Associations of Gestational Weight Gain With Offspring Body Mass Index and Blood Pressure at 21 Years of Age
Evidence From a Birth Cohort Study

Abdullah A. Mamun, PhD; Michael O’Callaghan, MBBS, FRANZCP; Leonie Callaway, PhD; Gail Williams, PhD; Jake Najman, PhD; Debbie A. Lawlor, PhD

Background—Maternal weight gain in pregnancy is positively associated with offspring body mass index (BMI) and obesity risk in childhood, but whether this increased risk extends into adulthood or results in increases in other cardiovascular risk factors such as elevated blood pressure (BP) is unclear.

Methods and Results—We used a population-based birth cohort of 2432 individuals (50% male) born in Brisbane, Australia, between 1981 and 1983 to prospectively examine the association between maternal gestational weight gain (GWG) and offspring BMI and BP at 21 years. On average, each mother gained 14.8 kg (SD, 5.1 kg) during her pregnancy. At 21 years of age, offspring mean BMI, systolic BP, and diastolic BP were 24.2 kg/m² (SD, 4.9 kg/m²), 116.4 mm Hg (SD, 14.5 mm Hg), and 67.7 mm Hg (SD, 8.5 mm Hg), respectively. Offspring BMI was on average 0.3 kg/m² (95% confidence interval, 0.1 to 0.4 kg/m²) higher for each 0.1-kg/wk greater GWG after adjustment for potential confounding factors. Systolic BP also was greater (0.2 mm Hg per 0.1 kg; 95% confidence interval, −0.2 to 0.6) in offspring whose mothers had higher GWG. Although this association was not statistically significant, it was consistent in magnitude with the association of maternal GWG with offspring BMI and of offspring BMI with BP.

Conclusions—Our findings show that greater GWG is associated with greater offspring BMI and of offspring BMI with BP.

Key Words: blood pressure ■ cardiovascular diseases ■ epidemiology ■ obesity ■ pregnancy ■ young adult

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The majority of studies to date have examined associations with offspring BMI assessed in childhood or adolescence. From a public health perspective, it is important to know whether this association persists into adulthood and whether it results in increased risk of other cardiovascular risk factors such as elevated blood pressure (BP) that are known to result from obesity. To the best of our knowledge, just 1 study has examined whether the association of maternal GWG with offspring obesity persists into adulthood, with that study finding an association with both childhood and adult obesity. Given the association of greater GWG with greater offspring BMI, one might also anticipate an association of greater maternal GWG with offspring elevated BP because it is influenced by greater BMI. In addition to the possibility...
that greater maternal GWG results in greater mean BP in offspring via an effect on the offspring’s BMI, other mechanisms could plausibly link the 2. Greater maternal GWG is associated with hypertensive disorders of pregnancy,10,11 which are in turn associated with elevated BP in offspring.12 Oken and colleagues4 reported a positive association between GWG and both offspring obesity and systolic BP (SBP) assessed at 3 years of age. The association with SBP was attenuated on adjustment for the child’s BMI at 3 years of age, providing support for the hypothesis that this mediated the association of GWG with the child’s SBP. The relevance of higher average SBP at 3 years of age to future cardiovascular health is unclear, whereas several studies have demonstrated that higher SBP in early adulthood (15 to 25 years of age) is positively associated with future cardiovascular disease risk.13–15 To the best of our knowledge, no previous study has examined the association of maternal GWG with offspring BP in early adulthood.

The aim of this study was to examine the association between maternal GWG and offspring BMI and BP at 21 years of age.

**Methods**

**The Study**

This study used data from the Mater-University Study of Pregnancy and its Outcomes (MUSP), a prospective study of 7223 women and their offspring who received antenatal care at a major public hospital in south Brisbane (Australia) between 1981 and 1983 and delivered a live singleton child who was not adopted before leaving the hospital.16,17 These mothers and their offspring have been followed up prospectively, with assessments done when the offspring were 6 months and 5, 14, and 21 years of age. In this study, the main analyses are restricted to 2432 mother-offspring pairs for whom we had information on weight gain during pregnancy and measured offspring height, weight, and BP at 21 years of age. Written informed consent from the mothers was obtained at all data collection phases and from the young adults at the 21-year follow-up of the study. Ethics committees at the Mater Hospital and the University of Queensland approved each phase of the study. Full details of the study participants and measurements have been previously reported.16,17

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

**Measurement of Exposure**

The main exposure is weight gain during pregnancy. A recent study that examined different methods of assessing GWG concluded that none was clearly superior with respect to neonatal outcomes (birth size and gestational age) and that, for maternal weight retention at 6 months, a simple difference (end of pregnancy weight minus beginning of pregnancy weight) was the superior measure, whereas for maternal weight retention at later time points (up to 36 months), the area under the curve method was superior.18 To the best of our knowledge, no such comparison of different methods of assessing GWG has been made with later offspring outcomes. Furthermore, in this study, we do not have serial measurements of maternal weight during pregnancy (only pre-pregnancy and maximum weight in pregnancy assessed at the end of pregnancy) and are therefore unable to assess area under the curve measurements. Therefore, we examined associations with 3 measures of GWG: a simple difference (maximum weight in pregnancy minus pre-pregnancy weight), average weekly gain (the simple difference divided by gestational age), and Institute of Medicine (IOM)19 categories (see Table 1). The results using a simple difference of pregnancy weight gain (maximum weight in pre-pregnancy minus pre-pregnancy weight) were identical to those using average weight gains per gestational week; therefore, we present here only the results for average weight gain per gestational week and for IOM categories.

Weight gain during pregnancy was calculated from measured maximum weight in pregnancy and self-reported prepregnancy weight. Maximum weight in pregnancy was abstracted from the medical chart by an obstetrician associated with the MUSP. At the first antenatal clinic visit, women were asked to report their prepregnancy weight; women were also weighed at this clinic (average gestational age at this clinic, 18 weeks). A high degree of correlation was found between maternal estimate of prepregnancy weight and the measured weight on the first antenatal clinic visit (Pearson correlation coefficient = 0.95). We found 22 women who did not appear to gain or lose weight during pregnancy and another 17 who appeared to gain >30 kg. Although these changes are not impossible, we assumed that they are extreme cases, and for the analytical purposes, we have excluded all 39 of these women from the analyses.

We calculated total GWG as the difference between maximum recorded weight during pregnancy and self-reported prepregnancy weight (determined at the first antenatal visit). We calculated average weight gain during pregnancy as this maximum weight minus the prepregnancy weight divided by gestational age to give a weight gain in 0.20 kg/wk gestation. We also categorized women as having gained inadequate, adequate, or excess weight according to IOM guidelines (see Table 1).19

**Measurement of Outcomes**

BP was assessed at 21 years of age with the participant rested and the arm supported at chest level. Two readings were taken 5 minutes apart with the OMRAN HEM-703C automatic BP device (Omron Corp, Tokyo, Japan) and with the appropriate cuff size for arm circumference. The mean of the 2 measurements was used in all analyses. On the basis of the SBP and diastolic BP (DBP), young adult subjects were classified as normotensive (SBP <120 mm Hg and DBP <80 mm Hg), hypertensive (SBP >140 mm Hg or DBP >90 mm Hg), and otherwise prehypertensive according to the guidelines of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High BP.20 Each young adult’s height was measured without shoes with a portable stadiometer to the nearest 1 cm. Weight was measured with the subject wearing light clothing using a scale accurate to 0.2 kg. Two measures of weight were taken with a 5-minute interval, and the mean of these 2 measures was used in all analyses. BMI (weight in

<table>
<thead>
<tr>
<th>Table 1. IOM Categories</th>
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<tbody>
<tr>
<td>**Prepregnancy BMI, kg/m²</td>
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<tr>
<td>----------------------------</td>
</tr>
<tr>
<td><strong>Adequate</strong></td>
</tr>
<tr>
<td>&lt;19.8</td>
</tr>
<tr>
<td>19.8 to 26.0</td>
</tr>
<tr>
<td>26.0 to 29.0</td>
</tr>
<tr>
<td>&gt;29.0</td>
</tr>
<tr>
<td><strong>Inadequate</strong></td>
</tr>
<tr>
<td>&lt;19.8</td>
</tr>
<tr>
<td>19.8 to 26.0</td>
</tr>
<tr>
<td>26.0 to 29.0</td>
</tr>
<tr>
<td>&gt;29.0</td>
</tr>
<tr>
<td><strong>Excessive</strong></td>
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<tr>
<td>&lt;19.8</td>
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<tr>
<td>19.8 to 26.0</td>
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<tr>
<td>26.0 to 29.0</td>
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<tr>
<td>&gt;29.0</td>
</tr>
</tbody>
</table>

Adapted from Institute of Medicine.19
kilograms by the square of height in meters) was categorized into normal (<25 kg/m²), overweight (25 to 29 kg/m²), and obese (≥30 kg/m²) using the World Health Organization classification of BMI cutoffs.21

Measurement of Confounders and Mediators

The confounders that we considered important to address in our associations were maternal age at birth (in years), maternal educational attainment (did not complete secondary school, completed secondary school, completed further/higher education), parental ethnicity origins (white, Asian, or Aboriginal/Islander), maternal pregnancy BMI, and tobacco consumption during pregnancy. These data were obtained from questionnaires at the first clinic visit and obstetric records. Maternal prepregnancy BMI was calculated on the basis of the maternal measured height at pregnancy and self-reported prepregnancy weight, which was recorded at the study initiation from maternal questionnaires. Maternal tobacco consumption during the last trimester of pregnancy (nonsmoker, 1 to 9 cigarettes per day, and ≥10 cigarettes per day) was recorded at 3 to 5 days after delivery.

To try to understand the possible mechanisms of any associations between maternal weight gain during pregnancy and offspring BMI and BP, we examined the effect of the following potential mediators on any associations: hypertensive disorder of pregnancy, birth weight (measured in grams but transferred into kilograms for the statistical analysis), placenta weight (measured in grams but transferred into kilograms for the statistical analysis), and breast-feeding. Hypertensive disorders of pregnancy were defined as a DBP >90 mm Hg on at least 2 occasions beyond 20 weeks’ gestation associated with proteinuria and/or excessive fluid retention (defined as generalized edema, including the face and hands, and excessive weight gain). Consultant obstetricians made this diagnosis. Birth weight and placental weight were obtained from obstetric records. Duration of breast-feeding (never, <4 months, or ≥4 months) was collected at the 6-month follow-up of the mothers.

Statistical Analyses

The associations of different measures of gestational weight by different characteristics of mother and offspring are presented in Table I of the online-only Data Supplement. We used ANOVA and different characteristics of mother and offspring are presented in Table I of the online-only Data Supplement. We used ANOVA and a χ² test for proportionality (Table 2).

Statistical evidence for a difference in effect between male and female participants was assessed by computing a likelihood ratio test of the interaction with sex. Some evidence was found of sex differences in the associations of GWG (continuous scale) with both BMI and BP (for interactions of exposures with sex, all P<0.05). When we used IOM categories of GWG as the exposure (which will have less statistical power than the continuous measurements), the statistical evidence for an interaction with sex was weaker (for interactions of exposures with sex, all P>0.187). We had no a priori evidence to suggest that these sex interactions would be present, and the direction of association was the same in both male and female subjects. Therefore, we presented all of our main analyses stratified by sex and with male and female subjects combined (the latter will have greater statistical power and therefore the greater estimate precision). Numbers were too small for us to explore whether associations differed by ethnic origins (see online-only Data Supplement Table I for numbers).

A series of multiple linear, logistic, and multinomial regression models (see footnotes to Tables 2 and 3) were used to determine the association of mean GWG with BMI and BP at 21 years of age assessed as continuous and categorical outcomes. In these analyses, we present results for a 0.1-kg/wk weight gain (just below the SD of average GWG). Similarly, a series of regression models were used to assess the association of IOM categories of weight gain with BMI and BP categories (see footnotes to Tables 4 and 5).

The observed associations of maternal GWG with offspring BP at 21 years of age were compared with the expected associations of maternal GWG through the pathways of maternal weight gain–offspring BMI and offspring BMI–BP associations. All analyses were undertaken with Stata version 10.0 (Stata Inc, College Station, Tex).

Results

The study included 2432 mother-offspring pairs for whom we have maternal self-reported GWG and offspring’s measured BMI and BP at 21 years of age. On average, each mother gained 14.8 kg (SD, 5.1 kg) of weight, with an average of 0.4 kg/wk (range, 0.0 to 0.8 kg/wk; SD, 0.1 kg/wk). At 21 years of age, offspring mean BMI, SBP, and DBP were 24.2 kg/m² (SD, 4.9 kg/m²), 116.4 mm Hg (SD, 14.5 mm Hg), and 67.7 mm Hg (SD, 8.5 mm Hg), respectively. According to the 1990 IOM recommendations, 34% women gained excessive weight, 41% gained adequate weight, and 25% gained inadequate weight. At 21 years of age, 21.17% of the young adults were overweight, and another 11.98% were obese. Although prevalence of overweight and prevalence of obesity were similar for young male and female adults, sex differences were found in mean BP and BP categories: Of 1287 male subjects, 33.88% had normal BP, 53.85% had elevated BP, and 12.28% were hypertensive; of 1292 female subjects, 83.98% had normal BP, 14.47% had elevated BP, and only 1.55% were hypertensive.

The unadjusted associations between GWG and characteristics of mother-offspring pairs around pregnancy and at 21 years of age are presented in online-only Data Supplement Table I. Women with male offspring tended to gain more weight during pregnancy than those with female offspring, and those with lower educational attainment were more likely to have excessive weight gain (as assessed by IOM categories) than those with higher education. Offspring birth weight was greater in women who gained more weight during pregnancy. Mothers who had greater prepregnancy BMI were more likely to gain excessive weight during pregnancy compared with other mothers. Mothers who had gained excessive weight during pregnancy were more likely to experience gestational hypertensive disorder, and their offspring were more likely to be overweight and obese at 21 years of age compared with their counterparts. No statistical evidence was found of an association of any measure of maternal GWG with offspring mean SBP and DBP or with BP categories.

Association of GWG With Offspring Obesity

Table 2 shows the mean differences in BMI, SBP, and DBP at 21 years of age by weight gain per week per 0.1 kg, with adjustment for potential confounding and mediating factors in a series of multiple regression models. The results are presented for the 2271 young adults with complete data on all variables in any of the multivariable models. In the age- and sex-adjusted model (when male and female subjects are combined), for 0.1-kg/wk greater increase in maternal gestational weight, young adults’ BMI at 21 years of age was greater on average by 0.3 kg/m² (95% confidence interval [CI], 0.1 to 0.4). With adjustment for potential confounding factors (maternal education, age, ethnicity, parity, prepregnancy BMI, and smoking during pregnancy), the association become somewhat stronger, with maternal prepregnancy BMI being the factor that resulted in this strengthening of associ-
weight gain in pregnancy (0.3 kg/m² higher for every 0.1-kg/wk greater maternal weight gain in pregnancy after adjustment for potential confounding factors). Thus, if the effect of maternal weight gain on offspring BMI were expected to directly translate into an effect on SBP, we would expect SBP to be on average 0.18 mm Hg greater for every 0.1-kg/wk greater maternal weight gain in pregnancy (0.3×0.6). This compares to a point estimate of 0.2 mm Hg for every 0.1-kg/wk greater maternal weight gain in pregnancy in our confounder-adjusted model (model 2, Table 2). Although this estimate is equivalent to the predicted association from the association of maternal weight gain with offspring BMI, in this sample, it is imprecisely estimated with wide CIs that include the null. As further evidence that the effect of GWG on adult BMI might result in greater SBP, when we additionally adjusted the confounder-adjusted association of GWG with SBP for offspring BMI at 21 years of age, it attenuated from 0.2 to 0.0 mm Hg per 0.1-kg/wk GWG (95% CI, −0.4 to 0.4) (model 6, Table 2). No association of maternal weight gain with DBP was found.

Associations of IOM-Recommended GWG Categories With BMI and BP in Offspring

Table 5 shows the mean differences in BMI, SBP, and DBP at 21 years of age by comparing IOM-recommended GWG categories with adjustment for potentially confounding and mediating factors in a series of multiple regression models. In the age- and sex-adjusted model, the offspring of those mothers with excess GWG had greater BMI compared with those whose mothers had inadequate GWG. A little attenuation of this association was found after adjustment for potential confounders. The IOM category of excessive weight gain was associated with modestly higher SBP in offspring, but again, this was imprecisely estimated and had 95% CIs consistent with the null.

Table 3. Cross-Sectional Association Between Offspring BMI and BP at 21 Years of Age (n=2271)

<table>
<thead>
<tr>
<th>Model</th>
<th>Male Participants (n=1134)</th>
<th>Female Participants (n=1137)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BMI</td>
<td>SBP (95% CI)</td>
</tr>
<tr>
<td>1</td>
<td>0.2 (0.0 to 0.4)</td>
<td>0.2 (−0.3 to 0.7)</td>
</tr>
<tr>
<td>2</td>
<td>0.3 (0.1 to 0.5)</td>
<td>0.3 (−0.2 to 0.8)</td>
</tr>
<tr>
<td>3</td>
<td>0.3 (0.1 to 0.5)</td>
<td>0.3 (−0.3 to 0.8)</td>
</tr>
<tr>
<td>4</td>
<td>0.3 (0.1 to 0.5)</td>
<td>0.3 (−0.2 to 0.9)</td>
</tr>
<tr>
<td>5</td>
<td>0.3 (0.1 to 0.5)</td>
<td>0.3 (−0.2 to 0.8)</td>
</tr>
<tr>
<td>6</td>
<td>...</td>
<td>0.0 (−0.5 to 0.5)</td>
</tr>
<tr>
<td>7</td>
<td>0.3 (0.1 to 0.5)</td>
<td>0.0 (−0.5 to 0.5)</td>
</tr>
</tbody>
</table>

Model 1: basic model; results adjusted for offspring age and sex (adjusted for only age for a specific sex). Model 2: confounder-adjusted model; results adjusted for offspring age, sex, maternal age, education, parity, cigarette smoking, and prepregnancy BMI. Model 3: model assessing possibility that maternal gestational hypertension mediates any association; results adjusted for as in model 2 and for gestational hypertensive disorder. Model 4: model assessing possibility that birth weight mediates any association; results adjusted for as in model 2 and for birth weight. Model 5: model assessing possibility that breast-feeding mediates any association as in model 2 and for breast-feeding. Model 6: model assessing possibility that BMI at 21 years of age mediates any association as in model 2 and for BMI at 21 years of age. Model 7: results adjusted for all of the above factors (including BMI at 21 years of age as a mediator for BP outcome). Values in parentheses are 95% CIs.

Predicted and Observed Association of GWG With Offspring BP

Offspring BMI at 21 years of age was positively associated with offspring BP at the same age (Table 4). As noted in Table 2, in our study, offspring BWI was on average 0.3 kg/m² higher for every 0.1-kg/wk greater maternal weight gain in pregnancy after adjustment for potential confounding factors. Thus, if the effect of maternal weight gain on offspring BMI were expected to directly translate into an effect on SBP, we would expect SBP to be on average 0.18 mm Hg greater for every 0.1-kg/wk greater maternal weight gain in pregnancy (0.3×0.6). This compares to a point estimate of 0.2 mm Hg for every 0.1-kg/wk greater maternal weight gain in pregnancy in our confounder-adjusted model (model 2, Table 2). Although this estimate is equivalent to the predicted association from the association of maternal weight gain with offspring BMI, in this sample, it is imprecisely estimated with wide CIs that include the null. As further evidence that the effect of GWG on adult BMI might result in greater SBP, when we additionally adjusted the confounder-adjusted association of GWG with SBP for offspring BMI at 21 years of age, it attenuated from 0.2 to 0.0 mm Hg per 0.1-kg/wk GWG (95% CI, −0.4 to 0.4) (model 6, Table 2). No association of maternal weight gain with DBP was found.

Table 2. Mean Difference in BMI, SBP, and DBP at 21 Years of Age by Weight Gain per Week per 0.1 kg With Adjustment for Potential Confounders and Mediators

<table>
<thead>
<tr>
<th>Model</th>
<th>Male Participants (n=1134)</th>
<th>Female Participants (n=1137)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Difference (95% CI) in SBP</td>
<td>Mean Difference (95% CI) in DBP</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Elevated</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Elevated</td>
</tr>
<tr>
<td>1</td>
<td>0.6 (0.5 to 0.8)</td>
<td>0.5 (0.5 to 0.6)</td>
</tr>
<tr>
<td>2</td>
<td>0.3 (0.1 to 0.5)</td>
<td>0.3 (−0.2 to 0.8)</td>
</tr>
<tr>
<td>3</td>
<td>0.3 (0.1 to 0.5)</td>
<td>0.3 (−0.3 to 0.8)</td>
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<td>4</td>
<td>0.3 (0.1 to 0.5)</td>
<td>0.3 (−0.2 to 0.9)</td>
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<tr>
<td>5</td>
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</tr>
<tr>
<td>7</td>
<td>0.3 (0.1 to 0.5)</td>
<td>0.0 (−0.5 to 0.5)</td>
</tr>
</tbody>
</table>

All results are adjusted for offspring age, sex, maternal age, education, parity, cigarette smoking, and prepregnancy BMI. Values in parentheses are 95% CIs.
Additional Analyses

Additional adjustment for placenta weight in any of our analyses did not alter the multivariable results that we present here (results available from authors on request). Given the previous interaction of maternal prepregnancy BMI and GWG with offspring BMI, we stratified these results by maternal prepregnancy BMI categories as underweight/normal and overweight or obese. We recognized that we had limited power for these analyses but thought that it was appropriate given the previous finding. Because of our limited statistical power, we examined this possible interaction only within our whole sample (ie, male and female subjects combined), and we examined it only for BMI measured on a continuous scale. We found some evidence that the association of maternal weight gain in pregnancy with offspring BMI was modified by maternal prepregnancy BMI, with a stronger association among underweight/normal weight mothers (as previously found). For underweight/normal weight mothers, for 0.1-kg/wk greater increase in maternal gestational weight, offspring BMI at 21 years of age was greater on average by 0.3 kg/m² (95% CI, 0.1 to 0.5); for overweight/obese mothers, the mean difference was −0.1 kg/m² (95% CI, −0.4 to 0.3). However, no strong statistical evidence was found that the association differed by maternal prepregnancy BMI (for interaction of maternal prepregnancy BMI with GWG, P=0.433).

Discussion

Consistent with several previous studies,2–8 we have shown that greater maternal weight gain during pregnancy is associated with greater BMI in offspring. This association was independent of a number of potential confounding and mediating factors. Our findings show that the association with offspring BMI extends into early adulthood. We also found that SBP was greater in offspring whose mothers had gained more gestational weight by an amount that was consistent with the association of maternal GWG with offspring BMI and of offspring BMI with their BP. However, in this study, this modest effect was imprecisely estimated; therefore, larger studies are required to confirm whether the effect of maternal GWG on offspring BMI translates into increased risk of higher BP.

Our work extends previous studies in several ways. First, our study has longer follow-up than previous studies. Thus, we have confirmed the finding from a previous study6 that the effect of greater maternal GWG on offspring adiposity extends into adulthood. This finding further highlights the importance of avoiding excessive weight gain during pregnancy for both the mother’s and her offspring’s future health. Second, we examined whether any association of maternal GWG with offspring BMI also resulted in greater BP. The similarity of the expected (from the association of maternal GWG on offspring BMI) and observed associations of maternal GWG with offspring BP suggests that the effect of maternal GWG during pregnancy on offspring BMI leads to increased offspring BP. However, in our study, the observed association was imprecisely estimated, and larger studies are required to examine this further.

A number of different pathways, which are not mutually exclusive, could explain the association between maternal GWG and offspring BMI later in life. First, the association could simply reflect the tracking in individual size across the life course. Maternal weight gain during pregnancy results from the growing fetus, the placenta, amniotic fluid, and increases in maternal fat stores. Greater increase in any of these will result in greater weight gain. Hence, women with larger babies will gain more weight, and because birth size is positively associated with later size, this could explain an association of maternal GWG and offspring BMI. However, in our study and 2 previous studies,3,4 adjustment for birth weight did not substantially alter the confounder-adjusted association. Additional adjustment for placental weight in our study had no effect on the association.

Second, offspring could inherit their mother’s genetic potential to gain weight or not,22 which might explain a link between greater maternal GWG and greater offspring BMI in later life. We are not able to assess this possibility in our study, nor have previous studies. Third, greater GWG might program greater adiposity in offspring as a result of greater delivery of glucose, amino acids, and free fatty acids to the developing fetus in utero and the developing infant postnatally (via breast-feeding). This phenomenon, called the developmental overnutrition hypothesis, has biological support and some support from epidemiological studies.23–26 Furthermore, a within-sibling comparison of offspring obesity in women who have substantial weight loss after surgery for very severe morbid obesity indicates that, in the case of extreme maternal obesity, evidence exists of developmental overnutrition.27 We did not find that either birth weight or breast-feeding mediated the association in our study, but this does not exclude a developmental overnutrition mechanism that affects later offspring adiposity via intrauterine mechanisms but does not result in greater birth weight. Finally, mothers who gain greater weight during pregnancy may engage in lifestyles (high-energy diet and low levels of...
The association between maternal GWG and offspring BMI was stronger in male than female subjects. We had no a priori reason to anticipate an interaction with sex, and such an interaction has not been reported in any previous studies. This finding needs to be replicated in other studies before we can conclude that weight gain in pregnancy really does have a difference effect on offspring BMI in male and female participants. Because 1 previous large study had found an interaction between maternal BMI at the start of pregnancy and maternal weight gain during pregnancy in their association with offspring BMI, we thought that it was appropriate to look at our results stratified by maternal prepregnancy BMI, although we acknowledge that we had limited statistical power to examine any interaction. The point estimates from these stratified analyses provide some support for the interaction found in the previous large studies in that they suggested that the association occurred primarily in women who were normal weight or underweight at the start of pregnancy. In this study, the numbers of participants from minority ethnic groups were too small to examine whether associations differed by ethnicity.

### Table 4. Mean Difference in BMI, SBP, and DBP at 21 Years of Age by IOM Categories

<table>
<thead>
<tr>
<th>Model</th>
<th>Male Participants (n=1134)</th>
<th>Female Participants (n=1137)</th>
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<tbody>
<tr>
<td></td>
<td>BMI</td>
<td>SBP</td>
</tr>
<tr>
<td>Model 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inadequate</td>
<td>0.1 (0.6 to 0.7)</td>
<td>0.0 (1.1 to 1.1)</td>
</tr>
<tr>
<td>Adequate</td>
<td>0.2 (0.9 to 0.9)</td>
<td>0.0 (1.8 to 1.8)</td>
</tr>
<tr>
<td>Excessive</td>
<td>0.9 (0.3 to 1.6)</td>
<td>0.4 (1.5 to 2.2)</td>
</tr>
</tbody>
</table>

Model 1: basic model; results adjusted for offspring age and sex (adjusted for only age for a specific sex). Model 2: confounder-adjusted model; results adjusted for offspring age, sex, maternal age, education, parity, cigarette smoking, and prepregnancy BMI. Model 3: confounder- and mediator-adjusted model; results adjusted for all factors in model 2 and for potential mediating by gestational hypertensive disorder, birth weight, and breast-feeding (and BMI at 21 years of age was included as a mediator for BP outcome). Values in parentheses are 95% CIs.

### Table 5. Odds Ratios of Becoming Overweight and Obese and of Experiencing Hypertension at 21 Years of Age by IOM Categories

<table>
<thead>
<tr>
<th>Model</th>
<th>BMI Categories</th>
<th>BP Categories</th>
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<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Overweight</td>
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<tr>
<td>Model 1</td>
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<tr>
<td>Inadequate</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Adequate</td>
<td>1.0</td>
<td>1.1 (0.8 to 1.4)</td>
</tr>
<tr>
<td>Excessive</td>
<td>1.0</td>
<td>1.6 (1.2 to 2.1)</td>
</tr>
</tbody>
</table>

Model 1: basic model; results adjusted for offspring age and sex (adjusted for only age for a specific sex). Model 2: confounder-adjusted model; results adjusted for offspring age, sex, maternal age, education, parity, cigarette smoking, and prepregnancy BMI. Model 3: confounder- and mediator-adjusted model; results adjusted for all factors in model 2 and for potential mediating by gestational hypertensive disorder, birth weight, and breast-feeding (and BMI at 21 years of age was included as a mediator for BP outcome). Values in parentheses are 95% CIs.
Table 4. Continued

<table>
<thead>
<tr>
<th>Female and Male Participants Combined (n=2271)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
</tr>
<tr>
<td>-----</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>0.1 (0.4 to 0.6)</td>
</tr>
<tr>
<td>1.2 (0.7 to 1.7)</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>0.3 (0.1 to 0.8)</td>
</tr>
<tr>
<td>0.8 (0.3 to 1.2)</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>-0.1 (1.3 to 1.1)</td>
</tr>
<tr>
<td>-0.3 (1.6 to 1.0)</td>
</tr>
</tbody>
</table>

Study Limitations

The loss to follow-up in the MUSP cohort was large, although similar to other prospective birth cohorts. Participants lost to follow-up were more likely to be of Asian and Aboriginal/Torres Strait Islander background; their mothers were more likely to have been teenagers at their birth, to be less educated, to be single or cohabitating, to have used tobacco and alcohol during pregnancy, and to have been anxious and depressed at their first antenatal visit. Our results would be biased if the associations we have assessed were markedly different in those who were lost to follow-up; we cannot test whether this is the case but cannot think of any reason why there should be an effect modification of the associations we have tested by loss to follow-up. We have compared our estimates of overweight at 20 to 24 years of age with the Australian National Nutritional Survey 1995 for a similar age category and found comparable results. At 21 years of age, the prevalence of overweight was 34% in MUSP. At 20 to 24 years of age, the prevalence of overweight in the Australian National Nutrition Survey was the same (34%).

One of the more important effects of loss to follow-up has been to limit the statistical power of the study. For the main effects examined, our associations are precisely estimated in analyses that combine male and female subjects. However, we had limited power for stratified analyses and limited power to precisely detect the modest association with SBP that would be anticipated from the effect of maternal GWG on offspring SBP.

In MUSP, we did not have serial measurements of maternal weight during pregnancy, so we could not look at area under curve or different patterns of weight gain during pregnancy that might be relevant to offspring obesity and BP. We have examined only 2 cardiovascular risk factors, BMI and BP; further large prospective studies are required to examine associations of maternal GWG with other risk factors such as dyslipidemia, insulin resistance, diabetes mellitus, and ultimately cardiovascular disease events.

Implications

This study found that greater GWG is independently associated with greater risk for offspring BMI in adulthood. We also found some suggestion that this association with greater offspring BMI might result in greater SBP but had limited power to demonstrate this with certainty. Our study supports other evidence suggesting that excessive pregnancy weight gain should be avoided for the health of both mother and offspring. The role of GWG in the obesity epidemic and its associated cardiovascular disease risk factors should be examined further in large studies. Future studies should include further examination of possible effect modification of these associations by maternal BMI at the start of pregnancy and by offspring sex, as well as the extent to which associations affect a range of cardiovascular risk factors in early and into middle-aged adulthood.

Acknowledgments

We thank all the participants in the study, the MUSP data collection team, and data manager at the University of Queensland who has helped manage the data for the MUSP.

Sources of Funding

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Table 6. Odds Ratios of Becoming Overweight and Obese and Experiencing Elevated BP and Hypertension at 21 Years of Age by Weight Gain per Week per 0.1 kg With Adjustment for Potential Confounders and Mediators (n=2271)

<table>
<thead>
<tr>
<th>Model</th>
<th>Normal</th>
<th>Overweight</th>
<th>Obese</th>
<th>Normal</th>
<th>Elevated</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>1.0</td>
<td>1.1 (1.0 to 1.2)</td>
<td>1.0 (0.9 to 1.1)</td>
<td>1.0</td>
<td>1.0 (0.9 to 1.0)</td>
<td>0.9 (0.9 to 1.1)</td>
</tr>
<tr>
<td>Model 2</td>
<td>1.0</td>
<td>1.1 (1.1 to 1.2)</td>
<td>1.1 (1.0 to 1.2)</td>
<td>1.0</td>
<td>0.9 (0.9 to 1.0)</td>
<td>1.0 (0.9 to 1.2)</td>
</tr>
<tr>
<td>Model 3</td>
<td>1.0</td>
<td>1.1 (1.0 to 1.2)</td>
<td>1.1 (1.0 to 1.2)</td>
<td>1.0</td>
<td>0.9 (0.9 to 1.0)</td>
<td>1.0 (0.8 to 1.1)</td>
</tr>
</tbody>
</table>

Model 1: basic model; results adjusted for offspring age and sex. Model 2: confounder-adjusted model; results adjusted for offspring age, sex, maternal age, education, parity, cigarette smoking, and prepregnancy BMI. Model 3: confounder- and mediator-adjusted model; results adjusted for all factors in model 2 and for potential mediating by gestational hypertensive disorder, birth weight, and breast-feeding (and BMI at 21 years of age was included as a mediator for BP outcome). Values in parentheses are 95% CIs.
Disclosures

None.

References

28. Mamun et al. Pregnancy Weight Gain and Offspring CV Risks 1727

CLINICAL PERSPECTIVE

Routine measurement of maternal weight during pregnancy is controversial. The practice was abandoned in many countries in the late 1990s because it was found to be a poor indicator of intrauterine growth retardation. However, this position is now being reconsidered as emerging evidence suggests that greater weight gain in pregnancy might indicate those women who are at increased risk of future cardiovascular and metabolic disease and may be a risk factor for future offspring health. In this study, we examined the association of maternal weight gain in pregnancy with offspring body mass index and blood pressure at 21 years of age. We found that greater weight gain during pregnancy was independently associated with greater risk for offspring body mass index and obesity. We also found some evidence that this association with greater body mass index might result in greater offspring systolic blood pressure. This study supports other evidence suggesting that excessive pregnancy weight gain should be avoided for the health of both mother and offspring. Further large studies are required to confirm these findings and to determine what should be considered healthy weight gain for the short- and long-term health of both mother and offspring. Ultimately, trials are required to explore whether routine monitoring of weight gain in pregnancy and provision of advice about healthy weight gain are effective at reducing obesity-related outcomes in mothers and offspring in the long term.
Associations of Gestational Weight Gain With Offspring Body Mass Index and Blood Pressure at 21 Years of Age: Evidence From a Birth Cohort Study
Abdullah A. Mamun, Michael O'Callaghan, Leonie Callaway, Gail Williams, Jake Najman and Debbie A. Lawlor

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http://circ.ahajournals.org/content/suppl/2009/03/24/CIRCULATIONAHA.108.813436.DC1

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Web-Table 1: The descriptive characteristics of mother-offspring pairs and their associations with gestational weight gain

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N</th>
<th>Gestational weight gain per week per 0.1 kg: mean (SD)</th>
<th>Gestational weight gain per Institute of Medicine Recommendation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inadequate (n=613)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>1212</td>
<td>3.8(1.3)</td>
<td>23.2</td>
</tr>
<tr>
<td>Females</td>
<td>1203</td>
<td>3.7(1.2)</td>
<td>27.6</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Maternal education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete high school</td>
<td>372</td>
<td>3.8(1.3)</td>
<td>29.0</td>
</tr>
<tr>
<td>Complete high school</td>
<td>1540</td>
<td>3.8(1.3)</td>
<td>24.4</td>
</tr>
<tr>
<td>Post high school</td>
<td>489</td>
<td>3.7(1.2)</td>
<td>25.6</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td></td>
<td>0.211</td>
</tr>
<tr>
<td>Parental racial origin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>2174</td>
<td>3.8(1.3)</td>
<td>25.2</td>
</tr>
<tr>
<td>Asian</td>
<td>86</td>
<td>3.6(1.2)</td>
<td>29.0</td>
</tr>
<tr>
<td>Aboriginal-Islander</td>
<td>95</td>
<td>3.7(1.4)</td>
<td>27.4</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td></td>
<td>0.617</td>
</tr>
<tr>
<td>Maternal smoking during pregnancy</td>
<td>None</td>
<td>1556</td>
<td>3.7(1.3)</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>------</td>
<td>------</td>
<td>----------</td>
</tr>
<tr>
<td>1-20 cigarettes/day</td>
<td>666</td>
<td>3.8(1.3)</td>
<td>26.7</td>
</tr>
<tr>
<td>20+/day</td>
<td>175</td>
<td>3.6(1.4)</td>
<td>31.4</td>
</tr>
<tr>
<td>p-value</td>
<td>0.123</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2199</td>
<td>3.7(1.3)</td>
<td>26.4</td>
</tr>
<tr>
<td>Yes</td>
<td>216</td>
<td>4.2(1.4)</td>
<td>15.3</td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breastfeeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>427</td>
<td>3.7(1.4)</td>
<td>29.5</td>
</tr>
<tr>
<td>&lt;4 months</td>
<td>856</td>
<td>3.8(1.3)</td>
<td>25.2</td>
</tr>
<tr>
<td>4+ months</td>
<td>1044</td>
<td>3.7(1.2)</td>
<td>23.7</td>
</tr>
<tr>
<td>p-value</td>
<td>0.234</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI category at 21 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1622</td>
<td>3.7(1.2)</td>
<td>26.8</td>
</tr>
<tr>
<td>Overweight</td>
<td>517</td>
<td>3.8(1.3)</td>
<td>22.2</td>
</tr>
<tr>
<td>Obese</td>
<td>276</td>
<td>3.7(1.4)</td>
<td>22.8</td>
</tr>
<tr>
<td>p-value</td>
<td>0.182</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1430</td>
<td>3.7(1.3)</td>
<td>26.3</td>
</tr>
<tr>
<td>Elevated</td>
<td>821</td>
<td>3.8(1.3)</td>
<td>24.5</td>
</tr>
<tr>
<td>Hypertension</td>
<td>164</td>
<td>3.8(1.3)</td>
<td>22.0</td>
</tr>
<tr>
<td>p-value</td>
<td>0.634</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean (SD) birth weight</td>
<td>Mean (SD) placenta weight</td>
<td>Mean (SD) maternal BMI</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>------------------------</td>
<td>---------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td></td>
<td>Mean difference (95% Confidence Interval)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2414</td>
<td>0.1(0.1, 0.1) *</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2334</td>
<td>0.0(0.0,0.0)*</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2415</td>
<td>-0.1(-0.1,-0.0)*</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2415</td>
<td>-0.3(-0.4,-0.1)*</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2415</td>
<td>0.1(-0.0,0.3)*</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2415</td>
<td>0.5 (0.0, 0.9)*</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>0.046</td>
<td>0.164</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2415</td>
<td>0.0 (-0.2,0.3)*</td>
</tr>
</tbody>
</table>
p-value indicates the significance level of the mean difference (continuous characteristics) or proportions (categorical characteristics) of characteristics by gestational weight gain per kg or gestational weight gain per IOM recommendation. We used an F test for a continuous data and a chi-squared test for categorical data.

* mean difference and 95% confidence interval