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ORIGINAL RESEARCH

Maternal body mass index, gestational weight gain, and early childhood growth: A register-based cohort study

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Abstract

Introduction: Childhood obesity is associated with maternal obesity, but the link to gestational weight gain (GWG) is not fully elucidated. We examined the relationship between early pregnancy maternal body mass index (BMI) and GWG on early childhood growth.

Material and Methods: Data from 30 197 mother–child pairs from Uppsala County Mother and Child Cohort were divided into 15 groups according to maternal BMI and GWG, based on World Health Organization classification and Institute of Medicine guidelines, respectively. Postnatal growth patterns were analyzed with linear mixed regression models within maternal BMI groups. Odds ratios of overweight and obesity at 4 years of age were assessed with logistic regression analyses. We treated children of mothers with normal weight and adequate GWG as the reference group, and all analyses were adjusted for potential confounders.

Results: GWG was associated with infant BMI *z*-score at birth, independent of potential confounding factors. Independent of GWG, we observed an overall decrease in BMI *z*-score from 18 months to 5 years in children of mothers who were underweight, while an increase in BMI *z*-score was seen in children of mothers who were overweight or obese. In children of normal- and overweight mothers, the risk of childhood overweight and obesity was associated with excessive compared to adequate GWG (adjusted odds ratio [aOR] 1.17, 95% confidence interval [CI] 1.01–1.36 for normal-weight mothers, and aOR 1.25, 95% CI 1.04–1.51 for overweight mothers, respectively). Children of mothers with obesity and excessive GWG had the highest risk of being overweight or obese at 4 years (aOR 2.88, 95% CI 2.40–3.44, and 4.38, 95% CI 3.37–5.67, respectively). Associations did not differ between children of mothers with obesity class 1 and 2–3 when comparing excessive and adequate GWG (aOR 1.33, 95% CI 0.96–1.85, and 1.12, 95% CI 0.74–1.70, respectively).

Conclusions: Maternal GWG affects infant birth size and growth until 18 months, although maternal BMI is more crucial for childhood growth beyond 18 months. Further,

Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; GWG, gestational weight gain; UCMC Cohort, Uppsala County Mother and Child Cohort.

children of mothers who are normal- or overweight and experience excessive GWG have an increased risk of obesity at 4 years.

KEYWORDS
childhood growth, early childhood obesity, gestational weight gain, maternal body mass index

1 | INTRODUCION

Overweight and obesity among children have risen during the last decades. In 2016, 18% of 5–19 year old children were overweight or obese, while the corresponding proportion in 1975 was 4%.[1] The growth pattern in early childhood is important for health later in life. Children with rapid weight gain in early childhood and early adiposity rebound have an increased risk of sustained obesity during childhood and adult life.[2,3] Children who are overweight or obese are at higher risk of sustained obesity, morbidity, and premature death in adulthood compared to children of normal weight.[4,5] It is crucial to identify children at risk of overweight and obesity early on to, if possible, prevent these conditions. Once overweight or obese is established, reducing and maintaining a lower body weight becomes much harder. Hence, early intervention can make a difference in long-term health outcomes.[6,7]

The development of childhood obesity is complex, and the underlying mechanisms are not fully understood. The intrauterine environment is important for the development and growth of the fetus and for the health of the newborn infant.[8] An unfavorable intrauterine environment may predispose the offspring to future morbidities, such as overweight and obesity in childhood as well as later in life.[9] Excessive gestational weight gain (GWG) and high maternal body mass index (BMI) are both associated with high birth weight and the risk of being born large for gestational age. Further, high maternal BMI and being born large for gestational age are risk factors for obesity later in life.[10–12] GWG has been linked to childhood obesity, both early in childhood and later on.[11,13] In sibling studies, GWG is associated with size at birth but not with risk of obesity at 3 years of age, where social factors or genetics are thought to play a greater role.[14] Furthermore, excessive GWG has been associated with obesogenic growth patterns from birth to 3 years of age.[15] the GWG-associated risk of obesogenic growth patterns and early childhood overweight may differ across maternal BMI strata. Studies examining the relation between excessive GWG and early childhood overweight or obesity across maternal BMI strata have found increased risks in children of mothers with normal weight. Further, children of mothers who are overweight or obese have a higher risk of being overweight and the risk increases with increasing GWG.[16,17] Still, early childhood growth patterns in relation to GWG across maternal BMI strata have not been fully elucidated. In addition, it is not clear if GWG is associated with the risk of childhood overweight and obesity in children of mothers with overweight and obesity.

Key message

Maternal gestational weight gain affects growth patterns in early childhood. Excessive gestational weight gain increases the risk of overweight and obesity in children of mothers with normal weight and overweight, while children of mothers with obesity are at increased risk of childhood overweight and obesity independent of gestational weight gain.

We leveraged a large population-based cohort of term-born children and their mothers to examine if the association between maternal GWG and childhood growth patterns from birth until 5 years of age differs by maternal BMI. Further, we assessed the risk of overweight and obesity at the age of four in relation to maternal early pregnancy BMI and GWG.

2 | MATERIAL AND METHODS

2.1 | Data sources and study population

This study is a registry-based cohort study based on data from the Uppsala County Mother and Child (UCMC) Cohort, originally based on a local register for child health care in Uppsala County, Sweden. The UCMC Cohort contains information about 57 000 children born at Uppsala University Hospital between 2000 and 2015 and their mothers. The UCMC Cohort has previously been described in detail.[18]

Children born preterm (gestational age less than 37 + 0) and post-term (gestational age more than 41 + 6) were excluded ($n = 6861$). We also excluded children born after multiple pregnancies ($n = 937$) and children of mothers lacking data on early pregnancy BMI or GWG ($n = 18\,757$), see Table S1 for characteristics of observations with and without data on GWG. We further excluded observations with an outlier value of GWG (GWG >40.0 kg and GWG <−15 kg, $n = 48$) and children lacking data on BMI *z*-score at birth ($n = 131$). Finally, we excluded children of mothers with preeclampsia ($n = 58$) and children of mothers lacking data on country of birth ($n = 11$). The final population consisted of 30 197 mother–child pairs (Figure 1).

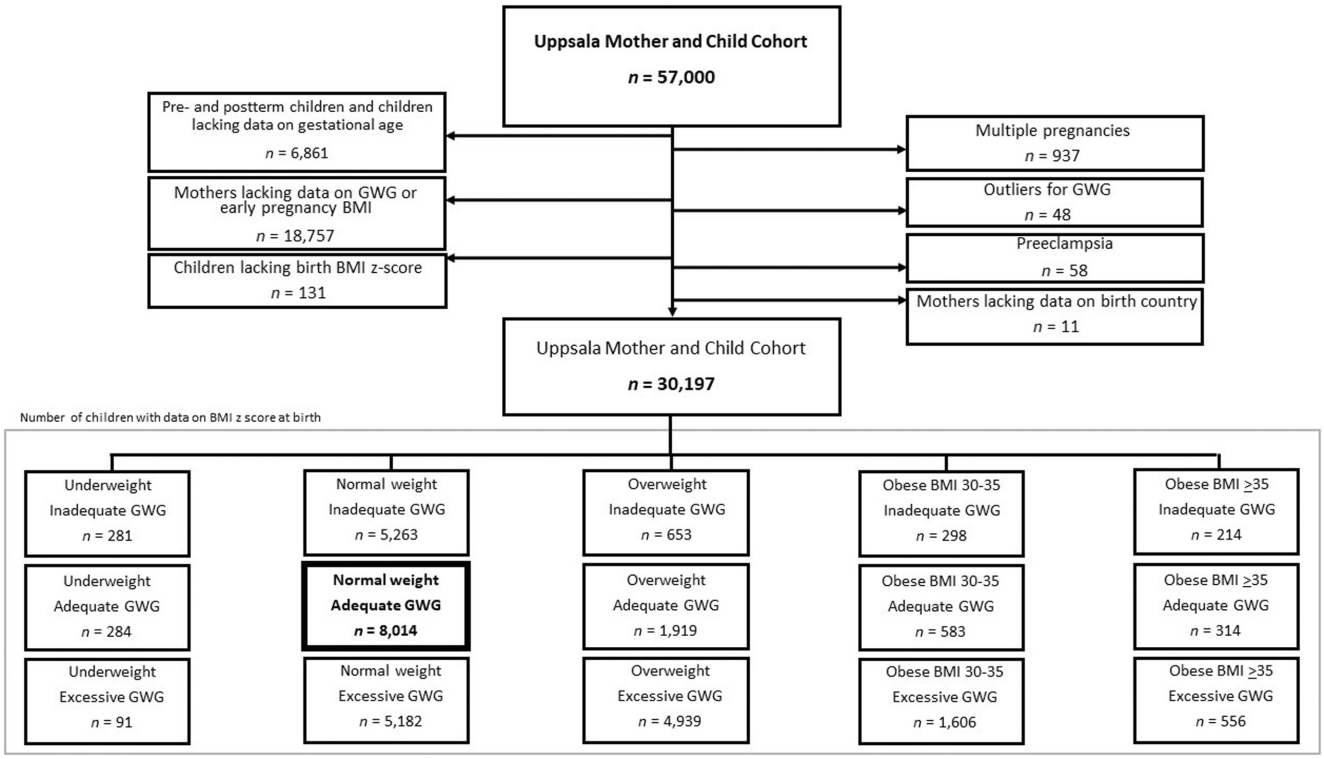

FIGURE 1 Study population. The flowchart shows causes and numbers of excluded observations and numbers of observations in the final study population. Numbers of mother-and-child pairs, with a value of BMI *z*-score at birth divided into maternal BMI-GWG groups according to weight status in the first trimester and gestational weight gain during pregnancy, are found at the bottom of the flowchart. BMI, body mass index; GWG, gestational weight gain; *n*, number of observations.

TABLE 1 Grouping of the study population based on early pregnancy maternal body mass index and gestational weight gain.

	Gestational weight gain[b]		
Weight category at first antenatal health care visit[a]	**Inadequate**	**Adequate**	**Excessive**
Underweight (BMI <18.5 kg/m^2)	UI	UA	UE
Normal weight (BMI 18.5–24.9 kg/m^2)	NI	NA (reference)	NE
Overweight (BMI 25–29.9 kg/m^2)	OvI	OvA	OvE
Obese class 1 (BMI 30–34.5 kg/m^2)	ObI class 1	ObA class 1	ObE class1
Obese class 2–3 (BMI ≥35 kg/m^2)	ObI class 2–3	ObA class 2–3	ObE class2-3

Abbreviation: BMI, body mass index.

[a]Weight classification according to the WHO classification. Underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2), obese class 1 (BMI 30–34.9 kg/m^2), and obese class 2–3 (BMI ≥35 kg/m^2).

[b]Gestational weight gain (GWG) classified according to Institute of Medicine guidelines 2009. Recommended GWG: 12.5–18 kg, 11.5–16 kg, 7–11.5 kg, and 5–9 kg for women with pre-pregnancy BMI classified as underweight, normal weight, overweight, and obese (≥ 30 kg/m^2), respectively. Adequate GWG, as recommended. Excessive GWG, above recommended; Inadequate GWG, less than recommended.

2.2 | Exposure, outcome and covariates

Maternal early pregnancy BMI and GWG were classified according to the World Health Organization classification and Institute of Medicine guidelines, respectively (Table 1).[19,20] Maternal early pregnancy weight was measured by trained midwives at the first antenatal care visit, taking place before pregnancy week 13. Maternal height was self-reported or measured by the midwife, and BMI was calculated by dividing weight by height in meters squared. Maternal weight at delivery was measured by a midwife or helping nurse in the maternity ward before delivery. GWG was calculated as weight at delivery minus early pregnancy weight. Mother-and-child pairs were divided into 15 groups depending on maternal early pregnancy BMI and GWG (Table 1).

The primary outcome was child growth trajectory expressed as BMI z-score from birth to 18 months, three, four, and 5 years. We did not have complete growth data at the time of study data collection since all children had not reached the age of the selected follow-up

points. The Swedish reference curves were used to calculate standard deviation scores (z-scores) of anthropometric data.[21,22] The secondary outcome was the risk of being overweight or obese at 4 years of age, defined according to the International Obesity Task Force (IOTF) criteria where boys with BMI ≥17.52 kg/m^2 and girls with BMI ≥17.36 kg/m^2 are classified as being overweight or obese.[23] Child BMI was calculated using weight in kg with two decimals at birth and at 18 months, and with one decimal at three, four, and 5 years of age, and height in meters with two decimals for all ages. Birth weight and length were measured by trained midwives or nurses in the delivery ward. At all the other follow-up points, weight and height were measured by trained nurses at child health care centers. We only included children with anthropometric data collected 2 months before or after the included follow-up points.

A directed acyclic graph (DAG) was created to select covariates for adjustment. The minimal sufficient adjustment set used in a secondary model included maternal age, height, parity, country of birth, educational level, and smoking at gestational weeks 30–32 (Figure S1A,B).

2.3 | Statistical analyses

For baseline characteristics, we used mean and standard deviation to describe continuous variables, and frequency and percentage to describe categorical variables.

To analyze the growth patterns of children in relation to GWG (inadequate, adequate, and excessive) taking repeated measurements into account, we ran linear mixed-effect regression models with an interaction term between the independent variable and the time variable (follow-up points). Each mother-and-child pair (i.e., subject) was treated as a random effect to allow the intercept to vary with the child. Child BMI *z*-score (continuous) was the dependent variable, and the maternal BMI-GWG group (categorical) was the independent variable. Linear mixed-effect regression analysis is considered appropriate when calculating trajectories due to its flexibility and robustness when analyzing longitudinal data. Specifically, the analysis accounts for correlations between repeated measures on the same subject and allows for individual differences in trajectories.

We performed separate linear mixed-effect regression model analyses for each maternal BMI group, comparing child BMI z-score trajectories (at birth, 18 months, three, four, and 5 years) across maternal GWG groups. Age and BMI-GWG group were handled as fixed effects, as were the covariates maternal age, height, parity, maternal country of birth, educational level, and smoking at gestational weeks 30–32. For all interactions between the maternal BMI-GWG group and child age, we used mothers of normal weight and adequate GWG as the reference. Growth trajectories from birth to the four follow-up points in the different BMI-GWG groups were compared to the growth trajectory of children of mothers with normal weight with adequate GWG (reference group). Estimates are presented by beta coefficients with a 95% confidence interval (CI).

The risks of overweight and/or obesity at 4 years were assessed by applying logistic regression analyses for each BMI-GWG group. Results were expressed as odds ratios (ORs) with 95% CI. Children of mothers of normal weight with adequate GWG were treated as the reference group. We also calculated the association between GWG and childhood overweight and/or obesity at 4 years, stratified by maternal early pregnancy BMI. Last, we assessed the risk of overweight and/or obesity at 4 years associated with GWG in children of mothers with overweight and obesity, respectively. In these analyses, children of mothers with overweight with adequate GWG constituted the reference in the overweight groups, and children of mothers with obesity with adequate GWG constituted the reference group in the obese groups. We performed both univariate and multivariate regression analyses.

Observations with missing data (maternal educational level [$n=126$] and smoking at gestational weeks 30–32 [$n=2083$]) were excluded in the adjusted analyses.

All statistical analyses were conducted with R Statistical Software (v 4.1.2; R core team 2021),[24] package lme4,[25] and ggplot2.[26]

3 | RESULTS

3.1 | Study participants

Data on BMI at birth were available for all 30 179 children and for 16 711 children at 5 years of age (Table S2). Baseline characteristics are presented in Table 2. Mothers with normal BMI in early pregnancy and with adequate GWG during pregnancy constituted the largest BMI-GWG group, $n=8014$ (26.6%). Early pregnancy BMI was comparable between included and excluded observations (Table S2). Among observations missing GWG, 23.1% were also missing data on early pregnancy BMI. Among the excluded observations, mothers were more likely to be smokers and born outside the Nordic countries.

3.2 | Child growth trajectory

In all primary outcome analyses, children of mothers with normal weight and adequate GWG were the reference group.

3.2.1 | Children of mothers with underweight

For children of mothers with underweight, those of mothers with inadequate or adequate GWG had lower BMI z-scores, while those of mothers with excessive GWG had equal BMI z-scores at birth compared to children in the reference group (mothers with normal weight and adequate GWG) (Figure 2; Table S3). Between birth and 18 months, children of mothers who were underweight and with inadequate GWG had an increase in BMI *z*-scores, while those with excessive GWG had a greater decrease in BMI *z*-scores, as compared to the reference group. Beyond 18 months, all children

TABLE 2 Characteristics of population.

		Early pregnancy maternal BMI (kg/m2)[a]				
	All	Underweight	Normal weight	Overweight	Obese class 1	Obese class 2–3
n (%)	30 197 (100.0%)	656 (2.2%)	18 459 (61.1%)	7511 (24.9%)	2487 (8.2%)	1084 (3.6%)
Age at pregnancy (years)	30.30 (5.04)	28.12 (4.99)	30.19 (4.89)	30.69 (5.21)	30.42 (5.36)	30.47 (5.24)
Primiparous (*n* (%))	13 345 (44.2)	357 (54.4)	8730 (47.3)	2978 (39.6)	909 (36.6)	371 (34.2)
Early pregnancy weight (kg)[b]	68.47 (13.39)	49.45 (4.42)	61.63 (6.43)	74.76 (6.82)	88.58 (7.60)	106.72 (12.12)
Height (cm)	166.64 (6.37)	166.65 (6.45)	166.91 (6.33)	166.19 (6.45)	166.14 (6.21)	166.19 (6.70)
Early pregnancy BMI (kg/m^2)	24.64 (4.53)	17.77 (0.68)	22.10 (1.65)	27.03 (1.38)	32.05 (1.39)	38.58 (3.13)
Gestational weight gain (kg)[c]	13.81 (5.41)	13.69 (4.62)	14.20 (4.77)	13.97 (5.91)	12.04 (6.73)	10.28 (6.89)
Gestational weight gain group (*n* (%))						
Inadequate	6709 (22.2)	281 (42.8)	5263 (28.5)	653 (8.7)	298 (12.0)	214 (19.7)
Adequate	11 114 (36.8)	284 (43.3)	8014 (43.4)	1919 (25.5)	583 (23.4)	314 (29.0)
Excessive	12 374 (41.0)	91 (13.9)	5182 (28.1)	4939 (65.8)	1606 (64.6)	556 (51.3)
Cesarean section (*n* (%))	5013 (16.6)	58 (8.8)	2549 (13.8)	1490 (19.8)	586 (23.6)	330 (30.4)
Smoking in third trimester (*n* (%))[d]						
1–9 cigarette daily	773 (2.6)	24 (3.7)	376 (2.0)	217 (2.9)	103 (4.1)	53 (4.9)
≥10 cigarettes daily	249 (0.8)	2 (0.3)	107 (0.6)	80 (1.1)	40 (1.6)	20 (1.8)
Missing data	2083 (6.9)	52 (7.9)	1137 (6.2)	552 (7.3)	236 (9.5)	106 (9.8)
Education level, post-secondary education (*n* (%))	17 302 (57.3)	399 (60.8)	11 600 (62.8)	3927 (52.3)	1016 (40.9)	360 (33.2)
Missing data	126 (0.4)	2 (0.3)	77 (0.4)	30 (0.4)	11 (0.4)	6 (0.6)
Maternal country of birth						
Nordic countries (*n* (%))	25 550 (84.6)	474 (72.3)	15 787 (85.5)	6249 (83.2)	2094 (84.2)	946 (87.3)
Europe, except Nordic countries, and North America (*n* (%))	1021 (3.4)	36 (5.5)	665 (3.6)	225 (3.0)	65 (2.6)	30 (2.8)
Other countries (*n* (%))	3626 (12.0)	146 (22.3)	2007 (10.9)	1037 (13.8)	328 (13.2)	108 (10.0)
Maternal diabetes (*n* (%))[e]	385 (1.3)	4 (0.6)	114 (0.6)	126 (1.7)	80 (3.2)	61 (5.6)
Male sex (*n* (%))	15 358 (50.9)	314 (47.9)	9404 (50.9)	3780 (50.3)	1292 (52.0)	568 (52.4)
Birthweight, g	3617.24 (481.27)	3375.91 (424.22)	3567.37 (459.40)	3694.36 (488.91)	3735.32 (518.18)	3807.02 (539.69)

Note: Data represent the mean (SD), unless otherwise indicated.

[a]Weight classification according WHO, underweight (BMI <18.5), normal weight (BMI 18.5–24.9), overweight (BMI 25–29.9), obese class 1 (BMI 30–34.9), and obese class 2–3 (BMI >35).

[b]First visit to maternal health care service in pregnancy week 9–12.

[c]Maternal weight gain from first maternal health care visit until delivery. Gestational weight gain classified according to Institute of Medicine guidelines 2009. Recommended GWG: 12.5–18 kg, 11.5–16 kg, 7–11.5 kg, and 5–9 kg for women with pre-pregnancy BMI classified as underweight, normal weight, overweight, and obese (≥30 kg/m^2), respectively. Inadequate GWG = less than recommended. Adequate GWG = as recommended. Excessive GWG = above recommended.

[d]Smoking at gestational weeks 30-32.

[e]Diabetes mellitus type 1, type 2, and gestational diabetes.

of mothers who were underweight had a general decrease in BMI z-scores.

3.2.2 | Children of mothers with normal weight

Children of mothers with normal weight and adequate GWG (the reference group) had a small decrease in BMI *z*-scores from birth to all follow-up points (Figure 2; Table S4). In comparison, children whose mothers had inadequate GWG had lower BMI *z*-scores at birth, with increasing BMI z-scores at all follow-up points (Table S4). Children of mothers with excessive GWG had higher BMI *z*-scores at birth, but a subsequent greater decrease in BMI *z*-scores compared to the reference group (Table S4).

3.2.3 | Children with mothers with overweight

Compared to the reference group (mothers with normal weight with adequate GWG), children of mothers with overweight and

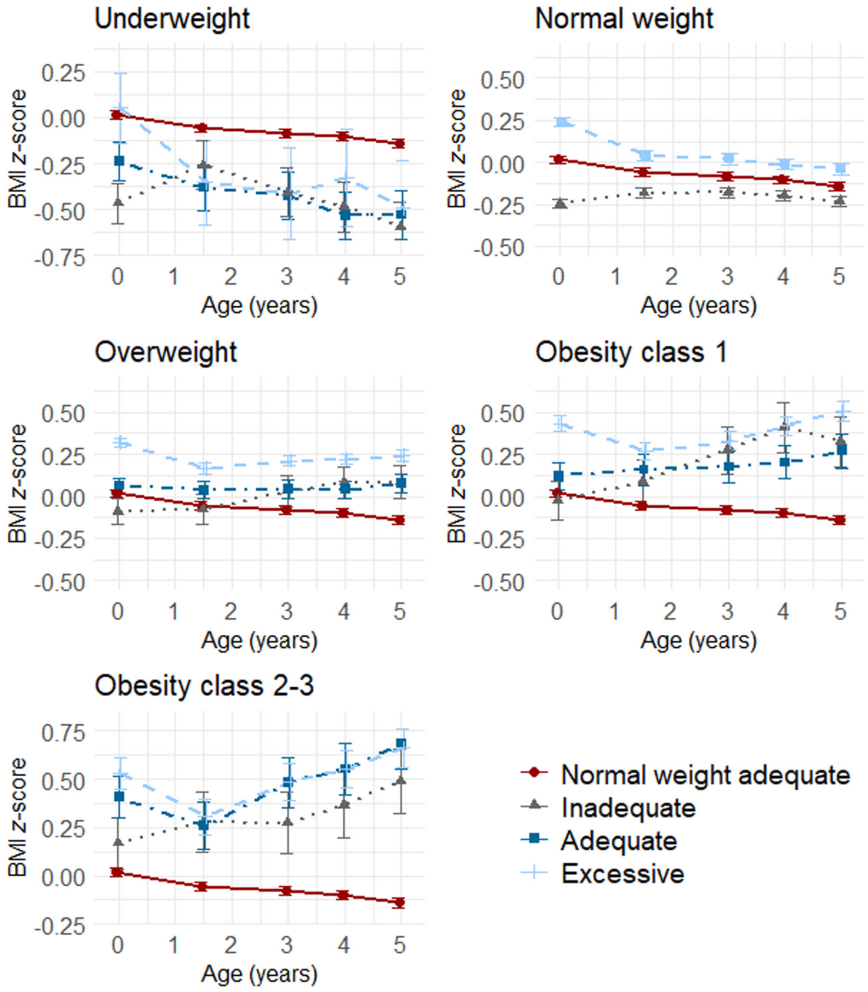

FIGURE 2 Growth from birth to five years of age in relation to maternal BMI-GWG groups. The cohort is divided into groups based on maternal BMI in early pregnancy (underweight, normal weight, overweight, obese class 1, obese class 2–3) and gestational weight gain during pregnancy (inadequate, adequate, excessive) adjusted for parity, maternal age and height, maternal educational level and country of birth, and smoking in pregnancy week 30–32. Child's growth is expressed as changes in BMI *z*-score from birth to one and a half, three, four, and 5 years of age in the different BMI-GWG groups. Children of mothers with normal weight with adequate GWG are the reference group. BMI, body mass index; GWG, gestational weight gain.

inadequate GWG had lower BMI *z*-scores at birth, with subsequent increased BMI *z*-scores (Figure 2; Table S5). Further, children of mothers with overweight and adequate GWG had higher BMI z-scores at birth and increased BMI *z*-scores from age 3 years compared to the reference group. Children of mothers with overweight and excessive GWG were larger at birth with an initial decrease, followed by an increase in BMI *z*-scores until 5 years of age.

3.2.4 | Children of mothers with obesity

There was no difference in BMI z-scores at birth between children of mothers with obesity class 1 and inadequate GWG and the reference group (mothers with normal weight and adequate GWG), whereas those with adequate or excessive GWG were larger at birth (Figure 2; Tables S6, S7). Children of mothers with obesity class 2–3 and adequate GWG and children of mothers with excessive GWG regardless of obesity class had a greater initial deceleration in growth compared to the reference group. From 18 months, there was a general increase in BMI *z*-scores in all children of mothers with obesity.

3.3 | Risk of being overweight or obese at 4 years of age

At 4 years, 2605 children (14.7%) were overweight or obese (Table S8). For all analyses (overall and stratified by BMI category), children of mothers with normal weight and adequate GWG were the reference group (normal weight reference). In additional analyses of children of mothers with overweight or obesity, children of mothers with overweight and adequate GWG were the reference group in analyses of children of mothers with overweight (overweight reference), and children of mothers with obesity class 1 and class 2–3, respectively, with adequate GWG were the reference groups (obese class 1 reference and obese class 2–3 reference) in analyses of children of mothers with obesity class 1 and class 2–3, respectively.

3.3.1 | Children of mothers with underweight

The risks of overweight or obesity at 4 years were lower in children of mothers with underweight and inadequate or adequate GWG compared to children in the normal weight reference group (Table 3). The risks of overweight or obesity in children of mothers

TABLE 3 Risk of overweight or obesity[a] at four years in children depending on maternal BMI[b] in early pregnancy and gestational weight gain[c].

	Unadjusted					Adjusted[d]				
		Child weight status		95% CI			Child weight status		95% CI	
Maternal weight status and level of GWG	*n* total	*n* = normal weight/ overweight or obese	OR	Lower	Upper	*n* total	*n* = normal weight/ overweight or obese	OR	Lower	Upper
Inadequate GWG	8782					8343				
Normal weight adequate GWG		4340/524	1.00 (ref)				4159/495	1.00 (ref)		
Underweight		151/9	0.49	0.23	0.92		138/8	0.49	0.22	0.95
Normal weight		2851/318	0.92	0.80	1.07		2715/297	0.91	0.78	1.06
Overweight		284/59	1.72	1.27	2.29		256/53	1.64	1.18	2.23
Obese class 1		113/29	2.13	1.38	3.18		102/25	1.85	1.15	2.86
Obese class 2–3		75/29	3.20	2.04	4.91		68/27	2.99	1.85	4.70
Adequate GWG	6695					6376				
Normal weight adequate GWG		4340/524	1.00 (ref)				4159/495	1.00 (ref)		
Underweight		157/9	0.47	0.22	0.88		147/9	0.51	0.24	0.96
Overweight		976/187	1.59	1.32	1.90		923/181	1.57	1.30	1.90
Obese class 1		257/73	2.35	1.78	3.08		236/63	2.07	1.52	2.78
Obese class 2–3		116/56	4.00	2.85	5.54		111/52	3.55	2.48	5.01
Excessive GWG	11 981					11 255				
Normal weight adequate GWG		4340/524					4159/495	1.00 (ref)		
Underweight		36/5	1.15	0.39	2.69		32/4	1.04	0.31	2.64
Normal weight		2565/370	1.19	1.04	1.38		2387/335	1.17	1.01	1.36
Overweight		2296/566	2.04	1.79	2.32		2145/525	2.04	1.78	2.33
Obese class 1		701/252	2.98	2.51	3.53		651/228	2.88	2.40	3.44
Obese class 2–3		207/119	4.76	3.73	6.06		192/102	4.38	3.37	5.67

Note: Children of mothers with normal weight with adequate gestational weight gain as reference.

Abbreviations: CI, confidence interval; GWG, gestational weight gain; OR, odds ratio.

[a]Overweight or obesity at four years of age defined according to the International Obesity Task Force (IOTF) criteria. Boys with BMI ≥ 17.52 kg/m^2 and girls with BMI ≥ 17.36 kg/m^2 classified as being overweight or obese.

[b]Weight classification according WHO, underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2), obese class 1 (BMI 30–34.9 kg/m^2), and obese class 2–3 (BMI >35 kg/m^2).

[c]Gestational weight gain classified according to Institute of Medicine guidelines 2009. Recommended GWG: 12.5–18 kg, 11.5–16 kg, 7–11.5 kg, and 5–9 kg for women with pre-pregnancy BMI classified as underweight, normal weight, overweight, and obese (≥ 30 kg/m^2), respectively. Inadequate GWG = less than recommended. Adequate GWG = as recommended. Excessive GWG = above recommended.

[d]Adjusted for parity, maternal age and height, maternal educational level and country of birth, and smoking in pregnancy week 30–32.

with underweight and excessive GWG were comparable to that of the normal weight reference group.

3.3.2 | Children of mothers with normal weight

Children of mothers with normal weight and inadequate GWG had a comparable risk of being overweight or obese at 4 years as the normal weight reference group (Table 3). Children of mothers with normal weight and excessive GWG had a 19% increased risk of being overweight or obese at 4 years compared to the normal weight reference group (adjusted OR [aOR] 1.19, 95% CI 1.04–1.38).

3.3.3 | Children of mothers with overweight

Overall, children of mothers with overweight had an increased risk of being overweight or obese at 4 years compared to the normal weight reference group, with the highest risk in the excessive GWG group (aOR 2.04, 95% CI 1.79–2.32, Table 3). When only including children of mothers with overweight, children of mothers with excessive GWG had a 29% increased risk of being overweight or obese at 4 years compared to those with mothers with adequate GWG (the overweight reference group) (aOR 1.29 95% CI 1.07–1.55, Table 4).

3.3.4 | Children of mothers with obesity

All children of mothers with obesity had an increased risk of overweight and obesity at 4 years, ranging from a two-fold risk (aOR 2.13, 95% CI 1.38–3.14) for children of obese class 1 mothers with inadequate GWG, to a four-fold risk (aOR 4.76, 95% CI 3.73–6.06) for children with obese class 2–3 mothers with excessive GWG, as compared to the normal weight reference group (Table 3). When only considering children of mothers with obesity, there was no impact of GWG on the risk of overweight and obesity at 4 years (Table 4).

4 | DISCUSSION

In this study, we identified different growth patterns in children depending on maternal early pregnancy BMI and GWG. We found associations of both GWG and maternal BMI with size at birth. Further, we observed different growth velocities from birth to 18 months depending on GWG, where inadequate GWG was associated with accelerating, whereas excessive GWG was associated with decelerating growth. Excessive GWG increased the risk of overweight or obesity at 4 years of age in children of mothers with normal- or overweight, whereas children of mothers with obesity had a higher risk of overweight and obesity regardless of GWG strata.

Children of mothers with underweight had an overall decrease in BMI z-scores from age 18 months to 5 years of age, while children of mothers with overweight or obese had a general increase in growth trajectory during the same age period. Similar growth trajectory patterns were seen across GWG strata independent of the maternal BMI group, suggesting that the growth trajectory is more dependent on maternal BMI than GWG. We speculate that the larger impact of maternal BMI reflects the importance of lifestyle and diet during childhood compared to the effect of fetal programming in utero through maternal GWG. Nonetheless, we observed an independent effect of GWG on childhood growth, and maternal care should recommend pregnant women avoid excessive GWG to promote healthy growth patterns in their offspring.

Our results are consistent with existing evidence regarding GWG and size at birth, where inadequate GWG is associated with small size and excessive GWG is associated with large size at birth.[10,11,27] Similar to our study, Fuemmeler et al observed a positive relationship between increasing GWG and size at birth regardless of maternal BMI.[28] It is well established that children born small for gestational age often display catch-up growth.[29] Catch-up growth can also be observed in children born appropriate for gestational age if the intrauterine environment is insufficient. For mothers with inadequate GWG, the intrauterine milieu may not fully support the fetus to grow along its genetically predetermined growth trajectory, supporting our findings of increasing BMI z-scores after birth in children of mothers with inadequate GWG.[30,31] Large for gestational age infants and children with macrosomia often display slower growth velocity during the first months of life, similar to children of mothers with excessive GWG in our study.[10,29,32] Our observation that GWG is of importance for the postnatal growth trajectory but maternal BMI seems to play a bigger role than GWG for childhood overweight and obesity after 18 months of age is in agreement with other studies.[15,33,34] Similarly, Gadon et al showed that GWG is associated with risk of obesity in early childhood,[14] but this association disappeared when they analyzed data between siblings. Thus, familial, social factors, and higher maternal BMI in early pregnancy (potentially caused by weight gain between pregnancies) may be of greater importance than GWG by itself.[14,35,36] In agreement with our results, other studies found an association between excessive GWG and risk of obesity in early childhood.[15,19] We extended this knowledge further by considering maternal BMI, showing that children of mothers with normal- and overweight and excessive GWG suffer increased risks of overweight and obesity. In a meta-analysis by Voerman et al, GWG was associated with childhood obesity, but to a lesser magnitude than maternal pre-pregnancy BMI, and to a lesser extent in children of mothers with overweight and obesity.[17] These findings are in line with our results.

A major strength of this study is the large cohort size, allowing us to consider both GWG and maternal early pregnancy BMI, thereby disentangling the importance of GWG and baseline BMI. To our knowledge, this is the first study of infants born at term to do so. Unfortunately, our sample size did not allow us to further stratify our analyses on parity. It is well known that parous women more often are overweight or obese than nulliparous women, a pattern that is seen in our study as well. We can not rule out that there is

TABLE 4 Risk of overweight or obesity[a] at four years in children in relation to maternal gestational weight gain.[b]

	Unadjusted					Adjusted[d]				
		Child weight status		95% CI			Child weight status		95% CI	
Maternal level of GWG	*n* total	*n* = normal weight/ overweight or obese	OR	Lower	Upper	*n* total	*n* = normal weight/ overweight or obese	OR	Lower	Upper
Children of mothers with overweight.[c] Mothers with overweight with adequate GWG as reference	4368					4083				
Inadequate GWG		284/59	1.08	0.78	1.49		256/53	1.00	0.71	1.39
Adequate GWG		976/187	1.00 (ref)				923/181	1.00 (ref)		
Excessive GWG		2296/566	1.29	1.07	1.55		2145/525	1.25	1.04	1.51
Children of mothers with obesity class 1.[c] Mothers with obesity class 1 with adequate GWG as reference	1425					1305				
Inadequate GWG		113/29	0.90	0.55	1.45		102/25	0.90	0.53	1.50
Adequate GWG		257/73	1.00 (ref)				236/63	1.00 (ref)		
Excessive GWG		701/252	1.27	0.94	1.71		651/228	1.33	0.96	1.85
Children of mothers with obesity class 2–3.[c] Mothers with obesity class 2–3 with adequate GWG as reference	602					552				
Inadequate GWG		75/29	0.80	0.47	1.36		68/27	0.86	0.49	1.49
Adequate GWG		116/56	1.00 (ref)				111/52	1.00 (ref)		
Excessive GWG		207/119	1.19	0.81	1.77		192/102	1.12	0.74	1.70

Abbreviations: CI, confidence interval; GWG, gestational weight gain; OR, odds ratio.

[a]Overweight or obesity at 4 years of age defined according to the International Obesity Task Force (IOTF) criteria. Boys with BMI ≥17.52 kg/m^2 and girls with BMI ≥17.36 kg/m^2 classified as being overweight or obese.

[b]Gestational weight gain classified according to Institute of Medicine guidelines 2009. Recommended GWG: 7–11.5 kg and 5–9 kg for women with pre-pregnancy BMI classified as overweight and obese (≥30 kg/m^2), respectively. Inadequate GWG, less than recommended, Adequate GWG, as recommended; Excessive GWG, above recommended.

[c]Weight classification according WHO, overweight (BMI 25–29.9 kg/m^2), obese class 1 (BMI 30–34.9 kg/m^2), and obese class 2–3 (BMI >35 kg/m^2).

[d]Adjusted for parity, maternal age and height, maternal educational level and country of birth, and smoking in pregnancy week 30–32.

an interaction between GWG and parity. This should be studied in future studies.

Another limitation is the large number of pregnancies that were excluded due to missing data. There is a risk that missing information on GWG was higher in women with high BMI, and further that large GWG was not randomly distributed across BMI groups, implying a risk of selection bias. Likewise, there is a risk that unmeasured potential confounders affecting fetal and postnatal growth were unevenly distributed due to selection bias, potentially leading to both over- and underestimation of the outcome. We cannot rule out residual confounding as we do not have any information on dietary and behavioral factors, such as physical activity, which might impact fetal and childhood growth as well as maternal early pregnancy BMI and GWG. Moreover, we do not have information on paternal BMI, which may reflect the family's lifestyle habits. However, previous research has shown that paternal BMI does not affect the infant's size at birth.[37]

Our study is based on data from the Swedish Medical Birth Register, which is regarded as a high-quality registry,[38] and all anthropometric data were obtained by skilled healthcare workers, increasing the credibility of the results of this study. We did not have access to maternal pre-pregnancy weight, and instead used first-trimester weight as a proxy in line with the WHO recommendations.[19] Thus, we may have overestimated the pre-pregnancy weight, especially so in the obese group where the recommended GWG is very small. This might potentially introduce a bias towards the null in the analysis of children of mothers with obesity since we might have erroneously classified GWG as adequate instead of excessive in our analysis comparing children whose mothers had excessive GWG to those with adequate GWG. Almost 94% of the mothers in our study were born in Nordic countries, and the proportion of childhood overweight and obesity in our study was similar to the prevalence of overweight and obesity among four-year-old children in Sweden, indicating that our results are representative of the entire Swedish population.[39] However, we cannot rule out that genetic or other differences may limit the generalizability of our results to other populations. We only identified 58 mothers with preeclampsia in our cohort, which is fewer than expected, raising the possibility that some mothers with preeclampsia were included in our final dataset. However, we do not think this affects the results of the study.

The proportion of overweight and obese children is steadily increasing worldwide, leading to both morbidity and preterm death.[2,4] The relationship between known risk factors for childhood obesity, such as high maternal BMI and excessive GWG, has not been fully explored.[10,11,27,40] In the present study, we found that maternal early pregnancy BMI is of great importance for offspring growth patterns, contributing to the growing evidence that large-scale efforts are needed to stop the ongoing global obesity epidemic. Children of mothers with normal- or overweight and excessive GWG have an increased risk of overweight and obesity at 4 years of age. Since GWG is a modifiable factor, lifestyle interventions during pregnancy resulting in reduced GWG might be a way both to prevent childhood obesity and prevent excessive maternal overweight in future pregnancies.[41]

5 | CONCLUSION

This study shows that GWG is important for size at birth and growth patterns from birth to 18 months of age. It also suggests that maternal BMI may have a greater impact than GWG on early childhood growth beyond 18 months of age. Last, excessive maternal gestational weight gain increases the risk of overweight and obesity at 4 years of age in children of mothers with normal and overweight.

AUTHOR CONTRIBUTIONS

Anders Forslund, Inger Sundström Poromaa, and Anna-Karin Wikström designed the study. Fredrik Ahlsson and Linda Lindström conducted the formulation of the research idea and developed the analysis plan. Per Wikman contributed to the analysis plan. Anna Österroos conceptualized the paper, analyzed the data, draw the figures, and wrote the first draft of the manuscript. All authors interpreted the data, critically revised the manuscript, and approved the final version of the manuscript for publication.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interest.

ETHICS STATEMENT

This study was endorsed by the Regional Ethical Review Board in Uppsala (no. 2014/353) on September 24, 2014. This study was performed following national and international guidelines for medical research. The registry data of the UCMC Cohort were merged and de-identified by Statistics Sweden before delivered to the research group. Participants were not identified or contacted during the study, therefore informed consent was not required.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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