International Journal of Epidemiology, 2020, 1682–1690
doi: 10.1093/ije/dyaa110
Advance Access Publication Date: 24 August 2020
Original article

Miscellaneous

Gestational weight gain, birthweight and early-childhood obesity: between- and within-family comparisons

Sylvia E Badon *, Charles P Quesenberry, Fei Xu, Lyndsay A Avalos and Monique M Hedderson

Kaiser Permanente Northern California Division of Research, Oakland, CA, USA

*Corresponding author. Kaiser Permanente Northern California Division of Research, 2000 Broadway, Oakland CA, USA. E-mail: sylvia.e.badon@kp.org

Editorial decision 26 May 2020; Accepted 28 May 2020

Abstract

Background: Associations of excessive gestational weight gain (GWG) with greater birthweight and childhood obesity may be confounded by shared familial environment or genetics. Sibling comparisons can minimize variation in these confounders because siblings grow up in similar environments and share the same genetic predisposition for weight gain.

Methods: We identified 96 289 women with live births in 2008–2014 at Kaiser Permanente Northern California. Fifteen percent of women ($N = 14\,417$) had at least two births during the study period for sibling analyses. We assessed associations of GWG according to the Institute of Medicine (IOM) recommendations with birthweight and obesity at age 3 years, using conventional analyses comparing outcomes between mothers and sibling analyses comparing outcomes within mothers, which control for stable within-family unmeasured confounders such as familial environment and genetics. We used generalized estimating-equations and fixed-effects models.

Results: In conventional analyses, GWG above the IOM recommendations was associated with 88% greater odds of large-for-gestational age birthweight [95% confidence interval (CI): 1.80, 1.97] and 30% greater odds of obesity at 3 years old (95% CI: 1.24, 1.37) compared with GWG within the IOM recommendations. In sibling analyses, GWG above the IOM recommendations was also associated with greater odds of large-for-gestational age [odds ratio (OR): 1.36; 95% CI: 1.20, 1.54], but was not associated with obesity at 3 years old (OR = 0.98; 95% CI: 0.84, 1.15).

Conclusions: GWG likely has a direct impact on birthweight; however, shared environmental and lifestyle factors within families may play a larger role in determining early-childhood weight status and obesity risk than GWG.

Key words: Pregnancy, weight gain, birthweight, paediatric obesity, siblings

Key Messages

- Gestational weight gain (GWG) above Institute of Medicine (IOM) recommendations was associated with greater birthweight using a conventional approach comparing pregnancies between mothers and using a sibling analysis controlling for stable within-family confounders, such as familial environment and genetics.
- GWG above IOM recommendations was associated with greater body mass index (BMI) and greater odds of obesity at 3 years old using a conventional approach comparing pregnancies between mothers, but was not associated with BMI or obesity at 3 years old in sibling analyses.
- GWG may directly impact birthweight; however, shared environmental and lifestyle factors and genetics within families may play a larger role in determining childhood weight status than GWG.

Introduction

Previous studies have reported associations between high gestational weight gain (GWG) and greater risk of high birthweight[1–4] and childhood obesity.[2,5–10] Mechanisms related to *in utero* exposure to over-nutrition, insulin resistance and fetal programming of obesity may underlie these previously observed associations.[11,12] However, these observed associations may also be explained by unmeasured confounding. Characteristics, such as environment, lifestyle behaviours and genetics, that influence a mother's weight and her GWG may have a similar influence on her child's birthweight and postnatal weight gain in childhood and beyond. These shared characteristics are difficult to accurately measure and control for using observational data, which results in residual confounding.

A sibling study design addresses confounding by shared familial characteristics that affect weight in a mother and her child, even if they are unmeasured. GWG, birthweight and childhood obesity can be compared across pregnancies to the same mother to control for unmeasured confounding factors that remain stable across time at the family level. However, this approach greatly reduces the sample size because it limits the study population to siblings and exaggerates bias due to unmeasured familial characteristics that change between pregnancies.[13] Several previous studies using a sibling design have reported associations of higher GWG with greater birthweight,[14–16] but few studies in contemporary cohorts have used a sibling design to assess the associations of GWG with early-childhood weight and obesity. The objective of this study was to assess associations of high GWG with birthweight and early-childhood obesity at 3 years old, integrating results from a conventional approach comparing pregnancies between mothers and a sibling-analysis approach comparing pregnancies within mothers.

Methods

Study setting

This study was conducted within Kaiser Permanente Northern California (KPNC), an integrated healthcare-delivery system that provides medical care for about one-third of the population in the Northern California region. KPNC members are representative of the underlying population of this region.[17]

Data collection

Data were extracted from KPNC electronic health records and included data collected during routine primary-care, prenatal-care and paediatric-care visits. This study was approved by the KPNC and the state of California institutional review board. The requirement for informed consent was waived.

GWG

Pre-pregnancy weight was defined as the last measured weight before conception up to 12 months prior to pregnancy (79% of analytic sample). If measured weight in the 12 months prior to pregnancy was not available, self-reported pre-pregnancy weight (14% of analytic sample) or measured weight before 10 weeks of pregnancy (7% of analytic sample) was used. Pre-pregnancy body mass index (BMI) was categorized using standard cut-points: underweight: $<18.5\,kg/m^2$, normal weight: $18.5–24.9\,kg/m^2$, overweight: $25–29.9\,kg/m^2$, obese: $\geq 30\,kg/m^2$.[18] Total GWG was calculated as the difference between the last measured prenatal weight within 4 weeks before delivery and the pre-pregnancy weight. Total GWG was categorized according to the 2009 Institute of Medicine (IOM) GWG recommendations: 28–40 lbs for underweight women, 25–35 lbs for normal-weight women, 15–25 lbs for overweight women, 11–20 lbs for obese women.[19]

Birthweight outcomes

Birthweight was collected from the electronic health record. Gestational age at birth was estimated based on first-trimester ultrasound data. Birthweight z-scores and percentiles were calculated using 2017 US sex-specific birthweight references curves.[20] We examined the distribution of birthweight and birthweight z-scores and did not exclude any infants for implausible birthweight-for-gestational-age values. Small-for-gestational age (SGA) was defined as birthweight ≤10th percentile for sex and gestational age. Large-for-gestational age (LGA) was defined as birthweight ≥90th percentile for sex and gestational age.

BMI at 3 years old outcomes

Weight and height measured within 3 months of a child's third birthday were used to calculate the BMI at 3 years old. BMI z-scores and percentiles were calculated using the 2000 sex-specific Centers for Disease Control and Prevention Growth Charts for the USA.[21] We examined the distribution of weight, height and BMI z-scores at 3 years old and did not exclude any children for implausible BMI z-score values. Childhood obesity was defined as BMI ≥95th percentile for age.

Covariates

Maternal age, race/ethnicity, parity, education and insurance type at delivery were obtained from the electronic health record. Maternal race/ethnicity and parity were confirmed against California birth-certificate data. Smoking during pregnancy was based on self-report of smoking on a self-administered Prenatal Substance Use Screening Questionnaire completed at entry into prenatal care and recorded in the electronic health record.

Study sample

KPNC members with at least one term live, singleton birth from 2008 to 2014 were identified from the KPNC electronic health-record database (*N* = 223 974 births among 184 148 women). For women with missing data for the exposure or covariates (7.8% missing IOM GWG category, 7.3% missing pre-pregnancy BMI, 7.2% missing smoking, 2.4% missing insurance type, 1.7% missing parity, 0.2% missing race/ethnicity), we used multiple imputation using the Markov Chain Monte Carlo method under the assumption of multivariate normality with 50 imputations to impute GWG according to IOM recommendations, pre-pregnancy BMI, race/ethnicity, parity, education, insurance type and smoking. After imputation, we excluded mother–child pairs with missing data for outcomes (*N* = 4109 missing birthweight-for-gestational age category and *N* = 110 624 missing obesity status at 3 years old),[22] for a total of 111 482 mother–child pairs (96 289 women). Of these, 14 417 mothers had at least two term, live singleton births from 2008 to 2014 (*N* = 29 610 mother–child pairs). Characteristics of pregnancies excluded due to missing outcome data are presented in Supplementary Table 1, available as Supplementary data at *IJE* online.

For sibling analyses of dichotomous outcomes, the analytic sample was restricted to mothers with discordant outcomes (*N* = 3499 mother–child pairs, 1689 mothers for SGA; 5076 mother–child pairs, 2421 mothers for LGA; 3881 mother–child pairs, 1862 mothers for obesity status at 3 years old).

Statistical analyses

Descriptive statistics are presented for mother–child pairs in the overall analytic cohort and in each of the discordant outcomes analytic cohorts and additionally presented separately for the first and second pregnancy during the study period in each of the four analytic cohorts. Mean and standard deviation were used to describe the distribution of continuous variables. Frequency and percentage were used to describe categorical variables.

We assessed associations of GWG categorized according to the IOM recommendations with outcomes using two approaches. First, we used generalized estimating-equations models accounting for the non-independence of outcomes in siblings. Linear regression was used to estimate mean differences and 95% confidence intervals (CIs) in birthweight z-score and BMI z-score at 3 years old. Logistic regression was used to estimate the odds ratios (ORs) and 95% CIs for SGA, LGA and obesity status at 3 years old. Second, we used fixed-effects regression models to control for within-family unmeasured confounders that remain constant across pregnancies, such as environmental factors and genetics. Fixed-effects linear models were used to estimate the mean differences and 95% CIs in birthweight z-score and BMI z-score at 3 years old within siblings. Conditional logistic regression was used to estimate ORs and 95% CIs for SGA, LGA and obesity at 3 years old within siblings with discordant outcomes.

For both approaches, we adjusted for confounders at the level of each individual pregnancy: gestational age at delivery (weeks), maternal race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic Asian/Pacific Islander, Hispanic, other; implicitly in fixed-effects models), maternal age at delivery (years), maternal pre-pregnancy BMI (kg/m^2), nulliparity (yes, no), smoking during pregnancy (yes, no), Medicaid coverage at delivery (yes, no), maternal education (years) and child's sex.

A multiplicative interaction term between the IOM GWG category and the pre-pregnancy BMI category was included in the model for each outcome to evaluate the effect-measure modification of the associations of the IOM GWG category with the outcomes by pre-pregnancy BMI category. In separate models, a multiplicative interaction term between the IOM GWG category and pregnancy order was included in the model for each outcome to test that the GWG and the outcome of the first pregnancy did not affect the GWG and outcome of the next pregnancy (carry-over effects).[23] We repeated generalized estimating-equations analyses in the discordant outcomes analytic cohorts to evaluate whether differences in the analytic population were contributing to differences between the general estimating-equations approach comparing pregnancies between mothers and the fixed-effects approach comparing pregnancies within mothers. We conducted a sensitivity analysis limited to pregnancies with a measured pre-pregnancy weight and a measured weight ≤2 weeks before delivery.

Regression models were run using each imputed data set. Results were combined using Rubin's rules.[24] Analyses were conducted in SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Our overall analytic cohort was 38% non-Hispanic White, 26% non-Hispanic Asian/Pacific Islander, 25% Hispanic, 6% non-Hispanic Black and 5% other race/ethnicity (Table 1). Twenty-four percent of women gained below the IOM GWG recommendations (GWG<IOM), 33% gained within the recommendations (GWG=IOM) and 43% gained above the recommendations (GWG>IOM). Characteristics of mother–child pairs excluded due to missing outcomes were similar to those of mother–child pairs included in the overall analytic cohort (Supplementary Table 1, available as Supplementary data at *IJE* online).

Most mothers in the overall analytic cohort had one birth during our study period (85%) and did not contribute to sibling analyses. Fourteen percent of women had two pregnancies during our study period and 1% had three or more pregnancies (maximum = 5 pregnancies). On average, there was a 2.7-year difference between a woman's first and second pregnancies in our cohort (Table 2). The majority (78%) of women were nulliparous during their first pregnancy in our cohort. Women had less GWG, were less likely to have GWG>IOM and were less likely to be overweight or obese prior to pregnancy in their second pregnancy. The distribution of race/ethnicity and pre-pregnancy BMI categories was different between women included in the overall analytic cohort and those included in the discordant outcome analytic cohorts (Supplementary Table 2, available as Supplementary data at *IJE* online), but similar differences in GWG and pre-pregnancy overweight/obesity were observed between the first and second pregnancies included in the discordant outcome analytic cohorts and those in the overall sibling cohort (Supplementary Table 3 to 5, available as Supplementary data at *IJE* online).

Table 1. Characteristics of term pregnancies with a singleton live birth, Kaiser Permanente Northern California 2008–2014 (*N* = 111 482 mother–child pairs)

Characteristics	
Maternal age at delivery (years), mean (SD)	30.8 (5.4)
Gestational age at delivery (weeks), mean (SD)	39.2 (1.1)
Race/ethnicity, *n* (%)	
Non-Hispanic White	42 137 (38)
Asian/Pacific Islander	28 470 (26)
Hispanic	27 933 (25)
Black	6912 (6)
Other	5949 (5)
Missing	81
Pre-pregnancy BMI category, *n* (%)	
Underweight	2684 (3)
Normal weight	52 125 (49)
Overweight	28 261 (27)
Obese	22 416 (21)
Missing	5996
Nulliparous, *n* (%)	53 267 (48)
Smoked during pregnancy, *n* (%)	2821 (3)
Missing	7230
Medicaid coverage at delivery, *n* (%)	5340 (5)
Missing	1345
Maternal education (years), mean (SD)	15.0 (2.3)
Missing	18 424
Female child, *n* (%)	54 775 (49)
Total gestational weight gain (kg), mean (SD)	13.8 (6.3)
Missing	5805
IOM gestational-weight-gain category, *n* (%)	
Below IOM	25 335 (24)
Within IOM	34 563 (33)
Above IOM	45 142 (43)
Missing	6442
Child's birthweight, mean (SD)	3445 (460)
Child's birthweight category, *n* (%)	
Small-for-gestational age	10 704 (10)
Appropriate-for-gestational age	89 727 (80)
Large-for-gestational age	11 051 (10)
Child's BMI at 3 years old (kg/m^2), mean (SD)	16.3 (1.6)
Child's obesity status at 3 years old, *n* (%)	10 433 (9)

BMI, body mass index; IOM, Institute of Medicine; SD, standard deviation.

Birthweight

Using all mother–child pairs in our cohort, accounting for the correlation of outcomes between siblings, GWG<IOM

Table 2. Characteristics of first and second pregnancies in the sibling cohort ($N = 14\,417$ mothers), Kaiser Permanente Northern California 2008–2014

	First pregnancy	Second pregnancy
Maternal age at delivery (years), mean (SD)	29.3 (4.6)	32.0 (4.6)
Gestational age at delivery (weeks), mean (SD)	39.3 (1.1)	39.1 (1.0)
Race/ethnicity, *n* (%)		
Non-Hispanic White	5998 (42)	
Asian/Pacific Islander	3821 (27)	
Hispanic	3177 (22)	
Black	638 (4)	
Other	779 (5)	
Missing	4	
Pre-pregnancy BMI category, *n* (%)		
Underweight	377 (3)	274 (2)
Normal weight	7330 (55)	6775 (47)
Overweight	3370 (25)	4038 (28)
Obese	2363 (18)	3195 (22)
Missing	977	135
Nulliparous, *n* (%)	11 204 (78)	0 (0)
Smoked during pregnancy, *n* (%)	319 (2)	145 (1)
Missing	1011	656
Medicaid coverage at delivery, *n* (%)	485 (3)	790 (6)
Missing	140	124
Maternal education (years), mean (SD)	15.3 (2.2)	15.4 (2.1)
Missing	2375	2355
Female child, *n* (%)	7453 (52)	7282 (51)
Total gestational weight gain (kg), mean (SD)	14.7 (6.2)	12.6 (5.8)
Missing	913	183
IOM gestational-weight-gain category, *n* (%)		
Below IOM	2747 (21)	4091 (29)
Within IOM	4486 (33)	4963 (35)
Above IOM	6169 (46)	5168 (36)
Missing	1015	195
Child's birthweight (g), mean (SD)	3425 (449)	3519 (449)
Child's birthweight category, *n* (%)		
Small-for-gestational age	1532 (11)	881 (6)
Appropriate-for-gestational age	11 737 (81)	11 712 (81)
Large-for-gestational age	1148 (8)	1824 (13)
Child's BMI at 3 years old (kg/m^2), mean (SD)	16.3 (1.5)	16.3 (1.5)
Child's obesity status at 3 years old, *n* (%)	1268 (9)	1133 (8)

BMI, body mass index; IOM, Institute of Medicine; SD, standard deviation.

was associated with 0.25 units lower birthweight z-score (95% CI: −0.27, −0.24), 59% greater odds of SGA (95% CI: 1.51, 1.68) and 43% lower odds of LGA (95% CI: 0.53, 0.60) compared with GWG=IOM (Table 3). GWG>IOM was associated with 0.28 units greater birthweight z-score (95% CI: 0.27, 0.30), 35% lower odds of SGA (95% CI: 0.61, 0.68) and 88% greater odds of LGA (95% CI: 1.80, 1.97) compared with GWG=IOM (Table 3). Using sibling fixed-effects analyses, associations remained but were attenuated. Within siblings, GWG<IOM was associated with 0.16 unit lower birthweight z-score (95% CI: −0.20, −0.13), 32% greater odds of SGA (95% CI: 1.11, 1.58) and 20% lower odds of LGA (95% CI: 0.68, 0.94) compared with GWG=IOM (Table 3). GWG>IOM was associated with 0.19 unit greater birthweight z-score (95% CI: 0.15, 0.22), 21% lower odds of SGA (95% CI: 0.65, 0.96) and 36% greater odds of LGA (95% CI: 1.20, 1.54) (Table 3).

BMI at 3 years old

Using all mother–child pairs in our cohort, accounting for the correlation of outcomes between siblings, GWG<IOM was associated with 0.10 unit lower BMI z-score (95% CI: −0.12, −0.09) and 13% lower odds of obesity at 3 years old (95% CI: 0.82, 0.93) (Table 4). GWG>IOM was associated with 0.11 unit greater BMI z-score (95% CI: 0.10, 0.13) and 30% greater odds of obesity at 3 years old (95% CI: 1.24, 1.37) (Table 4). Using sibling fixed-effects analyses, associations were strongly attenuated to the null. Within siblings, GWG>IOM was not associated with BMI z-score (mean difference: 0.01; 95% CI: −0.03, 0.05) or obesity at 3 years old (OR = 0.98; 95% CI: 0.84, 1.15) (Table 4).

Additional analyses

P-values for interaction suggested possible effect-measure modification of associations of IOM GWG categories with birthweight z-score and LGA outcomes by pre-pregnancy BMI category (Supplementary Table 6, available as Supplementary data at *IJE* online), but associations stratified by pre-pregnancy BMI category were not meaningfully different between pre-pregnancy BMI categories (Supplementary Table 7, available as Supplementary data at *IJE* online). We did not observe carry-over effects in our analysis (all *P* for interaction >0.10). Results of analyses using generalized estimating equations in each discordant outcome analytic cohort to evaluate whether differences in the analytic population were contributing to differences in results were attenuated compared with results using all term pregnancies for associations of GWG<IOM with SGA and LGA and associations of GWG>IOM with LGA and obesity at 3 years old (Supplementary Table 8, available as

Table 3. Associations of IOM gestational-weight-gain category and child's birthweight outcomes, Kaiser Permanente Northern California 2008–2014

	All term pregnancies	Term siblings
	Birthweight z-score	
	(N = 111 482 mother–child pairs; 96 289 mothers)	(N = 29 610 mother–child pairs; 14 417 mothers)
Gestational-weight-gain category	Mean difference[a] (95% CI)	Mean difference[b] (95% CI)
Below IOM	−0.25 (−0.27, −0.24)	−0.16 (−0.20, −0.13)
Within IOM	Referent	Referent
Above IOM	0.28 (0.27, 0.30)	0.19 (0.15, 0.22)
	Small-for-gestational age birthweight	
	(N = 111 482 mother–child pairs; 96 289 mothers)	(N = 3499 mother–child pairs; 1689 mothers)
Gestational-weight-gain category	OR[a] (95% CI)	OR[b] (95% CI)
Below IOM	1.59 (1.51, 1.68)	1.32 (1.11, 1.58)
Within IOM	Referent	Referent
Above IOM	0.65 (0.61, 0.68)	0.79 (0.65, 0.96)
	Large-for-gestational age birthweight	
	(N = 111 482 mother–child pairs; 96 289 mothers)	(N = 5076 mother–child pairs; 2421 mothers)
Gestational-weight-gain category	OR[a] (95% CI)	OR[b] (95% CI)
Below IOM	0.57 (0.53, 0.60)	0.80 (0.68, 0.94)
Within IOM	Referent	Referent
Above IOM	1.88 (1.80, 1.97)	1.36 (1.20, 1.54)

Model is adjusted for gestational age at delivery (weeks), maternal race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic Asian/Pacific Islander, Hispanic, other; implicitly in fixed-effects models), maternal age at delivery (years), maternal pre-pregnancy body mass index (kg/m^2), nulliparity (yes, no), smoking during pregnancy (yes, no), Medicaid coverage at delivery (Y/N), maternal education (years) and child's sex.

IOM, Institute of Medicine; OR, odds ratio.

[a]Generalized estimating-equations model accounting for correlation of outcomes in siblings.

[b]Fixed-effects model controlling for all measured and unmeasured time-stable covariates.

Table 4. Associations of IOM gestational-weight-gain category and child's BMI outcomes at 3 years old, Kaiser Permanente Northern California 2008–2014

	All term pregnancies	Term siblings
	BMI z-score	
	(N = 111 482 mother–child pairs; 96 289 mothers)	(N = 29 610 mother–child pairs; 14 417 mothers)
Gestational-weight-gain category	Mean difference[a] (95% CI)	Mean difference[b] (95% CI)
Below IOM	−0.10 (−0.12, −0.09)	−0.04 (−0.08, 0.00)
Within IOM	Referent	Referent
Above IOM	0.11 (0.10, 0.13)	0.01 (−0.03, 0.05)
	Obesity	
	(N = 111 482 mother–child pairs; 96 289 mothers)	(N = 3881 mother–child pairs; 1862 mothers)
Gestational-weight-gain category	OR[a] (95% CI)	OR[b] (95% CI)
Below IOM	0.87 (0.82, 0.93)	1.01 (0.85, 1.22)
Within IOM	Referent	Referent
Above IOM	1.30 (1.24, 1.37)	0.98 (0.84, 1.15)

Model is adjusted for gestational age at delivery (weeks), maternal race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic Asian/Pacific Islander, Hispanic, other; implicitly in fixed-effects models), maternal age at delivery (years), maternal pre-pregnancy BMI (kg/m^2), nulliparity (yes, no), smoking during pregnancy (yes, no), Medicaid coverage at delivery (Y/N), maternal education (years) and child's sex.

BMI, body mass index; IOM, Institute of Medicine; OR, odds ratio.

[a]Generalized estimating-equations model accounting for correlation of outcomes in siblings.

[b]Fixed-effects model controlling for all measured and unmeasured time-stable covariates.

Supplementary data at *IJE* online). Results of the sensitivity analysis limited to pregnancies with measured pre-pregnancy weight and measured weight $\leq$2 weeks before delivery were similar to the main results (Supplementary Tables 9 and 10, available as Supplementary data at *IJE* online).

Discussion

In our study, GWG>IOM was associated with greater birthweight, lower odds of SGA and greater odds of LGA using a conventional approach comparing pregnancies between mothers and using a sibling-analysis design controlling for stable within-family confounders. GWG>IOM was also associated with greater BMI and greater odds of obesity at 3 years old in the conventional approach comparing pregnancies between mothers, but was not associated with BMI or obesity at 3 years old in sibling analyses.

Our finding of an association between greater GWG and greater birthweight are consistent with previous studies using both conventional analyses and sibling study designs. A meta-analysis of 11 studies with SGA as the outcome and 13 studies with LGA as the outcome reported associations of GWG>IOM with 34% lower risk of SGA and 85% greater risk of LGA.[1] An individual participant-level meta-analysis of data from 196 670 participants from 25 studies also reported associations of greater GWG with lower risk of SGA and greater risk of LGA.[25] Using data from 354 945 siblings born to 167 977 mothers in Pennsylvania and Washington, Yan reported associations of GWG>IOM with 126 g greater birthweight and a 2% absolute increase (risk difference) in risk of LGA, controlling for maternal fixed effects.[14] Ludwig *et al.* reported a linear association of 1 kg greater GWG with 7 g greater birthweight in 1 164 750 siblings in 513 501 families after controlling for stable within-family unmeasured confounders in fixed-effects models.[15] Hutcheon *et al.* reported associations of 1 unit greater GWG z-score with 83–97 g greater birthweight, 15–22% lower risk for SGA and 32–58% greater risk for LGA in 44 457 siblings born to 21 680 women in Sweden.[16]

Our finding of an association between greater GWG and greater early-childhood-obesity risk is consistent with previous studies using conventional analyses. A meta-analysis of two studies reported associations of GWG>IOM with 91% greater risk of overweight and obesity at 3–4 years old.[6,26,27] Our finding that GWG was no longer associated with childhood-obesity risk using a sibling analysis is consistent with a previous sibling design study that assessed the association of GWG>IOM and childhood BMI using the Collaborative Perinatal Project cohort (5917 siblings from 2758 mothers, 1959–1974) and found that GWG>IOM was not strongly associated with BMI z-score at 4 years old after controlling for stable within-mother unmeasured confounders.[28] Our results are from a contemporary cohort, with greater racial/ethnic diversity, a higher prevalence of pre-pregnancy overweight and obesity, and lower prevalence of smoking than the Collaborative Perinatal Project cohort. In addition, we evaluated associations with childhood obesity, in addition to BMI.

Our results suggest that GWG>IOM may be causally related to greater birthweight, as GWG>IOM was consistently associated with greater birthweight in both conventional analyses comparing pregnancies between mothers and sibling analyses controlling for stable family environment, behaviours and genetic predisposition to weight gain that are shared between pregnancies. However, family environment, behaviours or genetic predisposition to weight gain that are shared between a mother and her children may explain a large portion of the association of GWG>IOM and early-childhood obesity that has been observed using conventional analyses in previous studies and our current study. Mothers and their young children tend to have similar lifestyle behaviours,[29] which may have a larger impact on early-childhood BMI and obesity risk than GWG. Increases in maternal BMI after pregnancy, which are related to familial-lifestyle habits and environment, are associated with childhood overweight/obesity at 11 years old,[30] further supporting stronger influences of common lifestyle, environmental or genetic determinants of weight gain than GWG in mothers and their children.

Strengths of our study include the use of both a conventional approach comparing outcomes between mothers and a sibling design controlling for shared familial factors that are stable across pregnancies and the use of clinically measured weights and heights to calculate GWG and maternal and child BMI. In addition, our study population was diverse and representative of the Northern California region. However, there are several limitations that should be considered when interpreting our study results. We did not have information about familial-lifestyle characteristics (diet, physical activity, stress) or environment (income, employment), which likely confound associations in conventional analyses. To the extent that familial-lifestyle characteristics were similar within siblings, the fixed-effects sibling analyses were able to control for these characteristics. However, it is possible that some of these familial characteristics changed from one pregnancy to another, and results from sibling analyses have greater bias due to confounding by these unstable unmeasured familial-lifestyle or environmental characteristics than results from conventional analyses.[13] Additionally, sibling analyses included 15% (birthweight z-score and BMI z-score analyses), 2% (SGA analysis), 3% (LGA analysis) and 2% (obesity analysis) of mothers in our overall analytic cohort, which may have introduced selection bias in our results. Characteristics of the mothers in the overall analytic cohort and the overall sibling cohort were similar; however, distributions of race/ethnicity and pre-pregnancy BMI categories differed between the overall analytic cohort and the discordant outcomes sibling cohorts. Some results using conventional analyses in the discordant outcomes analytic cohorts were attenuated compared with conventional analyses in the overall analytic cohort, suggesting that restriction of the analytic population to siblings with discordant outcomes contributed to the attenuation of associations. This may be due to a reduction in the variability of the familial environment in the discordant sibling samples or lower precision and higher variance in estimates of association due to the smaller sample sizes. Finally, obesity at 3 years old is associated with future cardiometabolic risk, including greater waist circumference and greater risk for obesity and metabolic syndrome in adulthood[31]; however, we were not able to assess the associations of GWG with child weight outcomes in later childhood or adulthood.

In conclusion, GWG>IOM was associated with greater birthweight using a conventional approach comparing pregnancies between mothers and using a sibling analysis controlling for stable within-family confounders. GWG>IOM was associated with greater BMI and greater odds of obesity at 3 years old using a conventional approach comparing pregnancies between mothers, but was not associated with BMI or obesity at 3 years old in sibling analyses. GWG may directly affect birthweight, whereas shared environmental, lifestyle or genetic factors within families may play a larger role in determining early-childhood weight status than GWG. Efforts to promote appropriate GWG are important for reducing the risk of LGA, as well as other adverse outcomes, such as preterm birth and caesarean delivery.[1] However, interventions that address behavioural and environmental factors that influence weight in families may be more successful in preventing early-childhood obesity and its sequelae than interventions that are focused on GWG.

Supplementary data

Supplementary data are available at *IJE* online.

Author contributions

S.E.B. contributed to the study design, conducted data analyses, interpreted results, and wrote and edited the manuscript. C.P.Q. and L.A.A. contributed to study design and interpreted results. F.X. compiled all study data from electronic health records. M.M.H. developed the study idea, contributed to study design, and interpreted results. All authors contributed to revising the manuscript critically for important intellectual content and approved the final version of the manuscript for publication.

Funding

This work was supported by the National Institute of Diabetes and Digestive and Kidney Diseases at the National Institutes of Health (grant T32DK11668401 to S.E.B.); the National Institute of Mental Health at the National Institutes of Health (grant K01MH103444 to L.A.A.); and the Kaiser Permanente Community Benefit grant programme (to M.M.H.).

Conflict of interest

None declared.

References

1. Goldstein RF, Abell SK, Ranasinha S *et al.* Association of gestational weight gain with maternal and infant outcomes: a systematic review and meta-analysis. *JAMA* 2017;**317**:2207–25.
2. Leonard SA, Petito LC, Rehkopf DH, Ritchie LD, Abrams B. Weight gain in pregnancy and child weight status from birth to adulthood in the United States. *Pediatr Obes* 2017;**12**:18–25.
3. Papazian T, Abi Tayeh G, Sibai D, Hout H, Melki I, Rabbaa Khabbaz L. Impact of maternal body mass index and gestational weight gain on neonatal outcomes among healthy Middle-Eastern females. *PLoS One* 2017;**12**:e0181255.
4. Zhao R, Xu L, Wu ML, Huang SH, Cao XJ. Maternal pre-pregnancy body mass index, gestational weight gain influence birth weight. *Women Birth* 2018;**31**:e20–25.
5. Hillier TA, Pedula KL, Vesco KK, Oshiro CE, Ogasawara KK. Impact of maternal glucose and gestational weight gain on child obesity over the first decade of life in normal birth weight infants. *Matern Child Health J* 2016;**20**:1559–68.
6. Mamun AA, Mannan M, Doi SAR. Gestational weight gain in relation to offspring obesity over the life course: a systematic review and bias-adjusted meta-analysis. *Obes Rev* 2014;**15**:338–47.
7. Lau EY, Liu J, Archer E, McDonald SM, Liu J. Maternal weight gain in pregnancy and risk of obesity among offspring: a systematic review. *J Obes* 2014;**2014**:1–16.
8. Sridhar SB, Darbinian J, Ehrlich SF *et al.* Maternal gestational weight gain and offspring risk for childhood overweight or obesity. *Am J Obstetr Gynecol* 2014;**211**:259.e1–59.e8.
9. Diesel JC, Eckhardt CL, Day NL, Brooks MM, Arslanian SA, Bodnar LM. Is gestational weight gain associated with offspring obesity at 36 months? *Pediatr Obes* 2015;**10**:305–10.
10. Tie HT, Xia YY, Zeng YS *et al.* Risk of childhood overweight or obesity associated with excessive weight gain during pregnancy: a meta-analysis. *Arch Gynecol Obstet* 2014;**289**:247–57.
11. Oken E, Gillman MW. Fetal origins of obesity. *Obes Res* 2003;**11**:496–506.
12. Committee on Obstetric Practice. *Weight Gain During Pregnancy: Reexamining the Guidelines*. Washington, DC: National Academies Press, 2009.
13. Frisell T, Oberg S, Kuja-Halkola R, Sjolander A. Sibling comparison designs: bias from non-shared confounders and measurement error. *Epidemiology (Cambridge, Mass)* 2012;**23**:713–20.
14. Yan J. Maternal pre-pregnancy BMI, gestational weight gain, and infant birth weight: a within-family analysis in the United States. *Econ Hum Biol* 2015;**18**:1–12.

15. Ludwig DS, Currie J. The association between pregnancy weight gain and birthweight: a within-family comparison. *Lancet* 2010; **376**:984–90.
16. Hutcheon JA, Stephansson O, Cnattingius S, Bodnar LM, Johansson K. Is the association between pregnancy weight gain and fetal size causal? A re-examination using a sibling comparison design. *Epidemiology (Cambridge, Mass)* 2019;**30**:234–42.
17. Gordon N. *Similarity of the Adult Kaiser Permanente Membership in Northern California to the Insured and General Population in Northern California: Statistics from the 2009 California Health Interview Survey*. Oakland, CA: Kaiser Permanente Division of Research, 2012.
18. Obesity: preventing and managing the global epidemic: report of a WHO consultation. *World Health Organization Technical Report Series* 2000;**894**:1–253; i–xii.
19. ACOG Committee opinion no. 548: weight gain during pregnancy. *Obstetr Gynecol* 2013;**121**:210–12.
20. Aris IM, Kleinman KP, Belfort MB, Kaimal A, Oken E. A 2017 US reference for singleton birth weight percentiles using obstetric estimates of gestation. *Pediatrics* 2019;**144**:e20190076.
21. Kuczmarski RJ, Ogden CL, Guo SS *et al.* 2000 CDC growth charts for the United States: methods and development. *Vital and Health Statistics Series 11, Data from the National Health* 2002; 1–190.
22. von Hippel P4. Regression with missing YS: an improved strategy for analyzing multiply imputed data. *Sociol Methodol* 2007; **37**:83–117.
23. Sjolander A, Frisell T, Kuja-Halkola R, Oberg S, Zetterqvist J. Carryover effects in sibling comparison designs. *Epidemiology (Cambridge, Mass)* 2016;**27**:852–58.
24. Rubin D. *Multiple Imputation for Nonresponse in Surveys*. New York: John Wiley, 1987.
25. Voerman E, Santos S, Inskip H *et al.* Association of gestational weight gain with adverse maternal and infant outcomes. *JAMA* 2019;**321**:1702–15.
26. Oken E, Taveras EM, Kleinman KP, Rich-Edwards JW, Gillman MW. Gestational weight gain and child adiposity at age 3 years. *Am J Obstet Gynecol* 2007;**196**:322.e1–22.e8.
27. Olson CM, Demment MM, Carling SJ, Strawderman MS. Associations between mothers' and their children's weights at 4 years of age. *Child Obes* 2010;**6**:201–07.
28. Branum AM, Parker JD, Keim SA, Schempf AH. Prepregnancy body mass index and gestational weight gain in relation to child body mass index among siblings. *Am J Epidemiol* 2011;**174**:1159–65.
29. Cameron AJ, Crawford DA, Salmon J *et al.* Clustering of obesity-related risk behaviors in children and their mothers. *Ann Epidemiol* 2011;**21**:95–102.
30. Risvas G, Papaioannou I, Panagiotakos DB, Farajian P, Bountziouka V, Zampelas A. Perinatal and family factors associated with preadolescence overweight/obesity in Greece: the GRECO study. *J Epidemiol Glob Health* 2012;**2**:145–53.
31. Graversen L, Sorensen TI, Petersen L *et al.* Preschool weight and body mass index in relation to central obesity and metabolic syndrome in adulthood. *PLoS One* 2014;**9**:e89986.