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Differences in risk factors for incident and recurrent small-for-gestational-age birthweight: a hospital-based cohort study

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Abstract

Objective—Examine whether small-for-gestational-age (SGA) risk factors differed by prior SGA birth.

Design—Hospital-based cohort study.

Setting—Utah, US.

Population—Electronic medical record data from 25,241 women who were nulliparous at study entry with 2 subsequent consecutive singleton deliveries (2002–2010).

Methods—Estimated adjusted relative risks (RR) and 95% confidence intervals (95% CI) for the association between second pregnancy characteristics and SGA risk. Tested for risk factor differences between recurrence and incidence ($P_{\text{difference}}$).

Main outcome measures—Second pregnancy incident (n=1,067) and recurrent SGA (n=484) determined using a population-based reference.

Results—SGA complicated 20.3% and 4.5% of deliveries to women with and without a prior SGA birth, respectively. Young maternal age ($P_{\text{difference}}=.01$) and pregnancy hypertensive diseases ($P_{\text{difference}}=.03$) were associated with incident, but not recurrent SGA. Significant risk

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factors for incidence and recurrence were smoking [Incident RR=1.64 (95% CI 1.22–2.19); Recurrent RR=1.59 (95% CI 1.17–2.17)], short stature [Incident RR=1.34 (95% CI 1.16–1.54); Recurrent RR=1.54 (95% CI 1.31–1.82)], prepregnancy underweight [Incident RR=1.32 (95% CI 1.07–1.64); Recurrent RR=1.30 (95% CI 1.03–1.64)], and inadequate weight gain [Incident RR=1.41 (95% CI 1.22–1.64); Recurrent RR=1.33 (95% CI 1.10–1.60)]. Race-ethnicity, marital or insurance status, alcohol, diabetes, asthma, thyroid disease, depression, or interpregnancy interval were not associated with incidence or recurrence.

Conclusion—There was considerable overlap in the risk factors for SGA recurrence and incidence. Recurrence and incidence risk factors included smoking, short stature, underweight, and inadequate weight gain. Maternal age and hypertensive diseases increased the risk for incidence only. Regardless of the SGA definition, some potentially modifiable risk factors for recurrence were identified.

Keywords

small-for-gestational-age; fetal growth restriction

INTRODUCTION

A history of a growth restricted neonate is a major risk factor for a subsequent growth restricted neonate in the next pregnancy, with reported risk estimates as high as 4–11 times. (1–7) There are many well-recognized risk factors for small-for-gestational-age (SGA) newborns.(8) Low prepregnancy weight,(2, 9) low weight gain during pregnancy,(2, 10) and maternal smoking(2, 9, 10) have been consistently reported across studies as risk factors for recurrence of growth restricted births. Maternal age, interpregnancy interval, hypertensive disorders and indicators of socioeconomic status have been inconsistently identified across studies as risk factors for recurrence,(2, 4, 9, 10) possibly due to differences in study populations, definitions of growth restriction, or classification of hypertensive disorders. Furthermore, it is unclear if such SGA risk factors differ for women with a previous SGA birth from women without a previous SGA birth. Only a few studies have distinguished between risk factors for incident and recurrent SGA cases(9, 10) and these studies have been limited in that one was based on case-control data with retrospective data collection of some key variable and included only term-SGA births(10) and the other based on vital records data with low birth weight (<2500 g) as the outcome.(9)

Using a longitudinal cohort of consecutive pregnancies with medical record data, we aimed to identify second pregnancy demographic and clinical risk factors for SGA recurrence and examine if the risk factors differed from women whose first pregnancy was non-SGA. We examined SGA using both a population-based birthweight reference and a customized definition. We also explored if the inclusion of first pregnancy risk factors further informed the recurrence risk above and beyond second pregnancy risk factors only.

MATERIALS AND METHODS

The Consecutive Pregnancies Study was a retrospective cohort study conducted by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development,

National Institutes of Health. Detailed information on 114,679 pregnancies from 51,086 women with two or more consecutive deliveries after 20 weeks of gestation from 2002–2010 at 20 Utah hospitals was extracted from the maternal and infant electronic medical records and supplemented with *International Classification of Diseases*, ninth revision (*ICD9*) discharge codes. We confirmed that all deliveries >20 weeks of gestation were consecutive, however, gravidity did increase more than parity, indicating that some women had a pregnancy loss <20 weeks. Pregnancies were linked using a unique maternal ID. Institutional review board approval was obtained by all participating institutions.

For this analysis we included only women who were nulliparous at study entry and had singleton deliveries in the first and second pregnancy ($n=27,077$). Women missing relevant data in the first or second pregnancy were excluded ($n=1,836$; 6.8%), leading to a total of 25,241 women with consecutive singleton deliveries.

Gestational age, according to the best obstetrical estimate (weeks), infant birthweight (g), and sex were obtained from the electronic medical record. We classified SGA using <10th percentile of a previously published population-based reference.(11) For secondary analyses, we also identified neonates <10th customized percentile utilizing previously published coefficients for physiologic parameters affecting birthweight according to the method of Gardosi and utilizing the intrauterine proportionality curves ($SGA_{\text{customized}}$).(12, 13)

Maternal age at delivery, race-ethnicity, parity, marital status, insurance status, smoking and alcohol intake during pregnancy, height, prepregnancy weight (kg), and weight at delivery (kg) were obtained from the patient electronic medical record. Short stature was defined as a height <160 cm.(14, 15) Prepregnancy body mass index (BMI; kg/m^2) was categorized as underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), or obese (>30.0 kg/m^2).(16) Total gestational weight gain (kg) was calculated as the difference between weight at delivery and prepregnancy weight. As previously described, (17) we classified women as having gained below, within, or above the 2009 Institute of Medicine (IOM) recommended range using rate of weight gain in the second and third trimester based on first trimester weight gain assumptions of 2 kg for underweight, normal weight and overweight women and 1.25 kg for obese women.(16) Interpregnancy interval was calculated as the time between delivery of first pregnancy and the last menstrual period of the second pregnancy.

Maternal pregnancy complications and medical history of pregestational diabetes, chronic hypertension, asthma, thyroid disease, depression or another mental health condition were obtained from the medical record and supplemented with *ICD9* codes. See **Appendix S1** for *ICD9* codes and percentage of cases identified from the medical record. Women were classified as having a condition if indicated on either source (chart or discharge code). Once classified with a chronic condition women were considered to have the condition at all subsequent pregnancies. Consistency checks were performed using repeated pregnancy data on all relevant covariates and conditions. The 3 cases of eclampsia were combined with preeclampsia.

Chi-square statistics were utilized for descriptive statistics. We estimated the percent of SGA deliveries at the second pregnancy according to first pregnancy SGA status (i.e. % incident and recurrent SGA). We used longitudinal transition models implemented with Poisson regression and robust variance(18) to estimate the risk of incident and recurrent SGA at the second pregnancy associated with risk factors at the second pregnancy. Transition models are similar to traditional risk models, but include first pregnancy SGA status in the model and multiplicative interactions between each risk factor and first pregnancy SGA status, allowing for the direct comparison between incident and recurrent SGA ($P_{difference}$). For these models, a significant interaction between a risk factor and first pregnancy SGA status indicated that the risk factor had a significantly different relationship for recurrent compared to incident SGA. The interaction, however, did not inform the overall significance of a given characteristics in predicting the risk of SGA and thus global p-values for each risk factor were reported separately according to first pregnancy SGA status. All models were adjusted for the full set of risk factors discussed above.

We also tested if non-disease related risk factors in the first pregnancy modified recurrence risk observed in relation to characteristics of women in their second pregnancy. We tested for the addition of first pregnancy status to the model and the interaction with second pregnancy status.

We used SAS version 9.3 (Cary, NC) for all analyses and considered P -values $<.05$ significant for main effects and interactions.

RESULTS

Of the 25,241 women, 2,393 (9.5%) had an SGA birth in the first pregnancy. Second pregnancy characteristics for women with a previous SGA birth differed from women without a previous SGA birth such that they were younger, less likely to be non-Hispanic white and more likely to be short, unmarried, or have public insurance (Table 1). Women with a previous SGA birth were also more likely to have smoked, drank alcohol during pregnancy, been underweight, and gained inadequately during pregnancy and were less likely to remain normotensive.

At the second pregnancy, 1,551 (6.1%) pregnancies were complicated by SGA, of which 1,067 (4.7%) occurred among the 22,848 women without a first pregnancy SGA birth (i.e. incident SGA) and 484 (20.2%) occurred among the 2,393 women with a first pregnancy SGA (i.e. recurrent SGA). The unadjusted risk ratio (RR) for SGA recurrence given a previous history was 4.33 [95% confidence interval (CI) 3.92, 4.78] compared to no previous history.

In the main sample ($n=25,241$), different adjusted risk patterns between second pregnancy incident and recurrent SGA were observed for maternal age ($P_{difference}=.01$) and hypertension ($P_{difference}=.03$) (Table 2). Young maternal age was associated with an increased risk for incident ($P=.01$), but not recurrent SGA ($P=.35$). This increased risk for incident SGA followed a linear pattern with the greatest risk observed among women who were 14–19 years of age at delivery of their second child. Development of gestational

hypertension, preeclampsia or superimposed preeclampsia during the second pregnancy was also associated with an increased risk for incident ($P<.001$), but not recurrent SGA ($P=.48$). Among normotensive women without a previous SGA birth, 4.5% had an SGA birth at the second pregnancy. Interestingly, women with chronic hypertension who did not have an SGA birth in the first pregnancy had a similar 4.3% incidence of second pregnancy SGA, which is in contrast to the 6.4% and 11.4% among women who developed gestational hypertension or preeclampsia, respectively. Once adjusted for maternal demographics and medical conditions, women who developed gestational hypertension had an adjusted 1.9-fold increased risk and women who developed preeclampsia or superimposed preeclampsia had a 3-fold increased risk for incident SGA. Significant differences were observed in the unadjusted percent of recurrent SGA cases across categories of maternal hypertension ($P<.001$) with recurrent SGA occurring among 22.6% and 25.0% of women with preeclampsia and superimposed preeclampsia, respectively, but only 20.2% of normotensive women. However, differences did not remain significant after adjustment ($P=.48$).

Smoking during pregnancy, short stature, prepregnancy underweight, and inadequate weight gain during pregnancy were significantly associated with a greater risk of both incident and recurrent SGA. While smoking was associated with a 1.6 times increased risk of recurrent and incident SGA ($P_{\text{difference}}=.90$), the excess risk was greater for recurrent SGA, where almost 30% of smokers had a recurrent SGA compared to 20% of non-smokers. Prepregnancy BMI and gestational weight gain followed approximately linear patterns with both incident and recurrent SGA such that the greatest risk was observed among women who were underweight or gained inadequately and the lowest risk was observed among obese women or women who gained excessively during pregnancy, respectively. Although non-Hispanic black race-ethnicity, unmarried status, public insurance, and depression were associated with an unadjusted increased percent of incident and recurrent SGA cases, these risk factors were not associated with recurrence or incidence once adjusted for all other maternal demographics and medical conditions.

We tested for the addition of first pregnancy risk factor status to aid the prediction of SGA at the second pregnancy as well as accounting for maternal characteristics in the second pregnancy. Including any of the first pregnancy risk factors did not appreciably change the risk estimates for SGA recurrence ($P>.05$).

Because some of the risk factors included in the main model were determined as the pregnancy progressed (i.e. gestational diabetes, hypertensive disease, and weight gain) and may have been caused by an underlying factor also causing SGA, we performed a sensitivity analysis using only risk factors known at the start of the pregnancy (e.g. pregestational diabetes or chronic hypertension). All findings were similar with no additional risk factors identified (data not shown).

We repeated our analyses using a customized definition of SGA. Compared to the population-based reference, a similar percentage of SGA_{customized} cases were identified at the first ($n=2,085$; 8.3%) and second ($n=1,450$; 5.8%) pregnancy, although customization identified a somewhat different group of neonates as only 66.1% and 62.0%, respectively, were concordant with those identified by the population-based reference. Among women

with a first pregnancy SGA_{customized} birth, only 16.2% recurred in the second pregnancy. When SGA_{customized} was used in risk factor models, we observed a few differences from the population-based findings. First, maternal age was no longer a risk factor for incident SGA_{customized} ($P=.24$). Second, smoking was a more significant risk factor for incident SGA_{customized} (RR=1.94; 95% CI 1.48, 2.55) rather than recurrent SGA (RR=1.24; 95% CI 0.82, 1.88), although the difference between recurrence and incidence did not reach statistical significance ($P_{\text{difference}}=.07$). Maternal short stature was associated with a decreased risk for incident (RR=0.81; 95% CI 0.69, 0.95), but not recurrent SGA_{customized}. The risk pattern with prepregnancy BMI was opposite of what was observed with the population-based reference, such that SGA_{customized} risk was highest among obese mothers for both incident (RR=1.49; 95% CI 1.27, 1.75) and recurrent (RR=1.55; 95% CI 1.22, 1.97) SGA_{customized}. Lastly, gestational diabetes was associated with a significant decreased risk in incident (RR=0.58; 95% CI 0.38, 0.87) and recurrent (RR=0.19; 95% CI 0.05, 0.75) SGA_{customized}. Results for hypertension were similar to the previous model such that development of gestational hypertension or preeclampsia during the second pregnancy were similarly associated with an increased risk for incident ($P=.006$), but not recurrent SGA ($P=.38$); however, in the model using SGA_{customized} superimposed preeclampsia was associated with a 2.66 times increased risk for recurrence (95% CI 1.13, 6.23).

DISCUSSION

Main findings

Women whose first pregnancy was complicated by an SGA birth had more than a four-fold increased risk for recurrence, but nearly 80% went on to have a non-SGA birth in their second pregnancy. In contrast, less than five percent of women without a previous SGA delivery had an SGA neonate in their second pregnancy. We found that there was considerable overlap in the risk factors for SGA recurrence and incidence, but there were some notable differences. Specifically, young maternal age and development of gestational hypertension or preeclampsia were significant risk factors for second pregnancy SGA incidence, but not recurrence. However, smoking, short stature, prepregnancy underweight, and inadequate weight gain were risk factors for both. Nonetheless, while the relative risk associated with the latter characteristics was similar between recurrence and incidence, the excess risk of SGA at the second pregnancy was much greater for recurrence than incidence given the overall increased baseline risk (20.2% recurrent SGA vs. 4.7% incident SGA). Our conclusions are based on the population-based SGA as it is currently not common to use customized SGA in clinical practice in the U.S. It should be noted, however, that different risk factors were identified using a customized definition of SGA which accounts for many characteristics of the mother when identifying cases and therefore fewer risk factors were associated with SGA using this definition. Thus the choice of SGA definition may impact which characteristics clinicians use when identifying at high risk women. Interestingly, first pregnancy risk factor status did not add additional information beyond the second pregnancy status. Our finding suggests that a woman's risk for SGA recurrence in the second pregnancy was influenced by her current height, smoking, prepregnancy weight and gestational weight gain alone. As such, recommendations for weight gain and smoking cessation may be particularly effective to avoid SGA recurrence in subsequent pregnancies.

Strengths and Limitations

In this study SGA was used as a proxy for fetal growth restriction. While we used a conservative classification of SGA, the 10th percentile of a population-based reference,(11) only 9% and 5% of first and second pregnancies were classified as SGA, likely because our sample was comprised of mostly healthy women. The risk factors identified may change with a more restrictive definition of SGA, such as the 5th or 3rd percentile, although we did not have a large enough sample to examine such changes. We did, however, also use the customized definition of SGA.(12) In this population smoking and alcohol intake were very rare and there may be reporting bias in such measures,(19) furthermore it is possible that we did not have the power to detect differences by alcohol intake, which was even less prevalent than smoking. The generalizability of our findings may be limited by the homogeneity of this cohort, having little racial diversity; none the less, residual confounding may be reduced among this sample. The major strength of our study was the detailed information from the patient medical record available for a large cohort of consecutive deliveries, which sets it apart from most linked cohorts that are based on vital statistics or registry data.

Interpretation

It is well established that women with a prior SGA birth have an increased risk for recurrence;(2–4, 9, 10, 20) however, few studies have examined how risk factors for SGA in high-risk women with a prior SGA delivery differ from women without a prior SGA delivery. In our study, smoking was associated with both incidence and recurrence, and notably was the strongest observed risk factor for SGA recurrence, with approximately 50% increased risk. Smoking is a well-known risk factor for fetal growth restriction as it is thought to cause reduced oxygen availability and blood flow to the fetus.(21) Smoking cessation interventions have been shown to reduce the risk of low birthweight.(22) Most, but not all, prior studies on SGA recurrence have reported an increased risk with current smoking.(2, 9, 10)

Maternal anthropometrics are also strong predictors of birthweight. In our study, short women had increased risks for recurrent and incident SGA. Some of the risk for SGA in short women may be due to their genetic potential, resulting in constitutionally small infants, (23) although short stature may have a pathologic influence as well, potentially through a constricted uterine environment at term.(15, 24) A prior study reported that the risk for SGA recurrence increased with low prepregnancy weight and low gestational weight gain,(2) and another observed that low birthweight risk decreased with increasing prepregnancy weight regardless of prior status.(9) However, these studies did not directly compare recurrence from incidence. In our study maternal underweight and inadequate pregnancy weight gain were identified as independent risk factors for both recurrence and incidence using the population-based reference. It is important to consider that both risk factors fall on a continuum and that as the risk for SGA is decreased the risk for the opposing condition of fetal macrosomia is potentially increased with maternal obesity and excessive weight gain. (16) Prepregnancy underweight and inadequate weight gain represent possible modifiable risk factors for SGA recurrence, though most weight gain intervention studies have focused on the prevention of excessive not inadequate weight gain.(25) Women with a prior SGA

birth may represent a particularly vulnerable population in which strategies are needed to prevent inadequate weight gain for the prevention of SGA recurrence. Furthermore, it has been suggested that women with a prior adverse birth outcome, including low birthweight, receive inter-pregnancy care and counseling.(26) Both incident and recurrent SGA were increased in underweight women, suggesting that they may represent an additional group of women who may benefit from counseling and care during the inter-pregnancy period regardless of the prior birth outcome.

Our findings related to incident SGA are valuable in that they are applicable to the larger population of women whose prior pregnancy was not complicated by SGA and thus are less likely to be constitutionally small. Indeed, we identified more risk factors for incident than recurrent SGA. The strongest risk factor for incident SGA was preeclampsia, which tripled the risk (i.e. 4.5% in normotensive women vs. 11% in preeclamptic women). It is important to highlight that this association is among women whose first pregnancy was non-SGA and therefore may not meet current criteria for higher level management in a second pregnancy. A previous case-control study reported that essential hypertension and preeclampsia were associated with incident but not recurrent term-SGA.(20) This finding that such risk factors were more important for SGA incidence than recurrence is similar to our study, as the prior SGA status was the strongest predictor of SGA in the second pregnancy and other risk factors offered little information above and beyond prior SGA status. We did not observe an increased risk for incident SGA with chronic hypertension. This difference from the prior study(20) may be due to different classifications of hypertensive diseases, as our study further classified women with chronic hypertension as to whether they developed superimposed preeclampsia. Also, chronic hypertension was relatively rare in this cohort of mostly healthy women and it may have been well managed. Lastly, the previous study included only full-term deliveries.(20) Others have reported that when severe chronic hypertension is distinguished from milder forms without preeclampsia the risk for neonatal morbidity is much lower.(27) Another study, which did not distinguish between types of hypertensive diseases, recently reported that SGA recurrence was stronger among nulliparous women with hypertension in the first pregnancy.(4) We also found that younger women had an increased risk for second pregnancy incident SGA. While we did not have information on changes in paternity, which is associated with an increased risk for intrauterine growth restriction,(28) this association is independent of marital status, hypertensive disorders and interpregnancy interval. This also potentially indicates that prior SGA is such a strong risk factor for SGA in the current pregnancy that young maternal age had little impact beyond prior history among these high risk women.

Our study was unique in that we examined recurrence using both population-based and customized SGA. We examined SGA using two definitions and found that results were similar with the exception of associations with maternal age, smoking, stature and prepregnancy BMI. The customized model takes constitutional variation in birthweight due to maternal height and weight into account, so it is not surprising that short maternal stature and underweight are not associated with SGAcustomized. However, it is unclear if customization,(29) particularly for weight,(30) aids in the identification of neonates at risk for adverse perinatal outcomes. Thus we presented results both ways, as there is wide interest in understanding the clinical utility of the more recently developed customized

birthweight centiles. Our findings further highlight the importance of identification of pathologic versus constitutional SGA as the risk factors identified in our models differed slightly based on the definition. For example, whether short stature has a pathological effect on birthweight is unclear(15, 24) and including maternal height in the customization also assumes that the mother herself was not stunted. Moreover, while some have suggested that SGA infants of obese mothers identified using customized percentiles may be at higher risk for perinatal mortality,(31) these results have yet to be replicated.

CONCLUSIONS

Our study suggests that the risk profiles for SGA in the second pregnancy differed according to women's first pregnancy SGA status. Recurrence was associated with smoking, short stature, underweight, and inadequate weight gain. Regardless of the SGA definition used, few risk factors informed a woman's risk for recurrence beyond her prior history. However, most observed risks are potentially modifiable (e.g. smoking, prepregnancy weight, and weight gain) suggesting avenues for intervention and possible prevention of SGA in subsequent pregnancies.

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Abbreviations

BMI	Body mass index
CI	Confidence interval
IOM	Institute of Medicine
ICD9	International Classification of Diseases, ninth revision
RR	risk ratio
SGA	small-for-gestational-age

References

1. Kinzler WL, Kaminsky L. Fetal growth restriction and subsequent pregnancy risks. *Semin Perinatol.* 2007; 31(3):126–34. [PubMed: 17531894]
2. Okah FA, Cai J, Dew PC, Hoff GL. Risk factors for recurrent small-for-gestational-age birth. *Am J Perinatol.* 2010; 27(1):1–7. [PubMed: 19670131]
3. Ananth CV, Kaminsky L, Getahun D, Kirby RS, Vintzileos AM. Recurrence of fetal growth restriction in singleton and twin gestations. *J Matern Fetal Neonatal Med.* 2009; 22(8):654–61. [PubMed: 19557663]
4. Voskamp BJ, Kazemier BM, Ravelli AC, Schaaf J, Mol BW, Pajkrt E. Recurrence of small-for-gestational-age pregnancy: analysis of first and. *Am J Obstet Gynecol.* 2013; 208(5):374, e1–6. [PubMed: 23419319]
5. Raine T, Powell S, Krohn MA. The risk of repeating low birth weight and the role of prenatal care. *Obstet Gynecol.* 1994; 84(4):485–9. [PubMed: 8090380]

6. Khoury MJ, Calle EE, Joesoef RM. Recurrence of low birth weight in siblings. *J Clin Epidemiol.* 1989; 42(12):1171–8. [PubMed: 2585008]
7. Bratton SL, Shoultz DA, Williams MA. Recurrence risk of low birthweight deliveries among women with a prior very low birthweight delivery. *Am J Perinatol.* 1996; 13(3):147–50. [PubMed: 8688104]
8. McCowan L, Horgan RP. Risk factors for small for gestational age infants. *Best Pract Res Clin Obstet Gynaecol.* 2009; 23(6):779–93. [PubMed: 19604726]
9. Bakewell JM, Stockbauer JW, Schramm WF. Factors associated with repetition of low birthweight: Missouri longitudinal. *Paediatr Perinat Epidemiol.* 1997; 11 (Suppl 1):119–29. [PubMed: 9018721]
10. Read AW, Stanley FJ. Small-for-gestational-age term birth: the contribution of socio-economic. *Paediatr Perinat Epidemiol.* 1993; 7(2):177–94. [PubMed: 8516191]
11. Kramer MS, Platt RW, Wen SW, Joseph KS, Allen A, Abrahamowicz M, et al. A new and improved population-based Canadian reference for birth weight for gestational age. *Pediatrics.* 2001; 108(2):E35. [PubMed: 11483845]
12. Gardosi J, Francis A. A customized standard to assess fetal growth in a US population. *Am J Obstet Gynecol.* 2009; 201(1):25, e1–7. [PubMed: 19576371]
13. Hadlock FP, Harrist RB, Martinez-Poyer J. In utero analysis of fetal growth: a sonographic weight standard. *Radiology.* 1991; 181(1):129–33. [PubMed: 1887021]
14. Fryar CD, Gu Q, Ogden CL. National Center for Health Statistics. Anthropometric reference data for children and adults: United States, 2007–2010. *Vital Health Stat.* 2012; 11(252)
15. Zhang X, Mumford SL, Cnattingius S, Schisterman EF, Kramer MS. Reduced birthweight in short or primiparous mothers: physiological or pathological? *BJOG.* 2010; 117(10):1248–54. [PubMed: 20618317]
16. *Weight Gain During Pregnancy: Reexamining the Guidelines.* Washington, DC: Institute of Medicine and National Research Council; 2009.
17. Bodnar LM, Hutcheon JA, Platt RW, Himes KP, Simhan HN, Abrams B. Should gestational weight gain recommendations be tailored by maternal characteristics? *Am J Epidemiol.* 2011; 15;174(2):136–46.
18. Zou G. A Modified Poisson Regression Approach to Prospective Studies with Binary Data. *Am J Epidemiol.* 2004; 159(7):702–6. [PubMed: 15033648]
19. Dietz PM, Homa D, England LJ, Burley K, Tong VT, Dube SR, et al. Estimates of nondisclosure of cigarette smoking among pregnant and nonpregnant women of reproductive age in the United States. *Am J Epidemiol.* 2011; 173(3):355–9. [PubMed: 21178103]
20. Read AW, Stanley FJ. A comparison of recurrent and isolated small-for-gestational-age term births. *Paediatr Perinat Epidemiol.* 1991; 5(2):138–56. [PubMed: 2052477]
21. Abbott LC, Winzer-Serhan UH. Smoking during pregnancy: lessons learned from epidemiological studies and experimental studies using animal models. *Crit Rev Toxicol.* 2012; 42(4):279–303. [PubMed: 22394313]
22. Lumley J, Chamberlain C, Dowswell T, Oliver S, Oakley L, Watson L. Interventions for promoting smoking cessation during pregnancy. *Cochrane Database Syst Rev.* 2009; (3):Cd001055. [PubMed: 19588322]
23. Zhang X, Cnattingius S, Platt RW, Joseph KS, Kramer MS. Are babies born to short, primiparous, or thin mothers “normally” or “abnormally” small? *J Pediatr.* 2007; 150(6):603–7. 7.e1–3. [PubMed: 17517243]
24. Overpeck MD, Hediger ML, Zhang J, Trumble AC, Klebanoff MA. Birth weight for gestational age of Mexican American infants born in the United States. *Obstet Gynecol.* 1999; 93(6):943–7. [PubMed: 10362159]
25. Hill B, Skouteris H, Fuller-Tyszkiewicz M. Interventions designed to limit gestational weight gain: a systematic review of theory and meta-analysis of intervention components. *Obes Rev.* 2013; 14(6):435–50. [PubMed: 23534901]
26. Johnson K, Posner SF, Biermann J, Cordero JF, Atrash HK, Parker CS, et al. Recommendations to improve preconception health and health care--United States. A report of the CDC/ATSDR Preconception Care Work Group and the Select Panel on Preconception Care. *MMWR Recomm Rep.* 2006; 55(Rr-6):1–23. [PubMed: 16617292]

27. McCowan LM, Buist RG, North RA, Gamble G. Perinatal morbidity in chronic hypertension. *Br J Obstet Gynaecol.* 1996; 103(2):123–9. [PubMed: 8616127]
28. Robillard PY, Dekker G, Chaouat G, Hulsey TC, Saftlas A. Epidemiological studies on primipaternity and immunology in preeclampsia--a statement after twelve years of workshops. *J Reprod Immunol.* 2011; 89(2):104–17. [PubMed: 21543120]
29. Larkin JC, Hill LM, Speer PD, Simhan HN. Risk of morbid perinatal outcomes in small-for-gestational-age pregnancies: customized compared with conventional standards of fetal growth. *Obstet Gynecol.* 2012; 119(1):21–7. [PubMed: 22183207]
30. Sjaarda LA, Albert PS, Mumford SL, Hinkle SN, Mendola P, Laughon SK. Customized large-for-gestational-age birthweight at term and the association with adverse perinatal outcomes. *Am J Obstet Gynecol.* 2013
31. Gardosi J, Clausson B, Francis A. The value of customised centiles in assessing perinatal mortality risk associated with parity and maternal size. *BJOG.* 2009; 116(10):1356–63. [PubMed: 19538413]

Table 1

Maternal characteristics in the second pregnancy by small-for-gestational-age birthweight status at the first pregnancy, Consecutive Pregnancy Study, 2002–2010, $n=25,241$.

Second Pregnancy Characteristics	First Pregnancy		P
	Non-SGA ($n=22,848$) <i>n</i> (%)	SGA ($n=2,393$) <i>n</i> (%)	
SGA^a			<.001
No	21,781 (95.3)	1,909 (79.8)	
Yes	1,067 (4.7)	484 (20.2)	
Age, years			<.001
14–19	728 (3.2)	117 (4.8)	
20–24	7246 (31.7)	803 (33.6)	
25–29	10693 (46.8)	1014 (42.4)	
30–34	3286 (14.4)	337 (14.1)	
35–49	895 (3.9)	122 (5.1)	
Race-ethnicity			<.001
Non-Hispanic white	20351 (89.1)	2027 (84.7)	
Non-Hispanic black	83 (0.4)	23 (1.0)	
Hispanic	1851 (8.1)	252 (10.5)	
Asian/Pacific Islander	468 (2.1)	74 (3.1)	
Other	95 (0.4)	17 (0.7)	
Marital status			<.001
Married	20617 (90.2)	2047 (85.5)	
Non-married	2231 (9.8)	346 (14.5)	
Insurance			<.001
Private	16959 (74.2)	1650 (69.0)	
Public	5889 (25.8)	743 (31.1)	
Smoking during pregnancy			<.001
No	22284 (97.5)	2259 (94.4)	
Yes	564 (2.5)	134 (5.6)	
Alcohol during pregnancy			.004
No	22506 (98.5)	2339 (97.7)	
Yes	342 (1.5)	54 (2.3)	
Short stature			<.001
No	18778 (82.2)	1705 (71.3)	
Yes	4070 (17.8)	688 (28.8)	
Prepregnancy weight status			<.001
Underweight	1148 (5.0)	201 (8.4)	
Normal weight	13172 (57.7)	1380 (57.7)	
Overweight	5056 (22.1)	484 (20.2)	
Obese	3472 (15.2)	328 (13.7)	
Gestational weight gain adequacy			<.001

Second Pregnancy Characteristics	First Pregnancy		P
	Non-SGA (n=22,848) n (%)	SGA (n=2,393) n (%)	
Inadequate	5097 (22.3)	788 (32.9)	
Within	6318 (27.7)	686 (28.7)	
Excessive	11433 (50.0)	919 (38.4)	
Diabetes			.07
None	21783 (95.3)	2298 (96.0)	
Gestational	694 (3.0)	53 (2.2)	
Prepregnancy	371 (1.6)	42 (1.8)	
Hypertension			.03
Normotensive	21600 (94.5)	2228 (93.1)	
Gestational hypertension	497 (2.2)	72 (3.0)	
Preeclampsia	413 (1.8)	53 (2.2)	
Chronic hypertension	282 (1.2)	36 (1.5)	
Superimposed preeclampsia	56 (0.3)	4 (0.2)	
Asthma			.08
No	20958 (91.7)	2170 (90.7)	
Yes	1890 (8.3)	223 (9.3)	
Thyroid disease			.34
No	21657 (94.8)	2279 (95.2)	
Yes	1191 (5.2)	114 (4.8)	
Depression or other mental health condition			.05
No	20342 (89.0)	2099 (87.7)	
Yes	2506 (11.0)	294 (12.3)	
Interpregnancy interval, months			<.001
<12	5948 (26.0)	742 (31.0)	
12–<18	6263 (27.4)	576 (24.1)	
18–23	4803 (21.0)	470 (19.6)	
>23	5834 (25.5)	605 (25.3)	

SGA, small-for-gestational-age.

^aSGA defined using the 10th percentile of a population-based reference.

Unadjusted percent and adjusted^c risk of second pregnancy incident and recurrent small-for-gestational-age birth by second pregnancy characteristics, Consecutive Pregnancy Study, 2002–2010, *n*=25,241.

Table 2

Second Pregnancy Risk Factors	Incident SGA ^b			Recurrent SGA ^b			<i>P</i> ^c	<i>P</i> ^d difference
	%	RR (95% CI)	<i>P</i> ^c	%	RR (95% CI)	<i>P</i> ^c		
Age, years			.01				.35	.01
14–19	(7.8)	1.48 (1.09, 2.02)		(19.7)	0.75 (0.50, 1.12)			
20–24	(5.5)	1.21 (1.06, 1.39)		(20.2)	0.89 (0.74, 1.08)			
25–29	(4.2)	1.00 (Referent)		(20.6)	1.00 (Referent)			
30–34	(3.9)	0.94 (0.78, 1.14)		(18.7)	0.93 (0.73, 1.19)			
35–49	(3.9)	0.91 (0.65, 1.27)		(23.0)	1.21 (0.87, 1.70)			
Race-ethnicity			.20				.46	.21
Non-Hispanic white	(4.5)	1.00 (Referent)		(20.0)	1.00 (Referent)			
Non-Hispanic black	(12.1)	2.25 (1.26, 4.01)		(30.4)	1.38 (0.75, 2.53)			
Hispanic	(5.8)	1.03 (0.83, 1.28)		(24.2)	1.01 (0.78, 1.30)			
Asian/Pacific Islander	(6.0)	1.32 (0.92, 1.89)		(17.6)	0.71 (0.44, 1.14)			
Other	(3.2)	0.67 (0.22, 2.01)		(23.5)	1.08 (0.51, 2.27)			
Marital status			.36				.97	.57
Married	(4.4)	1.00 (Referent)		(19.8)	1.00 (Referent)			
Non-married	(6.8)	1.10 (0.90, 1.35)		(22.5)	1.00 (0.78, 1.29)			
Insurance			.52				.08	.30
Private	(4.4)	1.00 (Referent)		(18.8)	1.00 (Referent)			
Public	(5.6)	1.05 (0.91, 1.21)		(23.4)	1.19 (0.98, 1.44)			
Smoking during pregnancy			.005				.01	.90
No	(4.5)	1.00 (Referent)		(19.7)	1.00 (Referent)			
Yes	(9.9)	1.64 (1.22, 2.19)		(29.9)	1.59 (1.17, 2.17)			
Alcohol during pregnancy			.57				.94	.65
No	(4.6)	1.00 (Referent)		(20.2)	1.00 (Referent)			
Yes	(6.4)	1.14 (0.75, 1.73)		(22.2)	0.98 (0.60, 1.60)			
Short stature			<.001				<.001	.20
No	(4.3)	1.00 (Referent)		(17.8)	1.00 (Referent)			

Second Pregnancy Risk Factors	Incident SGA ^b			Recurrent SGA ^b			<i>P</i> ^c	<i>P</i> ^d difference
	%	RR (95% CI)	<i>P</i> ^c	%	RR (95% CI)	<i>P</i> ^c		
Yes	(6.4)	1.34 (1.16, 1.54)	<.001	(26.6)	1.54 (1.31, 1.82)	.004	.77	
Prepregnancy weight status								
Underweight	(7.8)	1.32 (1.07, 1.64)		(30.9)	1.30 (1.03, 1.64)			
Normal weight	(5.0)	1.00 (Referent)		(21.2)	1.00 (Referent)			
Overweight	(4.1)	0.91 (0.77, 1.06)		(16.7)	0.84 (0.67, 1.05)			
Obese	(3.3)	0.64 (0.52, 0.78)		(14.6)	0.73 (0.55, 0.97)			
Gestational weight gain adequacy			<.001			<.001	.49	
Inadequate	(7.4)	1.41 (1.22, 1.64)		(28.1)	1.33 (1.10, 1.60)			
Within	(5.1)	1.00 (Referent)		(20.6)	1.00 (Referent)			
Excessive	(3.2)	0.63 (0.54, 0.74)		(13.3)	0.69 (0.55, 0.87)			
Diabetes			.11			.03	.13	
None	(4.7)	1.00 (Referent)		(20.4)	1.00 (Referent)			
Gestational	(4.0)	0.82 (0.57, 1.19)		(11.3)	0.48 (0.22, 1.01)			
Prepregnancy	(3.0)	0.64 (0.35, 1.15)		(21.4)	1.20 (0.67, 2.16)			
Hypertension			<.001			.48	.03	
Normotensive	(4.5)	1.00 (Referent)		(20.2)	1.00 (Referent)			
Gestational hypertension	(6.4)	1.90 (1.35, 2.67)		(20.8)	1.47 (0.94, 2.31)			
Preeclampsia	(11.4)	3.14 (2.38, 4.13)		(22.6)	1.34 (0.83, 2.17)			
Chronic hypertension	(4.3)	1.24 (0.71, 2.17)		(19.4)	1.25 (0.63, 2.44)			
Superimposed preeclampsia	(8.9)	2.98 (1.28, 6.94)		(25.0)	1.64 (0.39, 6.99)			
Asthma			.18			.91	.45	
No	(4.6)	1.00 (Referent)		(20.3)	1.00 (Referent)			
Yes	(5.3)	1.16 (0.95, 1.41)		(19.7)	1.02 (0.77, 1.33)			
Thyroid disease			.68			.99	.82	
No	(4.7)	1.00 (Referent)		(20.3)	1.00 (Referent)			
Yes	(4.4)	1.06 (0.81, 1.40)		(18.4)	1.00 (0.67, 1.51)			
Depression or other mental health condition			.16			.09	.03	
No	(4.6)	1.00 (Referent)		(20.6)	1.00 (Referent)			
Yes	(5.6)	1.14 (0.96, 1.37)		(17.8)	0.81 (0.62, 1.05)			
Interpregnancy interval, months			.07			.06	.47	

Second Pregnancy Risk Factors	Incident SGA ^b			Recurrent SGA ^b			<i>P</i> ^c	<i>P</i> ^d difference
	%	RR (95% CI)	<i>P</i> ^c	%	RR (95% CI)	<i>P</i> ^c		
<12	(4.6)	0.96 (0.80, 1.14)		(18.7)	0.91 (0.72, 1.14)			
12–<18	(4.7)	1.10 (0.92, 1.30)		(18.1)	0.90 (0.71, 1.15)			
18–23	(4.3)	1.00 (Referent)		(20.6)	1.00 (Referent)			
>23	(5.0)	1.17 (0.99, 1.40)		(23.8)	1.18 (0.94, 1.47)			

CI, confidence interval; RR, risk ratio; SGA, small-for-gestational-age.

^aModel adjusted for all characteristics shown in table.

^bSGA defined using the 10th percentile of a population-based reference.

^c*P* represents the global significance of the maternal characteristics within the respective recurrent or incident SGA group.

^d*P* difference represents the interaction between recurrent and incident SGA for the respective characteristic.