Diabetes, Metabolic Syndrome and Obesity

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Late Preschool BMI Acceleration as the Strongest Predictor of Childhood Cardiometabolic Risk at School Entry: A Dual-Trajectory Cohort Study

Shuang Zhang, Jinnan Liu, Weiqin Li, Jing Wang, Yijuan Qiao, Tao Zhang, Wei Dong, Junhong Leng, Lingyan Feng

Tianjin Women and Children's Health Center, Tianjin, People's Republic of China

Correspondence: Lingyan Feng, Tianjin Women and Children's Health Center, No. 96 Guizhou Road, Heping District, Tianjin, 300070, People's Republic of China, Email haiyangfly_2000@163.com

Objective: This study aimed to examine the independent and joint associations of maternal gestational weight gain (GWG) patterns and offspring BMI growth trajectories with lipid and glycemic profiles at age 6.

Methods: This analysis included 39,169 mother–child pairs from the Tianjin Women and Children Health Cohort. Maternal GWG was categorized into four trajectories: Adequate throughout (reference), Excessive early-only, Excessive late-only, and Excessive throughout. Offspring body mass index (BMI) trajectories from birth to age 6 were identified using group-based trajectory modeling, yielding four groups: Persistent Low, Normal (reference), Early Rapid, and Late Rapid. Multivariable linear regression assessed associations with triglycerides (TG), total cholesterol (CHO), and fasting glucose (GLU) at age 6. Interaction was tested via two-way ANOVA.

Results: Children with Late Rapid BMI growth (18.7%; accelerated gain after age 3) were almost universally overweight or obese by age 6 (99.7%). This trajectory was the strongest independent predictor of adverse metabolic outcomes. Compared to the Normal trajectory, the Late Rapid group had significantly higher TG (β = 0.193 mmol/L, 95% CI: 0.179–0.206) and GLU (β = 0.047 mmol/L, 95% CI: 0.030–0.064). The Persistent Low trajectory (12.3%) was associated with lower TG and GLU. Maternal GWG trajectories showed no independent association with offspring TG or GLU after adjustment for child's current BMI; only Excessive early-only GWG retained a weak association with higher CHO (β = 0.038, 95% CI: 0.011–0.064). A significant interaction was observed for TG (P = 0.012).

Conclusion: Late preschool BMI acceleration is the most influential factor for adverse cardiometabolic risk at school entry identified in this cohort, affecting one in five children with effect sizes five times larger than any maternal GWG pattern. Maternal GWG exerts minimal direct effects beyond shaping childhood growth. The preschool years represent a critical window for early BMI trajectory monitoring and targeted intervention.

Keywords: preschool, BMI trajectory, gestational weight gain, cardiometabolic risk, triglycerides, childhood obesity

Introduction

The developmental origins of health and disease (DOHaD) paradigm posits that prenatal and early postnatal exposures shape an individual's lifelong cardiometabolic trajectory.[1,2] Among these, maternal gestational weight gain (GWG) and offspring early childhood growth represent two sequential, modifiable, and closely intertwined risk factors.[3,4]

Excessive GWG, particularly during the first and second trimesters, has been consistently associated with adverse pregnancy outcomes and an increased risk of large-for-gestational-age (LGA) births.[4–6] Our previous work in the Tianjin Maternal and Child Health Cohort demonstrated that GWG at the end of the second trimester exhibits a nonlinear relationship with composite adverse outcomes, with optimal weight gain ranges varying by Chinese-specific body mass index (BMI) categories.[5] Furthermore, we reported that excessive GWG during the first half of pregnancy—rather than total GWG—conferred a higher risk of offspring adiposity persisting up to five years of age, independent of prepregnancy BMI and gestational diabetes.[4]

https://doi.org/10.2147/DMSO.S603371
Received: 13 February 2026
Accepted: 2 June 2026
Published: 18 June 2026

Separately, accelerated postnatal growth—often operationalized as rapid weight gain during infancy or upward crossing of BMI percentiles—is a well-established predictor of childhood obesity, insulin resistance, and dyslipidemia.[7–9] However, most existing studies have treated childhood growth as a static confounder or have focused exclusively on infancy.

Longitudinal modeling has refined our understanding of childhood BMI trajectories. The classic pattern comprises a rapid postnatal increase, a nadir at ages 5–7 years (adiposity rebound), followed by a progressive rise through adolescence.[10] Earlier adiposity rebound consistently predicts higher subsequent BMI and cardiometabolic risk.[10] Beyond timing, distinct trajectory patterns exist—some children exhibit persistently high BMI from infancy, while others show delayed acceleration after age 3.[11] Moreover, the genetic architecture of BMI varies across development, with distinct determinants operating in early childhood versus later life,[12] and the tempo of BMI maturation—rather than level alone—may differentiate children with similar weight status by revealing latent subgroups that differ in the timing of key inflection points.[13]

Several biological mechanisms underpin these associations. Adiposity rebound marks a critical transition in body composition, during which fat mass begins to increase relative to lean mass.[10] Accelerated preschool weight gain promotes adipose tissue expansion, triggering low-grade inflammation and insulin resistance.[14,15] The arginine–nitric oxide pathway has also been implicated in blood pressure regulation, with altered arginase expression observed in children with adverse growth trajectories.[16] Additionally, maternal prepregnancy BMI and GWG influence offspring BMI trajectories through both intrauterine programming and shared postnatal environments, with birth weight and early-life BMI trajectory serving as key mediators.[17] Together, these mechanisms highlight the preschool period as a critical window for metabolic programming.

The preschool period (ages 3–6 years) is a pivotal window for shaping long-term cardiometabolic health. BMI acceleration during this period strongly predicts obesity and metabolic risk at school entry and beyond.[11,18] This phase coincides with the transition from infant to childhood body composition, during which lean mass accrual substantially outpaces fat mass, rendering BMI an unreliable proxy for adiposity.[19,20] It is also marked by major shifts in diet, physical activity, and body composition, making it amenable to early intervention—arguably the last opportunity before obesity trajectories become entrenched.[21] This is particularly relevant as school environments introduce additional exposure heterogeneity.

Despite this body of evidence, critical gaps remain. First, the relative contributions of prenatal (maternal GWG) versus postnatal (childhood BMI trajectory) exposures to school-age metabolic risk have not been directly compared within a unified life-course framework. Second, while both excessive GWG and rapid childhood growth are individually harmful, their joint effects—whether additive, synergistic, or antagonistic—remain poorly characterized. Third, previous studies have largely relied on single-timepoint or total GWG measures, overlooking the distinct metabolic implications of early-only versus late-only excessive GWG patterns, as well as the heterogeneous childhood growth trajectories beyond the conventional "rapid catch-up" phenotype.

Furthermore, generalizability of existing findings is limited by the populations studied. Most trajectory-based research has been conducted in predominantly white European cohorts,[22,23] with scant evidence from Asian populations, who exhibit distinct body composition and metabolic risk profiles at lower BMI thresholds.[24,25] Family-level influences, particularly maternal prepregnancy weight status, have been shown to strongly shape child BMI trajectories, often surpassing modifiable factors such as diet and physical activity.[22] The Tianjin cohort—drawn from a large, geographically defined Chinese population—offers a valuable opportunity to examine these associations in an underrepresented population and to assess whether established patterns hold across diverse ethnic and environmental contexts.

To address these gaps, we leveraged a large, population-based prospective cohort with repeated anthropometric measurements from early pregnancy to age 6. Using group-based trajectory modeling, we: (1) identified distinct patterns of maternal GWG (classified by timing of excessive gain) and offspring BMI growth from birth to age 6; (2) quantified their independent and joint associations with fasting triglycerides (TG), total cholesterol (CHO), and glucose (GLU) at age 6; and (3) tested for statistical interaction between the two trajectory exposures. We hypothesized that childhood BMI trajectory would emerge as the strongest predictor identified in this cohort of cardiometabolic risk, with maternal GWG exerting effects largely mediated through, or modified by, postnatal growth patterns. Identifying specific high-risk dyadic combinations may inform precision prevention strategies targeting the mother–child dyad.

Methods

Study Design and Population

This study was a retrospective analysis of a large, population-based prospective cohort conducted in Tianjin, China. The sampling frame comprised all singleton pregnant women aged 18–45 years who registered for prenatal care between January 1 and December 31, 2015, within the Tianjin Women and Children Health Care system—a government-administered public health network that covers all community populations across urban, suburban, special economic zones, and rural areas of Tianjin. Antenatal care coverage in this system exceeds 95% of the local pregnant population. Women are enrolled from the first trimester and followed through delivery, with their children receiving scheduled health assessments from birth to age 6 years. All clinical and anthropometric measurements are conducted by trained healthcare practitioners and systematically recorded in an electronic health information system. From this base, we identified 39,169 mother-child pairs who participated in the 6-year follow-up visit and underwent fasting blood sampling for cardiometabolic assessment. All 39,169 children had at least one of the three outcome measurements (TG, CHO, or GLU) available; a very small number of individual assay results were excluded due to objective laboratory factors (detailed in the Missing Data Handling section).

Pregnant women were enrolled at their first antenatal visit ($\leq 13^{+6}$ gestational weeks). For the present analysis, we included singleton live births with available data on: (1) maternal prepregnancy BMI and GWG; (2) offspring anthropometrics at birth and at 3, 6, 8, 12, 18, 24, 30, 36, 48, 60, and 72 months of age; and (3) fasting TG, CHO, and GLU measured at the 6-year follow-up. Children with major congenital anomalies, genetic syndromes, or chronic conditions affecting growth (eg, thyroid dysfunction, severe congenital heart disease) were excluded.

All data were de-identified prior to analysis. The study protocol was approved by the Human Subjects Committee of Tianjin Women and Children's Health Center (approval number: TJWC20190305-6) and complied with the Declaration of Helsinki. The requirement for written informed consent was waived due to the retrospective use of routinely collected administrative data.

Exposure Definitions

Maternal Gestational Weight Gain (GWG) Trajectories

Prepregnancy BMI was calculated as weight (in kilograms) divided by squared height (in centimeters) measured at the first prenatal examination. Total GWG was defined as the difference between prepregnancy weight (measured at the initial prenatal visit in the first trimester) and delivery weight (measured before delivery in the third trimester). Early-mid GWG was defined as the difference between prepregnancy weight and mid-end weight (measured at the time of gestational diabetes screening between 24 and 28 weeks). According to the Recommended Weight Gain during Pregnancy of Chinese Women,[26] GWG was classified as "insufficiency", "adequate", or "excessive" across the prepregnancy BMI categories. We defined four mutually-exclusive GWG trajectory patterns based on the timing of excessive gain:

- Mom traj.-1. Adequate throughout (reference): Adequate early-mid GWG and adequate total GWG (implying adequate or insufficiency gain in each trimester).
- Mom traj.-2. Excessive early-only: Excessive early-mid GWG but non-excessive total GWG (implying excessive gain in the first and second trimesters, with adequate or insufficiency gain in the third trimester).
- Mom traj.-3. Excessive late-only: Non-excessive early-mid GWG but excessive total GWG (implying adequate or insufficiency gain in the 1st and 2nd trimesters and excessive gain in the 3rd trimester).
- Mom traj.-4. Excessive throughout: Excessive early-mid GWG and total GWG (implying excessive gain in each trimester).

Offspring BMI Growth Trajectories (0-6 Years)

Weight and length/height were measured at birth, 3, 6, 8, 12, 18, 24, 30, 36, 48, 60, and 72 months (6 years) by trained staff. BMI (kg/m^2) was calculated at each time point. To identify distinct BMI growth patterns from birth to 72 months

(0–6 years), we applied group-based trajectory modeling (GBTM) using the lcmm package (version 2.1.0) in R (version 4.2.3, R Foundation for Statistical Computing, Vienna, Austria).[27]

Models with one to five trajectory groups were fitted, each incorporating quadratic and cubic time terms to accommodate potential nonlinear growth patterns. Model selection was guided by the following criteria: (1) lower Bayesian Information Criterion (BIC); (2) minimum group proportion >5%; (3) average posterior probability (APP) per group >0.70; and (4) relative entropy (Ek) >0.50.

The model fit indices for all candidate models are presented in Supplementary Table S1. Among these, the four-group cubic model (m4_3) demonstrated superior performance, with the lowest BIC value (1,175,106.95), all group proportions exceeding 5% (40.8%, 42.3%, 6.5%, and 10.4%), APP values ranging from 0.74 to 0.87 (all >0.70), and a relative entropy of 0.616 (>0.50). To assess the robustness of the trajectory solution, we performed sensitivity analyses by varying the polynomial order (quadratic vs. cubic) and the number of trajectory groups (3 to 5). The four-group cubic solution was consistently identified as the optimal model based on the predefined criteria and clinical interpretability. All trajectory groups were derived empirically without imposing any prior constraints based on weight status. The four identified trajectories were as follows (Figure 1):

- Child Trajectory 1. Persistent Low: Consistently low BMI values throughout the follow-up period.
- Child Trajectory 2. Normal (Reference): Steady BMI increase, aligning with normative growth patterns and representing the largest subgroup.
- Child Trajectory 3. Early Rapid: Rapid BMI acceleration during infancy, typically exceeding the 85th percentile before age 2 years and thereafter maintaining a high plateau.
- Child Trajectory 4. Late Rapid: BMI progression similar to the Normal group until approximately age 3 years, followed by a pronounced upward shift, leading to overweight or obesity status by age 6 years.

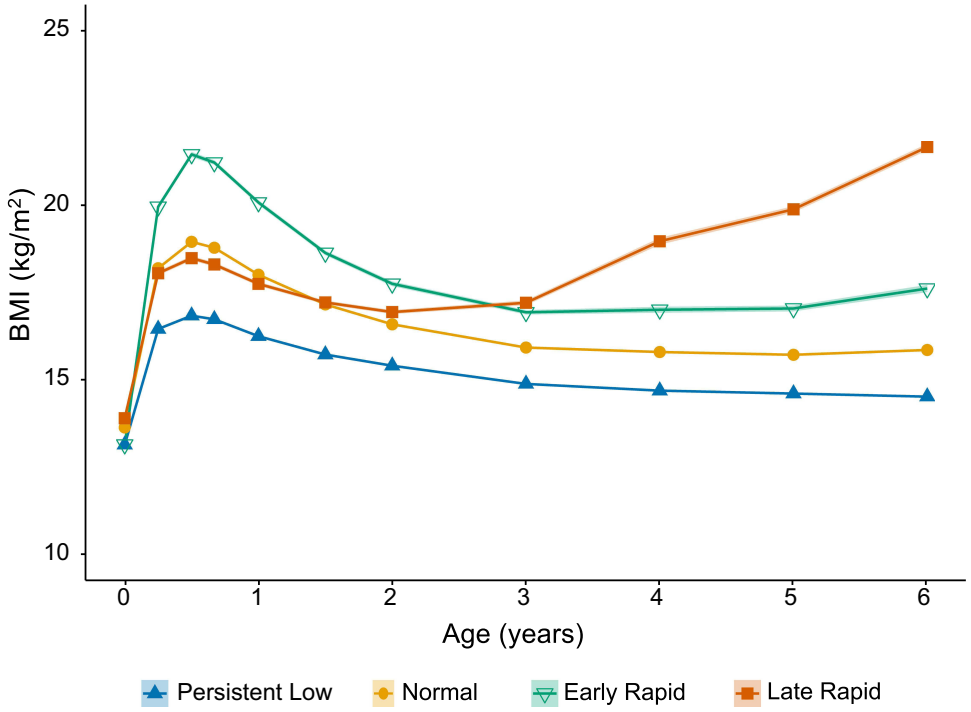

Figure 1 Four distinct body mass index (BMI) growth trajectories from birth to age 6 years identified by group-based trajectory modeling. Four distinct trajectories were identified: Persistent Low (consistently low BMI), Normal (steady increase, reference), Early Rapid (rapid gain before age 2), and Late Rapid (accelerated gain after age 3). Trajectory definitions are detailed in the Methods section.

Outcome Assessment

At the 6-year follow-up, children underwent a physical examination and peripheral blood sampling after an overnight fast. Serum TG and CHO were tested using GPO-PAP and CHOD-PAP method, respectively. GLU was measured using the enzyme electrode method. All assays were performed in the central laboratory of Tianjin Women and Children's Health Center with rigorous quality control.

Covariates

Potential confounders were selected a priori based on literature and included: maternal age at pregnancy (years), education level (≤12 years, >12 years), prepregnancy BMI (continuous, kg/m^2), gestational diabetes mellitus (GDM, yes/no), hypertensive disorders of pregnancy (HDP, yes/no), family history of diabetes/hypertension, offspring sex (male/female), gestational age at birth (weeks), birth weight category (SGA, AGA, LGA based on Chinese standards[28]), and feeding mode in the first 6 months (exclusive breastfeeding, mixed, formula).

Missing Data Handling

This retrospective cohort study included 39,169 mother-child pairs who participated in the 6-year follow-up visit and underwent fasting blood sampling for cardiometabolic assessment. All 39,169 children had at least one of the three outcome measurements (TG, CHO, or fasting GLU) available. However, due to objective laboratory factors (eg, hemolysis or values outside the clinically plausible range), a very small number of individual assay results were excluded. Specifically, the numbers of missing values were: TG n = 11 (0.03%), CHO n = 29 (0.07%), and GLU n = 49 (0.13%). Given the extremely low proportion of missing outcome data and the large sample size, we did not impute outcome variables; instead, we report effective sample sizes for each outcome in the results tables.

For covariates (eg, maternal education, maternal smoking), missingness ranged from 0% to 8.5%. To minimize bias and preserve statistical power, we performed multiple imputation by chained equations using the mice package in R (version 4.2.3) for covariates only.[29] The imputation model included all covariates, exposures, and outcomes as auxiliary variables. A total of 20 imputed datasets were generated, and Rubin's rules were applied to combine estimates.[30] Sensitivity analyses using complete-case analysis (ie, excluding participants with any missing covariate data) yielded consistent results, supporting the robustness of our findings against missing data. Key characteristics of the study population are summarized in Supplementary Table S2.

Statistical Analysis

Descriptive statistics were presented as mean ± SD or n (%). Differences across child BMI trajectory groups were tested using ANOVA or chi-square tests, as appropriate.

Our primary analysis employed multivariable linear regression to estimate β coefficients and 95% confidence intervals (CIs) for associations with TG, CHO, and GLU. We implemented a staged modeling strategy:

- Model 1 (Crude): Unadjusted.
- Model 2 (Demographically-adjusted): Adjusted for maternal age, education, and offspring sex.
- Model 3 (Fully adjusted): For maternal GWG trajectory: further adjusted for GDM, HDP, gestational age-based birth weight category, maternal prepregnancy BMI, and offspring BMI z-score at age 6.

For offspring BMI growth trajectory: further adjusted for GDM, HDP, gestational age-based birth weight category, maternal prepregnancy BMI but not offspring BMI z-score at age 6, to avoid over-adjustment for the trajectory outcome.

To address potential overadjustment concerns, we adopted a differentiated adjustment strategy based on causal assumptions.[31] For models estimating the direct effect of maternal GWG trajectories, we included child's BMI z-score at age 6 as a covariate to assess whether any residual association persisted independent of the child's current body size. For models estimating the effect of child BMI growth trajectories, we intentionally omitted adjustment for child's BMI at age 6 to avoid conditioning on a post-exposure variable that lies on the causal

pathway from growth trajectory to metabolic outcomes. This approach follows established recommendations for analyzing longitudinal exposure-outcome associations in the presence of potential mediators.[32]

To examine joint effects, we created a 16-category variable combining the four maternal GWG trajectories and four child BMI trajectories. Its association with outcomes was analyzed using Model 3 (without child's BMI at 6 years), with the dual-trajectory "Adequate throughout & Normal growth" as the reference. To test for effect modification, we performed a two-way factorial ANOVA including maternal GWG trajectory, child BMI trajectory, and their product term. A significant interaction term ($P<0.05$) was followed by simple effect analyses within strata of child growth trajectories.

All analyses were performed using IBM SPSS Statistics for Windows (Version 26.0, Armonk, NY: IBM Corp) and R statistical software (R version 4.2.3, R Foundation for Statistical Computing, Vienna, Austria). A two-tailed p-value <0.05 was considered statistically significant.

Results

Population Characteristics by Child BMI Trajectory

The final analytical sample comprised 39,169 mother-child pairs. The maternal age was 28.20±4.16 years, the prepregnancy BMI was 22.64±3.76, and the gestational age at delivery was 39.39±1.40 weeks. There were 20024 boys (51.21%) and 19145 girls (48.9%). Table 1 compares maternal and child characteristics across four distinct BMI trajectory groups from 0 to 6 years. Child BMI trajectories were strongly associated with multiple early-life and maternal factors, as well as with cardiometabolic markers at age 6. Children in the Late Rapid group had the highest mean prepregnancy maternal BMI (24.94 ± 4.37 kg/m^2), highest rates of GDM (13.1%) and cesarean delivery (59.5%), and were most often classified as LGA at birth

Table 1 Characteristics of Mothers and Children Stratified by the Child BMI Trajectory Groups

Factor	Child BMI Trajectory Groups (0–6 year)				*P*-value
	Persistent Low	Normal (Reference)	Early Rapid	Late Rapid	
n	15990	16,562	2536	4081	
Maternal age, years	**28.33±4.07***	28.15±4.17	28.06±4.34	28.01±4.32	<0.001
Ethnic Han	15331 (95.9%)	15,854 (95.7%)	2434 (96.0%)	3892 (95.4%)	0.487
Education >12 years	10912 (68.2%)	10,486 (63.3%)	1482 (58.4%)	2288 (56.1%)	<0.001
Prepregnancy BMI, kg/m^2	**21.84±3.43***	22.72±3.62	**23.46±3.85***	**24.94±4.37***	<0.001
Family history of diabetes	297 (1.9%)	299 (1.8%)	47 (1.9%)	122 (3.0%)	<0.001
Family history of hypertension	632 (4.0%)	620 (3.7%)	74 (2.9%)	197 (4.8%)	0.001
Smoking	54 (0.3%)	38 (0.2%)	8 (0.3%)	19 (0.5%)	0.067
Early-mid GWG, kg	7.65±3.40	7.72±3.54	7.81±3.71	**7.42±3.89***	<0.001
Total GWG, kg	**13.98±4.58***	14.10±4.71	14.14±4.87	**13.72±5.10***	<0.001
GDM	1537 (9.6%)	1579 (9.5%)	286 (11.3%)	533 (13.1%)	<0.001
HDP	398 (2.5%)	404 (2.4%)	125 (4.9%)	182 (4.5%)	<0.001
Cesarean delivery	7409 (46.3%)	8509 (51.4%)	1417 (55.9%)	2427 (59.5%)	<0.001
Gestational age at birth, week	39.44±1.39	39.44±1.28	**38.80±2.00***	**39.32±1.39***	<0.001
Premature birth	619 (3.9%)	539 (3.3%)	270 (10.6%)	169 (4.1%)	<0.001
Infant sex (male)	6652 (41.6%)	9340 (56.4%)	1580 (62.3%)	2452 (60.1%)	<0.001
Birthweight, g	**3289.19±435.37***	3448.32±428.20	**3312.58±597.27***	**3528.55±504.74***	<0.001

(*Continued*)

Table 1 (Continued).

Factor	Child BMI Trajectory Groups (0–6 year)				*P*-value
	Persistent Low	Normal (Reference)	Early Rapid	Late Rapid	
Birth weight category					<0.001
SGA	1156 (7.2%)	516 (3.1%)	154 (6.1%)	126 (3.1%)	
AGA	13553 (84.8%)	13,665 (82.5%)	1990 (78.5%)	3053 (74.8%)	
LGA	1267 (7.9%)	2373 (14.3%)	391 (15.4%)	901 (22.1%)	
Breastfeeding exclusively until 6 months	5793 (36.2%)	6004 (36.3%)	883 (34.8%)	1363 (33.4%)	0.016
BMI z_score at birth	**−0.15±0.95***	0.20±0.98	**0.03±1.07***	**0.43±1.12***	<0.001
BMI z_score at age 3	**−0.59±0.79***	0.22±0.81	**0.92±1.08***	**1.23±1.37***	<0.001
BMI z_score at age 6	**−0.66±0.93***	0.25±0.96	**1.20±1.27***	**3.10±1.10***	<0.001
Overweight/obesity at age 3	24 (0.2%)	274 (1.8%)	347 (14.6%)	817 (21.5%)	<0.001
Overweight/obesity at age 6	523 (4.1%)	2963 (22.7%)	1148 (56.5%)	2991 (99.7%)	<0.001
TG at age 6 (mmol/L)	0.82±0.33	0.82±0.34	**0.86±0.37***	**1.02±0.45***	<0.001
CHO at age 6 (mmol/L)	**4.21±0.70***	4.17±0.70	4.15±0.68	4.16±0.69	<0.001
GLU at age 6 (mmol/L)	**4.59±0.44***	4.62±0.44	**4.65±0.42***	**4.67±0.44***	<0.001

Notes: Data are presented as mean ± SD or n (%). For continuous variables, bold font (with *) indicates statistically significant differences compared to the Normal (reference) group based on ANOVA with post-hoc pairwise comparisons ($P < 0.05$); the overall ANOVA P-value is presented in the last column. For categorical variables, P-values are from overall chi-square tests; no pairwise comparisons were performed. Effective sample sizes: TG n = 39,158; CHO n = 39,140; GLU n = 39,120.
Abbreviations: BMI, body mass index; GWG, gestational weight gain; GDM, gestational diabetes mellitus; HDP, hypertensive disorders of pregnancy; SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age; TG, triglycerides; CHO, total cholesterol; GLU, glucose.

(22.1%). Their BMI z-score increased markedly from birth (0.43 ± 1.12) to age 6 (3.10 ± 1.10). Notably, this trajectory was identified solely by the longitudinal BMI pattern; the observation that 99.7% of children in this group met the criteria for overweight or obesity by age 6 is a post-hoc descriptive finding that reflects the trajectory's defining feature of rapid BMI acceleration after age 3, rather than a pre-specified selection criterion.

Critically, at age 6, the Late Rapid group exhibited the least favorable metabolic profile: significantly higher TG (1.02 ± 0.45 mmol/L), GLU (4.67 ± 0.44 mmol/L), and CHO (4.16 ± 0.69 mmol/L) levels compared to the Normal reference group (all $P < 0.001$). The Early Rapid group also showed elevated TG (0.86 ± 0.37 mmol/L) and GLU (4.65 ± 0.42 mmol/L) relative to the reference. In contrast, the Persistent Low trajectory group consistently demonstrated the most favorable metabolic values at age 6.

Independent Associations of Single Trajectories with Metabolic Outcomes

Table 2 shows the independent associations of maternal GWG and child BMI trajectories with metabolic markers at age 6.

Child BMI Trajectories

The "Late Rapid" trajectory was consistently and strongly associated with elevated TG and GLU across all models. In the fully-adjusted Model 3, compared to the "Normal" group, the "Late Rapid" group had β=0.193 mmol/L (95% CI: 0.179, 0.206) for TG and β=0.047 mmol/L (0.030, 0.064) for GLU. The "Early Rapid" group also showed significant but weaker associations. The "Persistent Low" group was associated with lower TG and GLU. No consistent association was found with CHO.

Table 2 Independent Associations of Maternal Gestational Weight Gain Trajectories and Offspring BMI Growth Trajectories with Metabolic Indicators at Age 6

Outcome Variable (Y)	Independent Variable (X)	β Coefficient (95% Confidence Interval)		
TG (mmol/L)		**Model 1**	**Model 2**	**Model 3**
	Maternal GWG Trajectory			
	Excessive throughout	0.006 (−0.003, 0.014)	0.006 (−0.002, 0.015)	−0.002 (−0.012, 0.009)
	Excessive early-only	0.001 (−0.010, 0.012)	0.002 (−0.009, 0.013)	0.002 (−0.012, 0.015)
	Excessive late-only	0.003 (−0.011, 0.017)	0.003 (−0.011, 0.017)	−0.007 (−0.024, 0.011)
	Adequate throughout	Ref.		
	Offspring BMI Growth Trajectory			
	Late Rapid	**0.193 (0.181, 0.205)****	**0.196 (0.184, 0.208)****	**0.193 (0.179, 0.206)****
	Early Rapid	**0.040 (0.025, 0.055)****	**0.045 (0.030, 0.059)****	**0.043 (0.026, 0.059)****
	Persistent Low	−0.007 (−0.014, 0.001)	**−0.017 (−0.025, −0.009)****	**−0.016 (−0.025, −0.008)****
	Normal	Ref.		
CHO (mmol/L)		**Model 1**	**Model 2**	**Model 3**
	Maternal GWG Trajectory			
	Excessive throughout	**0.017 (0.000, 0.033)***	0.016 (0.000, 0.032)	0.016 (−0.004, 0.037)
	Excessive early-only	**0.065 (0.044, 0.087)****	**0.041 (0.020, 0.062)****	**0.038 (0.011, 0.064)***
	Excessive late-only	**−0.056 (−0.084, −0.028)****	**−0.040 (−0.067, −0.012)***	**−0.039 (−0.073, −0.005)***
	Adequate throughout	Ref.		
	Offspring BMI Growth Trajectory			
	Late Rapid	−0.018 (−0.041, 0.006)	0.001 (−0.022, 0.025)	0.009 (−0.018, 0.035)
	Early Rapid	−0.020 (−0.049, 0.009)	−0.006 (−0.035, 0.023)	−0.002 (−0.034, 0.031)
	Persistent Low	**0.038 (0.023, 0.053)****	**0.018 (0.003, 0.033)***	0.014 (−0.003, 0.031)
	Normal	Ref.		
GLU (mmol/L)		**Model 1**	**Model 2**	**Model 3**
	Maternal GWG Trajectory			
	Excessive throughout	0.004 (−0.007, 0.014)	0.003 (−0.008, 0.013)	−0.003 (−0.017, 0.010)
	Excessive early-only	0.000 (−0.013, 0.014)	−0.001 (−0.014, 0.013)	0.009 (−0.009, 0.026)
	Excessive late-only	−0.002 (−0.020, 0.016)	−0.002 (−0.020, 0.015)	−0.020 (−0.042, 0.002)
	Adequate throughout	Ref.		
	Offspring BMI Growth Trajectory			
	Late Rapid	**0.053 (0.038, 0.068)****	**0.049 (0.034, 0.064)****	**0.047 (0.030, 0.064)****
	Early Rapid	**0.030 (0.012, 0.049)***	**0.025 (0.006, 0.043)***	**0.026 (0.005, 0.047)***
	Persistent Low	**−0.029 (−0.039, −0.020)****	**−0.016 (−0.025, −0.006)***	**−0.016 (−0.026, −0.005)***
	Normal	Ref.		

Notes: Data are presented as β coefficient (95% Confidence Interval). β represents the mean difference in the metabolic indicator compared to the reference group. Bold font indicates statistically significant associations, *$P < 0.05$, **$P < 0.001$. Model 1 (Crude): Unadjusted. Model 2 (Adjusted for demographics): Adjusted for maternal age, education, and offspring sex. Model 3 (Fully adjusted): For Maternal GWG Trajectory, further adjusted for gestational diabetes, hypertensive disorders of pregnancy, gestational age-based birth weight category, maternal prepregnancy BMI, and offspring BMI z-score at 6 years. For Offspring BMI Growth Trajectory, further adjusted for gestational diabetes, hypertensive disorders of pregnancy, gestational age-based birth weight category, maternal prepregnancy BMI (but NOT offspring BMI z-score at 6 years, to avoid over-adjustment for the trajectory outcome). Effective sample sizes: TG n = 39,158; CHO n = 39,140; GLU n = 39,120.
Abbreviations: BMI, body mass index; GWG, gestational weight gain; TG, triglycerides; CHO, total cholesterol; GLU, glucose.

Maternal GWG Trajectories

After full adjustment including child's BMI at 6 years (Model 3), maternal GWG trajectories showed no significant association with TG or GLU. For CHO, "Excessive early-only" and "Excessive late-only" trajectories remained associated (β=0.038 and −0.039 mmol/L, respectively), though effect sizes were small.

Joint Effects of Dual Trajectories

The joint effects of the 16 dual-trajectory combinations is summarized in Table 3; for complete estimates, see Supplementary Table S3). The reference group ("Adequate throughout" mother and "Normal" child) consistently showed the most favorable metabolic profile. The Late Rapid child BMI trajectory was consistently associated with elevated TG) and GLU across all maternal GWG patterns, with the strongest effects observed for children whose mothers had adequate GWG throughout pregnancy (TG: β = 0.225, 95% CI: 0.198–0.252; GLU: β = 0.058, 95% CI: 0.024–0.092). The Early Rapid trajectory was linked to moderately higher TG, though with smaller effect sizes. In contrast, only the Persistent Low trajectory combined with maternal excessive GWG showed a slight but significant increase in CHO. These results indicate that a Late Rapid BMI trajectory in early childhood is the strongest predictor identified in this cohort of adverse lipid and glycemic profiles at age 6, largely independent of maternal GWG pattern.

Interaction Between Maternal GWG and Child Growth Trajectories

Two-way ANOVA revealed a statistically significant multiplicative interaction between maternal GWG and child BMI trajectories for TG levels (F=2.36, P=0.012), whereas no significant interaction was observed for GLU or CHO (Table 4). Simple effect analysis (Supplementary Table S4) revealed that among children with a Late Rapid BMI trajectory, those whose mothers had Excessive throughout GWG showed significantly lower TG levels compared to the reference group with Adequate throughout GWG (mean difference: −0.049, P=0.002). No other within-trajectory comparisons reached statistically significant.

The child's BMI trajectory exerted strong independent main effects on TG (F = 244.067, $P < 0.001$), CHO (F = 8.604, $P < 0.001$), and GLU (F = 35.261, $P < 0.001$). In contrast, maternal GWG pattern showed a main effect only on CHO (F = 10.148, $P < 0.001$) and no significant effect on TG or GLU.

Collectively, these findings indicate that child BMI growth remains the strongest predictor identified in this cohort of cardiometabolic risk at age 6. Although a statistically significant interaction was detected for TG, the effect size was modest

Table 3 Associations of Maternal-Offspring Dual Trajectories with Cardiometabolic Risk Markers at Age 6

Dual Trajectory Group		**n**	**Cardiometabolic Risk Markers at Age 6**		
Maternal GWG Pattern	**Children's BMI Trajectory**		**TG**	**CHO**	**GLU**
Adequate throughout	Normal	4385	Ref.	Ref.	Ref.
High-Risk for TG					
Adequate throughout	Late Rapid	1017	**0.225 (0.198, 0.252)****	0.019 (−0.033, 0.072)	**0.058 (0.024, 0.092)***
Excessive early-only	Late Rapid	490	**0.216 (0.180, 0.252)****	0.043 (−0.028, 0.114)	**0.062 (0.017, 0.108)***
Excessive throughout	Late Rapid	2213	**0.183 (0.163, 0.203)****	0.012 (−0.027, 0.051)	**0.049 (0.024, 0.074)****
Excessive late-only	Late Rapid	361	**0.174 (0.133, 0.216)****	−0.066 (−0.148, 0.017)	0.036 (−0.016, 0.089)
Moderate-Risk for TG					
Excessive early-only	Early Rapid	350	**0.051 (0.009, 0.094)***	0.004 (−0.080, 0.088)	0.053 (0.000, 0.107)
Adequate throughout	Early Rapid	629	**0.050 (0.016, 0.083)***	0.000 (−0.067, 0.066)	**0.043 (0.000, 0.085)***
Excessive throughout	Early Rapid	1351	**0.045 (0.021, 0.069)****	0.009 (−0.039, 0.056)	0.022 (−0.008, 0.053)
Risk for CHO					
Excessive throughout	Persistent Low	7225	−0.007 (−0.021, 0.008)	**0.028 (0.000, 0.057)***	−0.005 (−0.023, 0.013)
Excessive early-only	Persistent Low	2871	−0.011 (−0.029, 0.007)	**0.041 (0.005, 0.076)***	−0.013 (−0.036, 0.009)

Notes: Data presented as: β coefficient (95% Confidence Interval) from multivariable linear regression (Model 3), using Group 16 as reference. β represents the mean difference in the metabolic marker compared to the reference group. Bold font indicates statistically significant associations, * $P < 0.05$, ** $P < 0.001$. Model 3 (Fully Model) was adjusted for: maternal age, education, offspring sex, gestational diabetes, hypertensive disorders of pregnancy, gestational age-based birth weight category, and maternal prepregnancy BMI. It was NOT adjusted for offspring BMI at 6 years to avoid over-adjustment for the growth trajectory outcome. This table mainly presents the statistically significant results. For complete joint effect estimates, see Supplementary Table S2.
Abbreviations: TG, triglycerides; CHO, total cholesterol; GLU, glucose.

https://doi.org/10.2147/DMSO.S603371

Table 4 Main Effects and Interaction Effects of Maternal GWG Trajectories and Offspring BMI Growth Trajectories on Cardiometabolic Markers (Two-Way ANOVA)

Outcome	Source	Type III Sum of Squares	df	Mean Square	*F*	*p*	Partial η^2
TG	Maternal GWG Pattern	0.447	3	0.149	1.209	0.305	<0.001
	Children's BMI Growth Trajectory	90.273	3	30.091	**244.067**	**<0.001**	**0.018**
	Maternal GWG Pattern × Children's BMI Growth Trajectory	2.622	9	0.291	**2.363**	**0.012***	**0.001**
	Error	4825.820	39,142	0.123			
CHO	Maternal GWG Pattern	14.696	3	4.899	**10.148**	**<0.001**	**0.001**
	Children's BMI Growth Trajectory	12.460	3	4.153	**8.604**	**<0.001**	**0.001**
	Maternal GWG Pattern × Children's BMI Growth Trajectory	2.996	9	0.333	0.690	0.719	<0.001
	Error	18886.743	39,124	0.483			
GLU	Maternal GWG Pattern	0.262	3	0.087	0.447	0.719	<0.001
	Children's BMI Growth Trajectory	20.653	3	6.884	**35.261**	**<0.001**	**0.003**
	Maternal GWG Pattern × Children's BMI Growth Trajectory	1.284	9	0.143	0.731	0.681	<0.001
	Error	7634.723	39,104	0.195			

Notes: Bold font indicates statistically significant main effects or interactions ($P < 0.05$). Analysis was performed using univariate analysis of variance (UNIANOVA). The model included maternal GWG trajectory (4 categories), offspring BMI growth trajectory (4 categories), and their multiplicative interaction term. * Statistical significance for the interaction term is indicated by $P < 0.05$. Partial η^2 indicates effect size (small: <0.01; medium: 0.06; large: >0.14, based on Cohen's conventions). Effective sample sizes: TG n = 39,158; CHO n = 39,140; GLU n = 39,120.

Abbreviations: GWG, gestational weight gain; BMI, body mass index; TG, triglycerides; CHO, total cholesterol; GLU, glucose.

and its clinical relevance warrants cautious interpretation. Maternal GWG may have a limited modifying influence on TG levels in children with a Late Rapid growth pattern, particularly when GWG is excessive throughout pregnancy.

Discussion

This prospective cohort study of nearly 40,000 mother–child pairs offers three principal findings. First, a late-onset rapid BMI trajectory—characterized by normative BMI in infancy followed by accelerated gain after age 3—was the strongest and most consistent predictor of adverse lipid and glycemic profiles at age 6. In this cohort, children in the Late Rapid trajectory exhibited mean TG levels of 1.02 mmol/L and GLU of 4.67 mmol/L at age 6, both significantly higher than the Normal trajectory group (0.74 mmol/L and 4.58 mmol/L, respectively; both $P < 0.001$). From a clinical perspective, these mean differences (ΔTG = 0.28 mmol/L, ΔGLU = 0.09 mmol/L) approach the thresholds used in pediatric dyslipidemia screening, where TG levels ≥1.13 mmol/L are considered elevated.[33] Nearly all (99.7%) children in this trajectory were overweight or obese by age 6. Second, maternal GWG patterns showed no direct association with offspring TG or GLU after adjustment for child's current BMI, and only weak, selective associations with CHO. Specifically, the Excessive early-only GWG trajectory retained a modest but statistically significant association with higher CHO (β= 0.038, 95% CI: 0.011–0.064) in fully adjusted models, whereas no GWG trajectory was independently associated with TG or GLU. Third, a suggestive interaction was observed between maternal GWG and child BMI trajectory for TG levels ($P = 0.012$), though the effect size was modest (partial $\eta^2 = 0.001$) and its clinical relevance requires cautious interpretation. Collectively, these findings reposition early childhood BMI trajectory—particularly the preschool period—as the strongest predictor identified in this cohort of cardiometabolic programming, while suggesting that the influence of maternal GWG is largely indirect, operating through the shaping of postnatal growth pathways.

Comparison with Previous Studies and Extension of Our Prior Work

Our findings both corroborate and substantially extend the existing literature. Consistent with previous meta-analyses,[34–36] we confirmed that excessive GWG is associated with an unfavorable offspring cardiometabolic profile. However, by decomposing GWG into timing-specific trajectory patterns, we demonstrated that once childhood BMI

trajectory is accounted for, the residual direct effect of maternal GWG on GLU and TG is negligible. In our fully adjusted models, the association between any excessive GWG pattern and offspring TG or GLU was attenuated to non-significance, with β estimates close to zero.

Importantly, the present study is not merely an extension of our 2022 report in this journal.[4] While our prior work established an association between first-half GWG and offspring obesity risk by age 5, it could not determine whether this effect was direct or mediated through the child's own growth trajectory—nor could it assess the relative contribution of prenatal versus postnatal exposures. By employing dual-trajectory modeling with formal interaction testing and direct quantification of mediation-by-growth, the current study provides the first evidence that the child's postnatal BMI trajectory is the strongest predictor identified in this cohort, and that the role of maternal GWG is largely indirect, operating through its influence on shaping childhood growth.

The weak but persistent association between excessive early-only GWG and higher offspring CHO—β= 0.038, an effect size equivalent to approximately one-fifth of the association observed for Late Rapid trajectory (β= 0.193)—merits attention. This finding aligns with our previous report that second-trimester GWG is optimally positioned for early risk stratification,[37] and suggests that CHO metabolism may be more sensitive to early-pregnancy nutritional programming than GLU or TG pathways.[38] Epigenetic modifications of hepatic LDL-receptor or HMG-CoA reductase genes represent a plausible mechanism warranting future investigation.[39]

The Preschool Period as a Critical Window for Metabolic Dysregulation

The graded metabolic risk across the four BMI trajectories—particularly the stark contrast between the Late Rapid and Persistent Low groups—underscores the preschool years (ages 3–6) as a critical window for metabolic programming. In the Persistent Low trajectory, which comprised 12.3% of the cohort, mean TG at age 6 was 0.62 mmol/L and GLU was 4.48 mmol/L—both significantly lower than the Normal reference group. The dose-response pattern across the four trajectories (Persistent Low < Normal < Early Rapid < Late Rapid) was consistent for all three metabolic outcomes. While the "early rapid" phenotype (obesity present by age 2) has received substantial research attention,[40,41] our data suggest that the "late rapid" phenotype is both more prevalent and metabolically more damaging in this Chinese population. The Late Rapid group comprised 18.7% of the cohort and exhibited the highest absolute levels of TG and GLU, with effect sizes (β = 0.193 for TG) substantially exceeding those of any prenatal exposure. This finding aligns with the "adiposity rebound" literature, where earlier rebound is a well-known risk factor for adult metabolic syndrome.[42] Our study advances this field by: (1) demonstrating that this effect is independent of birth weight and maternal metabolic status; and (2) quantifying its effect size relative to a major prenatal exposure (GWG). The near-universal overweight/obesity (99.7%) in the Late Rapid group at age 6 underscores the importance of early identification and intervention.

Interpretation of the Interaction Effect

A statistically significant but modest interaction was detected between maternal GWG trajectory and child BMI trajectory for TG levels (two-way ANOVA $P = 0.012$). Simple effects analysis revealed that, among children following the Late Rapid growth trajectory, those whose mothers had Excessive throughout GWG exhibited slightly lower mean TG levels at age 6 compared to those whose mothers had Adequate throughout GWG (mean difference: −0.049 mmol/L; 95% CI: −0.080, −0.018; $P = 0.002$). No significant within-trajectory differences were observed for other maternal GWG patterns or for the other metabolic outcomes (CHO, GLU).

The effect size of this interaction is modest (Δ= −0.049 mmol/L, partial $\eta^2 = 0.001$), representing less than one-tenth of the standard deviation of TG in this subgroup, and was observed in the absence of a pre-specified hypothesis. Given the large sample size, even small differences may achieve statistical significance, and the clinical relevance of this isolated finding remains uncertain. We therefore interpret this result as suggestive rather than definitive. Potential explanations—including residual confounding,[43] heterogeneity in the composition of GWG (fat vs. lean mass),[44] or chance—cannot be excluded. This finding requires independent replication in other cohorts before any mechanistic inference or clinical recommendation can be drawn.

Clinical and Public Health Implications

Our findings support a dual-generation, trajectory-informed preventive strategy.

1. Prenatal phase: While optimizing GWG remains important—particularly to prevent LGA and early-childhood obesity[45,46] —clinicians should recognize that a "perfect" GWG does not guarantee metabolic protection if the child subsequently follows a rapid BMI acceleration trajectory. In our data, even children of mothers with Adequate throughout GWG who developed a Late Rapid BMI trajectory had TG levels 0.225 mmol/L higher than the reference dyad—an effect size larger than that of any prenatal exposure alone.

2. Postnatal phase: The preschool period (ages 3–6) represents a second critical window for metabolic screening and intervention. Currently, most pediatric obesity programs focus on infancy or school-age children. Our data suggest that routine BMI trajectory monitoring from age 3 onward, with particular attention to upward crossing of percentiles, can identify the Late Rapid phenotype before overt obesity and dyslipidemia are fully established. By age 4, children in the Late Rapid trajectory already exhibited a mean BMI z-score of 1.52, crossing the 85th percentile, despite having been near-normal at age 2.

3. Risk communication: The joint trajectory combinations offer a clinically intuitive tool. For example, a child with LGA birth whose mother had excessive GWG and who shows rising BMI at age 4 should be prioritized for intensive family-based lifestyle counseling.

Strengths and Limitations

Major strengths include the large, population-based design; repeated anthropometric measurements enabling trajectory modeling; availability of fasting blood samples at age 6; and careful adjustment to avoid over-adjustment bias.

Several limitations should be acknowledged. First, the observational design precludes causal inference, although the temporal sequence (prenatal-early growth-outcome) strengthens the likelihood of a causal contribution. Second, cardiometabolic markers were assessed at a single time point (age 6), providing a cross-sectional snapshot rather than a longitudinal assessment of metabolic trajectory; extended follow-up is needed to determine whether these associations persist into adolescence and adulthood. We are currently extending cohort follow-up to address this. Third, despite adjustment for key covariates, residual confounding by unmeasured factor—including paternal BMI, dietary intake, physical activity and genetic susceptibility—cannot be fully excluded. Fourth, this study was conducted in a large, geographically and socioeconomically diverse population in Tianjin, China, encompassing urban, suburban, special economic zones, and rural areas—a setting that offers robust internal validity and broad representativeness within the Chinese context. However, replication in other ethnic and geographic populations is warranted, as body composition, cardiometabolic risk profiles, and GWG distributions vary across populations.

Conclusions

In this large prospective cohort, a late preschool BMI acceleration trajectory emerged as the strongest independent predictor of adverse cardiometabolic risk at school entry. Children following this trajectory—comprising nearly one-fifth of the cohort—exhibited TG and GLU levels substantially higher than peers with normative growth, independent of maternal GWG, birth size, and perinatal complications. Maternal GWG patterns exerted minimal direct effects on offspring GLU and TG, suggesting their impact operates primarily through postnatal growth trajectories rather than direct metabolic programming. These findings reframe the developmental programming narrative by highlighting the preschool years as a critical window during which metabolic trajectories become established, building upon the foundation set in utero. Given that cardiometabolic markers were assessed only at age 6, extended follow-up is needed to determine whether these associations persist into later life. Public health strategies must extend their focus beyond pregnancy to include vigilant monitoring of BMI velocity in early childhood and timely interventions aimed at moderating weight gain acceleration during this modifiable window.

Data Sharing Statement

The datasets generated and/or analyzed during the current study are not publicly available because the data in this study are public health data and are protected by government security laws and regulations but are available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

The study protocol was approved by the Human Subjects Committee of Tianjin Women and Children's Health Center (approval number: TJWC20190305-6) and complied with the Declaration of Helsinki. The requirement for written informed consent was waived due to the retrospective use of routinely collected administrative data.

Acknowledgments

The authors sincerely thank the obstetricians, pediatricians, and nurses in all community hospitals and delivery hospitals of Tianjin for their meticulous work in data collection and quality assurance.

Author Contributions

S.Z.: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Visualization, Validation, Writing–original draft, Writing–review & editing.

J.L.: Software, Formal analysis, Data curation, Writing–review & editing.

W.L. and J.W: Methodology, Formal analysis, Data curation, Writing–review & editing.

Y.Q., T.Z. and W.D.: Methodology, Investigation, Writing–review & editing.

J.L.: Project administration, Methodology, Resources, Writing–review & editing.

L.F.: Supervision, Conceptualization, Resources, Writing–review & editing.

All authors gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure

The authors report no conflicts of interest in this article.

References

1. Scheidl TB, Brightwell AL, Easson SH, Thompson JA. Maternal obesity and programming of metabolic syndrome in the offspring: searching for mechanisms in the adipocyte progenitor pool. *BMC Med*. 2023;21:50. doi:10.1186/s12916-023-02730-z
2. George AD, Wang T, Duong T, et al. Lipid pathways connecting maternal BMI with infant obesity risk. *Sci Rep*. 2025;16(1):438. doi:10.1038/s41598-025-30081-7
3. Wibaek R, Vistisen D, Girma T, et al. Body mass index trajectories in early childhood in relation to cardiometabolic risk profile and body composition at 5 years of age. *Am J Clin Nutrition*. 2019;110(5):1175–1185. doi:10.1093/ajcn/nqz170
4. Zhang S, Li N, Li W, et al. Increased gestational weight gain is associated with a higher risk of offspring adiposity before five years of age: a population-based cohort study. *Diab Metab Syndrome Obes*. 2022;15:2353–2363. doi:10.2147/DMSO.S374427
5. Zhang S, Li N, Dong W, et al. Identifying optimal ranges of weight gain at the end of the second trimester result from a population-based cohort study. *Public Health Nutrition*. 2023;26(10):2005–2013. doi:10.1017/S1368980023001490
6. Zhang S, Feng L, Li W, et al. Early gestational weight gain and birth weight outcome: a Chinese population-based cohort. *Pediatr Res*. 2025. doi:10.1038/s41390-025-04324-2
7. Guardamagna O, Abello F, Cagliero P, Lughetti L. Impact of nutrition since early life on cardiovascular prevention. *Ital J Pediatr*. 2012;38(1):73. doi:10.1186/1824-7288-38-73
8. Lanigan J, Singhal A. Early nutrition and long-term health: a practical approach. *Proc Nutr Soc*. 2009;68(4):422–429. doi:10.1017/S002966510999019X
9. Embleton ND, Korada M, Wood CL, Pearce MS, Swamy R, Cheetham TD. Catch-up growth and metabolic outcomes in adolescents born preterm. *Arch Dis Child*. 2016;101(11):1026–1031. doi:10.1136/archdischild-2015-310190
10. Rolland-Cachera MF, Deheeger M, Bellisle F, Sempe M, Guilloud-Bataille M, Patois E. Adiposity rebound in children: a simple indicator for predicting obesity. *Am J Clin Nutrition*. 1984;39:129–135. doi:10.1093/ajcn/39.1.129
11. Huang W, Meir AY, Olapeju B, et al. Defining longitudinal trajectory of body mass index percentile and predicting childhood obesity: methodologies and findings in the Boston birth cohort. *Precis Nutr*. 2023;2:e00037. doi:10.1097/PN9.0000000000000037
12. Wang G, McEwan S, Zeng J, et al. Distinct genetic profiles influence body mass index between infancy and adolescence. *Nat Commun*. 2026;17(1):1594. doi:10.1038/s41467-026-69310-6
13. Heiskala A, Tucker JD, Choudhary P, et al. Timing based clustering of childhood BMI trajectories reveals differential maturational patterns; study in the Northern Finland birth cohorts 1966 and 1986. *Int J Obesity*. 2025;49(5):872–880. doi:10.1038/s41366-025-01714-8
14. Després J-P, Lemieux I. Abdominal obesity and metabolic syndrome. *Nature*. 2006;444:881–887. doi:10.1038/nature05488

15. Weiss R, Dziura J, Burgert TS, et al. Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med*. 2004;350(23):2362–2374. doi:10.1056/NEJMoa031049
16. Perchard R, Garner T, Higgins LE, et al. Transcriptome and metabolome analyses uncover genes and pathways linking growth trajectories to cardiometabolic risk markers in childhood. *Curr Issues Mol Biol*. 2026;48(2):238. doi:10.3390/cimb48020238
17. Mao A, Yang SQ, Luo YJ, et al. Long-term impact of maternal pre-pregnancy BMI on the risk of overweight/obesity in preschool children: mediation by infant birth weight and BMI trajectory group from 0 to 2 years. *BMC Public Health*. 2024;24(1):3404. doi:10.1186/s12889-024-20914-x
18. Huang YD, Chen HC, Huang YS, Lee MC, Yeh CJ. Maternal pre-pregnancy BMI and early childhood adiposity trajectories: longitudinal evidence from the Taiwan birth cohort study. *BMC Public Health*. 2026;26(1). doi:10.1186/s12889-026-26762-1
19. de Fluiter KS, van Beijsterveldt I, Breij LM, Acton D, Hokken-Koelega ACS. Association between fat mass in early life and later fat mass trajectories. *JAMA Pediatr*. 2020;174(12):1141–1148. doi:10.1001/jamapediatrics.2020.2673
20. Rolland-Cachera MF, Deheeger M, Maillot M, Bellisle F. Early adiposity rebound: causes and consequences for obesity in children and adults. *Int J Obesity*. 2006;30 Suppl 4(S4):S11–17. doi:10.1038/sj.ijo.0803514
21. Geserick M, Vogel M, Gausche R, et al. Acceleration of BMI in early childhood and risk of sustained obesity. *N Engl J Med*. 2018;379 (14):1303–1312. doi:10.1056/NEJMoa1803527
22. Massara P, Keown-Stoneman CDG, Maguire JL, Bandsma R, Comelli EM, Birken CS. Understanding the association of longitudinal body mass index patterns in children and their parents: a data-driven study from the TARGet Kids! cohort. *Obes Res Clin Pract*. 2025;19(3):223–231. doi:10.1016/j.orcp.2025.04.011
23. Mattsson M, Maher GM, Boland F, Fitzgerald AP, Murray DM, Biesma R. Group-based trajectory modelling for BMI trajectories in childhood: a systematic review. *Obes Rev*. 2019;20(7):998–1015. doi:10.1111/obr.12842
24. Consultation WHOE. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*. 2004;363(9403):157–163. doi:10.1016/S0140-6736(03)15268-3
25. Nishida C, Ko GT, Kumanyika S. Body fat distribution and noncommunicable diseases in populations: overview of the 2008 WHO expert consultation on waist circumference and waist-hip ratio. *Eur J Clin Nutr*. 2010;64(1):2–5. doi:10.1038/ejcn.2009.139
26. CHina NHCotPsRo. Standard of recommendation for weight gain during pregnancy period. 2022.
27. Proust-Lima C, Philipps V, Liquet B. Estimation of extended mixed models using latent classes and latent processes: the R package lcmm. *J Statistical Softw*. 2017;78(2):1–56. doi:10.18637/jss.v078.i02
28. Zhu L, Zhang R, Zhang S, Shi W, Chen C. [Chinese neonatal birth weight curve for different gestational age] 中国不同胎龄新生儿出生体重曲线研制. *[Chin J Pediatr]* 中华儿科杂志. 2015;53:97–103.
29. van Buuren S, Groothuis-Oudshoorn K. mice: multivariate imputation by chained equations in R. *J Statistical Softw*. 2011;45:1–67. doi:10.18637/jss.v045.i03
30. Rubin DB. *Multiple Imputation for Nonresponse in Surveys*. New York: John Wiley & Sons; 1987.
31. Hernán MA, Robins JM. *Causal Inference: What If*. Boca Raton: Chapman & Hall/CRC; 2020.
32. Schisterman EF, Cole SR, Platt RW. Overadjustment bias and unnecessary adjustment in epidemiologic studies. *Epidemiology*. 2009;20 (4):488–495. doi:10.1097/EDE.0b013e3181a819a1
33. Expert Panel on Integrated Guidelines for Cardiovascular H, Risk Reduction in C, Adolescents, National Heart L, Blood I. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. *Pediatrics*. 2011;128 (Supplement_5):S213–S256. doi:10.1542/peds.2009-2107C
34. Wen J, Lv A, Aihemaitijiang S, Li H, Zhou Y, Liu J. The association of maternal gestational weight gain with cardiometabolic risk factors in offspring: a systematic review and meta-analysis. *Nutr Rev*. 2025;83:e106–e115. doi:10.1093/nutrit/nuae027
35. Tam CHT, RCW M, Yuen LY, et al. The impact of maternal gestational weight gain on cardiometabolic risk factors in children. *Diabetologia*. 2018;61(12):2539–2548. doi:10.1007/s00125-018-4724-x
36. Yuan N, Zhao D, Xu X, Zhang X. Maternal prepregnancy overweight: associations with maternal and offspring weight 4-7 years postpartum. *J Diab Res*. 2026;2026(1):9989579. doi:10.1155/jdr/9989579
37. Karachaliou M, Georgiou V, Roumeliotaki T, et al. Association of trimester-specific gestational weight gain with fetal growth, offspring obesity, and cardiometabolic traits in early childhood. *Am J Clin Exp Obstet Gynecol*. 2015;212(4):e501–514. doi:10.1016/j.ajog.2014.12.038
38. Zhang L, Zhang S, Zou W, et al. Maternal high-fat diet regulates offspring hepatic ABCG5 expression and cholesterol metabolism via the gut microbiota and its derived butyrate. *Clin Sci*. 2024;138(17):1039–1054. doi:10.1042/CS20240997
39. Friesen JA, Rodwell VW. The 3-hydroxy-3-methylglutaryl coenzyme-A (HMG-CoA) reductases. *Genome Biol*. 2004;5(11):248. doi:10.1186/gb-2004-5-11-248
40. Singhal A. Long-term adverse effects of early growth acceleration or catch-up growth. *Ann Nutr Metab*. 2017;70(3):236–240. doi:10.1159/000464302
41. Jain V, Singhal A. Catch up growth in low birth weight infants: striking a healthy balance. *Rev Endocr Metab Disord*. 2012;13(2):141–147. doi:10.1007/s11154-012-9216-6
42. Koyama S, Ichikawa G, Kojima M, Shimura N, Sairenchi T, Arisaka O. Adiposity rebound and the development of metabolic syndrome. *Pediatrics*. 2014;133(1):e114–119. doi:10.1542/peds.2013-0966
43. Tanaka H, Morisaki N, Harada S, Urayama KY. Obesity health screening in Japanese school-aged children and adolescents. *Cureus*. 2026;18(1): e100766. doi:10.7759/cureus.100766
44. Eto E, Kato M, Kirino S, et al. Relationship between maternal body composition during pregnancy and newborn birth weight in Japan. *JMA J*. 2026;9(1):189–197. doi:10.31662/jmaj.2025-0060
45. 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(21):2207–2225. doi:10.1001/jama.2017.3635
46. Sun Y, Shen Z, Zhan Y, et al. Effects of pre-pregnancy body mass index and gestational weight gain on maternal and infant complications. *BMC Pregnancy Childbirth*. 2020;20(1):390. doi:10.1186/s12884-020-03071-y