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Previous Adverse Outcome of Term Pregnancy and Risk of Preterm Birth in Subsequent Pregnancy

Rebecca J. Baer[1,2] · Vincenzo Berghella[3] · Louis J. Muglia[4] · Mary E. Norton[5] · Larry Rand[2,5] · Kelli K. Ryckman[6] · Laura L. Jelliffe-Pawlowski[2,7] · Monica R. McLemore[2,8]

Abstract

Objective Evaluate risk of preterm birth (PTB, < 37 completed weeks' gestation) among a population of women in their second pregnancy with previous full term birth but other adverse pregnancy outcome. *Methods* The sample included singleton live born infants between 2007 and 2012 in a birth cohort file maintained by the California Office of Statewide Health Planning and Development. The sample was restricted to women with two pregnancies resulting in live born infants and first birth between 39 and 42 weeks' gestation. Logistic regression was used to calculate the risk of PTB in the second birth for women with previous adverse pregnancy outcome including: small for gestational age (SGA) infant, preeclampsia, placental abruption, or neonatal death (≤ 28 days). Risks were adjusted for maternal factors recorded for second birth. *Results* The sample included 133,622 women. Of the women with any previous adverse outcome, 4.7% had a PTB while just 3.0% of the women without a previous adverse outcome delivered early (relative risk adjusted for maternal factors known at delivery 1.4, 95% CI 1.3–1.5). History of an SGA infant, placental abruption, or neonatal death increased the adjusted risk of PTB in their second birth by 1.5–3.7-fold. History of preeclampsia did not elevate the risk of a preterm birth in the subsequent birth. *Conclusions for Practice* The findings indicate that women with previous SGA infant, placental abruption, or neonatal death, despite a term delivery, may be at increased risk of PTB in the subsequent birth. These women may be appropriate participates for future interventions aimed at reduction in PTB.

Keywords Preterm birth · Poor adverse pregnancy outcome · Placental abruption · Small for gestational age · Neonatal death

✉ Rebecca J. Baer
  rjbaer@ucsd.edu

1 Department of Pediatrics, University of California, San Diego, 9500 Gilman Drive MC0828, La Jolla, CA 92093, USA

2 The California Preterm Birth Initiative, University of California, San Francisco, San Francisco, CA, USA

3 Department of Obstetrics and Gynecology, Sidney Kimmel Medical Center of Thomas Jefferson University, Philadelphia, PA, USA

4 Center for Prevention of Preterm Birth, Perinatal Institute, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

5 Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, San Francisco, CA, USA

6 Departments of Epidemiology and Pediatrics, University of Iowa, Iowa City, IA, USA

7 Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, USA

8 Department of Family Health Care Nursing, School of Nursing, University of California, San Francisco, San Francisco, CA, USA

Significance

What is already known on this subject? Preterm birth affects approximately 10% of live born infants in the United States and accounts for 17–34% of infant deaths within the first year of life. One understudied population of women to be considered for preterm birth interventions are women with a previous term birth and previous poor pregnancy outcome.

What this study adds? Our findings indicate that women with a previous poor outcome of pregnancy, despite a term delivery, may be at increased risk of preterm delivery in the subsequent birth. These women may be appropriate participates for future interventions aimed at reduction in preterm birth.

Introduction, Objectives, Purpose

Preterm birth affects approximately 10% of live born infants in the United States and accounts for 17–34% of infant deaths within the first year of life (Hamilton et al. 2017; Behrman and Stith Butler 2007). Identification of women at high risk for preterm birth early in pregnancy provides the most opportunity for intervention, high-risk prenatal management, and counseling. Few interventions exist for the prevention of preterm delivery and effective identification of women with the greatest response to current therapies (e.g. progesterone, aspirin) is ongoing (Norwitz and Caughey 2011). One of the primary populations targeted for current therapies are women with a previous preterm birth due to their known increased risk of a subsequent preterm birth (Jarde et al. 2017; Dodd et al. 2013).

One understudied population of women to be considered for preterm birth interventions are women with a previous full term birth and previous poor pregnancy outcome. Limited information suggests that previous preeclampsia, premature rupture of the membranes, placental abruption, and infant death increase a woman's risk of preterm birth in subsequent pregnancies (Wikstrom et al. 2011; Tandu-Umba et al. 2014; Salihu et al. 2013; Rasmussen et al. 2000; Lain et al. 2005). These studies lack the ability to examine preterm birth by timing (< 32 weeks, 32–36 weeks) and indication (preterm premature rupture of the membranes (PPROM), spontaneous labor with intact membranes, iatrogenic).

Here, we evaluated the risk of preterm birth among a population of women in their second pregnancy with previous term birth in the context of a previous small for gestational age (SGA) infant, preeclampsia, placental abruption, or neonatal death (within first 28 days of life) using a cohort of California births. We analyzed the risk of preterm birth by timing and indication. We hypothesized that women with previous complications would be at increased risk of a subsequent preterm birth.

Methods, Description

In this retrospective cohort study, the sample was drawn from a birth cohort file maintained by the California Office of Statewide Health Planning and Development which contains linked birth and death certificates, as well as detailed information on maternal and infant characteristics, hospital discharge diagnoses and procedures recorded as early as 1 year prior to delivery and as late as 1 year post-delivery (Jelliffe-Pawlowski et al. 2015; Yang et al. 2016; Felder et al. 2017). The sample included births in California between 2007 and 2012, women with gravidity and parity of two, and both pregnancies in the birth cohort file. The sample was further restricted to singletons for both pregnancies, linked to woman and infant hospital discharge records, and with birth weights within three standard deviations of the mean for sex and gestational age (Talge et al. 2014) (to improve gestational age accuracy), birth of the first infant between 39 and 42 completed weeks gestation (due to known association between preterm and early term birth and preterm birth in subsequent pregnancy) (Yang et al. 2016), and who had their second infant between 22 and 42 completed weeks gestation. Finally, women with infants with chromosomal abnormalities or major birth defects (Baer et al. 2014) in either birth were excluded (Fig. 1).

Gestational age at birth (best obstetric estimate) was obtained from birth certificate records. Preterm birth (before 37 completed weeks gestation) was grouped into PPROM, spontaneous labor with intact membranes, or iatrogenic preterm birth. As previously described (Jelliffe-Pawlowski et al. 2015), all preterm births with an indication of PPROM on the infant's birth certificate or in the woman's hospital discharge records were included in the PPROM group. Women with no indication of PPROM, but who had birth certificate or hospital discharge records with an indication of premature labor or tocolytic medication were included in the spontaneous labor with intact membranes group. Preterm births without an indication or PPROM or spontaneous labor or tocolytic medication, but had a code for medical induction, artificial rupture of membranes, or cesarean delivery were placed in the iatrogenic group. Preterm births were also subgrouped by gestational age as < 32 completed weeks and 32–36 completed weeks.

Poor previous pregnancy outcome was defined as: SGA, preeclampsia, placental abruption, or neonatal death. Infants were considered SGA when their birth weight below the 10th percentile for gestational age (Talge et al. 2014).
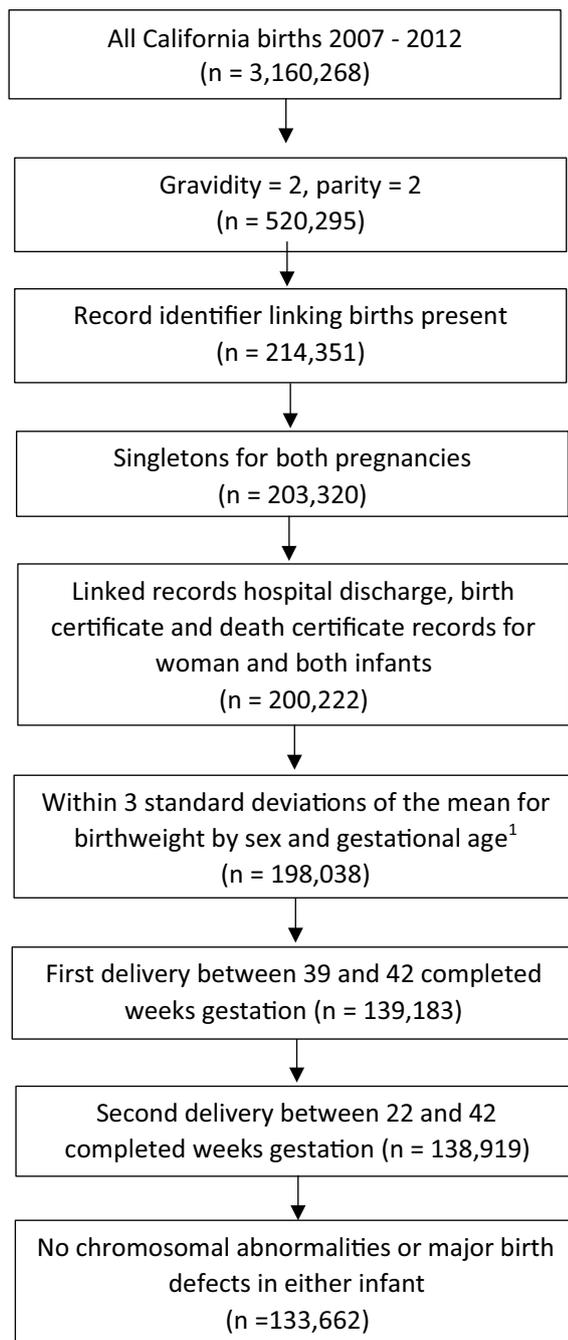
Fig. 1 Sample selection

Preeclampsia and placental abruption were obtained from hospital discharge ICD-9 diagnoses (Online Appendix) (American Medical Association 2008). Neonatal death was defined as death within the 28 days of life, regardless of cause. Death was obtained from linked death certificates and hospital discharge records.

Risk of preterm birth (< 32 weeks, 32–36 weeks, and any < 37 weeks gestation; PPROM, spontaneous labor with intact membranes, or iatrogenic) in the second delivery was evaluated by poor outcome in the previous pregnancy using women with no previous poor outcome delivering between 37 and 42 weeks as the referent group. Unadjusted risks were calculated using Poisson regression to calculate relative risks (RR) and 95% confidence intervals (95% CI). To provide risk assessment for women when entering prenatal care, calculations were adjusted (aRR) for second birth maternal factors known in the first trimester (race or ethnicity, maternal age, education, BMI, payment, smoking, preexisting hypertension, preexisting diabetes, interpregnancy interval). To provide fully adjusted risks assessments, calculations were made using maternal factors known at the time of delivery (race or ethnicity, maternal age, education, prepregnancy body mass index (BMI), payment for delivery, smoking, preexisting hypertension without progression to preeclampsia, preexisting hypertension with progression to preeclampsia, gestational hypertension without progression to preeclampsia, gestational hypertension with progression to preeclampsia, preexisting diabetes, gestational diabetes, infection, drug or alcohol use, mental illness, anemia, abruption, SGA or large for gestational age, interpregnancy interval).

Due to the disparities seen in rates of preterm birth by race or ethnicity and socioeconomic status (Jelliffe-Pawlowski et al. 2015), a sensitivity analysis was performed examining risk of preterm birth by previous poor outcome stratified by race or ethnicity and payer for delivery. Due to small sample sizes, American Indian, Hawaiian or Pacific Islander, other race, two or more races and unknown race or ethnicity were grouped together as 'other race or ethnicity'. For the payer for delivery stratification, public (Medi-Cal, California's Medicaid, proxy for low income) and private insurance coverage were examined.

All analyses were performed using Statistical Analysis Software version 9.4 (Cary, NC) and were based on data received by the California Preterm Birth Initiative at the University of California, San Francisco as of June 21, 2016. Methods and protocols for the study were approved by the Committee for the Protection of Human Subjects within the Health and Human Services Agency of the State of California.

Results, Assessment

The final population included 133,662 women, with 3.2% (n = 4303) experiencing a preterm birth in their second pregnancy. The majority of the population was Hispanic or White non-Hispanic (n = 97,841, 73.2%) and between 18 and 34 years old at their second birth (n = 111,710, 83.6%). A higher percent of the women delivering before 37 weeks were Hispanic, non-Hispanic Black, non-Hispanic Asian or non-Hispanic other races or ethnicities, < 18 years at their

Table 1 Maternal characteristics and obstetric factors for sample (n = 133,662)

Maternal characteristic or obstetric factor	Second birth	
	Preterm n (%)	Term n (%)
Sample	4303	129,359
Race/ethnicity		
Non-Hispanic White	1281 (29.8)	49,609 (38.4)
Hispanic	1666 (38.7)	45,285 (35.0)
Non-Hispanic Black	321 (7.5)	6036 (4.7)
Non-Hispanic Asian	692 (16.1)	19,107 (14.8)
Non-Hispanic other[a]	343 (8.0)	9322 (7.2)
Maternal age at second birth		
< 18 years	94 (2.2)	1084 (0.8)
18–34 years	3545 (82.4)	108,165 (83.6)
More than 34 years	664 (15.4)	20,109 (15.6)
Maternal education at second birth		
< 12 years	569 (13.2)	12817 (9.9)
12 years	1090 (25.3)	30,105 (23.3)
More than 12 years	2480 (57.6)	82,685 (63.9)
Pre-pregnancy body mass index at second birth		
Underweight (< 18.5 kg/m^2)	250 (5.8)	5394 (4.2)
Normal (18.5–24.9 kg/m^2)	2108 (49.0)	64,416 (49.8)
Overweight (25.0–29.9 kg/m^2)	916 (21.3)	29,801 (23.0)
Obese (≥ 30.0 kg/m^2)	773 (18.0)	23,793 (18.4)
Payment for second delivery		
Public[b]	2,364 (54.9)	80,700 (62.4)
Private	1,724 (40.1)	43,606 (33.7)
Self-pay	51 (1.3)	1,019 (0.8)
Other	154 (3.6)	3,899 (3.0)

[a]Includes: American Indian, Hawaiian or Pacific Islander, other race, two or more races, and unknown race

[b]Medi-Cal, California's Medicaid, health insurance for low-income persons

second delivery, had < 12 years education, and paid for delivery with public insurance (Table 1).

Over 87% (n = 117,068) of the population had no previous poor outcome of pregnancy and 3.0% (n = 3522) of those women delivered preterm (Table 2). Of the 16,594 women who had any previous poor outcome, 4.7% (n = 781) gave birth before 37 weeks gestation conferring a 1.4-fold higher risk of after adjusted for all maternal factors known at the time of delivery (95% CI 1.3–1.5). Women with any previous poor outcome of pregnancy were 1.4-times as likely to have a delivery before 32 weeks gestation after these adjustments (95% CI 1.0–1.8, p < 0.05) (Table 2).

Women with a previous SGA infant were at higher risk of preterm delivery before 32 weeks (aRR 1.7, 95% CI 1.2–2.2) and between 32 and 36 weeks (aRR 1.5, 95% CI 1.3–1.6) (Table 2). After full adjustment, a previous SGA infant did not increase the risk of preterm birth due to PPROM, but increased the risk 1.2-times for an iatrogenic preterm birth and 1.5-times for a preterm birth due to spontaneous labor with intact membranes (Table 3).

After adjusting for maternal factors known at delivery, women who previously had preeclampsia were not at elevated risk of preterm birth in their subsequent birth (Tables 2, 3).

Previous placental abruption increased the risk of a woman delivering between 32 and 36 weeks (1.8, 95% CI 1.3–2.5) in their second birth (Table 2). This risk of preterm birth was driven by births due to spontaneous labor with intact membranes or iatrogenic causes (aRR 1.9 spontaneous labor, aRR 2.4 iatrogenic) (Table 3).

Of the 70 women with a previous neonatal death, 12.9% (n = 9) gave birth in their second pregnancy between 32 and 36 weeks' gestation (aRR 4.1, 95% CI 2.1–7.9) (Table 2). Women with previous neonatal death were more likely to have a preterm birth due to spontaneous labor (aRR 4.5, 95% CI 1.9–10.9), and fewer than five women with a previous neonatal death had a preterm birth due to PPROM or provider initiation and risk calculations were not made (Table 3).

Table 2 Risk of preterm birth (by gestational age) by previous poor outcome

Previous poor outcome	Gestation at second birth			
	< 32 weeks	32–36 weeks	Any < 37 weeks	37–42 weeks
Sample (n = 133,662)				
n (row %)	**381 (0.3)**	**3922 (2.9)**	**4303 (3.2)**	**129359 (96.8)**
No previous poor outcome (n = 117,068)				
n (row %)	312 (0.3)	3,210 (2.7)	3,522 (3.0)	113,546 (97.0)
RR (95% CI)				Reference
Any previous poor outcome (n = 16,594)				
n (row %)	69 (0.4)	712 (4.3)	781 (4.7)	15,813 (95.3)
aRR1 (95% CI)	**1.5 (1.1–1.9)**	**1.5 (1.3–1.6)**	**1.5 (1.4–1.6)**	
aRR2 (95% CI)	**1.4 (1.0–1.8)**	**1.4 (1.3–1.5)**	**1.4 (1.3–1.5)**	
SGA in first birth (n = 13,122)				
n (row %)	62 (0.5)	574 (4.4)	636 (4.9)	12,486 (95.2)
aRR1 (95% CI)	**1.7 (1.3–2.2)**	**1.5 (1.4–1.7)**	**1.5 (1.4–1.7)**	
aRR2 (95% CI)	**1.7 (1.2–2.2)**	**1.5 (1.3–1.6)**	**1.5 (1.3–1.6)**	
Abruption in first birth (n = 568)				
n (row %)	3 (0.8)	31 (5.5)	34 (6.0)	534 (94.0)
aRR1 (95% CI)	[a]	**1.9 (1.4–2.8)**	**1.9 (1.4–2.7)**	
aRR2 (95% CI)	[a]	**1.8 (1.3–2.6)**	**1.8 (1.3–2.5)**	
Neonatal death (n = 70)				
n (row %)	0 (0.0)	9 (12.9)	9 (12.9)	61 (87.1)
aRR1 (95% CI)	[a]	**4.3 (2.2–8.3)**	**3.9 (2.0–7.6)**	
aRR2 (95% CI)	[a]	**4.1 (2.1–7.9)**	**3.7 (1.9–7.2)**	

Bold indicates p < 0.05

aRR adjusted relative risk, *SGA* small for gestational age

aRR1 adjusted relative risk—adjusted for Table 1 factors known in first trimester: race/ethnicity, age, education, pre-pregnancy body mass index, pre-existing hypertension, pre-existing diabetes, interpregnancy interval; aRR2 adjusted relative risk—adjusted for Table 1 factors known at delivery: race/ethnicity, age, education, pre-pregnancy body mass index, pre-existing hypertension, pre-existing diabetes, interpregnancy interval, payment for delivery, smoked during pregnancy, gestational hypertension, gestational diabetes, infection, drug/alcohol abuse, mental illness, anemia, placental abruption, cesarean delivery, small for gestational age, large for gestational age

[a]Not calculated when n < 5

When risk of preterm birth was examined among racial or ethnic groups, findings generally persisted for non-Hispanic White and Hispanic women. The most consistent finding was that women with a previous SGA infant were at elevated risk of preterm birth in their second delivery. This risk was elevated for non-Hispanic White and Black women, as well as Hispanic women (aRRs 1.4–1.7) (Supplemental Table 1).

Stratification by public and private insurance demonstrated similar patterns of risk (Supplemental Table 2). Among women with public insurance, 28 had a previous neonatal death. One (3.1%) of these women had a preterm birth therefore risk calculations were not made. Among women with private insurance, 37 women had a previous neonatal death. Nearly 19% (n = 7) of these women had a preterm birth (not tabled).

Discussion, Conclusions, Conclusions for Practice

Women with a previous SGA infant, placental abruption, or neonatal death were at increased risk of preterm birth in the subsequent live birth. Risk of delivery before 32 weeks was elevated for women with a previous SGA infant. Women with a previous abruption were at elevated risk of preterm birth due to spontaneous preterm labor or iatrogenic causes. Overall rates of preterm birth in this population were low (3.2%), likely because the cohort was parous women with no prior preterm or early term birth.

This study provides new insight into risk of preterm birth after other pregnancy complications. Likely due to the complexity of causes of intrauterine growth restriction, few have

Table 3 Risk of preterm birth (by indication) by previous poor outcome

	Gestation at second birth			
	< 37 weeks			37–42 weeks
Previous poor outcome	PPROM	Spontaneous labor	Iatrogenic	
Sample (n = 133,662)				
n (row %)	**965 (0.7)**	**2,268 (1.7)**	**758 (0.6)**	**129,359 (96.8)**
No previous poor outcome (n = 117,068)				
n (row %)	827 (0.7)	1,813 (1.6)	630 (0.5)	113,546 (97.0)
RR (95% CI)				Reference
Any previous poor outcome (n = 16,594)				
n (row %)	138 (0.8)	455 (2.7)	128 (0.8)	15,813 (95.3)
aRR1 (95% CI)	1.2 (1.0–1.4)	**1.7 (1.5–1.9)**	**1.4 (1.1–1.7)**	
aRR2 (95% CI)	1.1 (0.9–1.3)	**1.5 (1.3–1.7)**	**1.2 (1.0–1.5)**	
SGA in first birth (n = 13,122)				
n (row %)	117 (0.9)	367 (2.8)	98 (0.8)	12,486 (95.2)
aRR1 (95% CI)	**1.2 (1.0–1.5)**	**1.7 (1.5–1.9)**	**1.4 (1.1–1.7)**	
aRR2 (95% CI)	1.2 (1.0–1.5)	**1.6 (1.4–1.8)**	**1.4 (1.1–1.7)**	
Preeclampsia in first birth (n = 3,460)				
n (row %)	20 (0.6)	96 (2.8)	32 (0.9)	3,307 (95.6)
aRR1 (95% CI)	0.8 (0.5–1.3)	**1.7 (1.3–2.0)**	**1.5 (1.0–2.2)**	
aRR2 (95% CI)	0.7 (0.5–1.2)	1.2 (1.0–1.5)	0.9 (0.6–1.3)	
Abruption in first birth (n = 568)				
n (row %)	6 (1.1)	19 (3.4)	8 (1.4)	534 (94.0)
aRR1 (95% CI)	1.5 (0.7–3.3)	**2.1 (1.4–3.3)**	**2.6 (1.3–5.2)**	
aRR2 (95% CI)	1.4 (0.6–3.2)	**1.9 (1.2–3.0)**	**2.4 (1.2–4.9)**	
Neonatal death (n = 70)				
n (row %)	1 (1.4)	5 (7.1)	2 (2.9)	61 (87.1)
aRR1 (95% CI)	[a]	**4.3 (1.8–10.4)**	[a]	
aRR2 (95% CI)	[a]	**4.5 (1.9–10.9)**	[a]	

Bold indicates p < 0.05

aRR adjusted relative risk, *SGA* small for gestational age

aRR1 adjusted relative risk—adjusted for Table 1 factors known in first trimester: race/ethnicity, age, education, pre-pregnancy body mass index, pre-existing hypertension, pre-existing diabetes, interpregnancy interval; aRR2 adjusted relative risk—adjusted for Table 1 factors known at delivery: race/ethnicity, age, education, pre-pregnancy body mass index, pre-existing hypertension, pre-existing diabetes, interpregnancy interval, payment for delivery, smoked during pregnancy, gestational hypertension, gestational diabetes, infection, drug/alcohol abuse, mental illness, anemia, placental abruption, cesarean delivery, small for gestational age, large for gestational age

[a]Not calculated when n < 5

investigated the risk of preterm birth among women with a previous SGA infant. Despite the null findings after adjustments among women with previous preeclampsia, a previous SGA infant was a risk factor for all timings and indications for preterm delivery after each adjusted model. Our findings brings a new and important risk factor to light.

Previous preeclampsia, especially when onset occurs at 34 weeks or earlier, has been demonstrated to be a risk factor for preterm birth (Wikstrom et al. 2011; Lain et al. 2005). In our study, women with previous preeclampsia were not at elevated risk of preterm birth after adjustments were made for all maternal factors known at the time of delivery. We were unable to examine timing of the previous preeclampsia diagnosis, however, and therefore we were unable to replicate the study finding of early onset risk.

Previous abruption has been shown to be a risk factor for preterm birth, regardless of reoccurrence of the abruption (Rasmussen et al. 2000). Our study adds to this finding by demonstrating that the risk is most sizable for women with iatrogenic preterm birth or spontaneous labor with intact

membranes. The sample size became too small to consider risk among women with previous placental abruption by all races or ethnicities. When stratified by payer, risk of preterm birth after previous abruption was similar between women with public or private insurance.

In 2013, Salihu et al. (2013) demonstrated that women with a previous infant death (before 365 days) were at two-fold higher risk of preterm delivery. In our study evaluating women with previous neonatal death, women were three-times more likely to have a subsequent preterm birth. Salihu et al. (2013) also demonstrated that Black women were at 3.7-times higher risk of preterm birth after infant death. As no women with a previous neonatal death delivered before 32 weeks, the greatest risk was for a preterm birth between 32 and 36 weeks. Unfortunately our study numbers were too small to evaluate the risk among women of color or by payer for delivery.

This study has many strengths, including the ability to investigate preterm birth by timing and indication, the abundance of maternal factors needed to make appropriate adjustments, and the ability to evaluate risk as the pregnancy progresses and more information is elucidated. However, critical limitations must be considered when interpreting the findings. One such limitation was small numbers. Despite our large dataset beginning with over three-million pregnancies, we were limited to a final sample size of < 135,000 women. This limited our ability to evaluate risk for several rare occurrences, such as risk of birth before 32 weeks after previous neonatal death. Because of differences in risk of preterm birth by race or ethnicity and socioeconomic status (Braveman et al. 2015), we sought to evaluate risk stratified by these factors. Although findings by previous pregnancy outcome had differences across races and ethnicities, interpretation of these findings must be tempered due to small numbers after stratification. A prospective study evaluating the risk of preterm birth may have better power to examine these risk factors. Another limitation of this study is the applicability to other populations. We excluded women with more than two pregnancies because we felt it was important to assess the risk of preterm birth among women with specific previous adverse pregnancy outcomes. By including women with previous terminations, fetal demises, and multiple live births, the findings would be less clear due to multiple pregnancies with multiple outcomes. Further study is needed to assess if the findings from this work are consistent for women with more than two pregnancies.

Other limitations of this study relate to the nature of an administrative database. We aimed to have the best data, but in the process eliminated births that limit our findings. Because the sample is drawn from California, both births must have occurred in this state, meaning our sample may represent a more stable population. To better assess the impact of the sample restrictions, we looked at the rate of preterm birth in the excluded sample (women with all parities/gravidities, all gestations in previous birth, unlinked hospital discharge records, all birthweight for gestational age combinations, and infants with major anomalies: n = 498,640) and found that the rate of preterm birth was 11.8% in the most recent birth versus 3.2% in our sample. It is difficult to compare these numbers, as our intent was to focus on women who had a previous term delivery. However, our strict selection criteria should pull the findings toward the null if anything: therefore, risk of preterm birth among women with these previous adverse pregnancy outcomes may be more elevated than reported here. Additionally, the diagnoses used in this study relied on birth certificate and hospital discharge billing codes. Previous examination of California birth certificate documentation of gestational age suggests that preterm birth may be under ascertained (Barradas et al. 2014), justifying our exclusion criteria of unlikely birthweight and gestational age combinations. We are unaware of a study examining ascertainment of placental abruption or preeclampsia in the literature, however others who have examined maternal diagnoses in birth certificate and hospital discharge data in Washington state found that diagnoses such as preexisting diabetes or hypertension and placenta previa are well reported (Lydon-Rochelle et al. 2005). Finally, the most recent data available is from 2012. Changes in medical practice or hospital protocol may alter the outcomes both in the first and second pregnancy influencing the risk of preterm birth. A current, prospective study would be appropriate to further validate the findings presented here.

Our findings indicate that women with a previous SGA infant, placental abruption, or neonatal death, despite a term delivery, may be at increased risk of preterm delivery in the subsequent birth. Small for gestational age, preeclampsia, and placental abruption all suggest placental dysfunction (De Wolf et al. 1980; Olgan et al. 2015; Robertson et al. 1986). It is possible that this pathological factor has different clinical expressions for different pregnancies (Redline 1995). Identifying the biological link between these previous adverse pregnancy outcome and preterm birth in a subsequent pregnancy may suggest effective therapies to reduce preterm birth and maternal and infant morbidities.

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