

## **Association between maternal and paternal birth country and method of delivery: a cohort study in Washington state**

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**Introduction:** Rates of cesarean delivery in the United States have increased along with associated costs, although cesarean deliveries are risky and often medically unnecessary. Risk of cesarean delivery differs with demographic, medical, and systemic factors, but understanding of how parents' country of birth impacts risk is less clear. We compared Mexican-born women to United States-born women of Mexican descent to examine the relationship between maternal country of birth and risk of cesarean delivery, as well as the impact of paternal country of birth.

**Methods:** We conducted a retrospective cohort study using Washington state birth certificate data from 2003-2014. We included mothers who were born in Mexico and mothers of Mexican descent born in United States who were nulliparous and at low risk for cesarean delivery. Mothers were frequency matched 1:1 for a total of 12,100. The primary exposure was country of birth and the primary outcome was cesarean delivery. We used stratified analysis and logistic regression to estimate crude and adjusted relative risks for cesarean delivery by country of birth, adjusting for maternal age and education. We conducted a secondary stratified logistic regression to examine effect modification by paternal country of birth.

**Results:** Compared with women of Mexican descent born in the United States women born in Mexico were generally older, had less education, were more likely to be married, were more likely to be covered by Medicaid, and were less likely to have a partner born in the United States. Women born in Mexico had a slightly increased risk of cesarean delivery (RR=1.07; 95% CI=1.00-1.15). This association was stronger among women with a partner who was born outside of the United States (RR=1.22; 95% CI=1.06-1.40) and was not statistically significant among women with a partner who was born in the United States (RR=1.07; 95% CI=0.92-1.25).

**Discussion:** There was a significant association between being born in Mexico and cesarean delivery, largely restricted to women whose parenting partner was also foreign-born. This could be evidence of a "protective effect" of a partner born domestically. Alternatively, this might indicate acculturation

## **Maternal and Neonatal Outcomes in Physician Mothers Using a Population-Based Dataset from Washington State**

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**Introduction:** The proportion of physicians who are women is rising, yet the risks for adverse maternal and neonatal outcomes for physician mothers are poorly understood. Physicians work long hours and are at increased risk of preterm delivery and lower birth weight. Prior studies indicate that physicians have lower rates of unplanned c-sections, possibly related to increased medical knowledge. Prior studies have been limited due to sample size and survey-based data.

**Methods:** We studied a retrospective cohort of women based on Washington State birth certificate data from 2003-2014 and linked inpatient diagnosis and procedures codes. Our exposed group consisted of mothers who held a doctorate or professional degree and were listed as “physician/physician assistant.” Our unexposed group consisted of mothers in whom the mother or her partner had a doctorate or professional degree. Stratified analyses were performed to explore effect modification between variables and physician occupation. 4 multivariate logistic regression models were created, to assess the association between physician occupation and: (1) composite of maternal complications, (2) a composite of fetal complications, (3) non-surgical instrumented delivery, and (4) unplanned c-section. All models were adjusted for maternal age and race, smoking, body mass index (BMI), and diabetes. The composite fetal outcome was also adjusted for maternal height. Instrumented delivery and unplanned c-section were also adjusted for height and gestational hypertension. Unplanned c-section models were stratified by HMO as a payor source.

**Results:** There were 5,490 mothers. 1,474 were physicians and 4,016 were non-physicians. Physician mothers were older (33.9 vs. 32.3 years), less likely to have diabetes (5.3% vs. 7.5%), and had lower BMI (22.9 vs. 24.4). On multivariate analysis, there was no difference between physicians and non-physicians for maternal complications (OR=1.03, 95%CI=0.90-1.17), fetal complications (OR=0.89, 95%CI 0.78-1.03), or non-surgical instrumented delivery (OR=1.01, 95%CI 0.86-1.19). HMO payor source was found to exhibit significant interaction with physician occupation on the outcome of unplanned c-section (interaction term  $p=0.01$ ). Physician mothers were significantly less likely to have unplanned c-sections when the primary payor was an HMO (OR=0.47, 95%CI=0.29-0.77), however this was not statistically significant for non-HMO payors (OR=0.85, 95%CI=0.70-1.03).

**Discussion:** Physician mothers do not appear to be at increased risk of maternal or fetal complications compared to mothers with other extensive post-college training. While physicians were less likely to undergo an unplanned c-section, this association was not significant for mothers with non-HMO insurance. We found no evidence that operative vaginal delivery was associated with maternal physician occupation, despite physician mothers having a decreased rate of unplanned c-section.

## **Gestational Diabetes and Hypertension as Risk Factors for Postpartum Weight Retention**

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**Background:** Metabolic disorders of pregnancy (gestational hypertension and diabetes; MDPs) are associated with gestational weight gain (GWG). Excess GWG is a risk factor for developing obesity postpartum, and it also influences postpartum weight retention (PPWR). MDPs are associated with higher risk of developing maternal hypertension, diabetes and other cardiovascular and metabolic disorders later in life, disorders in which obesity plays a role. This study evaluated the association between MDPs and PPWR and examined whether this relationship varied by GWG.

**Methods:** Retrospective cohort study utilizing 2003-2014 Washington State birth and hospitalization records of 63,628 women (12,412 with MDPs and 51,216 without, frequency-matched 1:4 by birth year). We examined PPWR among women with two pregnancies during this time period, with an interpregnancy interval between nine months and four years. PPWR was defined as failure to return to within two BMI points of pre-pregnancy BMI, or as becoming overweight or obese. We examined whether MDPs were associated with PPWR, stratified by GWG and adjusting for pre-pregnancy BMI.

**Results:** Women with MDPs weighed more and were more likely to be obese before pregnancy. Adjusting for pre-pregnancy BMI, MDPs were weakly associated with PPWR among women with below-recommended GWG (failure to return: aRR 1.22 (1.07, 1.38); overweight/obese: aRR 1.38 (1.18, 1.60)). A marginal association was seen for women with excessive GWG. No association was seen among women within recommended GWG.

**Conclusions:** There may be a faint association between MDPs and PPWR, particularly among women with below-recommended GWG during the first pregnancy. This is unlikely to be clinically significant, but may serve as a signal for a biologically meaningful mechanism which could be explored in future studies.

## **No association between urinary tract infection in pregnancy and gestational or maternal weight gain**

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**Introduction:** Urinary tract infections (UTIs) are the most common bacterial infections during pregnancy. UTIs are associated with pre-term birth and low birth weight, leading to current recommendations for universal screening and treatment with antibiotics during pregnancy. Some studies suggest a connection between prenatal antibiotic use and higher body mass index (BMI) in childhood, but it is unclear whether there is an effect of UTI-related antibiotic use on birth weight or maternal weight gain in pregnancy, which may be precursors to high childhood weight.

**Methods:** We performed a population-based retrospective cohort study of term singleton, first pregnancies in Washington State between 2003 and 2014. Mothers with UTIs diagnosed in pregnancy, as determined by birth certificates and inpatient diagnosis codes taken from the Comprehensive Hospital Abstract Reporting System, were frequency matched by year in a 4:1 ratio to mothers without UTIs. Multivariable poisson regression with robust standard errors was performed to evaluate the association between UTI diagnosis and excess maternal weight gain during pregnancy, large for gestational age (LGA) infants, and small for gestational age infants (SGA). Confounders were defined *a priori* including pre-pregnancy BMI category, maternal age  $\geq 35$  years, use of private insurance, adequacy of prenatal care, and maternal diabetes.

**Results:** 28,671 mother-infant dyads were included in the analysis (5,025 with prenatal UTI; 23,646 without prenatal UTI). There was no association between maternal UTI and excess maternal weight gain in pregnancy (relative risk [RR] 1.02; 95% CI 0.99, 1.05) or with having an LGA infant (RR 0.99; 95% CI 0.87, 1.12). Mothers with UTIs in pregnancy had a 13% higher chance of having an SGA infant (RR 1.13; 95% CI 1.03, 1.23).

**Discussion:** Even in the era of strong recommendations for antibiotic treatment, mothers with UTIs in pregnancy were at increased risk of having SGA infants, which is consistent with prior studies. Diagnosis of UTI was not associated with excess maternal or fetal weight in term infants.

## **Evaluating the effectiveness of the Baby-Friendly Hospital Initiative on breastfeeding initiation: a quasi-experimental difference-in-differences analysis**

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**Introduction:** The Baby-Friendly Hospital Initiative (BFHI) is a worldwide ten-step program to promote, protect, and support breastfeeding. These steps include developing breastfeeding policies and training for hospital staff. But it is unclear how effective this initiative is, especially among marginalized populations.

**Methods:** We compared the change in breastfeeding initiation among singleton, live births pre- (2003-05) and post- (2010-12) implementation of the BFHI at the University of Washington Medical Center (UWMC) (pre: n=3,034, post: n=2,611) to the change in initiation over the same time periods for a non-BFHI group selected from other hospitals within King or Pierce counties that were not BFHI accredited before 2017 (frequency matched 6:1; sample: pre: n=17,562, post n=18,301) using a difference-in-differences analysis. Breastfeeding initiation data came from Washington State birth certificates. We excluded mothers and infants with severe impediments to breastfeeding (e.g. NICU admittance). Potential confounders considered were payer type and mother's education; neither confounded the association and therefore were not included in the final analysis. Since BFHI accreditation takes several years, sensitivity analyses were conducted using different time periods to assess the robustness of results.

**Results:** The non-BFHI group had a relatively steady increase in prevalence of breastfeeding initiation between 2003 and 2014 from 90% to 97%. Conversely, the change within the UWMC group was inconsistent, decreasing from 96% to 91% between 2005 and 2006 and increasing from 88% to 94% between 2011 and 2012. Overall, initiation of breastfeeding decreased more from pre- to post-accreditation at UWMC compared to the non-BFHI group (difference-in-differences: -11.4% 95% CI: -12.8, -10.0). Our sensitivity analyses results also showed a reduction in initiation, but were weaker than our primary analysis results.

**Discussion:** Our results were contrary to expected. It is improbable that the variation in breastfeeding initiation at UWMC was due to BFHI accreditation alone and may have been due to changes in data collection methodology. This study highlights the difficulties of policy evaluation using birth certificate data due to undocumented changes in data collection over time within and between hospitals.

## **The Impact of High School Educational Attainment Following Teenage Birth on Adverse Outcomes in Subsequent Birth: A Retrospective Cohort Study**

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**Introduction:** Preterm births (PTB), small for gestational age (SGA) births, and large for gestational age (LGA) births are associated with morbidity, mortality and disability in later life. Higher maternal education has been identified as a protective factor against adverse birth outcomes, but the impact of completing high school education on birth outcomes among infants of mothers with a previous birth during teenage years is unknown. The objective of this study was to assess the association between completion of high school education by mothers following an initial teenage birth and PTB, SGA, and LGA in the second birth and identify if those associations differ by race/ethnicity.

**Methods:** We conducted a population-based retrospective cohort study using Washington State birth and death certificate data from 2003 to 2014 for singleton live births of mothers with one previous teenage birth at ages 15–19 before completion of high school education. We utilized stratified analysis to examine the relationship between maternal high school educational attainment at the second birth and PTB, SGA, and LGA and for effect modification of this association by race/ethnicity.

**Results:** The incidence of PTB, SGA, and LGA in our sample (N=12,498) was 7.0%, 8.9% and 6.8% respectively. There was no association between high school educational attainment at second birth and PTB (RR=0.95; 95% CI:0.83–1.08) or SGA (RR=0.93; 95% CI:0.83–1.04) when compared with normal for gestational age (NGA) infants. After adjusting for birth-to-pregnancy interval, mothers who completed high school education at the second birth had a 20% higher risk of LGA (95% CI:1.05–1.37) compared to NGA infants. The overall race/ethnicity stratum-specific estimates were not statistically significantly different from another for PTB, SGA, or LGA. However, Native American mothers had a decreased risk of PTB (RR=0.56; 95% CI:0.36–0.89) and an increased risk of LGA (RR=1.94; 95% CI:1.25–3.02).

**Discussion:** Our study found that there is no substantial effect of maternal educational attainment at the second birth on adverse birth outcomes and maternal race/ethnicity did not modify this association. Research focused in different and more diverse populations may better elucidate the nature of this relationship.

## **Association between weekend deliveries and adverse birth outcomes in Washington State: A retrospective cohort study**

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**Background:** Poor health outcomes during weekends in obstetric care have been studied in different settings with inconclusive results. These outcomes may be due to differences health services provided during the weekends compared to weekdays. This study evaluated the association between weekend deliveries and neonatal mortality, neonatal sepsis, and perineal lacerations in Washington State. Effect modification by mode of delivery was also evaluated.

**Methods:** We conducted a retrospective cohort study from 2003 to 2014 in Washington State using linked data from the Comprehensive Hospital Abstract Reporting System (CHARS). Only live births (N=120,000 for weekend and 300,000 for weekday deliveries) were included. Neonates with congenital malformations and those not born in hospitals were excluded. Cesarean deliveries were excluded from the perineal lacerations analyses. The exposure, weekend delivery, was defined as hospital delivery between 7pm Friday to 6.59am Monday. Outcomes of interest were neonatal mortality, neonatal sepsis, and perineal lacerations. Stratified analysis was used to compute the crude relative risks and logistic regression for adjustments for maternal age, race, education level, marital status, and neonatal birth weight.

**Results:** Weekend deliveries were associated with higher risk of neonatal mortality among cesarean births (RR: 1.58, 95% CI: 1.29-1.93), however was no longer statistically significant after adjusting for the covariates (RR: 1.19, 95% CI: 0.95-1.49). Neonatal sepsis also presented higher risk on weekends for cesarean (RR: 1.34, 95% CI: 1.25-1.43) and vaginal deliveries (RR: 1.10, 95% CI: 1.04-1.17), after adjusting for covariates. Perineal lacerations presented minimal risk after adjustments (RR: 1.06, 95% CI:1.00-1.12).

**Conclusions:** Weekend deliveries were associated with high risk of neonatal sepsis and lacerations but not neonatal mortality. The risks for neonatal mortality and neonatal sepsis was higher in the cesarean than the vaginal deliveries. These findings could be due to differences between quality and safety of obstetric care between weekends and weekdays and also the circumstances surrounding cesarean deliveries.

## **Unspiraling maternal syphilis: Identifying populations at greatest risk for adverse perinatal outcomes**

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**Introduction:** Rates of syphilis increased by over 400% in the US from 2000-2016. Untreated syphilis infection is of particular concern among pregnant women, as it can cause adverse perinatal outcomes including low birth weight, preterm delivery, congenital syphilis, and infant death. The recent increase in diagnoses of congenital syphilis in the US indicates a remaining gap in syphilis screening and treatment during pregnancy. We sought to identify populations at greatest risk for syphilis-associated adverse perinatal outcomes.

**Methods:** We conducted a population-based retrospective cohort study in Washington State using birth certificate data linked with hospital admission records from 1987-2014. We examined the association between maternal syphilis infection and two perinatal outcomes: low birth weight and preterm birth. Mothers with syphilis were frequency-matched 1:10 by year of delivery and age (n=11,946). Results were stratified by maternal demographic factors including: race, ethnicity, prenatal care, socioeconomic status measured by education level and payer type, parity, and country of origin. Relative risks (RR) and 95% confidence intervals (CI) were calculated by stratification analysis.

**Results:** Maternal syphilis was positively associated with low birth weight (RR 1.58; 95% CI 1.29-1.93) and preterm birth (RR 1.44; 95% CI 1.19-1.74). Mothers at greatest risk for syphilis-associated low birth weight were non-Hispanic (RR 1.67; 95% CI 1.32-2.11), received inadequate prenatal care (RR 1.72; 95% CI 1.18-2.51), had multiple prior births (RR 2.06; 95% CI 1.49-2.86), or were born in the US (RR 1.80; 95% CI 1.43-2.28), compared with uninfected mothers. Mothers at greatest risk for syphilis-associated preterm birth were non-Hispanic (RR 1.03; 95% CI 1.01-1.06), received inadequate (RR 1.61; 95% CI 1.09-2.37) or intermediate prenatal care (RR 2.06; 95% CI 1.21-3.51), had multiple prior births (RR 1.74; 95% CI 1.31-2.31), or were born in the US (RR 1.52; 95% CI 1.21, 1.90).

**Discussion:** Mothers at greatest risk for adverse perinatal outcomes associated with syphilis were non-Hispanic, US-born, had poor prenatal care, or had multiple prior births. As syphilis rates increase, heightened risk of poor outcomes in these communities highlights the need to improve syphilis screening and treatment interventions for these populations.



## **Is the association between payer type and risk of cesarean delivery modified by maternal age, race/ethnicity, and rural or urban residence?**

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**Introduction:** Studies have shown an association between payer type and cesarean delivery. However, little is known about whether this association holds true across sociodemographic groups, including maternal groups by age, race/ethnicity, and rural/urban residence.

**Methods:** We studied the association between payer type and cesarean delivery using Washington State Birth Certificate data in a population-based cohort of 35,235 nulliparous women age 15 and above with low-risk pregnancies whose deliveries were insured either privately or through Medicaid between January 1, 2013 and December 31, 2014. We used logistic regression to examine the association between payer type and cesarean delivery while considering effect modification by maternal age, race/ethnicity, and rural/urban residence and adjusting for marital status and maternal education level.

**Results:** The risk of cesarean delivery was slightly higher among women insured by Medicaid than among privately insured women (RR=1.05, 95% CI: 0.99-1.11). There were no significant differences among maternal age categories. Non-Hispanic White women on Medicaid had a slightly higher risk of cesarean delivery compared to Non-Hispanic White women on private insurance (RR=1.09, 95% CI: 1.02-1.17), whereas there were no significant differences between risk of cesarean delivery comparing women on Medicaid to women with private insurance among other race/ethnicity categories (Non-Hispanic Black, Asian, and Hispanic). Women on Medicaid and living in rural areas had a slightly higher risk of cesarean delivery than women on private insurance living in rural areas (RR=1.13, 95% CI: 1.03-1.25), while there was no evidence of a significant difference among urban women.

**Discussion:** The risk of cesarean delivery among Medicaid users was higher for Non-Hispanic White women compared with women who identified as Non-Hispanic Black, Asian, or Hispanic, and among Medicaid users living in rural areas compared to urban areas. These findings are relevant to Medicaid enrollees in Washington State who are Non-Hispanic White women and women living in rural settings who may unknowingly be at a higher risk for cesarean delivery. Targeted education about the risk of medically unnecessary cesarean delivery among these Medicaid users could allow for greater maternal agency in choosing a delivery method.

## **Risk factors for precipitous delivery in Washington State mothers, 2003-2014**

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**Introduction:** Precipitous delivery, labor lasting less than three hours, is associated with adverse maternal and neonatal outcomes including vaginal lacerations, uterine rupture, and neonatal group B streptococcal infections. Our study aimed to evaluate risk factors for precipitous delivery. Identifying risk factors can be useful in preventing adverse maternal and neonatal outcomes.

**Methods:** Using Washington State birth certificate and maternally-linked hospital discharge data from 2003-2014, we performed a case-control study comparing women with precipitous labor to those without. In the primary analysis, cases were defined as precipitous delivery reported by both birth certificates and discharge codes due to low agreement between data sources (20% agreed). We evaluated the following exposures: hypertensive disorder, smoking during pregnancy, short interpregnancy period, fertility treatment, and small for gestational age. Odds ratios (OR) with 95% confidence intervals (CI) were calculated using a Mantel Haenszel approach adjusting for maternal age and parity.

**Results:** A total of 3,457 precipitous deliveries and 72,000 non-precipitous deliveries were included in the primary analysis. Compared to controls, women with precipitous deliveries were more commonly multiparous (88.7% vs. 50.6%) and less commonly <20 years old (3.9% vs. 9.2%). The odds of precipitous delivery were higher in mothers with small for gestational age infants (OR 1.50; 95% CI 1.34, 1.69) and with an interpregnancy interval <6 months (OR 1.58; 95% CI 1.30, 1.92). The odds of precipitous delivery was lower in women with hypertensive disorders (OR 0.70; 95% CI 0.60, 0.82).

**Discussion:** Small for gestational age, a proxy for intrauterine growth restriction, and shorter interpregnancy period were associated with a higher risk of precipitous delivery. This can be useful in helping identify high-risk mothers. However, low agreement on precipitous labor between hospitalization discharge codes and birth certificates suggests an opportunity for future validation studies to improve the capture of this outcome.

## **A population-based case-control study of maternal and infant factors and high school completion among teen mothers**

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**Introduction:** Teenage childbearing is a major contributor of reduced high school completion among teenage mothers. Better understanding maternal and infant factors that promote or hinder high school completion is necessary to develop impactful policies, programs, and interventions. Our objective was to estimate the association between maternal and infant factors and high school completion among prior teenage mothers in Washington State at the time of the birth of their second child.

**Methods:** We conducted a population-based case-control study of 14,617 prior teenage mothers who gave birth to their second child between 1993 and 2014, identified from Washington State Birth Certificates. Cases were prior teenage mothers who completed high school or equivalent degree by the birth of her second child (7,191 cases). Controls were prior teen mothers who did not complete high school or equivalent degree by the birth of her second child (7,426 controls). Controls were frequency-matched to cases on the birth year of the second child. All estimates were generated using stratified analysis.

**Results:** We identified seven maternal and infant exposures of interest associated with high school completion among prior teenage mothers by the birth of their second child. Four maternal exposures were estimated to be associated with lower odds of completing high school: receiving public assistance during first pregnancy (OR=0.79; 95% CI: 0.73–0.86), Hispanic race/ethnicity (OR=0.45; 95% CI: 0.42–0.49), and Inadequate or Intermediate utilization of prenatal care during first pregnancy (OR=0.82; 95% CI: 0.75–0.89) and (OR=0.86; 95% CI: 0.79–0.93), respectively. Being married at the second birth (OR=1.29; 95% CI: 1.21–1.38), longer birth interval between first and second births (OR=6.61; 95% CI: 5.13–8.51), and fetal macrosomia of first child (OR=1.21; 95% CI: 1.07–1.37) were estimated to be associated with higher odds of completing high school.

**Conclusions:** Our findings support previously identified associations between social and economic factors of teenage mothers and infant characteristics with lower educational attainment. The results of our study provide further evidence that policy and intervention efforts to promote high school completion among teenage mothers should be targeted towards those individuals exposed to potential risk factors.

## **Interpregnancy intervals after an unexplained fetal death: risks and recommendations**

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**Introduction:** In the United States an estimated 24,000 women experience fetal death each year and up to 60% of these have no identifiable cause. Women who had an unexplained fetal death are at higher risk of adverse outcomes depending on the duration of the interpregnancy interval (IPI). Current guidelines recommend a 15-24-month IPI but supporting evidence is inconsistent across studies. This study aimed to understand the risks associated with a more precise IPI.

**Method:** We conducted a retrospective cohort study from linked fetal death certificates and birth certificate data in Washington State from 1987-2014. We identified women (18-44 years of age) who experienced unexplained fetal death (>20 weeks' gestation) followed by a singleton live birth. We compared women with short <15 months (n= 795) and long  $\geq$ 15 months (n= 1,415) IPI and assessed their risk for low birth weight (LBW), small for gestational age (SGA), and preterm birth. We determined relative risk (RR) and 95% confidence interval (CI) using Mantel-Haenszel adjusting for mother's age.

**Results:** Infants born following a short IPI compared to long IPI had a reduced RR for LBW (RR= 0.67, 95% CI: 0.51 - 0.88) and SGA (RR= 0.76, 95% CI: 0.56 - 1.00) there was no association between IPI and preterm birth (RR= 0.93, 95% CI: 0.73 - 1.20). The association of IPI with LBW differed by mothers' marital status. Married women with short IPI were not associated with LBW (RR=0.91 95% CI: 0.63 - 1.3) whereas unmarried women with short IPI were associated with reduced relative risk of LBW (RR=0.49 95% CI: 0.31 - 0.78; p-value <0.05) The relative risk was different across subgroups of shorter IPI for LBW and SGA with the lowest relative risk in the 4-6 month group; SGA had the greatest difference (RR= 0.58, 95% CI 0.36-0.91).

**Discussion:** Women with a short IPI following a fetal death were at lower risk for LBW and SGA, this finding was consistent in the IPI subgroups which demonstrated the lowest risk in the 4-6-month group. Our findings may provide evidence to support shorter IPI recommendation for women after a fetal death.

## **Risk of Preterm Birth and Growth Restriction Following A First-born Son**

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**Introduction:** Previous studies found elevated risks of adverse outcomes among infants preceded by a first-born son, compared to infants preceded by a first-born daughter. Researchers have hypothesized that exposure to male-specific DNA or antigens in the first pregnancy may cause an immune response against subsequent pregnancies. Using a U.S. population, this study aimed to confirm associations of prior birth of a son with preterm birth and growth restriction in the second birth and evaluate whether associations differ by preterm birth subtypes, paternity change, or sex of the second-born.

**Methods:** We conducted a population-based retrospective cohort study using 2003-2014 Washington State birth certificate data. Participants were second live births preceded by a first-born son (n=58,704) or by a first-born daughter (n=58,704), frequency-matched on birth year. Stratified analysis was used to calculate relative risks for preterm birth, small for gestational age (SGA), and low birth weight (LBW), and to examine differences in associations for preterm birth subtypes, and effect modification by paternity change and sex of the second-born.

**Results:** Second-born infants preceded by a first-born son had a 13% higher risk of preterm birth (RR = 1.13, 95% CI: 1.08-1.19), 17% higher risk of LBW (RR=1.17, 95% CI: 1.10-1.24), and 13% higher risk of being SGA (RR=1.13, 95% CI: 1.08-1.18), compared with infants preceded by a first-born daughter. The risk estimate was higher for indicated preterm birth (RR=1.19, 95% CI:1.10-1.29) than for spontaneous birth (RR=1.12, 95% CI:1.04-1.20) and preterm premature rupture of membranes (RR = 1.15, 95% CI= 1.00-1.31). There was no effect modification by the second-born's sex or paternity change.

**Discussion:** This study confirmed that having a first-born son is associated with an increased risk of preterm birth and growth restriction in the subsequent birth. The highest risk estimate was observed for indicated preterm birth, consistent with our hypothesis that the association would be strongest for this subtype. Findings can inform clinicians' management of care for pregnant women with first-born sons.

## Examining the Association Between Hepatitis C and Pre-eclampsia

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**Background:** In the United States, an estimated 3.5 million people are infected with the Hepatitis C virus (HCV) with recent increases in women of childbearing age. Among pregnant women who report injection drug use, the prevalence of HCV is between 70 to 95%. Chronic HCV is associated with various adverse birth outcomes. Previous studies examining the association between HCV and pre-eclampsia were inconclusive. The aim of this study is to assess the relationship between HCV and pre-eclampsia in Washington State.

**Methods:** We conducted a population-based retrospective cohort study using Washington State birth certificates linked to inpatient hospitalization records. Our study sample included all cases of live singleton births that occurred to HCV-positive women ( $n = 2,732$ ) between 1995 to 2014 and a random sample of HCV-negative women ( $n = 22,073$ ), frequency-matched according to child birth year in a ratio of 8 HCV negative mothers to 1 HCV-positive mother. We used Poisson regression to estimate the risk ratio (RR) between HCV status and pre-eclampsia, after adjusting for potential confounding by parity. We also examined whether smoking modified the relationship between HCV and pre-eclampsia.

**Results:** A total of 1,736 women experienced pre-eclampsia (196 HCV-positive and 1,540 HCV-negative women). Smoking modified the association between HCV and pre-eclampsia. Adjusting for parity, among smokers, HCV-positive women had 0.93 times the risk of pre-eclampsia than HCV-negative women (95% CI: 0.74, 1.17). Among nonsmokers, adjusting for parity, HCV-positive women had 1.46 times the risk of pre-eclampsia compared to HCV-negative women (95% CI: 1.22, 1.75).

**Discussion:** Our observation of modification by smoking is similar to prior studies. HCV-positive women who smoked had lower risk of pre-eclampsia than HCV-negative women who smoked, but HCV positive women who did not smoke had higher risk of pre-eclampsia than HCV-negative women who did not smoke.

## **Hospital readmission and five-year mortality among survivors of multiple organ dysfunction syndrome in infancy: a retrospective cohort study**

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**Importance:** Multiple organ dysfunction syndrome (MODS) is a common and life-threatening condition in critically ill infants. Little is known about long-term sequelae for those who survive MODS. Better understanding of long-term morbidity and mortality risk after MODS is needed to help inform ongoing care among survivors.

**Objective:** To evaluate risk of repeat hospitalization and mortality over five years post-discharge for patients hospitalized in the first year of life with MODS versus isolated acute respiratory dysfunction (ARD)

**Design:** Retrospective cohort study

**Setting:** Washington State non-governmental hospitals

**Participants:** Infants <1 year who survived a first hospitalization for ARD from 1987-2009 with and without extrapulmonary organ dysfunction classified by ICD-9 codes

**Main outcomes and measures:** Re-hospitalizations and deaths were identified through the Comprehensive Hospital Abstract Reporting System and death certificate data. In each group of infants, the risk for both outcomes within five years following discharge from the first hospitalization for ARD was calculated, and the two risks were compared using stratified analysis with Mantel-Haenszel adjustment. Analyses were adjusted for gestational age and stratified by whether the first admission was the birth hospitalization. We used Poisson regression to assess risk for readmission and death with each additional organ dysfunction.

**Results:** MODS occurred in 7% (n=1484) of our 21,255 infant cohort. The proportion of infants who died was more than doubled in the MODS group (8.6% vs 3.9%). This association was stronger among patients with a non-birth first hospitalization (aRR 3.06, 2.29-4.10) compared to patients with a birth first hospitalization (aRR 1.34, 1.05-1.75). Risk of death increased with each additional organ system for patients in both strata, with a larger risk for those with non-birth first hospitalization (aRR 1.64, 1.32-2.05 for birth hospitalization; aRR 2.31, 1.97-2.70 for non-birth hospitalization). Adjusted risk of readmission was not significantly different between infants with MODS and those with ARD.

**Conclusions and relevance:** Development of MODS among infants with ARD was associated with increased risk of mortality in the five years post-discharge, suggesting the need for close follow-up and monitoring in this population.

## Risks of Recurrent Preterm Birth by Clinical Subtype

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Preceptor: Catherine Albright, MD

**Introduction:** Women with a history of preterm birth are at a higher risk for a subsequent preterm birth. Few studies have determined the risk of recurrent preterm birth by clinical subtype: *indicated*, with clinical risk requiring delivery prior to 37 weeks, and *spontaneous*, preterm delivery not prompted by obstetric intervention. We investigated differences in risk of recurrent preterm birth by subtype and assessed whether these differences vary by several covariates known to be associated with preterm birth.

**Methods:** We conducted a retrospective cohort study of birth certificate data linked to the Comprehensive Hospital Abstract Reporting System (CHARS) database from 2003–2014 in Washington State. A total of 85,536 women with their first live singleton birth (P1) and a consecutive live singleton birth (P2) in this time period were included: 6,032 spontaneous preterm P1, 3,035 indicated preterm P1, and 76,469 term P1. We conducted a stratified analysis examining exposure of preterm birth by subtype in P1 and associations with three outcomes: spontaneous preterm, indicated preterm, and term birth in P2. Associations were also examined by age, education, race, smoking status, BMI, interpregnancy interval, preeclampsia, and underlying hypertension or diabetes.

**Results:** Preterm birth in P1 was strongly associated with preterm birth in P2. Associations were strongest for concordant subtypes (spontaneous–spontaneous RR=6.0; 95% CI: 5.6–6.5, indicated–indicated RR=7.8; 95% CI: 7.1–8.6), but discordant subtypes were also associated (spontaneous–indicated RR=3.6; 95% CI: 3.3–4.1, indicated–spontaneous RR=2.4; 95% CI: 2.1–2.8). Associations were more pronounced for early preterm (<32 weeks gestation). In concordant subtypes, associations differed between strata of age, education, race, BMI, interpregnancy interval, preeclampsia, and underlying hypertension or diabetes.

**Discussion:** Women with a prior spontaneous or indicated preterm birth are at higher risk for both subtypes of preterm birth in a subsequent pregnancy. The strength of these associations varies by demographic and biological variables that should be considered when counseling women on their risk for a subsequent preterm birth.



## **Does adequacy of prenatal care modify the risk of adverse birth outcomes associated with hyperemesis gravidarum?**

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Preceptor: Rachel Winer, PhD.

**Introduction:** Hyperemesis gravidarum (HG) is associated with an increased risk of adverse birth outcomes including preterm birth (PTB), low birthweight (LBW), and small for gestational age (SGA). Prenatal care may provide an opportunity to intervene and prevent these outcomes. We evaluated whether associations between HG and adverse birth outcomes differ depending on adequacy of prenatal care utilization.

**Methods:** We conducted a population-based retrospective cohort study using linked Washington State birth certificate and hospitalization data from 1987 to 2014. We identified 5,798 women hospitalized for HG in the first 28 weeks of pregnancy who we frequency matched by birth year to 79,824 women without HG. The associations between HG and PTB, LBW, and SGA were evaluated using Mantel-Haenzel stratified analysis. Relative risks were determined in 4 categories of prenatal care utilization based on the Kotelchuck Index (KI): inadequate, intermediate, adequate, or adequate plus. We evaluated age, race/ethnicity, parity, maternal education, diabetes, smoking status during pregnancy, and infant sex as potential confounders.

**Results:** HG was associated with a higher relative risk (RR) of PTB (RR 1.60, 95% CI 1.24-2.07) and LBW (RR 1.59, 95% CI 1.17 - 2.15) but not SGA (RR 1.23, 95% CI 0.98-1.54) among women who received inadequate prenatal care. The associations between HG and each outcome in other prenatal care strata were not statistically significant. There was a modest dose response for all outcomes, with women receiving inadequate prenatal care having the highest risk of PTB, LBW, and SGA and progressively lower risk with increasing prenatal care utilization. Adjusting for potential confounders did not affect these associations.

**Discussion:** Our results demonstrate that HG increases the risk of PTB and LBW when women receive inadequate prenatal care. Women with HG who have poor outpatient follow-up or prenatal care access may benefit from enhanced outreach efforts by healthcare providers.

## **Craniosynostosis and risk of unplanned Cesarean delivery: Results from Washington State birth cohort data**

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Preceptor: Babette Saltzman, PhD

**Background:** Craniosynostosis, fusion of one or more cranial sutures in utero, may prohibit skull compression necessary for spontaneous vaginal birth, thereby increasing sequelae, including unplanned Cesarean section (C-section). Studies suggest elevated C-section risk in mothers delivering children with craniosynostosis compared to population averages. However, direct comparison of unplanned C-section risk in mothers delivering children with craniosynostosis to a comparable unexposed group has not been conducted, nor has interaction with maternal risk factors been evaluated. We aimed to examine the association between craniosynostosis and unplanned C-section overall as well as stratified by maternal risk factors.

**Methods:** Washington State birth certificate data was linked to hospitalization records between 2003 and 2014. The cohort included mother-infant pairs with attempted trial of labor who survived at least one year following birth. Women with planned or prior C-section were excluded. ICD-9 procedure and diagnosis codes were paired to identify infants with craniosynostosis (exposed; n = 624). Mother-infant pairs without craniosynostosis were frequency-matched by birth year to exposed at a 10:1 ratio (n = 6774). Other known C-section risk factors (maternal race, age, parity, pre-pregnancy BMI, hypertension or preeclampsia, gestational age at birth and size for gestational age) were used for stratified analysis. Analysis included overall and stratified relative risk (RR) estimates for unplanned C-section and 95% confidence intervals. No covariates met predefined confounding criteria; all RR are unadjusted.

**Results:** RR of unplanned C-section in exposed mother-infant pairs was 22% higher than in unexposed mother-infant pairs (RR 1.22; 95% CI 1.03, 1.46). Maternal factors associated with elevated risk of unplanned C-section among exposed relative to unexposed mother-infant pairs included: multiparity (RR 3.06; 95% CI 2.29, 4.09), advanced maternal age (RR 2.42; 95% CI 1.84, 3.18) and hypertension/preeclampsia (RR 1.99; 95% CI 1.42, 2.79). Multiparous women of advanced age had highest risk for unplanned C-section in exposed mother-infant pairs (RR 5.08, 95% CI 3.35, 7.71).

**Discussion:** Findings support previous studies showing elevated C-section risk associated with craniosynostosis. Multiparity, advanced maternal age and hypertension/preeclampsia further elevated risk among exposed mother-infant pairs, suggesting prenatal identification of craniosynostosis may have value in unplanned C-section prevention in women with these risk factors.