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Associations of Early and Late Gestational Weight Gain with Infant Birth Size

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Abstract

Objectives Associations of gestational weight gain (GWG) during specific periods of pregnancy with infant birth size have been inconsistent. Infant sex-specific differences in these associations are unknown

Methods Information on GWG (kg) [total, early (<20 weeks gestation), and late (≥20 weeks gestation)] and indices of infant birth size including birthweight (BW), ponderal index (PI), crown-heel length (CHL), and head circumference (HC) was collected from 3,621 pregnant women. We calculated adjusted mean differences and 95 % confidence intervals (CIs) relating total, early and late GWG to infant birth size using multivariable linear regression procedures. We used stratified analyses and interaction terms to test whether associations differed by infant sex.

Results One-kg increases in total, early or late GWG were associated with BW increases of 17.2 g (95 % CI 13.8–18.9), 14.1 g (95 % CI 10.3–18.0), and 21.0 g (95 % CI 16.7–25.4), respectively. Early GWG–BW and late GWG–BW associations were different ($p = 0.026$). Sex-stratified total GWG–BW associations were similar to overall results. There were sex-specific differences in early GWG–BW and late GWG–BW associations. Among females, early GWG–BW (12.0 g, 95 % CI 6.7–17.2) and late GWG–BW (24.2 g, 95 % CI 18.2–30.3) associations differed ($p = 0.0042$); the corresponding associations did not differ among males. Total, early, and late GWG were associated with CHL and HC, but not with PI. Associations did not differ for early or late GWG.

Conclusions for Practice For comparable GWG, late-GWG-related BW increase is greater than early-GWG-related BW increase, particularly among female infants.

Keywords Gestational weight gain · Birth weight · Infant sex · Fetal growth

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Significance

What is already known? Gestational weight gain is a potent determinant of infant size.

What this study adds? Gestational weight gain in the second half of pregnancy is associated with greater increases in birthweight than equivalent amounts of GWG in the first half of pregnancy, particulary among female infants.

Introduction

Birth size, a reflection of intrauterine growth and development, has consistently been associated with health and disease over the life course [1, 2]. While extremes of

birthweight are well known to be associated with higher risks of obesity, cardiovascular disease, and cancer [3], accumulating evidence also suggests lower birthweight, even within the normal range may be associated with a higher risk of cardiovascular disease [4]. Understanding determinants of birth size and related mechanisms may therefore have broad preventive implications. While risk factors for both macrosomia (e.g. multiparity and maternal diabetes) [5] and low birth weight (e.g. maternal smoking and pre-term delivery) [6] have been identified, our understanding of risk factors influencing birthweight across the normal range—particularly modifiable risk factors—and related mechanisms remains incomplete.

Overweight and obesity remain prevalent among women of childbearing age [7]. Measures of perinatal maternal size, including pre-pregnancy body-mass index (BMI) [8], and weight gain during pregnancy (GWG) [1], have been associated with infant birthweight. Associations of GWG with other birth size measures, such as head circumference (HC), crown-heel length (CHL), and ponderal index (PI), are less rigorously described, as are associations of birth size measures with weight gain at specific periods in gestation. Several previous reports suggest that associations of GWG that involve greater gain during the second half of pregnancy may be more strongly associated with birth size measures, especially BW [9, 10]. There is some inconsistency in reported findings however [11]. Secondly, sex-specific differences in fetal and placental growth and development patterns, trajectories of growth in response to intrauterine changes, gene-environment interactions, and eventual birth size are well established [12–15]. The National Institutes of Health have also highlighted the importance of sex-specific differences in recent policy changes [16]. To our knowledge, however, sex-specific associations of GWG (including early and late GWG) with birth size have not been systematically explored.

Using a large pregnancy cohort study, we investigated associations of total, early, and late GWG with birth size measures (BW, PI, CHL, and HC) and differences between early GWG-birth size and late GWG-birth size associations. We also examined whether these associations differed by infant sex.

Materials and Methods

Study Design and Setting

The study was conducted among participants of the Omega study, a pregnancy cohort study based at the Center for Perinatal Studies at Swedish Medical Center in Seattle, Washington. Study design and protocols have been published previously [17]. Briefly, the Omega study was designed to examine metabolic and dietary risk factors of preeclampsia, gestational diabetes, and other pregnancy outcomes. Participants were recruited (1996–2008) from prenatal care clinics affiliated with Swedish Medical Center in Seattle and Tacoma General Hospital in Tacoma, Washington.

Study Population

Pregnant women were eligible to participate in the Omega study if they were ≥18 years old at enrollment, initiated prenatal care prior to 16 weeks of pregnancy, were able to speak and read English, and planned to carry the pregnancy to term and deliver at one of the study hospitals. During the study period, approximately 80 % of eligible women who were approached consented to participate and >95 % were followed until delivery. All Omega study participants with singleton pregnancies and complete data on GWG and birth size were included in this analysis. From an initial sample of 4011 eligible subjects, 204 were excluded for multiple gestation, 183 were excluded due to missing data on infant sex, and 3 were excluded due to missing data on birthweight, leaving an analytic sample of 3621. The institutional review boards of Swedish Medical Center and Tacoma General Hospital approved the study, and all study participants provided written informed consent.

Data Collection

At an enrollment visit at approximately 15 weeks gestation, trained interviewers conducted in-person interviews (45–60 min in length) to collect data on mothers' age, height, pre-pregnancy weight, socioeconomic characteristics, reproductive and medical histories, tobacco consumption, dietary intake, and physical activity before and during pregnancy. Mothers were followed through delivery, and trained personnel abstracted data on course of pregnancy (e.g., GWG, pregnancy complications) and pregnancy outcomes (e.g., infant birth characteristics) from maternal and infant medical records. Information on dietary intake during the peri-conception period was obtained at the index visit using food frequency questionnaire data. Information on average weekly leisure-time physical activity during the year prior to conception was collected at the index visit using a structured questionnaire.

Gestational Weight Gain

Total gestational weight gain was calculated as the difference in weight (kilograms) between last recorded maternal weight within 4 weeks prior to delivery (abstracted from medical records) and self-reported pre-pregnancy weight during the 3 months prior to conception. Early GWG was calculated by subtracting pre-pregnancy

weight from weight at 20 weeks gestation. Late GWG was calculated by subtracting weight at 20 weeks from the last weight before delivery. Gestational age was determined using self-reported date of last menstrual period and confirmed by the earliest ultrasound, when available, or by physician's best estimate of last menstrual period.

Birth Size Measures

Information on BW (grams), PI (g/m^3*100), HC (cm), and CHL (cm) at birth, were obtained from medical records. Measurements were obtained immediately after birth and recorded to the nearest 1 g and 0.5 cm. CHL was measured by two trained nurses using a measuring board. PI was used in place of body-mass index as a length-normalized estimate of body size. Because it normalizes to the third power of length, it provides more valid comparisons among newborns [18].

Statistical Analysis

We used mean (standard deviation) and number (percent) for continuous and categorical variables, respectively, to describe study population characteristics, both overall and stratified by infant sex (Table 1). We used multivariable linear regression to test hypotheses that early and late GWG were independently associated with BW, PI, CHL, and HC. To determine whether associations of early GWG and late GWG with birth size were quantitatively different, we used a Wald test to examine differences between the coefficients for early GWG and late GWG.

To test our hypothesis that early GWG-birth size and late GWG-birth size associations might vary for male and female infants, we performed sex-stratified analyses. We also used a Wald test to examine differences between the coefficients for early GWG and late GWG in these stratified models. To evaluate the statistical significance of sex-GWG interactions, we fit linear regression models for all birth size measures with and without first-order interaction terms (i.e., terms for total GWG*infant sex, early GWG*infant sex, and late GWG*infant sex).We further modeled the expected change in infant size for women with excessive or inadequate GWG for pre-pregnancy size, using Institutes of Medicine guidelines [1], and used a likelihood ratio test to compare the equivalence of models with and without first-order interaction terms for category of GWG*infant sex (data not shown).

All models adjusted for maternal age (years), maternal pre-pregnancy body-mass index (kg/m^2), maternal height (m), nulliparous status (yes/no), marital status (married/unmarried), race (white/other), <12 years of education (yes/no), presence of any maternal hypertensive disorder including chronic hypertension, pregnancy-induced hypertension, or pre-eclampsia (yes/no), presence of

maternal glucose metabolism disorder (yes/no), maternal smoking during pregnancy (yes/no), infant sex (in non-infant sex stratified analyses) and gestational age at delivery (weeks).

In sensitivity analyses, we controlled for maternal dietary factors including total maternal caloric intake in the 3 months prior to pregnancy and early first trimester, percent of calories from fat, and maternal pre-pregnancy leisure-time physical activity. We also created sex-specific Z-scores for gestational weight gain [(GWG value—mean GWG)/standard deviation] and repeated our regressions with those terms in place of absolute early and late GWG. To check for the possibility of influential outliers, we estimated delta-betas from the regression equations. To address the possibility of non-linear GWG-birth size associations, we repeated all analyses using multinomial logistic regression to estimate the relative risk of giving birth to an infant in a higher (>1SD above the mean) or lower (>1SD below the mean) birth size category across categories of GWG (>1SD above the mean, within 1SD of the mean, and >1SD below the mean). To further address the possibility of a non-linear relationship between GWG and birthweight, we fit models with quadratic total, early, and late GWG terms, as well as linear spline-based models with knots at quartiles of total, early, and late GWG.

Analyses were performed using Stata 12.1 (College Station, TX). For all tests, a two-sided α of 0.05 was used.

Results

Study participants comprised predominantly married non-Hispanic white women (Table 1). They were 32.6 years old at time of enrollment, on average. Mean pre-pregnancy BMI was 23.7 kg/m^2. Average total, early (<20 weeks gestation), and late GWG (≥20 weeks gestation) were 16.2, 6.8, and 9.5 kg, with 54 % of women gaining in excess of Institutes of Medicine guidelines [1]. Average gestational age at delivery was 39 weeks, and 51 % of infants were male. Birth size measures were normally distributed. Mean BW was 3443 g (3513 g for males and 3382 g for females). Mean PI was 2.7 g/cm^3*100(2.7 g/cm^3*100 for males and 2.7 g/cm^3*100 for females). Mean HC was 35 cm (35 cm for males and 34 cm for females), and mean CHL was 51 cm (51 cm for males and 50 cm for females).

Overall, we found strong positive associations of total, early, and late GWG with birthweight, head circumference, and crown-heel length, but not ponderal index (Table 2). A 1 kg increase in total GWG was associated with a 17.2 g mean increase in BW (95 % CI 13.8–18.9). A 1 kg increase in early GWG was associated with a 14.1 g increase (95 % CI 10.3–18.0) in BW after adjustment for late GWG. A 1 kg increase in late GWG was associated

Table 1 Characteristics of mother-singleton infant pairs in the Omega birth cohort, overall and stratified by offspring sex (n = 3621)

	All (n = 3621)	Male (n = 1840)	Female (n = 1781)
Maternal characteristics			
Maternal age, years (SD)	32.6 (4.6)	32.6 (4.6)	32.5 (4.5)
Pre-pregnancy BMI, kg/m^2 (SD)	23.7 (5.1)	23.7 (5.1)	23.8 (5.0)
Maternal height, meters (SD)	1.7 (0.1)	1.7 (0.1)	1.7 (0.1)
Nulliparous % (n)	39 (1414)	38 (706)	40 (708)
Married, % yes (n)	85 (3247)	86 (1586)	86 (1539)
Less than 12 years of education, % yes (n)	4 (141)	4 (71)	4 (61)
Race			
Non-Hispanic white, % (n)	86 (3251)	85 (1561)	86 (1532)
African-American, % (n)	2 (74)	2 (37)	2 (34)
Asian, % (n)	8 (286)	8 (150)	7 (121)
Hispanic, % (n)	2 (65)	2 (34)	2 (29)
Other, % (n)	3 (110)	3 (53)	3 (56)
Smoked during pregnancy, % yes (n)	6 (214)	6 (107)	6 (97)
Maternal glucose metabolism disorder, % yes (n)	6.5 (234)	6.4 (118)	6.5 (116)
Gestational diabetes, % yes (n)	5 (188)	5 (94)	5 (93)
Pre-existing diabetes, % yes (n)	1 (56)	1 (25)	1 (23)
Maternal hypertensive disorder, % yes (n)	18.6 (668)	18.6 (339)	18.7 (329)
Chronic hypertension, % yes (n)	5 (185)	4 (77)	5 (95)
Pregnancy-induced hypertension, % yes (n)	12 (432)	13 (239)	11 (193)
Pre-eclampsia, % yes (n)	3 (109)	2 (42)	4 (67)
Median minutes of moderate or greater pre-pregnancy LTPA (IQR)	228 (111–388)	224 (111–388)	231 (111–390)
Total gestational weight gain, kg (SD)	16.2 (5.7)	16.5 (5.5)	15.9 (5.9)
Total GWG by IOM category, kg (SD)			
Inadequate, % (n)	14 (510)	10 (184)	12 (218)
Adequate, % (n)	32 (1202)	31 (569)	34 (608)
Excessive, % (n)	54 (2034)	59 (1067)	53 (943)
Early GWG, kg (SD)*	6.8 (3.9)	6.8 (3.7)	6.7 (4.0)
Late GWG, kg (SD)[a]	9.5 (3.7)	9.7 (3.7)	9.2 (3.7)
Infant characteristics			
Gestational age, weeks (SD)	39 (2)	39 (2)	39 (2)
Sex, % male (n)	51 (1840)	–	–
Outcome measures			
Birthweight, grams (SD)	3443 (576)	3513 (570)	3382 (540)
Ponderal index, g/cm^3*100 (SD)	2.7 (1.3)	2.7 (1.0)	2.7 (1.5)
Head circumference (cm)	35 (3)	35 (2)	34 (2)
Length (cm)	51 (4)	51 (3)	50 (3)

SD standard deviation, *BMI* body-mass index, *LTPA* leisure-time physical activity, *IQR* + interquartile range

* Early GWG was calculated by subtracting pre-pregnancy weight from weight at 20 weeks gestation

[a] Late GWG was calculated by subtracting weight at 20 weeks from the last weight before delivery

with a 21.0 g increase in BW (95 % CI 16.7–25.4) after adjustment for early GWG. The association differed for early versus late GWG ($p = 0.026$).

Sex-stratified results for total GWG were not different in male infants (17.1, 95 % CI 13.1–21.2) versus female infants (17.1, 95 % CI 14.5–20.9). Among males, early GWG–BW and late GWG–BW associations were similar (early 15.7, 95 % CI 10.0–21.4; late 18.2, 95 % CI 12.0–24.5; p for comparison = 0.579). In contrast, among females, a 1 kg increase in early GWG was associated with a 12.0 g increase in BW (95 % CI 6.7–17.2), while a 1 kg increase in late GWG was associated with a 24.2 g increase in BW (95 % CI 18.2–30.3; p for comparison = 0.0042). Terms for early and late GWG interactions with infant sex

Table 2 Infant birth size in relation to 1-kg increases in total, early, and late gestational weight gain (GWG), overall and stratified by infant sex

	All subjects n = 3621		Male n = 1840		Female n = 1781		Interaction model
	Coefficient (95 % CI)	p value	Coefficient (95 % CI)	p value	Coefficient (95 % CI)	p value	p for interaction*
Birthweight (g)							
Total GWG	17.2 (14.5–19.9)	<0.0001	17.1 (13.1–21.2)	<0.0001	17.1 (14.5–20.9)	<0.0001	0.973
Early GWG	14.1 (10.3–18.0)	<0.0001	15.7 (10.0–21.4)	<0.0001	12.0 (6.7–17.2)	<0.0001	0.549
Late GWG	21.0 (16.7–25.4)	<0.0001	18.2 (12.0–24.5)	<0.0001	24.2 (18.2–30.3)	<0.0001	0.354
Wald test (early vs. late)		0.026		0.5787		0.0042	
Ponderal index (g/cm)*100							
Total GWG	0.005 (−0.0001–0.010)	0.054	0.009 (−0.0004–0.019)	0.060	0.0009 (−0.004–0.005)	0.682	0.376
Total GWG, adjusted for BW	−0.0002 (−0.006–0.005)	0.937	0.005 (−0.006–0.016)	0.390	−0.005 (−0.010–0.001)	0.053	
Early GWG	−0.0005 (−0.008–0.008)	0.886	0.007 (−0.003–0.016)	0.161	−0.007 (−0.018–0.004)	0.187	0.062
Late GWG	0.012 (0.0002–0.024)	0.047	0.012 (−0.008–0.032)	0.224	0.012 (0.00004–0.024)	0.049	0.721
Wald test (early vs. late)		0.1331		0.6408		0.0718	
Head circumference (cm)							
Total gestational weight gain	0.040 (0.25–0.054)	<0.0001	0.045 (0.021–0.070)	<0.0001	0.034 (0.018–0.051)	<0.0001	0.636
Total GWG, adjusted for BW	0.006 (−0.008–0.019)	0.413	0.01 (−0.013–0.034)	0.373	0.001 (−0.013–0.016)	0.861	0.254
Early weight gain	0.038 (0.014–0.062)	0.002	0.052 (0.010–0.095)	0.016	0.024 (0.003–0.047)	0.047	
Late weight gain	0.042 (0.021–0.063)	<0.0001	0.040 (0.009–0.070)	0.011	0.047 (0.018–0.76)	0.001	0.483
Wald test (early = late)		0.8110		0.6725		0.2487	
Crown heel length (cm)							
Total GWG	0.060 (0.042–0.078)	<0.0001	0.050 (0.022–0.086)	0.001	0.069 (0.046–0.092)	<0.0001	0.634
Total GWG, adjusted for BW	0.009 (−0.007–0.025)	0.292	−0.003 (−0.028–0.022)	0.818	0.020 (−0.0008–0.040)	0.06	
Early GWG	0.052 (0.023–0.080)	<0.0001	0.039 (−0.05–0.082)	0.079	0.062 (0.026–0.098)	0.001	0.434
Late GWG	0.070 (0.042–0.097)	<0.0001	0.059 (0.018–0.100)	0.005	0.079 (0.04–0.12)	<0.0001	0.992
Wald test (early vs late)		0.4072		0.5261		0.5504	

Early GWG was calculated by subtracting pre-pregnancy weight from weight at 20 weeks gestation. Late GWG was calculated by subtracting weight at 20 weeks from the last weight before delivery. Models adjust for maternal age, maternal pre-pregnancy body-mass index, maternal height, nulliparous status, marital status, race, <12 years of education, presence of maternal hypertensive disorder, presence of maternal glucose metabolism disorder, maternal smoking status, and offspring sex and gestational age at delivery

* p value for multiplicative interaction taken from model specified above, weight gain modeled continuously

were not significant (*p* values 0.549 and 0.354, respectively), however.

Overall, total, early, and late GWG were associated with HC and CHL, but not PI. A 1 kg increase in total, early, or late GWG was associated with 0.038–0.042 cm higher HC and 0.052–0.070 cm higher CHL (all *p* values <0.002). Results were generally similar in sex-stratified models with no differences observed between males and females in the GWG–HC or GWG–CHL associations, although early GWG–CHL associations among male infants were not statistically significant. All the associations became non-significant after adjustment for BW. Further, tests for differences between early GWG–HC or CHL and late GWG–HC or CHL associations were not significant.

Findings from sensitivity analyses including analyses using Institutes of Medicine categories of GWG or categorized birth size measures (e.g. low birth weight) were similar to those reported above (data not shown). Results were also not quantitatively different when we controlled for pre-pregnancy maternal caloric intake, percent calories from fat, and LTPA, or when we used sex-specific GWG Z-scores in place of absolute values. Scatter plots of early GWG versus BW suggested the association might be non-linear at the extremes of the BW distribution. There were, however, very few values at those extremes. Scatter plots of studentized residuals versus total, early, and late GWG showed no trends.

Comments

We found strong associations of total GWG, early GWG, and late GWG with BW, HC, and CHL, but not PI. Associations of GWG with HC and CHL were not statistically significant after adjustment for BW. While we did not observe statistically significant differences in independent associations of early GWG and BW or late GWG and BW by infant sex (*p* values 0.549 and 0.354 respectively), the early GWG–BW association was quantitatively different from the late GWG–BW association overall (14.1 g/kg early GWG, 21.0 g/kg late GWG, *p* value for difference 0.026) and among female infants (12.0 g/kg early GWG, 24.2 g/kg late GWG, *p* value for difference 0.0042), but not among males (15.7 g/kg early GWG, 18.2 g/kg late GWG, *p* value for difference 0.5787).

Our findings are similar to some previous reports [9, 10], but not all [11]. In an African cohort of lean women, GWG after 32 weeks gestation was more strongly associated with BW than gain between 7 and 32 weeks. Among young women in 1950s Scotland, inadequate GWG during 20–30 and 30–36 weeks was associated with higher rates of low birth weight than inadequate gain during 13–20 weeks. On the other hand, Davenport et al. reported that mothers with

excess GWG prior to 16–20 weeks by Institutes of Medicine guidelines had greater BW than mothers with excess GWG after 16–20 weeks. To our knowledge, previous studies have not evaluated infant sex-specific associations or effect modification by infant sex.

There are a number of factors that could be expected to contribute to heterogeneity of results. Definitions of "early" and "late," as well as trimester cutpoints vary across study populations. In a sensitivity analysis, trends were similar when we stratified GWG by trimester. Differences in study population characteristics (e.g., pre-pregnancy overweight [19]) could also contribute to differences in findings across studies and to generalizability of findings. In our population, roughly 60 % gained in excess of Institutes of Medicine guidelines, similar to current weight patterns among reproductive-age American women. The probability of misclassification and measurement error were highly variable across these diverse cohort designs, with prospectively collected first-trimester weights available in some cohorts, while in others, the first objectively measured weights were recorded at nearly 18 weeks gestation. Finally, there was considerable variability in analytic approach (including formal testing of differences between early GWG–BW and late GWG–BW associations) and study power.

In the current study, the pattern of smaller gains in BW for corresponding increases in early GWG compared to similar increases in late GWG was observed in female infants (12.0 g/kg early GWG and 24.2 g/kg late GWG), but not male infants (15.7 g/kg and 18.2 g/kg, respectively). This observation is supported by mechanistic evidence of metabolic and hormonal changes occurring in the second half of pregnancy that may be more pronounced among female fetuses than males. Compared with women who are pregnant with male fetuses, women who were pregnant with female fetuses have higher serum placental growth hormone in the third trimester [20] and higher levels of insulin-like growth factor-1 at birth [21], two important regulators of fetal growth. Sex-specific differences in placental response to maternal factors have also been reported. For example, female placentas exhibit higher levels of expression of genes involved in placental growth [22]. Greater placental weight is also associated with increases in maternal fasting glucose among females but not males [23]. The female fetal growth pattern seems to mirror the maternal trajectory, in which the bulk of weight is gained in the second half of gestation [1]. Taken together, these observations suggest that effects of maternal energy balance (such as maternal GWG) at different points in the pregnancy may differ between male and female infants because of sex-specific sensitivities across gestational ages. Recent National Institutes of Health policy changes have highlighted growing awareness that females and males respond differently to chemical and microbial

stressors via mechanisms that are both hormonally independent and hormonally mediated [16]. Future studies further investigating mechanisms underlying these sex-specific effects are warranted.

GWG–HC and GWG–CHL associations appeared to remain stable across the course of pregnancy. Comparison of early GWG–PI and late GWG–PI associations in female infants did show a trend toward smaller gains in PI for similar increases for early compared to late GWG, but it did not reach statistical significance ($p = 0.0718$). In the case of both HC and CHL, quantitative differences in our sample from the smallest to the largest infants may have been so small that we were unable to detect a difference in early/late GWG patterns. Associations of GWG *rate* with birth size measures were similar to our primary findings. Because of the possibility that BW was collinear with other birth size measures, we used variance inflation factors to check for multicollinearity in models including birthweight. No individual VIF exceeded 1.83. Lack of statistical power may explain the fact that our tests of effect modification by sex were not significant, despite the fact that we saw evidence that early GWG–BW associations were quantitatively different than late GWG–BW in female infants but not male infants. On the other hand, in analyses where we found significant results, we cannot exclude the possibility we have falsely rejected a true null hypothesis, given the multiple statistical tests we performed. It will be important to replicate these findings in other cohorts.

This study is the largest, to our knowledge, to demonstrate that GWG after 20 weeks has a different, and likely stronger, association with BW, than GWG before 20 weeks. It is also the first to demonstrate infant sex-specific differences in the association. These findings are important in understanding early life determinants of health across the life course. This study has several strengths, including the prospective study design. Maternal weight was measured several times across the course of pregnancy, and women were followed prospectively until delivery. Other strengths include the large sample size and detailed information on potential confounders.

Several limitations of our study also deserve mention. We used self-reported retrospective measures of pre-pregnancy weight. Women tend to underestimate pre-pregnancy weight, and this behavior may be more exaggerated in women with greater pre-pregnancy BMI; however, reported pre-pregnancy weights rarely differ from measured values by more than 10 % even in the higher BMI categories [24, 25]. We also do not anticipate this to bias sex-specific differences in associations. Because weight at delivery was not captured in our study, we used the last recorded weight within 4 weeks of the delivery. Therefore, we were unable to assess variability, if present, in maternal weight in the final weeks prior to delivery. Another limitation of our study is our inability to estimate fetal weight contributions to measures of early and late GWG. Lastly, our study sample comprised largely of non-Hispanic white mothers with at least a high school education. Only few previous studies were conducted among racially/ethnically or low socio-economic status women [9, 26]. These studies generally reported measures that were not comparable to ours or findings that were similar. Similar studies are needed in more diverse study populations to ensure generalizability of findings.

In sum, our findings indicate that for a comparable GWG, late GWG-related BW increase tends to be higher than early GWG-related BW increase, particularly among female infants. Future studies with detailed measures of change in maternal body composition and fetal adiposity may help elucidate underlying mechanisms behind the observed associations and sex-specific differences. Further, potential implications of the observed associations on chronic disease risk in postnatal life are important targets of future research. A better understanding of these associations and mechanisms can be translated into improved clinical practice, helping clinicians identify at-risk pregnancies and guiding GWG-based interventions.

Conflicts of interest The authors report no conflicts of interest

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