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The association between parity and birthweight in a longitudinal consecutive pregnancy cohort

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Abstract

Background—Nulliparity is associated with lower birthweight, but few studies have examined how within mother changes in risk-factors impact this association.

Methods—We used longitudinal electronic medical record data from a hospital-based cohort of consecutive singleton live births from 2002–2010 in Utah. To reduce bias from unobserved pregnancies primary analyses were limited to 9,484 women who entered nulliparous from 2002–2004 with 23,380 pregnancies up to parity 3. Unrestricted secondary analyses used 101,225 pregnancies from 45,212 women with pregnancies up to parity 7. We calculated gestational age and sex-specific birthweight z-scores with nulliparas as the reference. Using linear mixed models, we estimated birthweight z-score by parity adjusting for pregnancy-specific sociodemographics, smoking, alcohol, prepregnancy body mass index, gestational weight gain, and medical conditions.

Results—Compared to nulliparas, infants of primiparas were larger by 0.20 unadjusted z-score units [95% confidence interval (CI) 0.18, 0.22]; the adjusted increase was similar at 0.18 z-score units [95% CI 0.15, 0.20]. Birthweight continued to increase up to parity 3, but with a smaller difference, (parity 3 vs. 0 $\beta=0.27$ [95% CI 0.20, 0.34]). In the unrestricted secondary sample, there was significant departure in linearity from parity 1 to 7 ($P<0.001$); birthweight increased only up to parity 4, (parity 4 vs. 0 $\beta=0.34$ [95% CI 0.31, 0.37]).

Conclusions—The association between parity and birthweight was non-linear with the greatest increase observed between first and second-born infants of the same mother. Adjustment for changes in weight or chronic diseases did not change the relationship between parity and birthweight.

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Keywords

pregnancy; birthweight; parity; siblings; birth order

Maternal parity is a well-recognized predictor of infant birthweight, with the lowest birthweights observed among infants born to nulliparous women.^{1–6} However, few epidemiological studies have addressed the biological reason behind such association. Some differences observed in birthweight by parity may be partially due to selection bias in prior cross-sectional studies, as some nulliparous women do not go on to have other children,¹ however, birthweight differences across parity have also been shown in prior sibling analyses.^{1–6} One prior study reported a birthweight difference of 118 g between first and second born infants; however, when limited only to sibling pairs the difference was even greater at 138 g.⁷ Another sibling study reported that the first birth was the lightest, but also that the correlation between sibling pairs was less for the first two births than subsequent sibling pairs.²

Lower birthweights among first born infants may be a direct consequence of physiological conditions associated with nulliparity.⁸ It has been hypothesized that the first pregnancy primes the body and with each subsequent pregnancy the body is more efficient.^{9, 10} Many other maternal and environmental factors are known to affect birthweight and many such factors also vary across a woman's reproductive lifespan. Maternal prepregnancy weight or weight gain during pregnancy,^{11, 12} medical conditions or pregnancy complications, which increase in risk with maternal age such as diabetes or hypertension,¹³ changes in other behavioral factors such as smoking, and paternity have all been reported to change with increasing parity.^{1, 14, 15} Most prior studies on parity and birthweight have been limited in the number and type of potential covariates that have been included in their analysis.⁷ Thus, it is unclear how much of the association between increasing parity and birthweight is due to within woman changes in risk factors between pregnancies. Given the importance of birthweight in predicting long-term health outcomes,¹⁶ it is important to better understand this association.

In the present study, we utilized a longitudinal cohort of women with consecutive pregnancies to comprehensively examine the relation between maternal parity and birthweight among siblings while including a wide range of potentially confounding variables. We hypothesized that differences in birthweight by parity would be attenuated after accounting for time-varying maternal and pregnancy characteristics within mothers.

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. The cohort included 51,086 women with 2 deliveries after 20 weeks of gestation from 2002–2010 at 20 Utah hospitals with parity at study entry ranging from 0 to 14. Detailed information was extracted for each delivery from the electronic medical records and *International Classification of Diseases, Ninth Revision (ICD9)* discharge codes. All successive pregnancies were linked using a unique maternal ID. Institutional review board approval was obtained by all participating institutions.

Of the 51,086 women, 39,974 contributed two pregnancies to the study, 9,792 contributed three, 1,247 contributed four, 71 contributed five, and 2 contributed six, resulting in 114,679 pregnancies. To ensure that unknown reproductive history (i.e. left censored data) did not bias our results, in our primary analyses we included only women who were nulliparous at

study entry ($n=27,741$). Similarly, because women who entered the study in the later years may have been more likely to have future pregnancies censored (i.e. right censored data), we further restricted the primary analyses to parity 0 to 3 pregnancies of nulliparas who entered the study in 2002–2004 ($n=10,727$). For this analysis we excluded women who at any point during the study had an observed multiple gestation pregnancy¹⁷ ($n=334$; 3.1%) or perinatal death¹⁸ ($n=117$; 1.1%). We also excluded women if infant birthweight was missing ($n=5$; 0.05%) or determined to be implausible based on the sex and gestational age ($n=3$; 0.03%) of the infant,¹⁹ or if there were missing covariate data ($n=795$; 7.7%) for any of their pregnancies. Of the women excluded for missing data, most were excluded due to missing height ($n=314$; 3.1%), prepregnancy weight ($n=373$; 3.6%), or weight at delivery ($n=288$; 2.8%), but there was no significant difference in the mean birthweight z-score ($P>0.05$). This primary sample comprised 23,380 pregnancies of parity 0 to 3 from 9,484 women.

Parity, defined as the number of previous deliveries after 20 weeks of gestation, infant birthweight (g), gestational age (weeks) estimated according to best obstetrical estimate,²⁰ and sex were recorded in the medical record. Infant gestational age and sex-specific birthweight z-scores were calculated with smoothed loess curves using infants of nulliparas as the reference, which made birthweights comparable across gestational ages. In this sample, at 40 weeks gestation, a 0.1 birthweight z-score change represented a birthweight change of 38 g for females and 39 g for males.

Maternal age, race-ethnicity, marital status, insurance status, smoking during pregnancy, alcohol intake during pregnancy, height, prepregnancy weight, and delivery weight were obtained from the medical record. Prepregnancy body mass index (BMI; kg/m^2) was calculated from height and prepregnancy weight and categorized $<18.5 \text{ kg}/\text{m}^2$, $18.5\text{--}24.9 \text{ kg}/\text{m}^2$, $25.0\text{--}29.9 \text{ kg}/\text{m}^2$, $30.0\text{--}34.9 \text{ kg}/\text{m}^2$, $35.0\text{--}39.9 \text{ kg}/\text{m}^2$, and $\geq 40.0 \text{ kg}/\text{m}^2$. As previously described,²¹ we calculated a ratio of total weight gain for gestational age and classified women as having gained below, within, or above the 2009 Institute of Medicine (IOM) recommended range using first trimester weight gain assumptions of 2 kg for mothers with a prepregnancy BMI $<30.0 \text{ kg}/\text{m}^2$ and 1.25 kg for mothers with a prepregnancy BMI $\geq 30.0 \text{ kg}/\text{m}^2$.²² Interpregnancy interval was calculated as the time between last menstrual period and delivery of the prior pregnancy.

Maternal medical history was obtained from the medical record and supplemented with ICD9 discharge codes (Appendix I). The following conditions were included: diabetes, hypertension, asthma, thyroid disease, depression or another mental health condition, and other chronic disease including kidney disease, gastrointestinal disease, heart disease, or HIV. 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 it at all subsequent pregnancies. Consistency checks were performed using repeated pregnancies.

Differences in birthweight z-score across sample characteristics were assessed using ANOVA. All modeling of the relation between parity and birthweight z-score was completed using linear mixed models specified with a random intercept and an unstructured covariance. The random intercept allowed the regression line to shift up or down by mother. Models were adjusted for time-invariant and updated pregnancy-specific covariates and fit with a categorical variable for parity as shown in equation 1:

$$\text{birthweight } z\text{-score}_{ij} = \beta_0 + \beta_1(\text{parity}=1)_{ij} + \beta_2(\text{parity}=2)_{ij} + \beta_3(\text{parity}=3)_{ij} + \beta_k X_{ij} + b_j + \varepsilon_{ij} \quad (\text{eq. 1})$$

for $i=1, \dots, 4^{\text{th}}$ pregnancy and $j=1, \dots, 9,484^{\text{th}}$ woman.

To better understand how the different types of variables impacted the association between parity and birthweight we presented the unadjusted model and three adjusted models: A) sociodemographic variables; B) Model A plus anthropometrics, smoking, and drinking during pregnancy; C) Model B plus medical conditions. We completed multiple sensitivity analyses. First, to ensure robustness of our results based on the complete-subject analysis, mothers with missing covariate data at some, but not all pregnancies were included in the sensitivity analysis ($n=9,948$). Second, because pregnancies of preterm deliveries (<37 gestational weeks) are more likely to be complicated or growth restricted,²³ only mothers of full-term infants were used in the sensitivity analysis ($n=8,192$).

To investigate the role of prepregnancy weight, interpregnancy interval, and maternal age at first delivery in the association between parity and birthweight, we classified women at each pregnancy (excluding the first in the study) according to their weight change or time between pregnancies and tested for a multiplicative interaction with parity.

Because few studies have examined the associations between parity and birthweight at higher order parity we relaxed our inclusion criteria for secondary analyses and included consecutive pregnancies up to parity 7 regardless of parity at study entry or year of entry. This secondary sample consisted of 101,225 pregnancies from 45,212 women. We examined the longitudinal unadjusted birthweight z-score by parity according to parity at study entry and the total number of pregnancies contributed to the study. Prior to modeling the association between parity and birthweight in this secondary sample, we confirmed that multiparous women entering the study had similar patterns with birthweight as nulliparous women regardless of their parity at entry ($P=0.34$) and that the relation between parity and birthweight did not differ for women with many pregnancies during the study period ($P=0.39$).

In the secondary analysis that included all women regardless of parity at study entry, we tested for a departure from linearity between parity 1 to 7 and birthweight z-score using a likelihood ratio test with the reduced model including only β_1 and β_2 and the full model that included a linear term for parity 1 and indicator variables for parity 3 to 7 as shown in equation 2:

$$\begin{aligned} \text{birthweight } z\text{-score}_{ij} = & \beta_0 + \beta_1(\text{parity} > 0)_{ij} + \beta_2(\text{parity} - 1 | \text{parity} > 1)_{ij} + \beta_3(\text{parity} = 3)_{ij} + \beta_4(\text{parity} = 4)_{ij} + \\ & \beta_5(\text{parity} = 5)_{ij} + \beta_6(\text{parity} = 6)_{ij} + \beta_7(\text{parity} = 7)_{ij} + \beta_k X_{ij} + b_j + \varepsilon_{ij} \end{aligned} \quad (\text{eq. } 2)$$

for $i=1, \dots, 6^{\text{th}}$ pregnancy and $j=1, \dots, 45,212^{\text{ed}}$ woman.

We used SAS version 9.3 (Cary, NC) and Stata version 12.1 (College Station, TX) and considered P -values <0.05 significant for main effects and interactions.

RESULTS

Overall, the primary study sample of women who were nulliparous and entered the study between 2002–2004 included predominantly white (89.3%), married (85.1%) women with private insurance (76.3%), who tended to be healthy, as few women smoked (1.4%) or drank alcohol (1.8%) during pregnancy, and most had a BMI between 18.5–24.9 (65.0%), and were normotensive (88.7%), or non-diabetic (97.5%). Birthweight z-score differed across most maternal characteristics (Table 1).

The unadjusted and adjusted associations between parity and birthweight z-score are presented in Table 2. The greatest increase in birthweight z-score was observed between parity 0 and 1 although birthweight continued to increase between parity 1 and 3. Adjusting for sociodemographic, lifestyle, anthropometrics, and medical conditions slightly attenuated

the association, but the patterns remained the same. No significant differences were observed when the sample was limited to women who never had an observed preterm delivery or had some missing covariate data, such that the difference between nulliparas and primiparas was 0.18 [95% CI 0.16, 0.20] and 0.19 [95% CI 0.17, 0.22] z-score units, respectively.

We explored prepregnancy weight changes, interpregnancy interval between pregnancies, and age at first delivery and the relation between parity and birthweight. Prepregnancy weight change between the first and second pregnancies was slightly skewed to the right with a median of 1.4 kg [interquartile range -0.9, 5.4], corresponding to an interpregnancy interval of 1.6 years [interquartile range 1.1, 2.4]. Women were classified at each pregnancy (starting at the second) into a category of weight change: lost >2 kg (19.3%), remained stable within 2 kg (35.8%), or gained >2 kg (44.9%). The association between parity and birthweight z-score did not depend on weight change status between pregnancies ($P=0.06$). However, compared to women whose prepregnancy weight remained stable between pregnancies, the association between parity and birthweight was lower by 0.03 [95% CI 0.01, 0.07] for women who became lighter and higher by 0.06 [95% CI 0.02, 0.10] z-score units for women who became heavier. The majority of women had an interpregnancy interval between 12–24 months (45.2%), while 20.5% and 34.2% had a short (<12 months) or long (>24 months) interval, respectively. The relationship between parity and birthweight z-score was modified by the interpregnancy interval between pregnancies ($P<0.001$). At parity 1, the mean birthweight z-score was highest among infants of women with an interval of 12–24 months at 0.26 units [95% CI 0.24, 0.29]. The mean birthweight z-score among women with a short and long interval was 0.18 units [95% CI 0.14, 0.21] and 0.24 units [95% CI 0.20, 0.28], respectively. There was a modest change from parity 1 to parity 3 for women with an interpregnancy interval of 12–24 months such that at parity 3 the mean z-score was 0.34 [95% CI 0.25, 0.43]. Comparatively, for women with a short interval birthweight z-score decreased with increasing parity such that the average z-score was 0.18 [95% CI 0.06, 0.29], but for women with a long interval birthweight z-score increased with increasing parity such that at parity 3 the mean z-score was 0.53 [95% CI 0.32, 0.73] (data not shown). Despite a large sample with substantial statistical power, no significant interaction between age at first delivery and parity was observed ($P=0.19$).

In the secondary analysis that included consecutive pregnancies up to parity 7 regardless of parity at study entry or year of entry, no significant differences were observed in the birthweight z-score patterns across parity according to either parity at study entry ($P=0.34$) or the number of pregnancies contributed to the study ($P=0.39$). The longitudinal unadjusted birthweight z-scores according to the number of pregnancies contributed and parity at study entry for the full secondary sample are demonstrated in Figure 1. The average z-score increased between parity 0 and 1, after which the change between pregnancies was less pronounced, but remained variable due to smaller sample sizes. We rejected the null hypothesis that the association was linear from parity 1 to 7 ($P=0.008$ for unadjusted; $P=0.01$ for adjusted models) and therefore all secondary sample models were fit with parity as a categorical variable. The mean unadjusted and adjusted birthweight z-score by parity in the secondary sample are shown in Table 3. Similar patterns between parity 0 to 3 were observed for the primary and secondary analysis. Adjustment for covariates had a greater impact at higher than lower parity and data indicated a slight plateau in birthweight z-score from parity 4 to 7.

COMMENTS

In a longitudinal cohort of women with consecutive pregnancies, the greatest increase in birthweight was observed between first and second-born infants of the same mother. While

we hypothesized that there would be a large degree of attenuation due to confounding factors, maternal demographic, medical conditions, and weight-related changes that occurred between pregnancies did not explain the observed association. To reduce the potential for bias due to unobserved past or future pregnancies, we used a subsample of the cohort for our main analyses that comprised only women who were nulliparous at study entry and entered in the first few years of the cohort. In this sample, parity continued to increase birthweight up to parity 3. We observed a similar pattern in the less restrictive full cohort and further found that the relationship between parity and birthweight was non-linear and appeared to stabilize between parity 4 and 7. The longitudinal nature of this cohort of consecutive pregnancies and the wide-range of covariates obtained from the electronic medical record allowed for determination of the association of parity on birthweight while accounting for the many changes that occur between a woman's pregnancies.

The difference in birthweight between nulliparas and primiparas has been reported in prior sibling studies;^{2-5, 7} however, few have adjusted for the many important within woman time-varying factors that may affect this relationship. One study which included the first two pregnancies of each mother adjusted for maternal race-ethnicity and changes in maternal age, prepregnancy weight and blood pressure, and infant gestational age and sex, and observed a mean adjusted difference of 156 g between nulliparas and primiparas.⁷ Our study adds to this body of knowledge by including adjustment for a wider-range of maternal medical and behavioral variables, and importantly prepregnancy weight and gestational weight gain. We observed a smaller fully-adjusted difference of 0.18 birthweight z-score units, which translates to approximately 68 g. Associations were slightly attenuated with adjustment for confounding variables that potentially changed across pregnancies. Lastly, our results were robust to multiple sensitivity analyses and similar when we utilized the full cohort or a restrictive sample designed to minimized bias from left and right censored data.

Importantly, parity was one of a number of factors which significantly impacted infant birthweight in this study. The effect size of nulliparity compared to primiparity (0.18 z-score units) was similar to the adjusted mean birthweight observed with preeclampsia (-0.23 z-score units), prepregnancy underweight (-0.19 z-score units), but was only about half of that observed with maternal smoking (-0.23 z-score units) (data not shown). Nonetheless, it is important to note that while the latter maternal conditions or behaviors are associated with pathological changes in birthweight that may lead to long-term neonatal morbidities, our study does not evaluate if increased birthweight between nulliparas and primiparas leads to better or worse long-term outcomes. Prior sibling studies have also reported an increased risk for congenital malformations,²⁴ sudden infant death syndrome,⁴ and perinatal mortality among infants born to nulliparous mothers.³ Interestingly, stratified analyses revealed that postpartum weight change did not modify the relationship between parity and birthweight. As expected,¹² neonates of women who returned to their prepregnancy weight before their next pregnancy weighed less on average than neonates born to women who retained or gained weight between pregnancies. While accounting for changes in chronic diseases or medical complications, similar to other studies we found that at parity 1 mean birthweight was highest among women with an interpregnancy interval of 12–24 months.^{25, 26} Interestingly, we found that interpregnancy interval modified the relationship with parity, such that birthweight decreased with increasing parity for women with a short interval, but also the gains with parity were even greater for women with a long interval. We did not, however, have information on paternity in this cohort, thus it is possible that the association with long interpregnancy intervals may be biased due to changes in paternity,^{14, 27} although a higher proportion of women in this cohort was married than the national average²⁸ and changes in marital status between pregnancies were rare.

The biological etiology for nulliparity causing lower birthweight may be that physiologic changes which occur during pregnancy to facilitate fetal growth incompletely reverse postpartum, thereby creating a more efficient basis for the establishment and growth of the subsequent pregnancy.^{29, 30} Specifically, uteroplacental blood flow, which is responsible for delivering oxygen and nutrients to the fetus, is greater during subsequent pregnancies compared to the nulligravid uterus.^{31, 32} In addition, there may be structural factors which limit uterine capacity in the first pregnancy,³³ after which increases in uterine size and protein content occur.³⁰ Furthermore, first born infants may be exposed to a different maternal immune environment, contributing to relative growth restriction, compared to subsequent pregnancies with consistent paternity.³⁴ Finally, although the variance was large at higher parity, our observation that birthweight continued to increase up to parity 4 and subsequently stabilized, is consistent with animal studies³⁵ and the biological hypothesis that uterine efficiency may increase up to a particular threshold, after which no additional gains in birthweight occur.

Our data suggest that the association between birthweight and parity is not an artifact of confounding or selection bias, which may have important clinical, policy, and research implications. First, there has been debate as to whether parity should be included in customized models of birthweight percentiles for the identification of abnormally small or large infants,^{36–39} designations which drive important clinical care decisions.⁴⁰ Our data suggest that the inherent biological differences between nulliparous and parous mothers deserve attention and therefore parity-specific birthweight references may need to be further examined, although this should be evaluated using estimated fetal weight and not birthweight, and longitudinal research on the relation between parity, birthweight, and neonatal morbidities will be a critical next step. Furthermore, these data may inform policy discussions regarding the need for parity-specific gestational weight gain recommendations.^{22, 41} It has been suggested that multiparas may benefit from lower weight gain than currently recommended to avoid postpartum weight retention.⁴¹ We have confirmed in a longitudinal cohort that nulliparas have the greatest risk for excessive weight gain, but also the smallest infants. Lastly, distinguishing nulliparous, primiparous, and multiparous women may be important for parameterization of parity in adjusted models, as opposed to a simple linear term, in perinatal epidemiological studies which include parity as a confounding variable.

Data for this study came from a demographically homogenous population of predominantly Caucasian women with high fertility rates and characteristics that suggest they may be healthier than the general population,²⁸ thereby limiting generalizability. Nonetheless, the high fertility and homogeneity of the sample likely reduced residual bias and provided an efficient study population for this research question. While most large databases lack comprehensive data on maternal medical conditions, data in our study came primarily from the medical chart abstraction and was supplemented administrative codes. Though the sensitivity of pre-gravid medical conditions and pregnancy complications from *ICD9* data may be lower than desired, some studies have found greater specificity by combining these data with medical chart abstraction.^{42, 43} In addition, data regarding socially sensitive behaviors, such as smoking or alcohol intake, may have been underreported. We also did not have any information on nutrition or physical activity, or other potential confounders such as stress that may have varied by parity. We did not have data on parous women who had only one observed pregnancy during the study period. Some women in our study had incomplete sibling data, either due to non-nulliparous entry into the study or censored future pregnancies. While it may be that the relationship between parity and birth weight differs for women with higher parity compared to women who only have two or three children due to underlying differences in highly fertile women, in the larger unrestricted sample we tested for and found no differences in the association between parity and birthweight by parity at

entry or the number of pregnancies during the study. Furthermore we found similar patterns with the restricted sample limited to consecutive deliveries of women who were nulliparous at study entry and entered between 2002–2004, suggesting that these potential biases were minimal. The major strengths of our study were the detailed information from the patient medical record which sets it apart from most linked cohorts that are based on vital statistics or registry data and the ability to explore these associations in women with higher parity.

In conclusion, using a longitudinal cohort of women with at least two consecutive pregnancies, our findings confirm that the greatest increase in birthweight was observed between nulliparas and primiparas. We demonstrate a non-linear association as birthweight continued to increase up to parity 4 and appeared to stabilize between parity 4 and 7. Most importantly, the observed associations between parity and birthweight were not explained by within mother changes in demographics, medical conditions, or weight that occurred between pregnancies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Abbreviations

CI	Confidence interval
BMI	body mass index
ICD9	International Classification of Diseases, ninth revision

References

1. Shah PS. Parity and low birth weight and preterm birth: a systematic review and meta-analyses. *Acta Obstetrica et Gynecologica Scandinavica*. 2010; 89:862–875. [PubMed: 20583931]
2. Beaty TH, Skjaerven R, Breazeale DR, Liang KY. Analyzing sibship correlations in birth weight using large sibships from Norway. *Genetic Epidemiology*. 1997; 14:423–433. [PubMed: 9271714]
3. Melve KK, Skjaerven R, Oyen N. Families with a perinatal death: is there an association between the loss and the birthweight of surviving siblings? *Paediatric and Perinatal Epidemiology*. 2002; 16:23–32. [PubMed: 11856452]
4. Oyen N, Haglund B, Skjaerven R, Irgens LM. Maternal smoking, birthweight and gestational age in sudden infant death syndrome (SIDS) babies and their surviving siblings. *Paediatric and Perinatal Epidemiology*. 1997; 11 (Suppl 1):84–95. [PubMed: 9018718]
5. Skjaerven R, Gjessing HK, Bakkeiteig LS. New standards for birth weight by gestational age using family data. *American Journal of Obstetrics and Gynecology*. 2000; 183:689–696. [PubMed: 10992194]
6. Pedersen CB, Sun Y, Vestergaard M, Olsen J, Basso O. Assessing fetal growth impairments based on family data as a tool for identifying high-risk babies. An example with neonatal mortality. *BMC Pregnancy and Childbirth*. 2007; 7:28. [PubMed: 18045458]
7. Wilcox MA, Chang AM, Johnson IR. The effects of parity on birthweight using successive pregnancies. *Acta Obstetrica et Gynecologica Scandinavica*. 1996; 75:459–453. [PubMed: 8677771]
8. Gluckman P, Hanson M. Maternal constraint of fetal growth and its consequences. *Seminars in Fetal and Neonatal Medicine*. 2004; 9:419–425. [PubMed: 15691778]
9. Khong TY, Adema ED, Erwich JJ. On an anatomical basis for the increase in birth weight in second and subsequent born children. *Placenta*. 2003; 24:348–353. [PubMed: 12657508]
10. Prefumo F, Ganapathy R, Thilaganathan B, Sebire NJ. Influence of parity on first trimester endovascular trophoblast invasion. *Fertility Sterility*. 2006; 85:1032–1036. [PubMed: 16580391]

11. Gunderson E. Childbearing and obesity in women: weight before, during, and after pregnancy. *Obstetrics and Gynecology Clinics of North America*. 2009; 36:317–332. ix. [PubMed: 19501316]
12. Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. *Lancet*. 2006; 368:1164–1170. [PubMed: 17011943]
13. Luo Z-C, An N, Xu H-R, Larante A, Audibert F, Fraser WD. The effects and mechanisms of primiparity on the risk of pre-eclampsia: a systematic review. *Paediatric and Perinatal Epidemiology*. 2007; 21:36–45. [PubMed: 17593196]
14. Trogstad LI, Eskild A, Magnus P, Samuelsen SO, Nesheim BI. Changing paternity and time since last pregnancy; the impact on pre-eclampsia risk. A study of 547 238 women with and without previous pre-eclampsia. *International Journal Epidemiology*. 2001; 30:1317–1322.
15. Miranda ML, Edwards SE, Myers ER. Adverse birth outcomes among nulliparous vs. multiparous women. *Public Health Reports*. 2011; 126:797–805. [PubMed: 22043095]
16. Harder T, Rodekamp E, Schellong K, Dudenhausen JW, Plagemann A. Birth weight and subsequent risk of type 2 diabetes: a meta-analysis. *American Journal of Epidemiology*. 2007:849–857. [PubMed: 17215379]
17. Corsello G, Piro E. The world of twins: an update. *Journal of Maternal-Fetal and Neonatal Medicine*. 2010; 23 (Suppl 3):59–62. [PubMed: 20807162]
18. Skjaerven R, Wilcox AJ, Lie RT, Irgens LM. Selective fertility and the distortion of perinatal mortality. *American Journal of Epidemiology*. 1988; 128:1352–1363. [PubMed: 3195572]
19. Alexander GR, Himes JH, Kaufman RB, Mor J, Kogan M. A United States national reference for fetal growth. *Obstetrics and Gynecology*. 1996; 87:163–168. [PubMed: 8559516]
20. Engle WA. Age terminology during the perinatal period. *Pediatrics*. 2004; 114:1362–1364. [PubMed: 15520122]
21. Bodnar LM, Hutcheon JA, Platt RW, Himes KP, Simhan HN, Abrams B. Should gestational weight gain recommendations be tailored by maternal characteristics? *American Journal of Epidemiology*. 2011:136–146. [PubMed: 21633118]
22. Institute of Medicine. *Weight Gain During Pregnancy: Reexamining the Guidelines*. Washington, D.C: National Academies Press; 2009.
23. Zeitlin J, Ancel PY, Saurel-Cubizolles MJ, Papiernik E. The relationship between intrauterine growth restriction and preterm delivery: an empirical approach using data from a European case-control study. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2000; 107:750–758. [PubMed: 10847231]
24. Melve KK, Skjaerven R. Families with birth defects: is birth weight of nonmalformed siblings affected? *American Journal of Epidemiology*. 2002; 155:932–940. [PubMed: 11994233]
25. Zhu BP. Effect of interpregnancy interval on birth outcomes: findings from three recent US studies. *International Journal of Gynecology & Obstetrics*. 2005; 89(Supplement 1):S25–S33. [PubMed: 15820365]
26. Zhu BP, Rolfs RT, Nangle BE, Horan JM. Effect of the interval between pregnancies on perinatal outcomes. *New England Journal of Medicine*. 1999; 340:589–594. [PubMed: 10029642]
27. Basso O, Christensen K, Olsen J. Higher risk of pre-eclampsia after change of partner. An effect of longer interpregnancy intervals? *Epidemiology*. 2001; 12:624–629. [PubMed: 11679788]
28. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Mathews TJ, Osterman MJ. *Births: final data for 2008*. National Vital Statistics Reports: from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System. 2010; 59:3–71.
29. Clapp JF 3rd, Capeless E. Cardiovascular function before, during, and after the first and subsequent pregnancies. *American Journal of Cardiology*. 1997:1469–1473. [PubMed: 9399724]
30. Woessner JF, Brewer TH. Formation and breakdown of collagen and elastin in the human uterus during pregnancy and post-partum involution. *Biochemical Journal*. 1963; 89:75–82. [PubMed: 14097370]
31. Prefumo F, Bhide A, Sairam S, Penna L, Hollis B, Thilaganathan B. Effect of parity on second-trimester uterine artery Doppler flow velocity and waveforms. *Ultrasound in Obstetrics and Gynecology*. 2004; 23:46–49. [PubMed: 14970999]

32. Hafner E, Schuchter K, Metzenbauer M, Philipp K. Uterine artery Doppler perfusion in the first and second pregnancies. *Ultrasound in Obstetrics and Gynecology*. 2000; 16:625–629. [PubMed: 11169368]
33. Sornes T, Bakke T. Uterine size, parity and umbilical cord length. *Acta Obstetrica et Gynecologica Scandinavica*. 1989; 68:439–441. [PubMed: 2520789]
34. Krulwich C, Herman A, Yu K, Johnson Y. Does changing paternity contribute to the risk of intrauterine growth retardation? *Paediatric and Perinatal Epidemiology*. 1997; 11:41–47. [PubMed: 9018714]
35. Gardner DS, Buttery PJ, Daniel Z, Symonds ME. Factors affecting birth weight in sheep: maternal environment. *Reproduction*. 2007; 133:297–307. [PubMed: 17244755]
36. Hutcheon JA, Walker M, Platt RW. Assessing the value of customized birth weight percentiles. *American Journal of Epidemiology*. 2011; 173:459–467. [PubMed: 21135027]
37. Anderson NH, Sadler LC, Stewart AW, McCowan LM. Maternal and pathological pregnancy characteristics in customised birthweight centiles and identification of at-risk small-for-gestational-age infants: a retrospective cohort study. *BJOG: An International Journal of Obstetrics and Gynaecology*. 2012; 119:848–856. [PubMed: 22469096]
38. Ego A, Subtil D, Grange G, Thiebaugeorges O, Senat MV, Vayssiere C, et al. Should parity be included in customised fetal weight standards for identifying small-for-gestational-age babies? Results from a French multicentre study. *BJOG: An International Journal of Obstetrics and Gynaecology*. 2008; 115:1256–1264. [PubMed: 18715411]
39. Gardosi J, Clausson B, Francis A. The value of customised centiles in assessing perinatal mortality risk associated with parity and maternal size. *BJOG: An International Journal of Obstetrics and Gynaecology*. 2009; 116:1356–1363. [PubMed: 19538413]
40. Gardosi J. Customised assessment of fetal growth potential: implications for perinatal care. *Archives of Disease in Childhood Fetal and Neonatal Edition*. 2012; 97:F314–317. [PubMed: 22684160]
41. Nohr EA, Vaeth M, Baker JL, Sørensen TI, Olsen J, Rasmussen KM. Pregnancy outcomes related to gestational weight gain in women defined by their body mass index, parity, height, and smoking status. *American Journal of Clinical Nutrition*. 2009; 90:1288–1294. [PubMed: 19759164]
42. Lydon-Rochelle MT, Holt VL, Cardenas V, Nelson JC, Easterling TR, Gardella C, et al. The reporting of pre-existing maternal medical conditions and complications of. *American Journal of Obstetrics and Gynecology*. 2005; 193:125–134. [PubMed: 16021070]
43. Andrade S, Moore Simas T, Boudreau D, Raebel M, Toh S, Syat B, et al. Validation of algorithms to ascertain clinical conditions and medical procedures used during pregnancy. *Pharmacoepidemiology and Drug Safety*. 2011; 20:1168–1176. [PubMed: 22020902]

Figure 1.

Longitudinal trends in gestational age and sex-specific birthweight z-score by maternal parity (parity at entry, number contributed). Groups with $n < 50$ not shown (e.g. only 1 person started at entered the study at parity 0 and contributed 6 pregnancies). No differences observed by parity at study entry ($P=0.34$) or number of pregnancies contributed to the study ($P=0.39$). Consecutive Pregnancies Study, 2002–2010, $n=45,212$.

Table 1

Birthweight z-score at the first pregnancy according to characteristics of the primary study sample of women who were nulliparous at study entry and entered the study from 2002–2004, Consecutive Pregnancies Study, 2002–2010, $n=9,484$.

Characteristics at first pregnancy	<i>n</i> (%)	Birthweight z-score	
		Mean (SD)	<i>P</i>
Age, years ^b			0.07
13–24	5,987 (63.1)	0.01 (0.99)	
25–34	3,360 (35.4)	0.04 (1.00)	
34–49	137 (1.4)	0.15 (1.12)	
Race-ethnicity			<0.001
Non-Hispanic white	8,465 (89.3)	0.05 (0.99)	
Non-Hispanic black	32 (0.3)	−0.47 (0.67)	
Hispanic	748 (7.9)	−0.14 (0.98)	
Asian/Pacific Islander	204 (2.2)	−0.28 (1.02)	
Other	35 (0.4)	−0.03 (1.06)	
Married			<0.001
No	1,418 (15.0)	−0.18 (0.97)	
Yes	8,066 (85.1)	0.06 (0.99)	
Private insurance			<0.001
No	2,249 (23.7)	−0.07 (0.97)	
Yes	7,235 (76.3)	0.05 (1.00)	
Smoked during pregnancy			<0.001
No	9,351 (98.6)	0.03 (0.99)	
Yes	133 (1.4)	−0.40 (0.92)	
Drank alcohol during pregnancy			0.09
No	9,311 (98.2)	0.02 (1.00)	
Yes	173 (1.8)	−0.10 (0.90)	
Height ^b , cm			<0.001
<160	1,745 (18.4)	−0.24 (0.95)	
160	7,739 (81.6)	0.08 (0.99)	
Prepregnancy BMI, kg/m ²			<0.001
<18.5	658 (6.9)	−0.26 (0.90)	
18.5–24.9	6,166 (65.0)	−0.02 (0.96)	
25.0–29.9	1,702 (18.0)	0.17 (1.05)	
30.0–34.9	631 (6.7)	0.19 (1.10)	
35.0–39.9	219 (2.3)	0.28 (1.13)	
40.0	108 (1.1)	0.31 (1.23)	
Gestational weight gain			<0.001
Inadequate	1,825 (19.2)	−0.30 (0.94)	
Adequate	2,495 (26.3)	−0.11 (0.94)	
Excessive	5,164 (54.5)	0.20 (1.00)	

Characteristics at first pregnancy	n (%)	Birthweight z-score	
		Mean (SD)	P
Diabetes			<0.001
None	9,246 (97.5)	0.01 (0.98)	
Gestational	152 (1.6)	0.35 (1.21)	
Prepregnancy	86 (0.9)	0.55 (1.33)	
Hypertension			0.05
Normotensive	8,413 (88.7)	0.02 (0.98)	
Unspecified hypertensive disease	44 (0.5)	0.24 (1.13)	
Gestational hypertension	542 (5.7)	0.02 (1.07)	
Preeclampsia/eclampsia	425 (4.5)	−0.08 (1.10)	
Chronic hypertension	39 (0.4)	−0.08 (1.12)	
Superimposed preeclampsia	21 (0.2)	0.47 (1.48)	
Asthma			0.33
No	8,856 (93.4)	0.02 (0.99)	
Yes	628 (6.6)	0.06 (1.00)	
Thyroid disease			0.12
No	9,182 (96.8)	0.02 (0.99)	
Yes	302 (3.2)	0.11 (1.04)	
Mental health condition			0.33
No	9,212 (97.1)	0.02 (1.00)	
Yes	272 (2.9)	−0.04 (0.95)	
Other chronic disease ^d			0.10
No	9,230 (97.3)	0.02 (0.99)	
Yes	254 (2.7)	−0.08 (1.04)	

Abbreviations: BMI, body mass index.

^e Gestational age- and sex-specific birthweight z-score.

^d Includes heart disease, kidney disease, gastrointestinal disease, and HIV.

Table 2

Birthweight-for-gestational-age z-score by maternal parity estimated using linear mixed models among the primary sample of women who were nulliparous at study entry and entered the study from 2002–2004, Consecutive Pregnancies Study, $n=9,484$.

Gestational Age- and Sex-Specific Birthweight Z-Score				
Parity	Unadjusted β [95% CI]	Model A β [95% CI]	Model B β [95% CI]	Model C β [95% CI]
0	0.0 Reference	0.0 Reference	0.0 Reference	0.0 Reference
1	0.20 [0.18, 0.22]	0.17 [0.15, 0.19]	0.19 [0.16, 0.21]	0.18 [0.15, 0.20]
2	0.26 [0.23, 0.29]	0.21 [0.17, 0.24]	0.23 [0.19, 0.26]	0.22 [0.18, 0.25]
3	0.32 [0.25, 0.39]	0.26 [0.19, 0.33]	0.28 [0.21, 0.35]	0.27 [0.20, 0.34]

Abbreviations: CI, confidence interval.

^a Model A adjusted for maternal age, race-ethnicity, marital status, and insurance type

^b Model B adjusted for model A variables and smoking during pregnancy, alcohol during pregnancy, height, prepregnancy weight status, and gestational weight gain adequacy

^c Model C adjusted for model B variables and diabetes, hypertension, asthma, thyroid disease, depression and mental health, and other chronic conditions.

Table 3

Association between maternal parity and infant birthweight-for-gestational-age z-score among the second sample estimated using linear mixed models, Consecutive Pregnancies Study, $n=45,212$.

Gestational Age- and Sex-Specific Birthweight Z-Score				
Parity	Unadjusted β [95% CI]	Model A β [95% CI]	Model B β [95% CI]	Model C β [95% CI]
0	0.0 Reference	0.0 Reference	0.0 Reference	0.0 Reference
1	0.20 [0.19, 0.21]	0.17 [0.15, 0.18]	0.19 [0.18, 0.21]	0.18 [0.17, 0.20]
2	0.28 [0.26, 0.29]	0.22 [0.20, 0.23]	0.25 [0.23, 0.27]	0.24 [0.22, 0.26]
3	0.33 [0.31, 0.35]	0.25 [0.23, 0.27]	0.29 [0.26, 0.31]	0.28 [0.25, 0.30]
4	0.41 [0.39, 0.44]	0.31 [0.28, 0.35]	0.35 [0.32, 0.38]	0.34 [0.31, 0.37]
5	0.41 [0.37, 0.46]	0.30 [0.25, 0.34]	0.34 [0.29, 0.39]	0.33 [0.28, 0.37]
6	0.47 [0.40, 0.54]	0.33 [0.26, 0.41]	0.38 [0.31, 0.45]	0.36 [0.29, 0.44]
7	0.43 [0.31, 0.55]	0.28 [0.16, 0.40]	0.33 [0.21, 0.44]	0.31 [0.20, 0.43]

Abbreviations: CI, confidence interval.

^aModel A adjusted for maternal age, race-ethnicity, marital status, and insurance type

^bModel B adjusted for model A variables and smoking during pregnancy, alcohol during pregnancy, height, prepregnancy weight status, and gestational weight gain adequacy

^cModel C adjusted for model B variables and diabetes, hypertension, asthma, thyroid disease, depression and mental health, and other chronic conditions.