codes 343.X and Department of Disabilities and Special Needs program (452 cases), contributing 1061 (51%), 57 and 64 unique cases respectively. Trends and average annual changes (AAC, 95% confidence interval) were calculated in negative binominal regression. **Results:** Three CP prevalence measures show significantly downward trends at means of: 2.7/1,000 live births [AAC: -3.0% (-4.4, -1.6)]; 46.0/1,000 very low birth weight (VLBW, <1500 g at birth) live births [-2.9% (-5.2, -0.5)]; and 53.0/1,000 for VLBW 1-year survivors [-2.7% (-4.9, -0.5)]. Disparities persisted over time between non-Hispanic Black infants and non-Hispanic White infants [prevalence ratio 1.60 (1.46, 1.75)]; and significant reductions occurred over time ($P < 0.02$). However, CP prevalence was unchanged in Hispanic infants ($P = 0.98$). CP trends were downward in males and females by means of 3.1 cases and 2.4 cases /1,000 live births, respectively ($P = < 0.035$). Disparities persisted between male and female [prevalence ratio 1.30 (1.19, 1.42)]. **Conclusion:** Downward trends and disparities persisted in CP prevalence across race and gender from 1996 to 2009 in South Carolina, which differed from those in Atlanta, but were consistent with findings from Europe and Australia. The methods using claims data can overcome roadblocks to set-up passive public health surveillance systems. Further efforts include on-going monitoring, methodological validation then evaluation of clinical practice and disparities.

HOW ARE NEW DADS SLEEPING? A PROSPECTIVE STUDY TO IDENTIFY PATTERNS AND DETERMINANTS OF SLEEP QUALITY IN FIRST-TIME FATHERS

Deborah Da Costa, Phyllis Zelkowitz, Kaberi Dasgupta, Ilka Lowensteyn, Kelly Hennegan, Rebecca Wickett, Michael Raptis, Samir Khalife

Sleep deprivation and poorer sleep quality are common in women during the perinatal period and have been associated with maternal postpartum depression. Less is known about changes in sleep patterns in men during the transition to parenthood. This study aimed to examine sleep duration and quality in men 2 months following their infant's birth and to identify factors associated with poor sleep quality. Men expecting their first child were recruited from local prenatal classes and university affiliated obstetric clinics. During their partner's third trimester of pregnancy and 2 months following their infant's birth, 459 men (mean age = 34.3 years, \pm 5.5 years) completed standardized online self-report questionnaires measuring depressed mood, physical activity, marital adjustment, life events, financial stress and demographics. Sleep was assessed using the Pittsburgh Sleep Quality Index (PSQI) and a measure of parental stress was added to the postnatal assessment. Multiple linear regression examined correlates of poorer sleep quality at postpartum. Sleep duration was reduced by 48 minutes to 6.2 hours at postpartum, and mean sleep efficiency was reduced from 90.9% to 83.1%. The prevalence of poor sleep quality (defined as PSQI global score > 5) increased from 29.6% during the third trimester to 44.7% at 2 months postpartum. Poorer antenatal sleep quality ($\beta = 0.38$, 95% CI [0.30, 0.46]), greater postnatal depressive symptoms ($\beta = 0.17$, 95% CI [0.05, 0.18]) and higher parental stress ($\beta = 0.20$, 95% CI [0.03, 0.09]) were significant determinants of poorer sleep quality in the postpartum. Sleep is compromised in new fathers following the birth of a child. The findings suggest that sleep hygiene counseling, psychosocial strategies aimed at improving depressed mood, and pre ration skills to manage the challenges of parenting are important components to include in prenatal interventions aimed at enhancing the transition to parenthood.

TRENDS AND DISPARITIES IN CEREBRAL PALSY IN PERIVIALE BIRTHS IN SOUTH CAROLINA, 1996 TO 2009

Qing Li, Dorothea Jenkins, Melbourne Hovell, Rita Ryan

Objectives: Despite the long-term goal of survival without disability, no data in the U.S. monitor trends and disparities in cerebral palsy (CP) in periviable births (PB, born at 20-25 weeks of gestation) to inform population-based preventive interventions. The objective of this study was to monitor trends and racial and gender disparities in the birth prevalence of CP in infants. **Study Design:** This is a population-based historical prospective cohort study using claims data. Among 755,433 live births from 1996 to 2009 in South Carolina (SC), we identified 2,080 CP patients (44% died) up to age 4 based on ICD-9 codes 343 from Medicaid and Hospital Discharge abstracts and diagnoses from Department of Disabilities and Special Needs program. This analysis compared 169 CP cases of 1,949 survivors from 2,815 to 462 of 10,867 survivors of 11,271 infants born at 26-31 weeks. Birth prevalence was calculated as the number of children with CP for each birth year per 1,000 neonatal survivors to 28 days. Trends were calculated in negative binominal regression. **Results:** The mean age of in SC was 23.9 weeks and mean birth weight was 720 grams. CP prevalence was stable at 86.7 in , ranging from 55.2 in 2004 to 159.7 in 2008 at average annual change of -9% (95% confidence interval: -5, 3; $P = 0.69$); and it decreased from 68.1 in 1998 to 20.9 in 2006 [-5%: -8, -1; $P < 0.01$] averaging at 42.5 in infants born at 26-31 weeks. In , CP prevalence was stable in non-Hispanic Black infants (65.0 in 2002 to 139.8 in 2000) and non-Hispanic White infants (42.6 in 2003 to 214.3 in 2008) and across genders (all $P > 0.05$). However, in those born 26-31 weeks, prevalence in non-Hispanic Black infants decreased from 60.1/1,000 in 1998 to 24.8/1,000 in 2006, [-5% (-8, -2), $P < 0.01$]. Compared to significant disparities in neonatal survivors born at 26-31 weeks, disparities in CP prevalence between males and females [prevalence ratio 1.23 (0.92, 1.65), $P = 0.17$] and between non-Hispanic Black and White infants [0.90 (0.66, 1.22), $P = 0.49$] did not reach statistical significance. **Conclusions/Significance:** Among neonatal survivors in from 1996 to 2009 in SC, stable trends and no racial or gender disparities in CP prevalence persisted, in contrast to downward trends in Europe or Australia. Further efforts should include monitoring more states, validation of CP diagnosis and coverage, and evaluation of clinical practice and disparities in disease propensity and access to care.

SLEEP DURATION IS INVERSELY ASSOCIATED WITH BIRTH-WEIGHT IN A COHORT OF BRAZILIAN PREGNANT WOMEN

Ana Beatriz Franco-Sena, Linda Kahn, Dayana Farias, Aline Ferreira, Ilana Eshriqui, Amanda Figueiredo, Michael Schlüssel, Pam Factor-Litvak, Gilberto Kac

Background: High proportions of births of macrosomic or large for gestational age neonates are observed worldwide. Studies on sleep duration suggest it may play a role in weight control. Thus, we hypothesize that the duration of sleep throughout pregnancy may be associated with birthweight (BW). **Objective:** To evaluate the effect of sleep duration throughout pregnancy on BW in nulliparous and parous women. **Methods:** A prospective cohort of 173 pregnant women was followed at the 5-13th, 20-26th and 30-36th gestational weeks. The outcome was the z-score of BW for gestational age and sex, according to the International Fetal and Newborn Growth Consortium for the 21st Century (Intergrowth-21st) curves. The effects of sleep duration (number of hours) in the first trimester of pregnancy, as well as the effects of the variations in sleep duration from 1st to 2nd (value in the 2nd minus value in the 1st) and 2nd to 3rd (value in the 3rd minus value in the 2nd) trimesters, were assessed using linear regression models adjusted by maternal age, pre-gestational BMI, smoking, Edinburgh Postnatal Depressive Scale, gestational weight gain, education, marital status, per-capita family income and planned pregnancy. Analyses were stratified by parity status. **Results:** In nulliparous women, sleep duration in the first trimester of pregnancy was inversely associated ($\beta = -0.29$, p-value=0.001) with BW z-score. We also detected associations between the variations in sleep duration across pregnancy trimesters (1st to 2nd: [$\beta = -0.28$, p-value=0.005]; 2nd to 3rd: [$\beta = -0.15$, p-value=0.039]) and BW z-score. No associations were detected among parous women. **Conclusion:** Sleep duration presented an effect on BW z-score in nulliparous but not in parous women. Our results indicate that, in nulliparous women, longer periods of sleep in the first trimester are associated with lower BW z-scores and the same is true for women who present lower decreases in the duration of sleep throughout pregnancy.

PREVALENCE OF UNSAFE SLEEP FACTORS AMONG DEATHS CLASSIFIED AS EXPLAINED SUFFOCATION AND UNEXPLAINED POSSIBLE SUFFOCATION

Carrie Shapiro-Mendoza

Background. Little is known about the presence of unsafe sleep factors and mechanisms most frequently attributed to sleep-related infant deaths. We describe the prevalence of these unsafe sleep factors and mechanisms among infant deaths classified as explained suffocation or possible suffocation. **Methods.** We analyzed data from the National Center for the Review and Prevention of Child Deaths Case Reporting System. Deaths from 10 states participating in the CDC's Sudden Unexpected Infant Death Case Registry during 2011–2012 were included. Cases were categorized and assigned a mechanism using the Registry's classification system. Frequencies and percentages of the prevalence of selected unsafe sleep factors and mechanisms attributed to death were reported for explained suffocation and possible suffocation deaths. **Results.** Among deaths in the explained suffocation ($n=95$) and possible suffocation ($n=132$) categories, soft bedding was the most prevalent mechanism (52% and 68%, respectively), followed by wedging (23% and 9%) and overlay (22% and 18%). The most prevalent unsafe sleep factor was non-supine sleep position (82% and 80%), followed by not sleeping in a crib or bassinet (72% and 73%) and sleeping on a shared-surface (56% and 56%). A new or different sleep environment than usual was reported for >15% of deaths. **Conclusions.** Contrary to widespread belief, being overlaid was not the most frequently reported mechanism for deaths classified as suffocation or possible suffocation in our study population. Instead, soft bedding (e.g., airway occlusion by a pillow) accounted for more than half of the cases examined. Quantifying the frequency of mechanisms and factors associated with accidental sleep-related suffocation can inform prevention strategies. Greater emphasis on educating caregivers about the importance of removing potentially hazardous bedding from the sleeping environment may strengthen safe sleep interventions and reduce infant suffocation deaths.

OUTCOMES OF BREECH BY MODE OF DELIVERY: A POPULATION LINKAGE STUDY

Yu Sun Bin, Christine Roberts, Jane Ford, Michael Nicholl

Background: Trial evidence supports a policy of caesarean section for singleton breech presentations at term but vaginal breech birth is considered a safe option for selected women. **Aims:** To provide recent Australian data on outcomes associated with intended mode of delivery for term breech singletons in women who meet conservative eligibility criteria for vaginal breech birth. **Materials and Methods:** Birth and hospital records from 2009 to 2012 in New South Wales were used to identify women with non-anomalous pregnancies who would be considered eligible for vaginal breech birth. Intended mode of delivery was inferred from labour onset and management. **Results:** Of 10,133 women with term breech singleton pregnancies, 5,160 (51.4%) were considered eligible for vaginal breech delivery. Of these, 6.7% intended vaginal breech birth, 76.5% planned caesarean section, and intention could not be determined for 16.8%. Rates of neonatal morbidity (6.3% vs. 2.5%), birth trauma (7.5% vs. 0.9%), Apgar <4 at 1 minute (10.7% vs. 1.1%), Apgar <7 at 5 minutes (4.3% vs. 0.5%), and NICU/SCN admissions (16.7% vs. 6.6%) were higher among women intending vaginal delivery than those planning caesarean section. Increased perinatal risks remained after adjustment for maternal characteristics. Severe maternal morbidity (1.2% vs. 0.7%) and postpartum readmission (4.6% vs. 4.0%) were also higher in the intended vaginal compared to planned caesarean births although these were differences not statistically significant. **Conclusions:** In a population of women considered eligible for vaginal breech birth, intended vaginal delivery was associated with higher rates of neonatal morbidity than planned caesarean section.

POPULATION-BASED STUDY OF SLEEP APNEA IN PREGNANCY AND MATERNAL AND INFANT OUTCOMES

Yu Sun Bin, Peter Cistulli, Jane Ford

Study Objectives: To examine the association between sleep apnea and pregnancy outcomes in a large population-based cohort. **Methods:** Population-based cohort study using linked birth and hospital records was conducted in New South Wales, Australia. Participants were all women who gave birth in hospital from 2002 to 2012 ($N=636,227$). Sleep apnea in the year before pregnancy or during pregnancy was identified from hospital records. Outcomes of interest were gestational diabetes, pregnancy hypertension, planned delivery, caesarean section, preterm birth, perinatal death, 5-minute Apgar score, admission to neonatal intensive care or special care nursery, and infant size for gestational age. Maternal outcomes were identified using a combination of hospital and birth records. Infant outcomes came from the birth record. Modified Poisson regression models were used to examine associations between sleep apnea and each outcome taking into account maternal age, country of birth, socioeconomic disadvantage, smoking, obesity, parity, pre-existing diabetes and hypertension. **Results:** Sleep apnea was significantly associated with pregnancy hypertension (adjusted RR 1.68; 95% CI 1.40 – 2.07), planned delivery (1.15; 1.07 – 1.23), preterm birth (1.50; 1.21 – 1.84), 5-minute Apgar <7 (1.60; 1.07 – 2.38), admission to neonatal intensive care/special care nursery (1.26; 1.11 – 1.44), large-for-gestational-age infants (1.27; 1.04 – 1.55) but not with gestational diabetes (1.09; 0.82 – 1.46), caesarean section (1.06; 0.96 – 1.17), perinatal death (1.73; 0.92 – 3.25), or small-for-gestational-age infants (0.81; 0.61 – 1.08). **Conclusions:** Sleep apnea is associated with higher rates of obstetric complications and intervention, as well as preterm delivery. Future research should examine if these are independent of obstetric history.

SLEEP QUALITY BUT NOT DURATION IS ASSOCIATED WITH TESTOSTERONE LEVELS: A PILOT STUDY OF MEN FROM AN URBAN FERTILITY CLINIC

Linda Kahn, Pam Factor-Litvak, Mark Sauer

Prior research suggests that poor sleep quality and short sleep duration are associated with reduced testosterone (T) in men. T levels peak during the first REM cycle, approximately 3–4 hours after falling asleep, and remain elevated until awakening. Men with extreme sleep deprivation and those who do not attain deep sleep are vulnerable to low T, which may increase their risk of clinical symptomatology and reduced fecundity. In this pilot study, we tested associations between sleep quantity/quality and serum T. Men ($n=65$) age 30–50 years were recruited from the Center for Women's Reproductive Care at Columbia University and given a self-administered survey that asked about sleep quantity, sleep quality, and use of sleep medication. Those who reported <6.5 hours of sleep/night were coded as having short sleep duration (SSD) and those who reported "very bad" sleep quality or use of any sleep medication within the past month were coded as having poor sleep quality (SQ). Blood samples were taken simultaneously. The outcome measure, serum T (ng/dL), was log-transformed to normalize its distribution. Linear regression was performed 1) unadjusted, 2) semi-adjusted for age (continuous), income (categorical), and alcohol consumption (dichotomous), and 3) fully adjusted for the above covariates plus body mass index (BMI). In an analysis of 59 complete cases, SSD was not significantly associated with T in any of the three models. However, poor SQ was inversely associated with T in both unadjusted and semi-adjusted models ($\beta=-0.35$, 95% CI [-0.58, -0.12]; $\beta_{\text{semiadj}}=-0.38$, 95% CI [-0.62, -0.14]). The relationship was attenuated but still statistically significant in the fully adjusted model, $\beta_{\text{fulladj}}=-0.31$, 95% CI [-0.56, -0.07], implying partial confounding by BMI. Our study provides additional evidence for an association between poor SQ and reduced serum T levels. These results suggest that sleep hygiene may be a valuable addition to the clinical management of men with low T.

GESTATIONAL DIABETES RISK IN RELATION TO SLEEP DURATION AND NAPPING DURING THE 1ST AND 2ND TRIMESTER OF PREGNANCY: A PROSPECTIVE COHORT STUDY

Shristi Rawal, Stefanie N. Hinkle, Yeyi Zhu, Paul S. Albert, Cuilin Zhang

Both short and prolonged sleep duration have been linked to type 2 diabetes due to their adverse impact on insulin sensitivity. Sleep difficulty is common in pregnancy, but prospective data on its relation to gestational diabetes (GDM) is limited. In the NICHD Fetal Growth Studies-Singletons (n=2584), a prospective, multiracial cohort of healthy women without diabetes before pregnancy, we examined the relation of sleep duration and napping frequency to GDM risk. GDM (n=107) was diagnosed by medical record review. In the 1st (8-13 gestational weeks) and 2nd (16-22 weeks) trimesters, women reported their typical sleep duration (5-6, 7, 8-9 or 10+ hours) and napping frequency (most times, sometimes or rarely/never) in the preceding weeks. Adjusted relative risks (aRRs) [95% confidence interval (CI)] for GDM were estimated with Poisson regression, adjusting for demographics, pre-pregnancy body mass index, and other risk factors. From the 1st to 2nd trimester, women were less likely to sleep for 10+ hours (24.4% vs. 14.7%) or to nap some/most times (80.4% vs. 54.4%). Sleep duration in the 1st trimester was not associated with GDM risk. The relation of 2nd trimester sleep duration and GDM differed significantly by obesity status (p for interaction=0.04). Only among non-obese women, both sleeping more or less than 8-9 hours was significantly associated with GDM risk; aRRs were 2.53 (95% CI:1.28-4.99) for 5-6 hours, 1.98 (95% CI:1.08-3.64) for 7 hours, and 2.37 (95% CI: 1.15-4.88) for 10+ hours. Napping frequency in either the 1st or 2nd trimester was not associated with GDM risk. Our data suggest a U-shaped relation between 2nd trimester sleep duration and GDM risk, specifically among non-obese women, with the highest risk among women who sleep 5-6 hours.

BIOMARKERS OF IRON STATUS AND SUBSEQUENT RISK OF GESTATIONAL DIABETES: FINDINGS FROM A PROSPECTIVE, MULTI-RACIAL COHORT

Shristi Rawal, Wei Bao, Yeyi Zhu, Stefanie N. Hinkle, Jagteshwar Grewal, Paul S. Albert, Michael Y. Tsai, Cuilin Zhang

Increased oxidative stress resulting from high body iron stores has been implicated in the pathogenesis of type 2 diabetes. Yet, longitudinal studies examining iron status during pregnancy in relation to the risk of gestational diabetes (GDM) are few and findings are inconsistent. We aimed to address these data gaps in a case control study of 107 GDM cases and 214 controls (matched 1:2 on age, race/ethnicity, and gestational age at blood draw) within the multi-racial NICHD Fetal Growth Studies. GDM diagnosis was based on medical record review. Plasma ferritin, soluble transferrin receptor and hepcidin were measured at two visits prior to GDM diagnosis (gestational weeks 8-13 and 16-22), and at weeks 24-29 and 34-37. Adjusted odds ratios (aORs) [95% confidence intervals (CIs)] for GDM were estimated using conditional logistic regression adjusting for demographics, pre-pregnancy BMI, and other major risk factors. As the pregnancy progressed, ferritin and hepcidin levels declined whereas soluble transferrin receptor concentrations increased. Ferritin levels were significantly higher among women who subsequently developed GDM than those who didn't and were positively related to GDM risk; aOR (95% CI) comparing the highest vs. lowest quartile of ferritin was 2.43 (1.12, 5.28) during weeks 8-13 and 3.95 (1.38, 11.3) during weeks 16-22. Hepcidin levels were significantly higher in cases than controls and were positively related to GDM risk during weeks 16-22 but not earlier; aOR (95% CI) comparing the highest vs. lowest quartile was 2.61 (1.07, 6.36). In contrast, ratio of soluble transferrin receptor to ferritin, an indicator of iron deficiency, was significantly and inversely related to GDM risk; aOR (95% CI) comparing the highest vs. lowest quartile was 0.33 (0.14, 0.80) at weeks 8-13 and 0.15 (0.05, 0.48) at weeks 16-22. Our data suggest that high maternal iron stores may play a role in the development of GDM starting from early pregnancy.