

## OBSTETRICS

# Pregnancy as a window to future health: maternal placental syndromes and short-term cardiovascular outcomes

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**BACKGROUND:** Cardiovascular disease is the leading cause of death among women. Identifying risk factors for future cardiovascular disease may lead to earlier lifestyle modifications and disease prevention. Additionally, interpregnancy development of cardiovascular disease can lead to increased perinatal morbidity in subsequent pregnancies. Identification and implementation of interventions in the short term (within 5 years of first pregnancy) may decrease morbidity in subsequent pregnancies.

**OBJECTIVE:** We identified the short-term risk (within 5 years of first pregnancy) of cardiovascular disease among women who experienced a maternal placental syndrome, as well as preterm birth and/or delivered a small-for-gestational-age infant.

**STUDY DESIGN:** We conducted a retrospective cohort study using a population-based, clinically enhanced database of women in the state of Florida. Nulliparous women and girls aged 15-49 years experiencing their first delivery during the study time period with no prepregnancy history of diabetes mellitus, hypertension, or heart or renal disease were included in the study. The risk of subsequent cardiovascular disease was compared among women who did and did not experience a placental syndrome during their first pregnancy. Risk was then reassessed among women with placental syndrome and preterm birth or delivering a small-for-gestational-age infant vs those without these adverse pregnancy outcomes.

**RESULTS:** The final study population was 302,686 women and girls. Median follow-up time for each patient was 4.9 years. The unadjusted rate of subsequent cardiovascular disease among women with any placental

syndrome (11.8 per 1000 women) was 39% higher than the rate among women without a placental syndrome (8.5 per 1000 women). Even after adjusting for sociodemographic factors, preexisting conditions, and clinical and behavioral conditions associated with the current pregnancy, women with any placental syndrome experienced a 19% increased risk of cardiovascular disease (hazard ratio, 1.19; 95% confidence interval, 1.07–1.32). Women with >1 placental syndrome had the highest cardiovascular disease risk (hazard ratio, 1.43; 95% confidence interval, 1.20–1.70), followed by those with eclampsia/preeclampsia alone (hazard ratio, 1.42; 95% confidence interval, 1.14–1.76). When placental syndrome was combined with preterm birth and/or small for gestational age, the adjusted risk of cardiovascular disease increased 45% (95% confidence interval, 1.24–1.71). Women with placental syndrome who then developed cardiovascular disease experienced a 5-fold increase in health care–related costs during follow-up, compared to those who did not develop cardiovascular disease.

**CONCLUSION:** Women experiencing placental syndromes and preterm birth or small-for-gestational-age infant are at increased risk of subsequent cardiovascular disease in short-term follow-up. Strategies to identify and improve cardiovascular disease risk in the postpartum period may improve future heart disease outcomes.

**Key words:** cardiovascular disease, preeclampsia, preterm birth, small for gestational age

## Introduction

Cardiovascular disease (CVD) is the leading cause of death among women in the United States.<sup>1</sup> An increasing body of evidence indicates that pregnancy-related morbidities, including preeclampsia, placental infarction, and abruptio, are associated with the development of subsequent CVD and can be referred to as maternal placental syndromes (PS).<sup>2-5</sup> Furthermore, the adverse pregnancy outcomes of preterm delivery, and infants born small for

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## EDITORS' CHOICE

gestational age (SGA), resulting from intrauterine growth restriction, may be referred to as fetal PS and also appear to confer CVD risk.<sup>4,6-10</sup>

Both retrospective and prospective epidemiological studies have reported associations between hypertensive disorders of pregnancy, preterm birth (PTB), and maternal PS and an increased risk of future CVD.<sup>4,7-9,11</sup> While most of these studies focus on long-term CVD risk, up to 15 years after giving birth, limited data exist regarding the short-term risk of CVD. CVD occurring within the first 5 years of the index delivery will likely occur in the mother's reproductive lifespan and therefore lead to further morbidity in subsequent pregnancies. No prior research investigates the impact of PS and

subsequent CVD on health care utilization or costs. We hypothesized that the short-term risk of CVD (within 5 years of first pregnancy) would be increased among women with maternal PS. Additionally we examined health care utilization and direct medical costs in the years immediately following pregnancy with and without placental complications.

## Materials and Methods

### Design, data source, and study population

We conducted a population-based retrospective cohort study using a statewide maternal and infant longitudinally linked database.<sup>12,13</sup> For Florida-resident births from 1998 through 2009, birth certificates were linked both to infant birth and maternal delivery hospitalization discharge records using a

hierarchical deterministic linking strategy.<sup>14</sup> After establishing events that occur at birth, we then linked in death certificates and all subsequent infant and maternal inpatient, outpatient, and emergency department discharge records available through the end of follow-up (Dec. 31, 2010). For mothers, we also linked to all hospital discharge data preceding the index pregnancy, as far back as Jan. 1, 1998. Details of the data linkage process, which achieved >92% linkage rate, and an evaluation of the validity and reliability of database have been published previously.<sup>14</sup> The study population consisted initially of 318,362 nulliparous pregnant women and girls aged 15–49 years who gave birth

to a live born singleton infant from Jan. 1, 2004, through Dec. 31, 2007 (Figure 1). This time frame was chosen to review medical history in the 5-year period before pregnancy, incorporate potential confounders present only on the new version of the Florida birth certificate, and allow for a minimum of 3 years of follow-up after the index delivery. Women diagnosed with prepregnancy CVD, hypertension, diabetes, or renal disease in the 5-year period before the index delivery hospitalization (n = 14,165) and those giving birth to infants with implausible gestational age–birthweight combinations based on national fetal growth curves<sup>15</sup> (n = 416) were excluded. The final study

population consisted of 302,686 women and girls.

### PS and adverse infant outcomes

Using *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* diagnosis codes from discharge records, supplemented with birth certificate indicators to improve sensitivity, we determined whether each mother had a PS—pre-eclampsia (642.4, 642.5), eclampsia (642.6 or birth certificate indicator), gestational hypertension (642.3 or birth certificate indicator), placental infarction (656.7), or placental abruption (641.2)—diagnosed during her index delivery hospitalization. Three exposures were used in analyses: (1) a 2-level “any PS” variable; (2) a 5-level variable to capture the nature and number of PS conditions; and (3) a 4-level variable that combined PS with PTB (20–37 weeks’ gestation) and SGA (birthweight <10th percentile for gestational age).

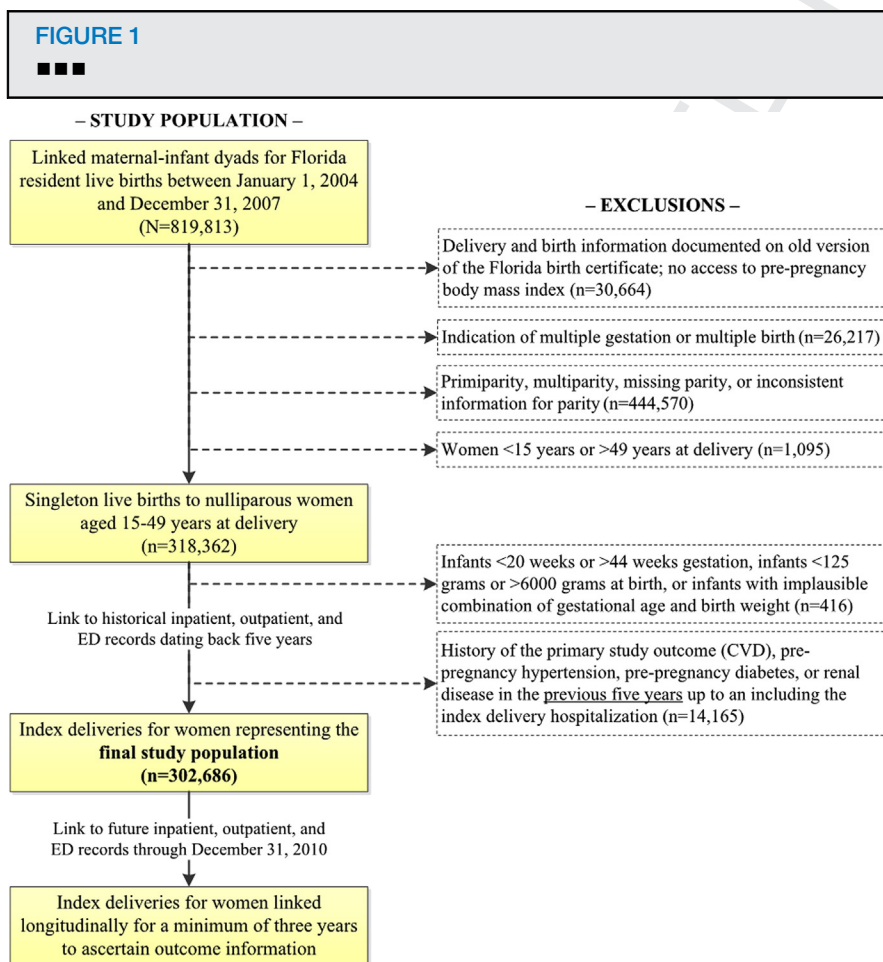
### Cardiovascular health outcomes

The primary outcome was incident CVD, operationalized as presence of  $\geq 1$  ICD-9-CM diagnosis codes indicative of coronary heart disease, cerebrovascular disease, peripheral artery disease, or congestive heart failure, or an ICD-9-CM procedure code for cardiac or peripheral arterial revascularization. To prevent capturing the immediate effect of the index delivery on risk of CVD,<sup>4</sup> assessment of CVD included encounters taking place  $\geq 90$  days after discharge from the index delivery hospitalization. Follow-up continued through Dec. 31, 2010. A detailed list of the ICD-9-CM codes used to define CVD is presented in the Appendix.

### Health care utilization indices

We explored the associations between PS and 3 indicators of health care utilization: (1) number of encounters, (2) length of stay (LOS) across encounters, and (3) cost of providing direct medical care. The number of encounters was calculated as the number of unique inpatient, outpatient, and emergency department discharge records with date of admission  $\geq 90$  days after discharge

FIGURE 1



Flow diagram representing final determination of study population of nulliparous, Florida-resident women and girls aged 15–49 years whose first singleton live birth occurred from 2004 through 2007.

CVD, cardiovascular disease; ED, emergency department.

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