Gestational weight gain and risk of overweight in the offspring at age 7 y in a multicenter, multiethnic cohort study

Brian H Wrotniak, Justine Shults, Samantha Butts, and Nicolas Stettler

ABSTRACT

Background: The earliest determinants of obesity may operate during intrauterine life, and gestational weight gain may influence the intrauterine environment in a way that may affect the risk of overweight in the offspring.

Objective: The purpose of this study was to examine the association of gestational weight gain with offspring overweight.

Design: This was a retrospective cohort study of 10,226 participants from the Collaborative Perinatal Project (1959–1972). Anthropometric and sociodemographic variables were assessed during gestation, at birth, and at age 7 y. The association between gestational weight gain and offspring overweight at 7 y was examined after adjustment for important confounding factors.

Results: The odds of overweight in offspring at age 7 y increased by 3% for every 1 kg of gestational weight gain (adjusted odds ratio: 1.03; 95% CI: 1.02, 1.05). When gestational weight gain was examined using Institute of Medicine guidelines, the odds of overweight were 48% greater for children of mothers who gained more than the weight gain recommendations than for children of mothers who met the weight gain guidelines (adjusted OR: 1.48; 95% CI: 1.06, 2.06). The association remained significant after additional adjustment for birth weight. The association between gestational weight gain and overweight in the offspring was strongest for women who were underweight before pregnancy (P for interaction < 0.01).

Conclusion: Helping pregnant women to meet the recommended weight gain during pregnancy may be an important and novel strategy for preventing pediatric obesity. Am J Clin Nutr 2008;87:1818–24.

INTRODUCTION

Childhood obesity continues to be a serious public health problem. Children who are overweight are at risk of health conditions that include dyslipidemia, hypertension, and type 2 diabetes (1). Childhood obesity is also a risk factor for obesity in adulthood (2) and associated diseases such as cardiovascular disease and cancer (3). A life course approach to chronic disease epidemiology and prevention suggests that the development of excessive weight may be the result of complex interactions between environmental, genetic, and psychological variables that occur throughout the life span (4). By understanding the early determinants of obesity, it may be possible to influence the course of excessive weight gain and help curtail the obesity epidemic.

The earliest influences on human development may occur within the intrauterine environment (5–7). The concept that chronic health conditions may be programmed in early life has been demonstrated in research examining intrauterine exposures that influence fetal growth, such as maternal smoking (8) and gestational diabetes (9). Similarly, the amount of weight a woman gains during pregnancy may be a potentially important modifiable risk factor that influences the growth and health of the fetus as well as outcomes later during childhood and adulthood. Excessive gestational weight gain may be complicated by insulin resistance or even gestational diabetes, which is associated with fetal macrosomia and health risks in the offspring (9, 10). The Institute of Medicine (IOM) provides recommendations that weight gain for pregnant women be based on prepregnancy body mass index (BMI; in kg/m²) (11) (Table 1).

Previously, there has been an emphasis to promote sufficient weight gain during pregnancy in an effort to reduce low-birthweight deliveries and adverse perinatal outcomes (12). However, despite the increase in the obesity epidemic and the increase in the percentage of women gaining more than the IOM weight gain recommendations (from 37% to 46% between 1993 and 2003; 11), the role of gestational weight gain in obesity in the offspring has received relatively limited attention. Most studies examining the potential role of intrauterine factors on future obesity have examined factors other than gestational weight gain, such as birth weight, maternal parity, maternal smoking, and gestational age (13, 14). The few studies that have examined gestational weight gain as a determinant of future obesity in the offspring have reported mixed results (15–19).

The purpose of this study was to examine the association of gestational weight gain with the risk of overweight in offspring at 7 y of age in a multicenter, multiethnic cohort study design. It was hypothesized that gestational weight gain would be positively associated with overweight in offspring at age 7 y after the...
TABLE 1
Recommended maternal gestational weight gain based on prepregnancy BMI, as defined by the Institute of Medicine (12)

<table>
<thead>
<tr>
<th>BMI category</th>
<th>Recommended gestational weight gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;19.8 kg/m²</td>
<td>12.5–18</td>
</tr>
<tr>
<td>19.8–26.0 kg/m²</td>
<td>11.5–16</td>
</tr>
<tr>
<td>≥26.0–29.0 kg/m²</td>
<td>7–11.5</td>
</tr>
<tr>
<td>≥29.0 kg/m²</td>
<td>≥6.8</td>
</tr>
</tbody>
</table>

Subjects

The National Collaborative Perinatal Project was a multicenter cohort study initiated in 1959 to investigate risk factors for cerebral palsy at 12 US sites (20). Between 1959 and 1965, 58,760 women with singleton pregnancies presenting for prenatal care in these centers were enrolled in the study after informed consent was obtained. Among them, 6454 were lost to follow-up before delivery or experienced fetal death, resulting in a cohort of 52,306 live births. Follow-up data were collected for the children on multiple occasions up to age 7 y. For the present study, the baseline sample was restricted to the 27,889 children with birth documented to be at term gestation to eliminate the potential for confounding by differences in the duration of pregnancy on gestational weight gain. For participants that were excluded, gestational age was <37 wk for 2973 participants, ≥42 wk for 1494 participants, and unavailable for 19,950 births, primarily from children born before 1962, when this information began to be widely recorded as part of the research protocol. An additional 2 participants with mothers diagnosed with gestational diabetes were also excluded. At the 7-y time point, 8121 participants were lost to follow-up, and gestational weight gain data were missing for 9540 subjects, which resulted in an overall sample for these analyses of 10,226 (37% of the eligible sample). The study was approved by the Institutional Review Board of The Children’s Hospital of Philadelphia.

Measurements

Maternal data were collected at enrollment by using a questionnaire and included maternal prepregnancy weight, age, race, number of cigarettes smoked per day, number of siblings in the household, and number of previous pregnancies. Maternal weight and height were measured at the time of delivery and used to calculate gestational weight gain. Gestational weight gain was determined as the difference between measured weight at delivery and reported prepregnancy weight. Prepregnancy BMI was computed by dividing reported prepregnancy weight (in kg) by height (in m²), measured at the time of delivery. All obstetric examinations and procedures in study participants were conducted by trained study staff. Recommended, excess, and insufficient gestational weight gain was determined on the basis of the IOM recommendations for healthy weight gain for pregnant women, by prepregnancy BMI category (12) (Table 1). Because the IOM does not identify an upper healthy gestational weight gain boundary for women with a BMI ≥ 29 before pregnancy, we conservatively set it at 11.5 kg, the upper limit recommended for women with a prepregnancy BMI between 26 and 29 (21).

Variables collected by trained research staff for the children included sex, gestational age at birth, weight at birth, and weight and height at the 7-y visit. Gestational age was determined by the senior physician who assumed responsibility for the delivery using all clinical and historical information. Study labor and delivery records were completed by the delivering obstetrician immediately after delivery. Children were considered as first born if the mother reported no previous delivery or no other children living in the household at the time of delivery, depending on which question was asked at that time. Children ≥95th BMI percentile of a reference population for age and sex at the 7-y pediatric examination visit were considered to be overweight (22).

Analyses

Most variables were skewed, as has been shown in other populations for biological variables (23, 24) and are, therefore, described using medians, 2.5th, and 97.5th percentiles. Categorical variables are reported as proportions in percentage. Baseline characteristics for participants who were followed up and for those with incomplete data were compared by using the chi-square or Wilcoxon’s rank-sum test, as appropriate. For the main analysis, the primary dichotomous outcome variable was childhood overweight status. Childhood overweight was considered to be a BMI ≥ 95th percentile for age and sex, and the reference category of nonoverweight was a BMI < 95th percentile for age and sex. A categorical measure of childhood overweight was selected rather than a continuous outcome because there is no strong evidence that variations within the normal range affect long-term health. Additionally, because only 5.7% of offspring at 7 y of age were overweight in our sample, most of the variability would be in the healthy range if a continuous measure of BMI was used, which we were not interested in predicting. Of 10,226 women, 530 (5.2%) were included more than once (519 twice and 11 three times) because they had more than one child enrolled in the study. Because the percentage of women who were included more than once was relatively small, we used logistic regression for our primary analyses. However, we also assessed the sensitivity of our findings to the fact that we have duplicate measurements on some women by adjusting the SEs in our analyses using the cluster option in STATA (Stata Corp, College Station, TX). The findings were not changed when we adjusted for clustering of observations by mother, so the results reported in this article are based on the primary analyses. Our analytic plan involved a 3-tier approach. First, a single univariate logistic regression model was used to examine the unadjusted association between the continuous measure of gestational weight gain and childhood overweight. Next, overweight status was regressed on gestational weight gain after adjustment for potential confounding variables chosen a priori: maternal race, age, prepregnancy BMI, number of cigarettes smoked per day, gestational age, child sex, age, first-born status, and study site. Finally, birth weight was added to the adjusted model to assess its influence as a potential mediator of the association between gestational weight gain and overweight status. Unadjusted and
adjusted ORs and 95% CIs for overweight status were calculated, and statistical significance was assessed by using a Wald’s test. All analyses were then repeated by using a model that included indicator variables for “excessive weight gain” and “insufficient weight gain,” with “healthy weight gain” as the referent group, as defined by the IOM, instead of the continuous measure of gestational weight gain.

Additional analyses were performed to test possible interactions between excessive or insufficient weight gain and offspring overweight by offspring’s sex and race in the logistic regression models. To test whether the association between gestational weight gain and overweight in the offspring was modified by maternal prepregnancy BMI, we used stepwise regression on IOM prepregnancy weight categories and pregnancy weight gain categories and their interaction terms. The logistic model included indicator variables for maternal prepregnancy underweight (BMI < 19.8), overweight (BMI = 26–29.0), and obese IOM categories (BMI > 29.0), with normal weight (BMI = 19.8–26.0) as the reference category. In addition, the model included indicator variables for insufficient and excessive maternal weight gain, with healthy weight gain as the reference category. The model also included BMI categories by maternal weight gain interaction terms that were constructed as the product of the indicator variables for IOM prepregnancy and maternal weight gain categories. Backwards stepwise logistic regression and a manual backwards stepwise logistic regression procedure were used to select the final model, and terms with a significance level of <0.10 were retained as potential predictor variables; both procedures resulted in the same model. After a final model was obtained that showed one significant interaction, the model was modified to include additional covariates, including child sex, gestational age, first-born status, child age, mother’s race, maternal age, smoking, and study site. The Hosmer-Lemeshow test (25) was used to test the hypothesis of reasonable fit for all logistic regression models. Analyses stratified by prepregnancy BMI categories were then conducted, as prepregnancy BMI coding modified the association between excessive weight gain and overweight in the offspring. All statistical tests were 2-tailed and a P value < 0.05 considered statistically significant. Analyses were conducted using STATA version 8.2 (Stata Corp) (26).

RESULTS

Maternal baseline characteristics for the participants in the original cohort who were not analyzed because of loss to follow-up or missing gestational weight gain data (n = 17 661) were not significantly different from the sample studied (n = 10 226) in maternal smoking, first-born status, or child sex. However, mothers with complete data were more likely to have a slightly higher prepregnancy BMI (22.9 compared with 22.8; P = 0.01), to be slightly younger (aged 24.0 versus 24.1 y, P = 0.03), have a different racial distribution (black: 48% compared with 45%; white: 50% compared with 44%; Hispanic: 1% compared with 10%; other: 1% compared with 1%; P < 0.001), and have a child with a slightly higher birth weight (3.25 kg compared with 3.22 kg; P < 0.001) and with a slightly higher gestational age (39.8 wk compared with 39.7 wk; P < 0.001).

Characteristics of the women and their offspring included in this analysis are listed in Table 2. Twenty-two percent of the women had a prepregnancy BMI < 19.8, 60% had a prepregnancy BMI of 19.8–26.0, 9% had a prepregnancy BMI of 26.0–29.0, and 9% had a prepregnancy BMI > 29. According to the current IOM recommendations and on the basis of these prepregnancy BMI categories, 11% of women gained excessive weight, 24% gained adequate weight, and 65% gained insufficient weight. The percentage of women who gained excessive, recommended, and insufficient weight during gestation by prepregnancy BMI category differed between categories (χ² = 670.0, P < 0.001) and are displayed in Table 3. The prevalence of overweight in the offspring at 7 y by prepregnancy BMI category was as follows: BMI < 19.8, 2.2%; BMI of 19.8–26.0, 5.4%; BMI of 26.0–29.0, 7.6%; BMI > 29.0, 13.2% (χ² = 153.0, P < 0.001). Of the gestational weight gain categories, the prevalence of offspring overweight differed for women with a prepregnancy BMI < 19.8 (χ² = 15.7, P < 0.001) and with a prepregnancy BMI of 19.8 to 26.0 (χ² = 8.0, P = 0.02) (Figure 1). The risk of overweight in the offspring was lowest for mothers with a BMI < 19.8 who gained an insufficient amount of weight during pregnancy (prevalence of childhood overweight = 1.7%) and greatest for mothers with a BMI > 29 who had gained an excessive amount of weight during pregnancy (prevalence of childhood overweight = 14.5%) (Figure 1).

The unadjusted and adjusted associations between gestational weight gain and childhood overweight at 7 y are reported in Table 4. The unadjusted frequency of offspring overweight represents 10 cases per 100 women with excessive weight gain compared with 6 cases per 100 women who meet the weight gain recommendations. A strong predictor of childhood overweight was maternal prepregnancy BMI (unadjusted OR: 1.10; 95% CI: 1.09, 1.12; adjusted OR: 1.14; 95% CI: 1.11, 1.16). The relation between gestational weight gain and overweight in the offspring was not modified by sex or race. However, this association was modified by maternal prepregnancy BMI categories. After the
The use of backward stepwise regression to test a model that included indicator variables for maternal weight gain and prepregnancy BMI categories, the significant terms remaining in the final model included maternal overweight (OR: 0.35; 95% CI: 0.25, 0.50), maternal obesity (OR: 1.38; 95% CI: 1.03, 1.83), maternal underweight (OR: 2.56; 95% CI: 2.04, 3.23), and maternal underweight X excessive versus healthy gestational weight gain interaction (OR: 3.18; 95% CI: 1.34, 7.59), which indicated that the association between gestational weight gain and overweight in the offspring is strongest for children of underweight mothers. These associations and interaction remained significant after the model was further adjusted for child sex, gestational age, first-born status, child age, mother’s race, maternal age, smoking, and study site. To assess the importance of catch-up-growth in the development of childhood obesity, additional analyses were conducted to examine the association between gestational weight gain and birth weight, and then the interaction of this association with prepregnancy BMI. A positive association between birth weight and gestational weight gain was found (adjusted β = 18.26 g of birth weight per every 1 kg gain in gestational weight; 95% CI: 16.5, 20.0; P < 0.001), but there was no significant interaction by prepregnancy BMI. The Hosmer Lemeshow test indicated good fit for all logistic regression models (χ² > 0.05). Because of the significant interaction by prepregnancy BMI, the main analyses were repeated after stratifying by underweight status (Table 4).

### DISCUSSION

The results of this study indicate that gestational weight gain is associated with overweight in the offspring at 7 y of age even after adjustment for maternal race, age, prepregnancy BMI, cigarette smoking, gestational age, child sex, age, first-born status, and study city. Compared with children of mothers who met the gestational weight gain recommendations, children of mothers who gained excessive weight during pregnancy had a 48% greater odds of overweight at 7 y of age. The magnitude of the association between excessive gestational weight gain and childhood overweight decreased after infant birth weight was added to the logistic regression model, suggesting that birth weight is likely on the pathway between gestational weight gain and child adiposity, but is unlikely to entirely explain this association.

Our findings are consistent with other research that support a positive association between gestational weight gain and overweight in the offspring (15–17, 27). Oken et al (15), using the same IOM gestational weight gain recommendations, but where the outcome was measured at 3 y of age, found a stronger association between gestational weight gain and offspring overweight compared with our findings. This suggests that the association between gestational weight gain and offspring overweight may decrease as children grow older. In contrast with Oken et al’s findings we did not find an association between overweight in the offspring of mothers who had recommended compared with insufficient gestational weight gain. This may be because in Oken et al’s study the reference group was children with a BMI < 50th percentile. An additional explanation could be influences of different environmental exposures on cohorts from 2 different time periods. Mothers who experience undernutrition and insufficient weight gain during pregnancy may conserve energy by suppressing metabolic rate and gaining little fat as a means of protecting fetal growth and theoretically preventing potential future morbidity in the offspring (28).

The association between gestational weight gain and overweight in the offspring was strongest for women who were underweight before pregnancy, and may reflect the fact that pregnancy weight gain has a greater impact in underweight women. Birth weight has been shown to be more strongly related to gestational weight gain in women of lower BMI compared with higher BMI (29). A greater likelihood of childhood overweight among underweight mothers who gain more weight during pregnancy is consistent with a published preliminary report (30). A possible explanation for why the odds of offspring overweight is

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**TABLE 3**

Percentage of women who gained insufficient, recommended, and excessive weight during gestation by prepregnancy BMI†

<table>
<thead>
<tr>
<th>Prepregnancy BMI</th>
<th>Insufficient weight gain</th>
<th>Recommended weight gain</th>
<th>Excessive weight gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;19.8 kg/m² (n = 2137)</td>
<td>74</td>
<td>22</td>
<td>4</td>
</tr>
<tr>
<td>19.8–26.0 kg/m² (n = 5794)</td>
<td>67</td>
<td>24</td>
<td>9</td>
</tr>
<tr>
<td>26.0–29.0 kg/m² (n = 816)</td>
<td>39</td>
<td>33</td>
<td>28</td>
</tr>
<tr>
<td>&gt;29.0 kg/m² (n = 886)</td>
<td>45</td>
<td>29</td>
<td>26</td>
</tr>
</tbody>
</table>

† Excessive, recommended, and insufficient gestational weight gain were defined based on criteria from the Institute of Medicine (12). The percentage of women who gained excessive, recommended, and insufficient weight during gestation by prepregnancy BMI category differed between categories (χ² = 670.0, P < 0.001).

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**FIGURE 1.** Prevalence of childhood overweight at 7 y by maternal prepregnancy BMI categories and gestational weight gain categories. In chi-square analyses, the prevalence of offspring overweight differed (P < 0.02) between gestational weight gain categories for women with a prepregnancy BMI < 19.8 and with a prepregnancy BMI of 19.8 to 26.0. The risk of overweight in the offspring was lowest for mothers with a BMI < 19.8 who gained an insufficient amount of weight during pregnancy (prevalence of childhood overweight = 1.7%) and greatest for mothers with a BMI > 29 who had gained an excessive amount of weight during pregnancy (prevalence of childhood overweight = 14.5%). Excessive, recommended, and insufficient gestational weight gain are defined based on criteria from the Institute of Medicine (12).
Excessive gestational weight gain and hyperglycemia may over- 
the offspring. From a life course perspective, intrauterine devel-

opment association between gestational weight gain and overweight in 
have the greatest odds of offspring overweight (data not shown). 

women who are underweight and gain more gestational weight 
testistically significant interaction and support the finding that 
in relation to childhood overweight. The results revealed a sta-
tistical significance in the association between gestational 
weight gain by prepregnancy BMI category. To explore this 
association between maternal gestational weight gain and overweight in the offspring at 7 yo fa g e

| TABLE 4 |

Association between maternal gestational weight gain and overweight in the offspring at 7 y of age.

<table>
<thead>
<tr>
<th>Main analyses</th>
<th>Unadjusted</th>
<th>Adjusted</th>
<th>Adjusted with additional adjustment for birth weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational weight gain by 1 kg of weight gain</td>
<td>1.02 (1.00, 1.03) [10,226]</td>
<td>1.03 (1.02, 1.05) [7,191]</td>
<td>1.03 (1.01, 1.05) [7,191]</td>
</tr>
<tr>
<td>Excessive weight gain vs recommended weight gain</td>
<td>1.62 (1.25, 2.12) [3,491]</td>
<td>1.48 (1.06, 2.06) [2,572]</td>
<td>1.40 (1.00, 1.95) [2,572]</td>
</tr>
<tr>
<td>Insufficient weight gain vs recommended weight gain</td>
<td>0.82 (0.67, 1.01) [8,707]</td>
<td>0.88 (0.68, 1.14) [6,365]</td>
<td>0.93 (0.72, 1.21) [6,365]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stratified analyses</th>
<th>Unadjusted</th>
<th>Adjusted</th>
<th>Adjusted with additional adjustment for birth weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mothers with prepregnancy BMI &lt; 19.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational weight gain by 1 kg of weight gain</td>
<td>1.08 (1.02, 1.14) [2,137]</td>
<td>1.09 (1.01, 1.16) [1,412]</td>
<td>1.07 (0.99, 1.15) [1,412]</td>
</tr>
<tr>
<td>Excessive weight gain vs recommended weight gain</td>
<td>2.90 (1.12, 7.48) [563]</td>
<td>3.36 (1.01, 11.16) [331]</td>
<td>3.26 (0.95, 11.16) [331]</td>
</tr>
<tr>
<td>Insufficient weight gain vs recommended weight gain</td>
<td>0.59 (0.30, 1.16) [2,045]</td>
<td>0.46 (0.19, 1.10) [1,352]</td>
<td>0.55 (0.22, 1.37) [1,352]</td>
</tr>
<tr>
<td>Mothers with prepregnancy BMI ≥ 19.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational weight gain by 1 kg of weight gain</td>
<td>1.02 (1.00, 1.03) [8,089]</td>
<td>1.02 (1.00, 1.04) [5,984]</td>
<td>1.01 (0.99, 1.03) [5,984]</td>
</tr>
<tr>
<td>Excessive weight gain vs recommended weight gain</td>
<td>1.45 (1.10, 1.91) [2,928]</td>
<td>1.59 (1.14, 2.23) [2,156]</td>
<td>1.48 (1.05, 2.08) [2,156]</td>
</tr>
<tr>
<td>Insufficient weight gain vs recommended weight gain</td>
<td>0.89 (0.71, 1.10) [6,662]</td>
<td>0.88 (0.68, 1.14) [4,958]</td>
<td>0.95 (0.73, 1.24) [4,958]</td>
</tr>
</tbody>
</table>

1 Odds ratios and 95% CIs were computed by using simple and multivariate logistic regression analyses. The dependent variable was childhood overweight status defined as a BMI ≥ 95% percentile for age and sex compared with a reference category defined as a BMI < 95th percentile for age and sex (34). Excessive, recommended, and insufficient gestational weight gain were defined based on criteria from the Institute of Medicine (12). The analyses were stratified by prepregnancy BMI (< 19.8 and ≥ 19.8) because of the significant (P < 0.01) interaction of maternal underweight by excessive gestational weight gain.

2 Adjusted for child sex, gestational age, first-born status, child’s exact age at the 7-y assessment, mother’s race, maternal age, maternal prepregnancy BMI, smoking, and study site. Stratified adjusted analyses were adjusted for the same covariates, except for maternal prepregnancy BMI.

strongest in underweight women who gain excessive weight gain during pregnancy is that there are different cutoffs for excessive weight gain by prepregnancy BMI category. To explore this possibility, we investigated the interaction between prepregnancy BMI and gestational weight gain as a continuous variable in relation to childhood overweight. The results revealed a statistically significant interaction and support the finding that women who are underweight and gain more gestational weight have the greatest odds of offspring overweight (data not shown).

There are a number of possible mechanisms responsible for the association between gestational weight gain and overweight in the offspring. From a life course perspective, intrauterine development may be a critical time period during which maternal weight gain may contribute to the programming of future risk of childhood overweight, perhaps through insulin resistance (15). Excessive gestational weight gain and hyperglycemia may over-stimulate fetal pancreatic β cells and consequently bring about fetal hyperinsulinism. Insulin itself is a growth hormone for the fetus, resulting in higher birth weight (9, 31) and in impaired glucose tolerance and obesity in adolescence (31). In animal studies, fetal hyperinsulinism can elevate the expression of neuropeptide Y neurons in the arcuate hypothalamic nucleus (32), which results in hyperphagia and weight gain in postnatal life (33). An alternative explanation for the association of gestational weight gain with offspring overweight is that mothers with greater gestational weight gain may have children who gain more weight through shared mechanisms that may include genetics, dietary preferences, and physical activity patterns. It is not possible to distinguish between those possibilities based on this study. However, the strength of the association between gestational weight gain and offspring overweight was only slightly reduced after adjustment for variables that included prepregnancy BMI, which suggests that shared genes and extraterine exposures may not primarily mediate the relation. This finding, in addition to the experimental data from animal models reported above, tends to support a causal association between gestational weight gain and overweight in the offspring.

There are several limitations of this study. Prepregnancy weight was self-reported and therefore may have been underreported. However, if some women who were overweight were incorrectly misclassified as normal weight, this would have biased estimates toward the null. Thus, our estimates of risk are conservative. A second limitation was that the analyses were based on a cohort of individuals born in US cities during the 1960s whose behavioral practices and environmental exposures may be different from those experienced by individuals today. However, if these associations are based on physiologic mechanisms, it is unlikely that the associations observed in the present study would be different now. The historical nature of this cohort may however explain the fact that only 11% of mothers in the sample gained an excessive amount of weight and that such a large proportion of women (65%) gained insufficient weight during pregnancy. Because of the percentage of women gaining excessive weight during pregnancy is significantly higher today, if the association described in the current study is confirmed in a contemporary cohort, the public health importance of excessive gestational weight gain for childhood obesity may be larger than can be estimated here. Additional limitations of this study include the amount of missing data due to changes in the data collected over the study, and that the individuals lost to follow-up had a higher prepregnancy BMI and birth weight. These potential limitations would only create a biased estimate of the results if the association of gestational weight gain with offspring overweight was different among those with complete and missing data. Additionally, there were no differences between the groups in maternal smoking, first-born status, or child sex, and the differences in characteristics reported between the samples were statistically significant because of the large sample size, but were small in
magnitude. Another limitation of this study was that, because all cases of preeclampsia could not be definitively identified at the time the data were collected (20), there may have been some cases in the data set that could have influenced the findings. Likewise, the reason for the apparently low prevalence of gestational diabetes in the data set was unclear, but was likely related to the fact that our study was restricted to full-term infants that lived to 7 y of age. During the time period of the study cohort, there was a higher incidence of perinatal deaths, stillbirths, neonatal deaths, and prematurity among mothers with gestational diabetes. Thus, the effects of medical complications of gestational diabetes on the offspring may have resulted in the exclusion of many offspring of women with gestational diabetes. However, there may have been some cases of gestational diabetes mellitus that were not identified at the time the data were collected, and this limitation could also have influenced the findings. Finally, because BMI is not a measure of adiposity, having a more direct estimate of adiposity, such as skinfold thickness, would have been more clinically relevant.

There are unique strengths of this research. The sample studied was a multiethnic cohort from 12 sites throughout the United States that was followed for 7 y. It is the largest study to have examined the relation between gestational weight gain and overweight in the offspring using criteria defined by the IOM. Because the research was retrospective and part of a research protocol investigating other health outcomes, the potential for reporting bias was reduced. The number and quality of the measures also allowed for meaningful adjustment for a large number of potential confounders. Other than another preliminary report (30), this is the only study to suggest that the relation between gestational weight gain and childhood overweight is strongest among underweight mothers. This finding requires further research before being translated into recommendations, because it is possible that a large pregnancy weight gain among underweight mothers may confer some benefits to the offspring and the mother.

In conclusion, additional research is needed to clarify whether the association between greater gestational weight gain and increased odds of overweight in the offspring is causal and exists in today’s obesogenic environment. If our findings are confirmed, improving compliance with pregnancy weight gain recommendations may be an important and novel strategy in preventing childhood obesity, because almost half of US women exceed these recommendations.

The authors’ responsibilities were as follows—BHW and NS: participated in the design of the present retrospective study, in the analysis and interpretation of the data, and in the writing of the manuscript; JS: participated in the analysis and interpretation of the data and contributed to the writing of the manuscript; and SB: participated in the interpretation of the data and contributed to the writing of the manuscript. None of the authors had a conflict of interest.

REFERENCES