Association between Prepregnancy Body Mass Index and Gestational Weight Gain with Size, Tempo, and Velocity of Infant Growth: Analysis of the Newborn Epigenetic Study Cohort

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Abstract

Background: The first 1000 days of life is a critical period of infant growth that has been linked to future adult health. Understanding prenatal factors that contribute to variation in growth during this period could inform successful prevention strategies.

Methods: Prenatal and maternal characteristics, including prepregnancy obesity and gestational weight gain were evaluated in relation to weight growth trajectories during the first 24 months of life using the SuperImposition by Translation and Rotation (SITAR) method, which provides estimates of infant size, timing to peak velocity, and growth velocity. The study sample included 704 mother-infant dyads from a multiethnic prebirth cohort from the Southeastern United States. The total number of weight measures was 8670 (median number per child = 14).

Results: Several prenatal and maternal characteristics were linked with infant growth parameters. The primary findings show that compared to women with a prepregnancy BMI between 18 and 24.9, women with a prepregnancy BMI ≥ 40 had infants that were 8% larger during the first 24 months, a delayed tempo of around 9 days, and a slower velocity. Mothers who had greater than adequate gestational weight gain had infants that were 5% larger even after controlling for prepregnancy BMI and several other covariates.

Conclusions: The findings contribute new data on the associations between gestational weight gain and aspects of early growth using the SITAR method, and support a growing consensus in the literature that both prepregnancy BMI and gestational weight gain relate independently to risk for greater postnatal weight growth.

Introduction

The first 1000 days of life, from conception through 24 months, is a critical period of infant growth.¹ Among healthy infants, there is typically an initial loss of birth weight during the first 2 weeks followed by an increase in weight-for-height gain (or mass—otherwise weight alone increases with no decline) and a peak around 6 weeks. Subsequently, there is a decline and leveling off of

weight growth around 6 months.² Variation in this pattern of infant growth has been related to future risk for childhood obesity and adult health.^{1,3,4} Infants that reach a peak growth earlier, gain weight or mass more rapidly, or are larger during the first 2 years are at greater risk for obesity and chronic disease later in life.⁵ It is not fully understood what factors are uniquely associated with variation in infant growth during this period. Thus, a more complete accounting of these factors could advance

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our understanding of early childhood obesity etiology and inform prevention strategies.

A range of prenatal exposures are associated with gestational age, birth weight, and subsequent child BMI.^{6–9} Recent studies have linked some of these same exposures with early postnatal growth. For instance, smoking during pregnancy has been linked both directly with rapid growth and indirectly to rapid growth by low birth weight.¹⁰ Prepregnancy BMI and gestational weight gain (GWG) have also been associated with rapid weight gain between birth and 6 months.¹¹ It is important to clarify the factors associated with growth during early postnatal growth as well as those related to birth weight given that birth weight and infant growth have been shown to independently predict future childhood obesity.^{4,12}

Effectively modeling early postnatal growth is critical to understanding factors that may contribute to variation in growth. Extant studies have modeled infant growth by examining changes between two time points during infancy. Although useful in some circumstances, this method does not fully account for the dynamic growth patterning during these early months. Researchers have recently developed and proposed the use of a novel random effects modeling method for assessing dynamic growth during infancy called SuperImposition by Translation and Rotation (SITAR).¹³ The SITAR method allows for examining factors that may be associated with biologically important growth parameters: namely, *size*—an expression of weight; *tempo*—an expression of the timing of maximum growth velocity; and *velocity*—an expression of the rate of growth. To better understand the relationship between prenatal factors and early life growth, the SITAR method was applied to the study of infant growth in three birth cohorts (from Portugal, Italy, and Chile).¹⁴ Investigators showed that maternal smoking, prepregnancy BMI, parity, and gestational hypertension were all associated with various aspects of infant growth.¹⁴ These results were fairly consistent across the cohorts. The study, however, did not examine gestational weight gain, which is also a risk factor for later childhood obesity independent of prepregnancy BMI.^{15–18}

In this study, we aimed to examine the associations among maternal characteristics, prenatal factors—including gestational weight gain—and size, tempo, and velocity. We hypothesized that maternal smoking, parity, and gestational hypertension would be related to infant growth parameters derived using SITAR. We further hypothesized that both prepregnancy obesity and GWG would be associated with infant growth parameters.

Methods

Study Sample

Data were from the Newborn Epigenetic Study (NEST). NEST is a prebirth cohort based in the Southeastern United States that was initiated in 2005. The institutional review board approved studies involving these participants, and

informed written consent was obtained from all mothers. Participant identification and enrollment procedures have been previously described in detail elsewhere.^{19,20} Briefly, 2595 pregnant women were recruited from prenatal clinics serving Duke University Hospital and Durham Regional Hospital Obstetrics facilities from April 2005 to June 2011. Eligibility criteria were as follows: age ≥ 18 years, English speaking, pregnant, and intention to use one of the two obstetrics facilities for the index pregnancy to enable access to labor and birth outcome data. These analyses were limited to a subset of participants from whom data were available on maternal prenatal characteristics and infant weight data for at least two data points needed for estimated growth trajectories ($n = 740$). The total number of weight measures was 8670 (median number per child = 14). The 740 children included were comparable to the sample not used in the analyses with respect to maternal prepregnancy obesity and GWG. There were some differences between the two groups with respect to birth weight and percent born full term. The analysis cohort had offspring with a slightly higher mean birth weight than the full cohort (mean [M] = 3234.4 g; standard deviation [SD] = 540.9 vs. M = 3128.2; SD = 722.3; $p < 0.001$) and fewer in the low-birth-weight category of 2500 g or less (9% vs. 15%; $\chi^2 = 16.0$). The effect size for the mean difference in birth weight between the groups was small (Cohen's $d = 0.17$).²¹ There were no mean differences in number of weeks of gestation between the groups (M = 38.9; SD = 1.6 vs. M = 38.2; SD = 2.9), but there was a slightly higher percentage of infants born full term (gestational weeks ≥ 37) in the analysis cohort than the overall cohort (89% vs. 82%; $\chi^2 = 16.6$). Data for infant weight were retrieved from the infant's electronic medical record, which is based upon measured weight during clinic visits.

Maternal Characteristics and Prenatal Exposures

Background characteristics abstracted from medical records included the following: sex, race/ethnicity, maternal age, parity, maternal height, and total gestational days. Health-related variables included gestational diabetes and pregnancy hypertension abstracted from medical records and smoking status from self-report on the enrollment survey. Prepregnancy BMI was computed from self-reported weight at last menstrual period and measured height. Prenatal clinics use the same model of stadiometers and weight scales (seca GmbH & Co. KG, Hamburg, Germany) with height accurate within one eighth of 1 inch and weight accurate within 0.1 lbs. GWG was computed as the difference between the weight at the last menstrual period and the last weight taken up to 7 days before or at delivery from medical records. The Institute of Medicine (IOM) GWG categories²² were calculated because this method defines clinically relevant categories of weight gain (more than recommended, recommended, and less than recommended) in relation to prepregnancy BMI.

Table 1. Sample Characteristics

	N or Mean	% or SD
Child Characteristics		
<i>Gestation</i>		
Gestational age (days)	272.94	11.10
>= 37 weeks	656	89
<37 weeks	84	11
<i>Gender</i>		
Male	385	52
Female	355	48
<i>Race/Ethnicity</i>		
African American	368	50
Hispanic	156	21
Other	41	6
Caucasian	175	24
Maternal Characteristic		
Maternal height (meters)	1.62	0.08
Maternal age	27.96	6.05
<i>Maternal Education</i>		
College graduate	178	25
High school or some college	340	48
Less than high school	184	26
<i>Parity (# of live births)</i>		
none	240	32
1–3	461	62
4 or more	38	5
<i>Gestational diabetes</i>		
Yes	47	7
No	676	93
<i>Hypertension (pregnancy induced)</i>		
Yes	43	6
No	694	94
<i>Maternal smoking during pregnancy</i>		
Yes	162	23
No	534	77
<i>BMI Categories</i>		
<18.5	36	5
18.5–24.9 (referent)	270	37
25–29.9	178	24
30–34.9	124	17
35–39.9	57	8
>= 40	69	9

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Table 1. Sample Characteristics continued

	N or Mean	% or SD
<i>Gestational weight gain (IOM categories)</i>		
Less than adequate	163	22
Adequate	158	22
More than adequate	413	56
Gestational weight gain (mean)	14.26	8.21

Statistical Analyses

We examined prepregnancy obesity and IOM gestational weight gain categories in relation to infant weight growth trajectories from birth to 24 months. Specifically, we estimated three parameters of early life growth believed to have a lasting effect on child and adult health: infant size, timing to peak velocity (tempo), and velocity. A larger size, earlier peak velocity, and greater velocity are believed to be high risk.²³ These parameters were estimated using the SITAR model, a shape invariant model with a single fitted curve.^{13,24} The SITAR R program fits cubic splines and was fit with log transformation of weight measurements.²⁵ For these analyses, three internal knots were used at quantiles of the age distribution. The three parameters estimated from the SITAR model represent the adjustments (*i.e.*, shifting and scaling random effects) needed to match individual growth to reference curves within the sample. *Size* (α_i) indicates how much larger or smaller a child is, and a positive value would indicate a larger size or heavier child; *tempo* (β_i) denotes how much earlier or later a child reaches peak growth, and a negative value would indicate growth that is more advanced and peaks at an earlier age; and *velocity* (γ_i) reflects how much faster or slower a child's weight trajectory is, and a positive value would indicate faster growth.

Results

Descriptive Results

Table 1 displays the full listing of sample characteristics. In brief, 50% were African American, 21% Hispanic, 24% Caucasian, and 6% other. Mean age of mothers at delivery was 28 years (SD = 6.05). The percentage of women with a prepregnancy BMI in the obese range was 34%. As defined by IOM categories, 22% of women gained less weight during pregnancy than what is considered adequate, 22% had adequate weight gain, and 56% had greater than adequate weight gain.

Explanatory Variables for Growth Trajectories

Table 2 displays the association between prepregnancy BMI, IOM GWG, and other prenatal covariates and infant size, tempo, and velocity parameters in the NEST cohort. Model 1 presents the parameters minimally adjusted for sex, race, maternal height, maternal age, parity, total

Table 2. SITAR Growth Parameter Estimates, 95% Confidence Interval, and p-value for Selected Covariates

	Size % (95% CI) p-value	Tempo β^a (95% CI) p-value	Velocity % (95% CI) p-value
Model 1			
Gestational age (days)	0.002 (0.00, 0.003) 0.05	-0.02 (-0.03, -0.01) 0.00	-0.00 (-0.01, 0.00) 0.24
Gender			
Male (referent)			
Female	2.4 (-1.0, 5.8) 0.17	0.33 (0.19, 0.48) 0.00	-18.2 (-25.5, -10.9) 0.00
Race/Ethnicity			
Caucasian (referent)			
African American	-3.0 (-7.9, 1.9) 0.23	0.03 (-0.18, 0.25) 0.75	5.7 (-4.8, 16.2) 0.29
Hispanic	-3.4 (-9.6, 2.7) 0.28	-0.27 (-0.54, -0.01) 0.05	13.6 (0.4, 26.9) 0.05
Other	-13.0 (-21.3, -4.7) 0.00	-0.36 (-0.71, 0.00) 0.05	22.1 (4.2, 40.0) 0.02
Maternal height	0.50 (0.26, 0.74) 0.00	0.84 (-0.20, 1.88) 0.12	-0.52 (-1.04, 0.00) 0.05
Maternal age	0.01 (0.00, 0.01) 0.00	0.02 (0.00, 0.03) 0.02	-0.01 (-0.02, 0.00) 0.04
Maternal Education			
Less than High School (referent) College	-8.6 (-14.9, -2.2) 0.01	-0.33 (-0.61, -0.06) 0.02	16.7 (3.0, 30.3) 0.02
High School or Some College	-0.4 (-4.8, 4.0) 0.85	-0.04 (-0.23, 0.16) 0.71	1.5 (-7.9, 11.0) 0.75
Parity (# of live births)			
0 live births (referent)			
1-3 live births	-2.7 (-6.5, 1.1) 0.17	-0.14 (-0.31, 0.02) 0.09	3.7 (-4.5, 11.9) 0.38
4 or more live births	0.0 (-8.9, 9.0) 0.94	-0.24 (-0.63, 0.15) 0.22	-2.4 (-21.7, 16.8) 0.80
Model 2^b			
Gestational diabetes			
No (referent)			
Yes	13.2 (6.4, 20.0) 0.00	0.47 (0.18, 0.75) 0.00	-29.4 (-43.6, -15.2) 0.00
Hypertension (pregnancy induced)			
No (referent)			
Yes	-6.1 (-13.1, -0.8) 0.08	-0.06 (-0.34, 0.23) 0.70	10.9 (-3.7, 25.4) 0.15
Maternal Smoking During Pregnancy			
No (referent)			
Yes	2.0 (-2.1, 6.2) 0.34	0.22 (0.05, 0.39) 0.01	-5.7 (-14.4, 3.0) 0.20
BMI Categories			
<18.5	-6.5 (-14.2, 1.2) 0.10	-0.16 (-0.47, 0.20) 0.31	12.0 (-4.1, 28.2) 0.14
18.5-24.9 (referent)			
25-29.9	1.0 (-3.4, 5.3) 0.66	-0.05 (-0.23, 0.12) 0.55	0.6 (-8.6, 9.8) 0.90
30-34.9	2.9 (-1.9, 7.8) 0.24	0.04 (-0.16, 0.23) 0.73	-0.8 (-11.0, 9.4) 0.87
35-39.9	2.7 (-4.0, 9.4) 0.44	-0.01 (-0.28, 0.26) 0.95	2.0 (-12.0, 16.0) 0.78
>40	7.8 (1.5, 14.0) 0.02	0.30 (0.05, 0.56) 0.02	-15.6 (-28.6, -2.5) 0.02

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Table 2. SITAR Growth Parameter Estimates, 95% Confidence Interval, and p-value for Selected Covariates *continued*

	Size % (95% CI) p-value	Tempo β^a (95% CI) p-value	Velocity % (95% CI) p-value
Model 3^c			
Gestational weight gain (IOM categories)			
Less than adequate	−3.4 (−8.5, 1.7) 0.19	−0.10 (−0.31, 0.12) 0.34	7.9 (−2.8, 18.6) 0.15
Adequate (referent)			
More than adequate	4.5 (0.3, 8.6) 0.04	0.06 (−0.12, 0.24) 0.54	−5.7 (−14.5, 3.1) 0.20

^aTempo is on the age unit months due to transformation of weight on the log scale. Beta values can be converted to days by multiplying the value by 31 days (e.g., .30*31 = 9.3 days); ^bModel 2 includes covariates in Model 1; ^cModel 3 includes covariates in Model 1 and Model 2; Bold font indicates statistical significant result.

Figure 1. Fitted growth curves for NEST data. (A) Curves based on IOM gestational weight gain categories. Curves for children of mothers in the greater than recommended weight category are above that of children of mothers in the recommended weight category; the differences between the two increase over time. Timing to peak growth is similar among the groups. (B) Curves for infants born to women with prepregnancy BMI 18.0–24.9 versus women with prepregnancy BMI >40. Curves of children born to mothers with prepregnancy BMI >40 are similar to children born to healthy weight mothers through the first months of life, but diverge and become greater around 8–9 months. Timing to peak growth is delayed among children born to mothers with prepregnancy BMI >40 compared to children born to healthy weight mothers. IOM, Institute of Medicine; kg, kilograms; NEST, Newborn Epigenetic Study.

gestational days, and education obtained from the SITAR model. Model 2 presents an adjusted model specifically focusing on BMI categories with adjustment for covariates in model 1. Model 3 presents a fully adjusted model specifically focusing on GWG categories with adjustment for covariates in models 1 and 2.

As shown in model 2, infants born to women with gestational diabetes were 13% larger in size ($\delta_\alpha = 13.2$; $p < 0.0001$), had a delayed tempo of around 14 days ($\delta_\beta = 0.47$; $p = 0.002$), and a slower growth velocity ($\delta_\gamma = -29.4$; $p < 0.0001$). Smoking status was unrelated to infant size or velocity, but infants of mothers who smoked had delayed tempo of around 6.8 days ($\delta_\beta = 0.22$; $p = 0.01$). Model 2 also shows that compared to women with a prepregnancy BMI between 18 and 24.9, women with a prepregnancy BMI ≥ 40 had infants that were 8% larger during the 24 months ($\delta_\alpha = 7.8$; $p = 0.02$), a delayed tempo of around 9 days ($\delta_\beta = 0.30$; $p = 0.02$), and a slower velocity ($\delta_\gamma = -15.6$; $p = 0.02$).

As shown in model 3, independent of prepregnancy BMI, GWG was also associated with infant growth. Mothers who had greater than adequate gestational weight gain had infants that were 4.5% larger ($\delta_\alpha = 4.5$; $p = 0.04$). GWG was not significantly associated with tempo and velocity parameters.

In a sensitivity analysis, we excluded women with type 2 diabetes from the analyses ($n = 14$). Excluding these women resulted in a slight attenuation of the effects of prepregnancy BMI and GWG. In these analyses, compared to women with a prepregnancy BMI between 18 and 24.9, women with a prepregnancy BMI ≥ 40 had infants that were 7% larger during the 24 months ($\delta_\alpha = 6.8$; $p = 0.05$), a delayed tempo of around 9 days ($\delta_\beta = 0.29$; $p = 0.06$), and a slower velocity ($\delta_\gamma = -14.6$; $p = 0.05$). With respect to GWG, women who had greater than adequate GWG had infants that were 4% larger ($\delta_\alpha = 3.9$; $p = 0.07$). The effect of gestational diabetes remained largely the same: Infants born to women with gestational diabetes were 13% larger in size ($\delta_\alpha = 13.9$; $p < 0.0001$), had a delayed tempo of around 17 days ($\delta_\beta = 0.54$; $p = 0.001$), and a slower growth velocity ($\delta_\gamma = -31.1$; $p < 0.0001$).

Figure 1 displays the trajectories predicted for children born to mothers who differed based on prepregnancy BMI categories (Fig. 1A) and GWG categories (Fig. 1B) corresponding to models 2 and 3 above. In both cases, children in the exposed groups differ from the nonexposed. Thus, for example, if predicted weight at 24 months is ~ 12 kilograms (kg) among mothers with a BMI in the normal range, then children of class 2 obese mothers (BMI > 40) would be ~ 12.9 kg. If predicted weight at 24 months is ~ 12 kg among mothers with adequate GWG, then children of mothers with greater than adequate weight gain would be ~ 12.5 kg.

Discussion and Conclusions

In this multiethnic sample of infants born in the Southeastern United States, we aimed to examine the extent to

which maternal characteristics and prenatal factors relate to parameters of growth during the first 2 years of life. We did so using the novel SITAR method, which facilitated simultaneous estimation of covariate effects related to three biologically relevant growth parameters: infant size, timing to peak growth, and growth velocity. Although the field has increasingly called for a better understanding of early infant growth, few studies have examined predictors of dynamic growth during early childhood. The findings here add to the growing evidence and suggest that prepregnancy obesity and greater than adequate GWG are both significant predictors of infant weight growth even after accounting for other relevant variables. The use of longitudinal data and modeling with the SITAR method further highlight a meaningful effect of maternal weight on infant growth during the first 2 years of life.

One of the main goals of this article was to contribute new data on the associations between GWG and early growth, and to replicate and extend the work of Pizzi and colleagues, who examined maternal and prenatal characteristics in relation to SITAR-derived parameters of infant growth in two European cohorts (Portugal and Italy) and one South American cohort (Chile).¹⁴ In that study, consistency was observed across the three cohorts with respect to maternal height, parity, and prepregnancy overweight/obesity being positively associated with infant size from birth to 24 months. They also observed that prepregnancy overweight/obesity and gestational hypertension were associated with delayed tempo (timing to peak velocity). Similarly, our data show a positive relationship between maternal height and infant size, but we did not observe a relationship with parity. Also consistent, we show that prepregnancy obesity was associated with a larger size and delayed tempo. Whereas Pizzi and colleagues observed no effect of gestational diabetes and an effect of gestational hypertension (for a delayed tempo only), we found that gestational diabetes was related to an overall larger size, delayed tempo, and less-rapid growth velocity, as well as a consistent, but not statistically significant, effect of gestational hypertension on reduced size ($p = 0.08$). We further also show that greater than adequate GWG, regardless of prepregnancy BMI, was associated with an overall larger size.

Prepregnancy obesity and greater than adequate GWG are known to be associated with subsequent childhood obesity.^{12,26,27} Recently, greater attention has been directed at understanding how these and other factors are associated with early childhood weight.¹⁶ The findings are consistent with a growing body of literature showing prepregnancy obesity and GWG to be associated with weight outcomes, variously measured, during early childhood.¹² Specifically, our results show that infants of mothers with a prepregnancy BMI greater than 40 were 8% larger than infants of women with a prepregnancy BMI in a “healthy” range (18.5–24.9). Also, relative to infants of healthy weight mothers, infants of heavier mothers were delayed by around 9 days in reaching their peak velocity and demonstrated a slower pace of growth. Pizzi and colleagues reported a very similar

pattern among infants from a Portuguese cohort—an 8% larger size and delay of 8 days in reaching peak velocity. The delay in tempo and less-rapid weight gain may relate to a “ceiling effect”—larger infants experience a delay in growth to peak velocity and slower overall growth than their lighter counterparts. A unique contribution of our study was that it is the first to examine GWG in relation to infant gain using the SITAR method. The findings here show that GWG remains a significant predictor of infant weight growth even after taking into account prepregnancy BMI are supported by other studies.^{4,12}

Beyond the associations observed for prepregnancy obesity and GWG, we also found significant effects for gestational diabetes. Children born to mothers who had gestational diabetes were 13% larger during infancy (controlling for other factors), had a delay of 14 days in reaching peak velocity, and a significantly less-rapid infant weight growth relative to their healthy counterparts. Thus, the findings here align with previous results showing a high risk of macrosomia and later obesity among children born of mothers with gestational diabetes.^{28,29} We further show that infants of mothers with diabetes are markedly larger during the first 24 months. Continued research is needed in other cohorts to verify the findings here given that others have shown that whereas children of mothers with diabetes are heavier, these patterns are not observed during infancy.²⁹

In our data, we did observe a counterintuitive finding with respect to maternal smoking. In a Portuguese cohort, Pizzi and colleagues found that mothers who smoked past the first trimester (but not those who quit around the first trimester) had offspring with a positive and significant value for velocity (14% greater velocity than nonsmokers). Nonsignificant, but negative, parameter values were observed for size and tempo. Our data show that size and tempo were positive and statistically significant for the tempo parameter among mothers who reported smoking. The velocity parameter in our data was negative and nonsignificant. The reasons for these differences are not clear. They may be attributed to the different method for quantifying smoking. In our data, we are unable to distinguish whether participants quit during pregnancy and when. The counterintuitive finding may also reflect potential postnatal clinical interventions received among women smokers in our cohort. All of the women and children in the analyses are observed at the university clinics, and these clinics spend a lot of resources intervening with mothers and their infants with risk factors that have the potential to affect birth weight (*e.g.*, prenatal smoking). Replication of these findings in other regional cohorts would help to further corroborate our findings.

A unique feature of this study was that we used the SITAR method to quantify growth during early postnatal growth, which has only been applied in a few studies. If serially collected data are available, there are some unique advantages to using the SITAR method for assessing early postnatal growth. First, relative to calculating a difference score between two points in time, the SITAR method better

captures nonmonotonic outcomes, such as changes in infant weight during the first 24 months. Second, covariates can be examined in relation to three clinically interpretable growth parameters—size, timing to peak growth, and growth velocity. Finally, the SITAR method can be applied to data where there may be irregularity in the spacing of weight data collection or amount at any one point in time. Notably, the SITAR method is fairly new to the field of childhood obesity, and there are few studies that have linked the SITAR-derived growth parameters to later life health outcomes. To date, only one study has examined SITAR growth parameters as predictors of later health outcomes.²³ When examining the relationship between size, tempo, and velocity during infancy as predictors of subsequent childhood obesity, investigators found that only size predicted subsequent obesity.²³ Further study is needed to help determine to what degree these different postnatal growth patterns (size, tempo, and velocity) relate to later life health and chronic disease outcomes.

The findings should be interpreted in the context of some methodological caveats. First, the focus here was on maternal and prenatal characteristics. Thus, we are not able to determine how other postnatal factors, such as breastfeeding, may moderate, mediate, or independently relate to growth parameters. Parent feeding practices, such as timing to introduction of solids or pressuring infants to eat beyond satiety, could also play a role in modifying the growth trajectory during these early years. We also did not have data on other important prenatal factors that may be relevant to infant weight outcomes, such as maternal diet and physical activity levels. Future research is needed that examines salient prenatal and postnatal factors and how they work together in order to provide a more complete understanding of the factors that contribute to infant weight.

A second caveat that should be considered when interpreting these results is the inherent variability in weight data obtained from a combination of study measurements and electronic medical records. Weight data were based on office-based measurements, and differences in measurement protocols from clinic to clinic could have introduced noise in the data. The SITAR method is ideal for this type of data that is irregularly measured with a high degree of frequency and statistical methods are available to filter biologically implausible data. Ideally, however, using externally valid measures for weighing and measuring infants could improve the precision of the estimates we observed here. Nevertheless, use of electronic medical records for weight data as well as other risk factors observed here may result in nondifferential misclassification with respect to maternal obesity, likely biasing the estimates toward the null.

A third caveat is that our measurement of gestational weight gain was limited in that we only had access to prepregnancy weight and weight at the last weight taken up to 7 days before or at delivery from medical records. As indicated by Lawlor,³⁰ it is unclear to what degree this measure reflects weight gain of the mother or the contribution of

placenta, amniotic fluid, and the growing fetus. Other issues are: (1) IOM categories do not properly account for the effects of maternal prepregnancy BMI given that women who were overweight and obese before pregnancy are more likely to be over the recommended GWG level than those with a normal weight; and (2) there is dependence between GWG and gestational age.³⁰ We did include prepregnancy BMI and gestational age in the models that included GWG to statistically control for these effects. Nevertheless, we cannot completely rule out the confounding effects of these variables. Ideally, having multiple measures of maternal weight throughout pregnancy would help improve precision, and future studies are needed that include this level of detail in order to more fully determine the effect of GWG.

Finally, as noted, our analysis cohort was a subset of the larger prebirth cohort. The cohort overall was fairly representative of the sample population, but there were some small differences between the analysis cohort and those excluded with respect to birth weight and percent born full term. Thus, there is the possibility of a selection bias that favors slightly more healthy weight infants. The small differences in birth weight, however, favor an interpretation that this bias toward inclusion of more healthy weight infants on postnatal growth trajectories may be nominal. Future studies that include a full range of birth weight observed in community-based samples would further extend the findings from this analysis cohort.

Despite these limitations, our findings support a growing consensus in the literature that both prepregnancy BMI and GWG relate independently to risk for greater early postnatal weight growth. Weight management before and during pregnancy may be effective in altering infant weight trajectories during the first 2 years of life. The aim of developing approaches to reduce childhood obesity across the life course is indeed supported by leading public health agencies, such as the World Health Organization.³¹ Yet, with some exceptions, there are few early life cycle studies that aim to address early childhood obesity by intervening during the prenatal phases of development.³² Observational studies that follow children born of mothers who were participants in lifestyle interventions targeting gestational weight gain or gestational diabetes have not found a “spillover” effect on childhood obesity or metabolic profile.^{32–34} Grounding interventions in life course theoretical models and developing solution-focused intervention strategies that cover both prenatal and early postnatal behavioral changes may be needed to advance the evidence base in this area.¹ In short, comprehensive and effective childhood obesity prevention will require targeting factors at different developmental windows in order to meaningful affect the prevalence of obesity in the population.

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Author Disclosure Statement

No competing financial interests exist.

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