Early Pregnancy Weight Gain Exerts the Strongest Effect on Birth Weight, Posing a Critical Time to Prevent Childhood Obesity

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Objective: Gestational weight gain (GWG) is associated with infant birth weight and childhood obesity; however, the patterns of GWG on infant birth weight are poorly understood.

Methods: This analysis in 16,218 mother-child dyads from Tianjin, China, determined the risk of infant size at birth according to GWG occurring throughout the first and second trimester (early GWG) or during the third trimester (late GWG), according to maternal prepregnancy BMI and the 2009 Institute of Medicine recommendations.

Results: Excessive GWG in early and late pregnancy had an increased risk for large-for-gestational-age (LGA) infants (odds ratio [OR]: 2.4; 95% confidence interval [CI]: 1.5-4.0, \(P < 0.001\)). Regardless of prepregnancy BMI, excessive GWG early in pregnancy (<24 weeks) was associated with an increased risk of LGA infants (OR: 2.5; 95% CI: 2.1-3.1, \(P < 0.001\)), and inadequate early GWG was associated with a higher risk of small-for-gestational-age (SGA) infants (OR: 1.4; 95% CI: 1.2-1.7, \(P < 0.001\)).

Conclusions: The pattern of GWG early in pregnancy, regardless of GWG later in pregnancy, had the greatest impact on infant size at birth. Interventions initiated early in pregnancy may facilitate better adherence to the GWG guidelines and minimize the risk of LGA and SGA infants, a potential precursor for childhood obesity.

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Introduction

Obesity prevalence continues to rise worldwide, and women of childbearing age are not an exception (1). The recent increase in maternal prepregnancy BMI has brought to light several studies showing that infant outcomes are worsened with increasing degrees of maternal BMI at conception (2,3). Gestational weight gain (GWG) also influences infant outcomes such as increased risks of preterm birth, macrosomia, and childhood obesity (4,5). Because of the significant health care costs required to manage these outcomes (6), greater attention is being directed toward preventive measures, including the development and testing of interventions to better manage GWG in pregnant women.

Although excessive and/or inadequate total GWG can influence neonatal outcomes, recent observations suggest that the timing of GWG may also be important. A study of 650 pregnant women who were primarily African American, and with low income and obesity first identified this hypothesis and reported that in comparison to women with adequate GWG throughout pregnancy, excess GWG prior to 20 weeks, regardless of weight change later in pregnancy, significantly increased the risk of large-for-gestational-age (LGA) infants (7). Furthermore, a physical activity intervention for healthy management of GWG found that neonates born to women with excessive GWG early in pregnancy (<20 weeks) were not only heavier at birth but had more body fat compared with neonates exposed to...
excessive GWG only late in pregnancy or adequate GWG throughout pregnancy (8). These studies suggest the a priori hypothesis that GWG early in pregnancy may exert the largest influence on intratuerine programming of infant size at birth. However, these findings are limited and there is a need to further explore this hypothesis with larger cohorts. The aim of the present study was to utilize a well-described cohort (2.5) of more than 16,000 pregnant women and infants to evaluate the effect of early versus late GWG on infant size at birth.

Methods

Electronic health care records for both pregnant women and infants were collected from the Women’s and Children’s Health Center system of Tianjin, China, between June 2009 and May 2011 (2.9,10). Prenatal care was established within the first 12 weeks of pregnancy. Abstracted records included general patient information (age, occupation, education, date of first visit, number of pregnancy/infants, last menstrual period, expected delivery date, smoking habits), maternal and family history of disease, clinical measurements (height, weight, blood pressure, gynecological examinations, ultrasonography, gestational diabetes mellitus screening test), pregnancy outcomes (delivery mode, labor complications), and postnatal exams occurring <42 days after delivery (2,10). Pediatric health records include information from neonates (date of birth, sex, gestational weeks of birth, birth weight, birth recumbent length, Apgar score, etc.), family history of diseases, and feeding modality (10). Between June 2009 and May 2011, all available maternal and pediatric records were abstracted (n = 66,285). Application of a priori exclusion criteria to exclude records with missing data pertinent for our analysis plan, with multiple gestation (n = 506), that were missing the complete set of maternal weight data (n = 46,547), and that were missing mother-infant pairs data required for this analysis (n = 3,014) revealed 16,218 mother-infant dyads with complete data and clinical measurements for this analysis. The maternal and infant characteristics were not different between the entire set of extracted data and the complete data set used in this analysis.

The present study included 16,218 records of mother-infant dyads with complete data and clinical measurements and live-born infants born between June 2009 and May 2011. The study and analysis plan were approved by the Tianjin Women’s and Children’s Health Center Institutional Review Board.

Clinical measurements

Specially trained gynecologists in the hospital system obtained anthropometric data of mothers during pregnancy using the same devices. Weight and height were measured on a balance beam scale in light clothing and no shoes (RGZ-120, Jiangsu Shuhong Medical Instruments Co., China). Birth weight was measured to the nearest 0.01 kg using a digital scale (TCS-60, Tianjin Weighing Apparatus Co., China). Length was measured to the nearest 0.1 cm using a recumbent length stadiometer (YSC-2, Beijing Guowangxingda, China). Internal validity comparing the electronic data of birth weight (n = 454) and maternal height and weight (n = 200) found a high level of agreement with the hospital measurement, r = 0.991, 0.998, and 0.997, respectively.

Prepregnancy BMI was calculated using the measured weight (baseline weight) and height recorded at the first prenatal visit occurring within the first 12 weeks of gestation. This was used to categorize women as having underweight (BMI < 18.5 kg/m²), normal weight (18.5 kg/m² ≤ BMI < 24.0 kg/m²), overweight (24.0 kg/m² ≤ BMI < 28.0 kg/m²), or obesity (BMI ≥ 28.0 kg/m²) using Chinese classifications (11). Prepregnancy weight is often inferred when the first measured weight in pregnancy occurs in the first trimester, and several groups have demonstrated good validity and a high correlation (0.95, P = 0.0001) between first measured weight in pregnancy and prepregnancy weight (12,13). The decision to use the Chinese (or Asian) classification for BMI is guided by a World Health Organization report advising to lower cutoff points for Chinese populations (14). Lower BMI cutoff points for Asians with overweight or obesity are required because the observed disease risk in these different populations occurs at 22 to 25 kg/m² (overweight) and at 26 to 31 kg/m² (obesity) for high risk.

Total GWG was calculated as the difference between prepregnancy and delivery weight. The second trimester pregnancy weight gain, defined in this study as “early GWG,” was calculated as the difference between the first measured weight recorded in the first trimester (<12 weeks) and the weight measured between 24 and 27 weeks. The third trimester pregnancy weight gain, defined as “late GWG,” was calculated as the difference between weight measured at weeks 24-27 and weight measured at weeks 32-36. The adequacy of GWG was defined for each woman according to the Chinese maternal prepregnancy BMI classification and the 2009 Institute of Medicine (IOM) recommendations (1): 12.5 to 18 kg (prepregnancy BMI < 18.5 kg/m²), 11.3 to 16 kg (BMI 18.5-23.9 kg/m²), 7 to 11.5 kg (BMI 24.0-27.9 kg/m²), and 5 to 9 kg (BMI > 28 kg/m²) and adjusted for the length of gestation. The adequacy of rates of weight gain during the second and third trimesters was defined according to the Chinese maternal prepregnancy BMI status and the 2009 IOM GWG recommendations (1): 0.453592 to 0.589670 kg (prepregnancy BMI < 18.5 kg/m²), 0.362874 to 0.453592 kg (BMI 18.5-23.9 kg/m²), 0.226796 to 0.317515 kg (BMI 24.0-27.9 kg/m²), and 0.181437 to 0.272155 kg (BMI > 28 kg/m²). We used the translation of US IOM GWG recommendations because no official recommendations exist in China.

Small-for-gestational-age (SGA) infants were identified as a standardized birth weight <10th percentile, whereas LGA infants were identified as a standardized birth weight >90th percentile. Infants who were appropriate for gestational age in the existing population were used as the standard. Low birth weight was defined as <2500 g and macrosomia was defined as birth weight ≥4000 g.

Statistical analyses

Characteristics of mothers and children based on maternal prepregnancy BMI and GWG at early and late gestation were compared using the general linear models and χ² tests. Logistic regression was used to assess the single and joint associations of maternal prepregnancy BMI, early GWG, and late GWG with the risks of infant birth outcomes. All models included maternal age, height, education, smoking status, occupation, family income, and gestational age as covariates. The trend over different categories of maternal prepregnancy BMI and GWG was tested in each model by giving an ordinal numeric value for each dummy variable. All statistical analyses were performed with PASW for Windows, version 21.0 (SPSS Statistics, version 21, IBM Corp., Armonk, New York).

Results

Of the 16,218 mothers studied (Table 1), 12% had underweight, 64% had normal weight, 18% had overweight, and 6% had obesity prior to pregnancy. In accordance with the IOM guidelines, there was an inverse relationship between prepregnancy BMI and total
## TABLE 1
Characteristics of study participants among 16,218 mother-infant pairs according to maternal prepregnancy BMI and gestational weight gain categories in Tianjin, China

| Prepregnancy BMI (kg/m²) | Institute of Medicine categories at early weight gain | Institute of Medicine categories at later weight gain |
|-------------------------|------------------------------------------------------|-----------------------------------------------------|
|                         | Inadequate  | Adequate  | Excessive | P         | Inadequate  | Adequate  | Excessive | P         |
| <18.5                   | 1,872       | 10,446    | 2,982     | 918       | 1,966       | 2,147     | 12,105     | 0.034     |
| 18.5-23.9               |             |           |           |           |             |           |           |           |
| 24.0-27.9               |             |           |           |           |             |           |           |           |
| ≥ 28                    |             |           |           |           |             |           |           |           |
| Maternal characteristics |
| Age, y                  | 26.8 (2.9)  | 27.7 (3.1) | 28.1 (3.4) | 27.8 (3.3) | <0.001     | 27.5 (3.2) | 27.8 (3.1) | 27.7 (3.2) | 0.034 |
|                         | 21.5 (0.8)  | 21.1 (1.5) | 25.6 (1.1) | 30.4 (2.4) | <0.001     | 21.5 (3.5) | 21.0 (3.4) | 22.3 (3.3) | <0.001 |
| Gestational age at delivery, wk | 39.2 (1.2) | 39.2 (1.3) | 39.2 (1.3) | 39.1 (1.3) | 0.015     | 39.3 (1.3) | 39.2 (1.3) | 39.1 (1.3) | <0.001 |
| Caesarean delivery, %   | 55.9        | 62.8      | 75.5      | 85.9      | <0.001     | 60.3       | 59.5      | 67.6      | <0.001 |
| Blood pressure at second trimester, mmHg |
| Systolic                | 103 (9.7)   | 106 (9.9) | 110 (10.1) | 114 (10.9) | <0.001     | 105 (10.1) | 105 (10.1) | 108 (10.3) | <0.001 |
| Diastolic               | 66 (6.8)    | 68 (7.1)  | 71 (7.5)  | 73 (7.9)  | <0.001     | 67 (7.2)   | 67 (7.4)  | 69 (7.3)  | <0.001 |
| Blood pressure at third trimester, mmHg |
| Systolic                | 105 (9.9)   | 108 (10.2) | 112 (10.5) | 115 (11.1) | <0.001     | 106 (10.3) | 107 (10.6) | 109 (10.5) | <0.001 |
| Diastolic               | 67 (7.1)    | 69 (7.3)  | 72 (7.7)  | 75 (8.4)  | <0.001     | 68 (7.4)   | 69 (7.6)  | 70 (7.6)  | <0.001 |
| Education, %            | <0.001      |           |           |           | 0.188      |           |           |           | 0.190 |
| University and above    | 45.6        | 48.9      | 40.8      | 32.7      |           | 45.5       | 48.3      | 45.9      |           |
| Junior college          | 27.0        | 26.7      | 28.3      | 27.8      |           | 26.6       | 25.4      | 27.4      |           |
| High school and under   | 27.4        | 24.4      | 30.9      | 39.5      |           | 27.9       | 26.3      | 26.7      |           |
| Family income, yuan/month, % |
| ≥ 3,000                 | 55.9        | 58.0      | 51.4      | 46.4      | <0.001     | 54.7       | 56.6      | 56.0      | 0.212 |
| 2,000-2,999             | 23.0        | 21.5      | 25.5      | 24.2      |           | 23.2       | 20.9      | 22.8      | 0.188 |
| < 2,000                 | 21.1        | 20.5      | 23.1      | 29.4      |           | 22.1       | 22.5      | 21.2      |           |
| Smoking during pregnancy, % | 1.4   | 0.9      | 1.5      | 1.7      | 0.009      | 1.0        | 1.0      | 1.2      | 0.666 |
| Passive smoking, %      | 47.3        | 49.5      | 50.4      | 53.8      | 0.011      | 48.3       | 47.1      | 50.3      | 0.010 |

Data presented as mean (standard deviation).
GWG (Figure 1). Mothers with obesity gained the least amount of total weight in early and late pregnancy (7.1 ± 3.7 kg and 3.7 ± 2.3 kg, respectively) when compared with overweight (8.2 ± 3.4 kg and 4.1 ± 2.2 kg), normal weight (8.8 ± 3.1 kg and 4.4 ± 2.2 kg), and underweight (8.8 ± 2.8 kg and 4.3 ± 2.0 kg) mothers (P < 0.001).

Gestational weight gain
The weight used to calculate GWG in early and late pregnancy was first measured between 2 and 13 weeks of gestation (mean gestational age 11.0 ± 1.7 wk) and between 24 and 27 weeks of gestation (mean gestational age 25.7 ± 1.0 wk). The final weight measurement was recorded between 32 and 36 weeks of pregnancy (mean gestational age 32.4 ± 0.9 wk). Figure 1 shows the total (panel A) and rate of GWG stratified by the IOM guidelines in each prepregnancy BMI group and for both early pregnancy (panel B) and late pregnancy (panel C). Considering all mothers together, those with excess GWG had the highest rate of GWG, which was two to three times higher than mothers with inadequate GWG (P < 0.001). Mothers with excess early GWG had the highest rate of GWG, which was 37% and 61% higher than mothers with adequate and inadequate GWG early in pregnancy (0.7 ± 0.2 kg/wk, 0.4 ± 0.1 kg/wk, and 0.3 ± 0.1 kg/wk; P < 0.001), respectively. Mothers with excess early GWG also had the highest rate of GWG during late pregnancy compared with mothers with adequate or inadequate early GWG (0.7 ± 0.3 kg/wk, 0.6 ± 0.3 kg/wk, and 0.6 ± 0.3 kg/wk, respectively; P < 0.001).

Early in pregnancy, GWG was inadequate in 12% (n = 1,966), adequate in 13% (n = 2,147), and excessive in 75% (n = 12,105) of mothers. Similarly, in late pregnancy, 13% (n = 2,183) had inadequate GWG, 10% (n = 1,579) had adequate GWG, and 77% (n = 12,456) had excess GWG according to the IOM guidelines. Mothers with excess early GWG had a total GWG that was greater than mothers with either adequate or inadequate GWG early in pregnancy (14.1 ± 3.5 kg, 10.5 ± 2.6 kg, 8.2 ± 2.9 kg, respectively; P < 0.001). Similarly, mothers who exceeded the IOM guidelines late in pregnancy had a total GWG that was greater than mothers who had adequate or inadequate GWG in late pregnancy (13.7 ± 3.7 kg, 10.9 ± 3.2 kg, 9.7 ± 3.4 kg, respectively; P < 0.001).

Effect of early and late GWG on infant birth weight
Effect of early GWG. In all analyses, the reference group was mothers with a normal prepregnancy BMI and adequate GWG in early and/or late pregnancy. In comparison with normal-weight mothers prior to pregnancy (Figure 2A), infants born to underweight mothers were 1.7 times (95% CI: 1.5-2.0) more likely to be SGA (P < 0.001) compared with infants born to mothers who had overweight (OR: 0.7; 95% CI: 0.6-0.9, P < 0.001) and obesity (OR: 0.55; 95% CI: 0.4-0.7, P = 0.005). Compared with infants born to mothers with adequate early GWG, infants born to mothers with inadequate early GWG had a 40% increase (OR: 1.4; 95% CI: 1.2-1.7, P < 0.001) in being SGA.
at birth, whereas infants born to mothers with excessive early GWG had a decreased likelihood of being SGA at birth (OR: 0.54; 95% CI: 0.5-0.6, \( P < 0.001 \)). For early GWG and LGA (Figure 2B), infants born to mothers with obesity were three times more likely (OR: 3.0; 95% CI: 2.5-3.6, \( P < 0.001 \)) to be born LGA compared with infants born to mothers with overweight (OR: 1.7; 95% CI: 1.5-1.9, \( P = 0.001 \)) or underweight (OR: 0.34; 95% CI: 0.3-0.4, \( P = 0.002 \)). Infants born to mothers with adequate early GWG were 50% less likely to be LGA than infants born to mothers with excessive early GWG (OR: 1.5; 95% CI: 1.3-1.9, \( P = 0.001 \)). Infants born to mothers with inadequate early GWG did not have an increased risk of being born LGA (OR: 1.1; 95% CI: 0.9-1.4, \( P = 0.239 \)). This same pattern of early GWG was evident for both low birth weight and macrosomia, respectively (data not shown).

**Effect of late GWG.** Considering only maternal prepregnancy BMI, infants born to mothers who were underweight prior to pregnancy had a 70% increased risk for being born SGA (95% CI: 1.5-2.0, \( P = 0.01 \)), whereas no risk existed for infants born to mothers with overweight (OR: 0.72; 95% CI: 0.6-0.9, \( P = 0.76 \)) and obesity (OR: 0.55; 95% CI: 0.4-0.7, \( P = 0.79 \)) (Figure 3A). Conversely, the risk of an infant being born LGA was positively associated with maternal BMI prior to pregnancy (\( P < 0.001 \)) (Figure 3B). Infants born to mothers with obesity had a threefold increased risk of being born LGA (OR: 3.0; 95% CI: 2.5-3.6, \( P < 0.001 \)), whereas no increased risk existed for infants born to mothers with overweight (OR: 1.7; 95% CI: 1.5-1.9, \( P = 0.87 \)) or underweight (OR: 0.34; 95% CI: 0.3-0.4, \( P = 0.16 \)). Considering the pattern of late GWG, in comparison with mothers with adequate late GWG, infants born to mothers...
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Patterns of GWG across the entire pregnancy. Infants born to mothers with inadequate GWG in both early and late pregnancy (OR: 2.0; 95% CI: 1.3-3.0; P = 0.001) had the greatest risk of being born SGA (Figure 4A), whereas mothers with inadequate early GWG but excessive late GWG only had a 15% increased risk of their infant being born SGA (OR: 1.2; 95% CI: 0.8-1.6). In contrast, infants born to mothers with excess GWG in both early and late pregnancy (OR: 2.4; 95% CI: 1.5-4.0) pregnancy had the highest risk (P = 0.001) for being born LGA (Figure 4B), whereas infants born to mothers who had excessive early GWG followed by either inadequate (OR: 1.9; 95% CI: 1.1-3.2) or adequate late GWG (OR: 1.7; 95% CI: 1.0-3.0) had a reduced risk of being born LGA (P < 0.001). Therefore, regardless of prepregnancy BMI, a U-shaped association between early GWG and infant birth weight is evident such that excessive early GWG was associated with a higher risk of LGA infants, whereas inadequate early GWG was associated with a higher risk of SGA infants. We observed the same findings for macrosomia and low birth weight, respectively (data not shown).

Discussion

Timing of GWG has implications for the future health of women and children. We observed that GWG occurring early in pregnancy that exceeds the IOM recommendations, regardless of the pattern of weight gain later in pregnancy, increases the risk of an infant born LGA or with macrosomia. Conversely, early GWG that is below the IOM recommendations increases the risk for having an infant born SGA; however, this effect was attenuated by increasing weight gain to optimal levels later in the pregnancy.

Historical examinations of weight gain in pregnancy conclude that very little weight gain occurs in the first trimester and weight thereafter increases linearly until delivery (1). Following the publication of the IOM recommendations for weight gain in pregnancy, the impact of total GWG on maternal and infant outcomes has received increasing attention (1). Epidemiological studies show that excessive GWG across the entire pregnancy increases the risk for LGA infants (15,16), whereas inadequate GWG increases the risk for SGA infants (2,4,17), and our cohort concurs with these previous observations. Much less attention is given to the patterns of GWG and whether weight gain early and/or late in pregnancy is more or less problematic. It has been suggested that a 2-pound weight gain in excess of the IOM guidelines in women with obesity during the first trimester is a strong predictor for excess GWG throughout pregnancy (18). Similar findings with excess weight gained even earlier, at 8 to 12 weeks, were reported (19,20). Identifying the most important windows of GWG will allow prevention strategies to be better designed and targeted toward health outcomes in mothers and infants.

The present study suggests that early pregnancy is a vital period for ensuring that mothers receive advice and close monitoring of GWG. Longitudinal studies support this idea, with reports that early GWG (between 0 and 20 weeks) is associated with a greater risk for childhood obesity (21,22). Unfortunately, behavioral interventions with the goal of reducing total GWG and adverse outcomes in infants have achieved underwhelming results, particularly in women with obesity, where the impact of early and late GWG has the most profound effect on infant size at birth. For example, the Fit for Delivery Study, which delivered a lifestyle intervention during pregnancy, was successful in reducing GWG in normal-weight women only (13). Similarly, the UPBEAT trial, which enrolled women with obesity in a diet and physical activity intervention, found no effect on GWG between the intervention and control groups and no differences in prevalence of LGA infants (23). Of note, both of these large randomized controlled trials initiated their interventions after week 16 of pregnancy, and therefore if the hypothesis that early GWG programs infant size at birth is true, it appears that the critical window for the programming of neonatal size at birth and adiposity was missed in these studies. In support of this idea, the most successful intervention targeting GWG in women with obesity was initiated as early as 7 weeks and led to a reduction in LGA and macrosomia in the offspring (24). Collectively, these intervention studies support
the idea that women should receive counseling regarding optimal weight gain early in pregnancy, and ideally at the first prenatal appointment, which would likely occur in a critical window for neonatal size at birth.

One possible explanation for the increased risk for LGA with maternal obesity and excess GWG is that the infant metabolism in utero could be compromised by the obesity milieu of the mother. Energy expenditure, one of the two major determinants of body weight, has been shown to be lower in infants at 3 months of age born to mothers with obesity when measured over several days by doubly labeled water (25). The obvious maternal behavior that could contribute to excess GWG is changes in energy intake. Maternal energy intake in the early stages of pregnancy is usually prescribed as minimal increases of ~150 kcal/d to upwards of 350 into the second trimester (26). We used a publicly available maternal energy intake calculator to estimate the energy intake in women in this study, determined by prepregnancy weight, height, and measured weights throughout the three trimesters (27). Using the mean data, the calculator suggests that those women who had excessive GWG in early and late pregnancy were consuming ~200 kcal/d more than women in the reference group (those who had adequate GWG in both early and late pregnancy). Studies of the determinants of GWG in mother-infant dyads are warranted because the potential for developmental programming of energy intake and energy metabolism is not known, and these factors probably play a key role in the development of postnatal adiposity in offspring.

The strength of this study was the use of a large well-characterized cohort of mother-infant dyads to explore GWG in early and late gestation and the use of the IOM rate of gain guidelines to classify weight gain rather than the use of total net weight gain. One limitation was that this study includes only Chinese women, although the women studied resided in both rural and urban regions and therefore would likely encompass varying levels of physical activity and patterns of dietary intake. Importantly, routine obstetrical care in China is identical to the United States, with establishment of care in the first trimester followed by monthly checkups, then biweekly, and finally weekly through to delivery. It should also be noted that the abstracted data include gestational diabetes and hypertension diagnoses but do not preeclampsia. We acknowledge that these pathologies can influence both GWG and infant size at birth, but because of low incidence in our cohort, we did not explore these in regards to infant outcomes. Finally, all available maternal and pediatric records were initially abstracted from 66,285 women, but a final sample size of 16,218 records was used, which may influence the generalizability of some of the outcomes.

In summary, excess GWG early in pregnancy regardless of weight gain that occurs later increases the risk of LGA in the infant. Because this period of pregnancy could influence the development of increased adiposity in the child, this is the opportune time to initiate lifestyle interventions in pregnant women. Data on unintended pregnancy in the United States suggest approximately 49% of pregnancies are unplanned (28), and therefore capturing couples who are planning pregnancy is a critical strategy for public health programs targeting intergenerational obesity prevention. Further, longitudinal research and lifestyle interventions are merited on infants born to mothers with excess GWG, specifically those mothers with excess GWG early in pregnancy, to learn whether this period is associated with more profound obesity in childhood. Finally, lifestyle interventions targeting women prior to pregnancy need to be developed and tested.

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