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Association of maternal metabolic risk factors with offspring body mass index (BMI) trajectories in early childhood: a retrospective cohort study

Ting Lai ,[1] Ang Mao,[2] Liu Yang,[1] Yan Ren,[1] Xiao Yang,[3] Wei Song,[4] Yingjuan Luo[1]

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TL, AM and LY contributed equally.

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For numbered affiliations see end of article.

Correspondence to
Dr Yingjuan Luo;
55580253@qq.com

ABSTRACT

Objective This study aimed to identify body mass index (BMI) growth trajectories from birth to 24 months of age and examine the independent and additive effects of four maternal metabolic risk factors, namely prepregnancy BMI, the rate of gestational weight gain, gestational diabetes mellitus (GDM) and gestational hypertension, on offspring growth trajectories in childhood in China.

Design A retrospective cohort study was conducted.

Setting The study used Maternal and Child Health Management Database in Chengdu, China, including the mothers' antenatal care data, birth certificate records and 0–3-year-old children's healthcare data.

Participants The study included mothers who gave birth between January 2014 and December 2014, and followed their offspring through 31 December 2016. The final analysis included 4492 mother-child pairs.

Primary outcome measures The primary outcomes were children's BMI measurements from birth to 24 months of age. We performed group-based trajectories modelling to identify children's BMI growth trajectories. Then, we applied logistic regression to examine the associations between maternal metabolic risk factors and offspring BMI trajectories in childhood.

Results Four distinct trajectories were identified: stable low (16.83%), stable average (40.69%), stable high (32.06%) and early increase (10.42%) trajectories. Relative to the stable average trajectory, maternal prepregnancy overweight (adjusted OR (aOR)=2.001, 95% CI 1.482–2.702, p<0.001), an excessive rate of gestational weight gain (aOR=1.496, 95% CI 1.138–1.966, p=0.004) and GDM (aOR=1.470, 95% CI 1.097–1.970, p=0.010) were positively associated with their offspring being in the early increase trajectory. In addition, the children's risk of being included in the early increase trajectory showed an increasing trend with an increasing number of adverse maternal metabolic risk factors.

Conclusion Exposure to maternal prepregnancy overweight, excessive rate of weight gain and GDM resulted in a greater risk of offspring exhibiting an early increase trajectory for BMI. Decreasing maternal metabolic risk before and during pregnancy and monitoring childhood growth trajectories may prevent or delay the onset of childhood obesity.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This retrospective design with Chinese birth cohort data permitted the collection of repeated body mass index (BMI) measurement data from the children and evaluation of childhood BMI trajectories by the group-based trajectory modelling.
⇒ This study assessed the independent and additive effects of maternal metabolic adverse factors on the offspring's growth trajectories, providing intervention strategies to prevent childhood obesity.
⇒ Maternal prepregnancy weights were self-reported, which introduces the possibility of recall bias.
⇒ Lack of information on the maternal blood lipids, offspring dietary intake and physical activity levels, which could be important contributors shaping child growth trajectories, is a limitation.

INTRODUCTION

The increasing incidence of childhood obesity has emerged as a significant public health challenge worldwide.[1] The worldwide prevalence of overweight or obesity among children aged 5–19 years increased from approximately 4% to over 18% from 1975 to 2016.[1] In 2015, 10.4% of preschool children in China were overweight or obese when referring to Chinese body mass index (BMI) criteria.[2] Childhood obesity often persists into adolescence and has been demonstrated to increase susceptibility to adulthood obesity, cardiovascular disease, asthma, type 2 diabetes and psychological or behavioural consequences.[3–6] These findings indicate that physical development in early life can largely predict the risk of obesity and chronic diseases in adulthood.

Mounting evidence strongly suggests that childhood obesity may originate in the 'first 1000 days' from conception to age 2,[7] when tissue is forming and when the epigenetic system is most sensitive to environmental perturbations.[8] The identification of modifiable risk factors before and during pregnancy

is essential for the early prevention of childhood obesity. Indeed, maternal metabolic factors, such as prepregnancy BMI, gestational diabetes mellitus (GDM) and gestational weight gain (GWG), have been associated with a greater risk of obesity or overweight in offspring.[9–11] These associations may be explained by shared genetic susceptibility between the mother and fetus, and the alteration of intrauterine environment that stimulates fetal metabolic programming.[12] However, most previous studies focused on assessing only one factor, and few have simultaneously assessed both the factors and their joint effects.

The metabolic syndrome was first conceptualised by the WHO.[13] To date, there are no obligatory components to define it, but rather a cluster of inter-related conditions that encompass obesity, insulin resistance, dyslipidaemia and hypertension,[14] which are inter-related and share underlying mediators, mechanisms and pathways.[15] Recent evidence has found maternal metabolic syndrome during pregnancy is associated with more pregnancy complications and adverse birth outcomes,[16] but less is known about the subsequent effects on their offspring's development, showing the need to understand these associations as early on as possible.

To date, most cross-sectional studies have focused on physical attributes at a specific time point, but BMI and BMI changes over time in children are highly heterogeneous. Longitudinal BMI growth trajectories consider the dynamics of BMI variations over time and integrate repeated growth measurements to identify distinctive developmental patterns, offering new perspectives for identifying young children who may be at greater risk of obesity.[17 18] However, the associations between maternal metabolic risk factors and offspring BMI trajectories have rarely been explored, especially in the Asian population. Therefore, this study, which was based on a Chinese birth cohort from Chengdu City, Sichuan Province, aimed to explore the distinct BMI growth trajectory classes from birth to 24 months of age and elucidate the individual and additive effects of four maternal metabolic health factors and offspring BMI trajectories.

METHODS

Study design

Our study was based on a retrospective and longitudinal birth cohort study of mother-child pairs obtained from the Maternal and Child Health Management Database (MCHD) in Chengdu, China. This database was established by the Chengdu Women's and Children's Central Hospital in 2003. It primarily serves the purpose of collecting data from primary, secondary and tertiary healthcare institutions in Chengdu and provides systematic evidence support for clinical practice, medical research and healthcare administration. Mothers' antenatal care data, birth certificate records and 0–3-year-old children's healthcare data were extracted from the MCHD and linked by a unique ID number. Providing free-of-charge health check-ups for children aged 0–3 years is one of the national basic public health services projects funded by the government. The children's heights and weights were measured during regular check-ups at community health centres in Chengdu at the ages of 1–24 months. A computer engineer abstracted the data from the MCHD by using structured query language. A blinded reviewer visually inspected all of the data to check for missing information or other implausible measurements, and we excluded participants with missing key information.

Population

We applied a strict set of inclusion and exclusion criteria to avoid confounding factors. The inclusion criteria were as follows: women with a singleton pregnancy; generally healthy pregnant individuals aged 18–35 years without major diseases, congenital anomalies and known pregnancy complications; children with a gestational age of 37–42 weeks at delivery and children with a minimum of five assessment points. The exclusion criteria for mothers included pregestational diabetes; prepregnancy chronic hypertension; a history of mental illness; missing data on prepregnancy weight, weight at first check-up, or predelivery and missing key information such as prepregnancy BMI, rate of gestational weight gain (rGWG), GDM, gestational hypertension or gestational age. The exclusion criteria for children were a postpartum 1 min Apgar score <7 or congenital abnormalities or medical conditions known to affect growth and development. Ultimately, our final analysis cohort included 4492 children born between January 2014 and December 2014, with complete maternal data. Based on the principle of 10 events per variable, this cohort has a sufficient sample size.

Maternal metabolic risk factors

The maternal metabolic risk factors evaluated in this study included prepregnancy BMI, the rGWG, GDM and gestational hypertension. The rGWG was used in this study to eliminate the confounding bias caused by gestational age. Maternal prepregnancy BMI was estimated from self-reported height and weight prior to pregnancy at the first prenatal check-up. BMI was calculated as weight (kg) divided by the square of height (m^2) and categorised into the following four groups according to the guidelines for the prevention and control of overweight and obesity in China[19]: underweight, <18.5 kg/m^2; normal weight, 18.5–23.9 kg/m^2; overweight, 24.0–27.9 kg/m^2; and obesity, ≥ 28.0 kg/m^2. The rGWG was calculated as follows: (weight before delivery (or weight at last visit) (kg) – weight at 13th gestational weeks (kg))/(weeks of gestation at delivery – 13), which was based on prepregnancy BMI and the standard of recommendation for weight gain during pregnancy in China[20]: underweight, 0.37–0.56 kg/week; normal weight, 0.26–0.48 kg/week; overweight, 0.22–0.37 kg/week; and obesity, 0.15–0.30 kg/week. A maternal rGWG above or below the above thresholds was defined as excessive or insufficient, respectively. In China, pregnant individuals are routinely screened for GDM at 24–28 weeks of gestation by a 2-hour oral glucose

tolerance test with a 75 g glucose load. If a mother's blood glucose level met any of the criteria (fasting glucose level≥5.1 mmol/L, 1-hour glucose level≥10.0 mmol/L or 2 hour glucose level≥8.5 mmol/L) based on the Guidelines for the Diagnosis and Treatment of Gestational Hyperglycemia,[21] a diagnosis of GDM was established. Gestational hypertension was diagnosed if the systolic blood pressure was≥140 mm Hg or if the diastolic blood pressure was ≥90 mm Hg during pregnancy.[22]

Childhood BMI trajectories

Childhood BMI trajectories from birth to 24 months were the primary outcomes of interest. Birth weight and length were measured by a trained physician and recorded on the birth certificate records of the MCHD. The anthropometric measurements were performed by trained nurses at each check-up for children dressed in only light clothing, without caps, shoes and coats. Each child's weight and recumbent length were measured to the nearest 0.1 kg and 0.1 cm, respectively. BMI (kg/m^2) measurement was standardised into sex- and age-specific BMI *z*-scores according to the WHO Child Growth Standards.[23]

Covariates for adjustment

Covariates were selected a priori based on their clinical significance and were extracted from the MCHD. Maternal characteristics included age (18–25, 25–30 or 30–35 years), ethnicity (Han or other), occupation type (enterprises and institution staff, self-employed, unemployed or other), education level (junior school or below, high school or junior college, university or above), folic acid supplementation (prepregancy, pregnancy or never) and delivery mode (caesarean section or vaginal delivery). Child characteristics included gestational age (continuous, week), sex (male or female), low birth weight (yes or no) and exclusive breastfeeding up to 6 months of age (insufficient, normal, or excessive). We used directed acyclic graphs to select maternal and offspring sociodemographic characteristics as potential confounders (online supplemental figure S1). Covariates that resulted in more than 10% change in model parameter estimates for at least one exposure factor were retained in the final models. These included maternal age, ethnicity, occupational type and educational level. However, folic acid supplement, gestational age, low birth weight and exclusive breastfeeding up to 6 months were not included in the final adjustment sets, which may mediate the causal pathways between maternal metabolic factors and offspring growth trajectory.

Statistical analysis

The identification of BMI trajectories from 0 to 24 months of age was achieved by performing group-based trajectory modelling using the SAS procedure PROC TRAJ. The optimal number of latent trajectory groups was determined by the Bayesian information criterion (BIC), the difference in the BIC between the two models (ΔBIC), the average posterior probability and the relative entropy. The posterior probability is an estimate of the probability of individuals' membership in each of the possible groups. Entropy is a statistic that ranges from 0.00 to 1.00, and high values (entropy >0.80) indicate that individuals are classified with confidence.[24] We also required the sample size in each trajectory to contain a minimum of 5% of the total sample.[25] Initially, we conducted linear, quadratic and cubic term fitting on two, three, four and five groups of trajectory models to identify the latent classes (online supplemental figure 2)and compared the fitting metrics of each model and interpretability of trajectories' morphology. Ultimately, the above procedures indicated that the four-group trajectory was the best-fitting model with an adequate separation between the latent classes. The model selection process is presented in online supplemental table S1, and the model adequacy assessments of the optimal trajectory model are presented in online supplemental table S2. The parameter estimates and equations of the optimal trajectory model are shown in online supplemental tables S3 and S4. To further validate the model's reliability, we fitted the model using raw BMI scores for children grouped by sex, and we found four trajectories was still the optimal model. To maximise comparability, we primarily used the BMI z-score trajectory in the subsequent primary analysis.

The N (%) and median (IQR) were calculated for categorical and continuous variables, respectively. Comparisons of maternal and child characteristics among BMI trajectory groups were performed using the χ^2 test or Fisher's exact test for proportions and the Wilcoxon rank-sum test for medians. Multivariable logistic regression was performed to evaluate the associations between maternal metabolic risk factors and child BMI trajectories. We tested two models for maternal metabolic factors: unadjusted and adjusted for potential confounders. We also used a cumulative score to assess the additive effects of the four maternal metabolic factors on BMI *z*-score trajectories, and we assigned scores to each factor in online supplemental table S5. To test the robustness of our results, sensitivity analyses were conducted to evaluate the associations of each metabolic risk factor and offspring BMI trajectories in subgroups. All the data analyses were performed with SAS V.9.4 (SAS Institute, Cary, North Carolina, USA), and a two-tailed p value<0.05 was considered to indicate statistical significance.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

In total, the study population included in the analysis consisted of 4492 mother-child pairs. The average number of the BMI measurements among children was 9.56, and the average length of follow-up among children was 23.1 months. Four distinct BMI *z*-score trajectory

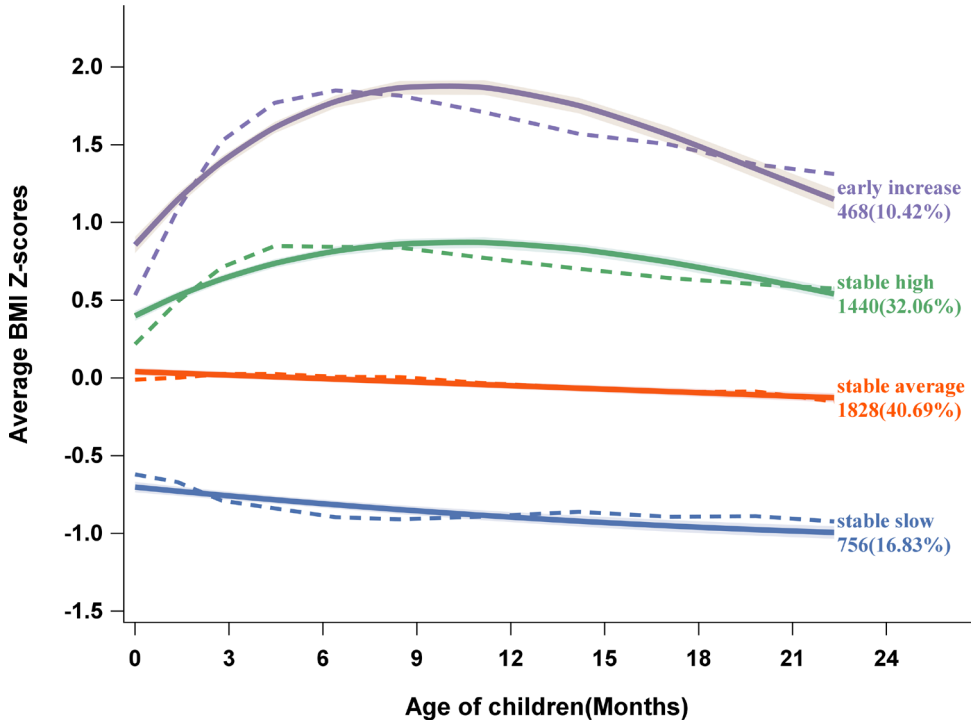

Figure 1 Child body mass index (BMI) *z*-score trajectories from 0 to 24 months of age in Chengdu, China. Dashed lines represent the measured values, and solid lines represent the predicted values. Greater overlap of the lines indicates a better fit of the model.

groups were identified based on children's BMI *z*-scores (figure 1). In group 1, the 'stable low' trajectory group included children who had relatively lower birth sizes and who maintained the lowest average BMI throughout the developmental trajectory (with *z*-scores ranging from −0.5 to −1), these children accounted for 16.83% of the cohort. In group 2, most of the children (40.69%) were classified into the 'stable average' trajectory characterised by average birth size followed by a stable *z*-score over time close to zero. In group 3, the 'stable high' trajectory (32.06%) began from a relatively larger birth size, followed by a stable increase throughout the observation period (for which the *z*-score ranged from 0 to 1). In group 4, the 'early increase' trajectory demonstrated that the remaining 10.42% of children who had the highest birth size followed by an accelerated *z*-score gain; this trajectory appeared as a relatively steeper curve.

To explore the curve of raw BMI value trajectories by sex, we identified four distinct raw BMI trajectory groups for 2299 boys and 2193 girls. Four trajectory groups were found to constitute the best-fitting model for both boys and girls. The trajectory curves of the boys and the girls were roughly similar in shape. Groups 1, 2 and 3 were named 'stable slow', 'stable average' and 'stable high', respectively. Group 4 was named the 'early increase' trajectory for both boys and girls, exceeded the overweight threshold curve but was below the obesity threshold throughout the observation period (figures 2,3).

The characteristics of the mothers and children in the four BMI *z*-score trajectory groups are illustrated in table 1. There were significant differences in maternal delivery mode, child sex and low birth weight among the four trajectory groups. The early increase trajectory group was more likely to include children born by caesarean section and male children and was less likely to include children with low birth weight. Prepregnancy BMI and rGWG significantly varied among the child BMI *z*-score trajectory groups. Children born to mothers with overweight/obesity and an excessive rGWG had greater risks of being in the stable high trajectory and early increase trajectory groups. According to the multivariable logistic regression models (table 2), with the stable average trajectory as the reference category, after we adjusted for maternal age, ethnicity, occupational type and educational level, maternal prepregnancy overweight was positively associated with the stable high trajectory (adjusted OR (aOR) (95% CI)=1.601 (1.272–2.014)) and the early increase trajectory (aOR (95% CI)=2.001 (1.482–2.702), whereas maternal prepregnancy underweight was negatively associated with these two trajectories. A significant association was observed between an excessive rGWG and early increase trajectory (aOR (95% CI)=1.496 (1.138–1.966)). Maternal GDM was also associated with the early increase trajectory (aOR (95% CI)=1.470 (1.097–1.970)). We also evaluated the additive effects of the four maternal metabolic factors on the child BMI *z*-score trajectory groups. The children's risk of being in the early increase trajectory was stronger with an increasing number of adverse maternal metabolic factors (table 3). Sensitivity analyses found that the associations between each metabolic risk factor and

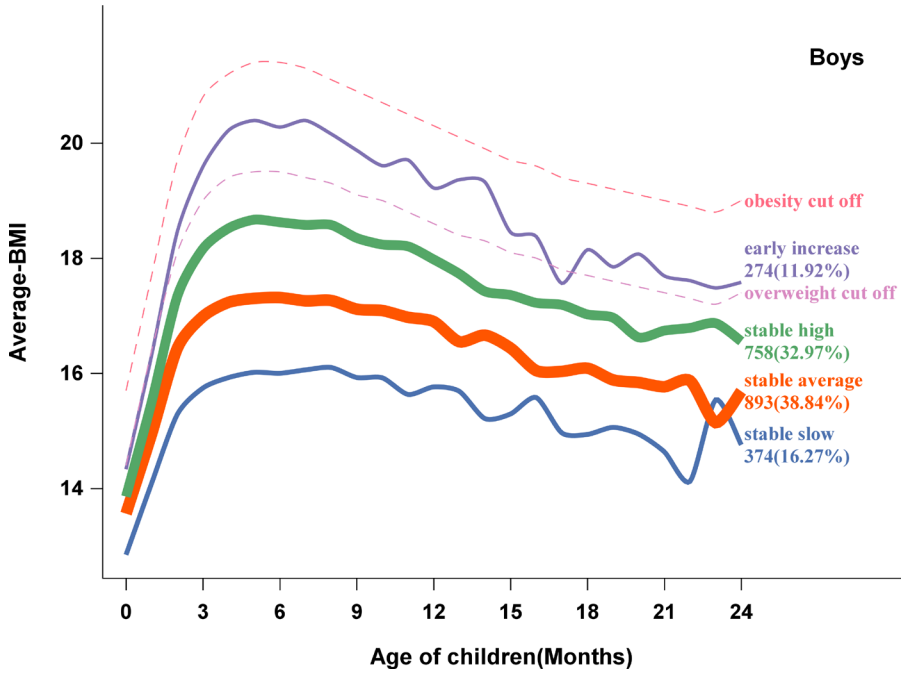

Figure 2 Body mass index (BMI) trajectories for boys aged 0–24 months. Solid lines depict the raw BMI trajectory groups, and dashed lines indicate the overweight cut-off and obesity cut-off.

the children's BMI trajectory in subgroups were similar to our results from the primary analysis (online supplemental tables S6–S10).

DISCUSSION

In this study, we identified four distinct raw BMI growth trajectory groups grouped by child sex, and the early increase trajectories of boys and girls were between the thresholds for obesity and overweight throughout the observation period. Furthermore, we identified four distinct BMI *z*-score trajectory groups for all children aged 0–2 years. Among the prepregnancy BMI, rGWG, GDM and gestational hypertension, maternal overweight had the greatest association with children being in the early increase trajectory, followed by a maternal excessive rGWG and GDM. Conversely, mothers who were

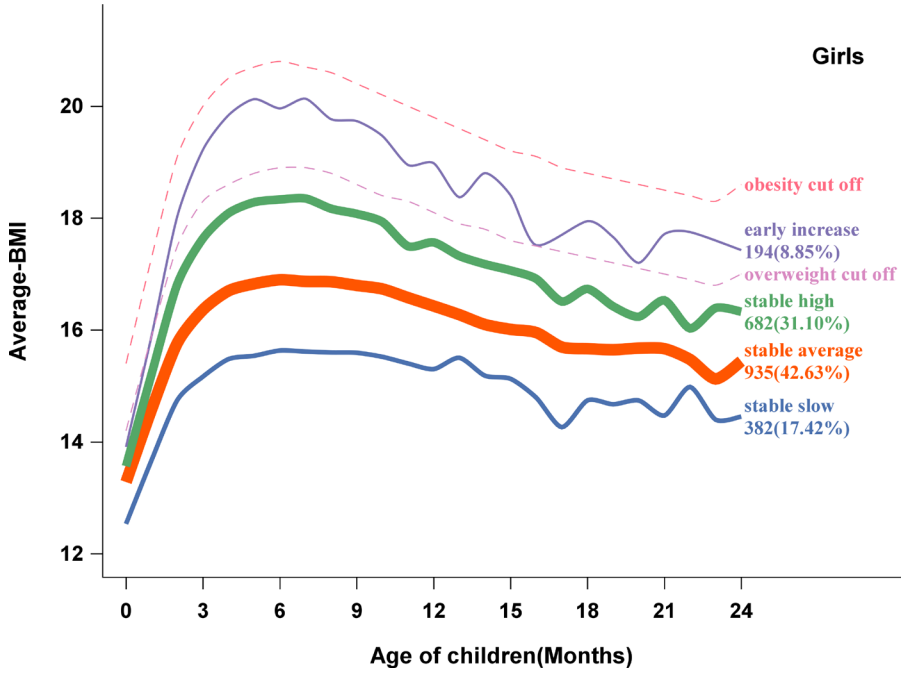

Figure 3 Body mass index (BMI) trajectories for girls aged 0–24 months. Solid lines depict the raw BMI trajectory groups, and dashed lines indicate the overweight cut-off and obesity cut-off.

Table 1 Characteristics of mothers and children according to child body mass index *z*-score trajectory group

Variables	All	Group 1, stable low	Group 2, stable average	Group 3, stable high	Group 4, early increase		
N (%) or M (P25, P75)	n=4492	n=756	n=1828	n=1440	n=468	$\chi^2/t/Z$	P value
Maternal age, years							
18–25	871	150 (19.84)	339 (18.54)	304 (21.11)	78 (16.67)	7.53	0.275
25–30	2623	438 (57.94)	1070 (58.53)	838 (58.19)	277 (59.19)		
30–35	998	168 (22.22)	419 (22.92)	298 (20.69)	113 (24.15)		
Race/ethnicity							
Han	4365	739 (97.75)	1777 (97.21)	1398 (97.08)	451 (96.37)	2.08	0.557
Other	127	17 (2.25)	51 (2.79)	42 (2.92)	17 (3.63)		
Occupational type							
Enterprises and institutions staff	2597	443 (58.60)	1066 (58.32)	819 (56.88)	269 (57.48)	5.66	0.463
Self-employed	1031	182 (24.07)	397 (21.72)	349 (24.24)	103 (22.01)		
Unemployed or other	864	131 (17.33)	365 (19.97)	272 (18.89)	96 (20.51)		
Education level							
Junior school or below	472	82 (10.85)	180 (9.85)	159 (11.04)	51 (10.90)	2.74	0.841
High school or junior college	2101	359 (47.49)	872 (47.70)	655 (45.49)	215 (45.94)		
University or above	1919	315 (41.67)	776 (42.45)	626 (43.47)	202 (43.16)		
Folic acid supplementation							
Prepregnancy	322	54 (7.14)	138 (7.55)	98 (6.81)	32 (6.84)	6.55	0.365
Pregnancy	4070	686 (90.74)	1657 (90.65)	1308 (90.83)	419 (89.53)		
Never	100	16 (2.12)	33 (1.81)	34 (2.36)	17 (3.63)		
Delivery mode							
Caesarean section	2587	385 (50.93)	1030 (56.35)	864 (60.00)	308 (65.81)	31.28	<0.001*
Vaginal delivery	1905	371 (49.07)	798 (43.65)	576 (40.00)	160 (34.19)		
Child sex							
Male	2299	374 (49.47)	893 (48.85)	758 (52.64)	274 (58.55)	16.24	0.001*
Female	2193	382 (50.53)	935 (51.15)	682 (47.36)	194 (41.45)		
Gestational age (weeks)		39.2 (38.4,40.0)	39.3 (38.5,40.1)	39.3 (38.5,40.1)	39.3 (38.5,40.1)	6.29	0.099
Low birth weight							
No	4442	725 (95.90)	1817 (99.40)	1433 (99.51)	467 (99.79)	74.22	<0.001*
Yes	50	31 (4.10)	11 (0.60)	7 (0.49)	1 (0.21)		
Exclusive breastfeeding during the first six months							
No	3626	604 (80.86)	1498 (82.17)	1162 (81.26)	362 (77.85)	4.61	0.203
Yes	839	143 (19.14)	325 (17.83)	268 (18.74)	103 (22.15)		
Prepregnancy body mass index							
<18.5	986	226 (29.89)	430 (23.52)	264 (18.33)	66 (14.10)	95.43	<0.001*
18.5–23.9	2931	466 (61.64)	1205 (65.92)	952 (66.11)	308 (65.81)		
24.0–27.9	478	53 (7.01)	155 (8.48)	191 (13.26)	79 (16.88)		
≥28	97	11 (1.46)	38 (2.08)	33 (2.29)	15 (3.21)		
Rate of gestational weight gain							
Insufficient	195	39 (5.31)	83 (4.65)	52 (3.70)	21 (4.58)	17.97	0.006*
Normal	927	176 (23.95)	400 (22.40)	276 (19.62)	75 (16.34)		
Excessive	3265	520 (70.75)	1303 (72.96)	1079 (76.69)	363 (79.08)		
Gestational diabetes							

Continued

Table 1 Continued

Variables	All	Group 1, stable low	Group 2, stable average	Group 3, stable high	Group 4, early increase		
N (%) or M (P25, P75)	n=4492	n=756	n=1828	n=1440	n=468	$\chi^2/t/Z$	P value
No	3961	671 (88.76)	1625 (88.89)	1270 (88.19)	395 (84.40)	7.55	0.056
Yes	531	85 (11.24)	203 (11.11)	170 (11.81)	73 (15.60)		
Gestational hypertension							
No	4340	726 (96.03)	1772 (96.94)	1391 (96.60)	451 (96.37)	1.45	0.693
Yes	152	30 (3.97)	56 (3.06)	49 (3.40)	17 (3.63)		

Body mass index *z*, age- and sex-specific body mass index *z*-score.
The p value denotes the comparison of the mean or percentage of each characteristic by growth trajectory class.
*P < 0.05, statistically significant difference between the groups (tested two-tailed).

underweight had a lower probability of having children who were in the stable high trajectory or the early increase trajectory. We also found that children's risk of being included in the early increase trajectory was stronger with an increasing number of adverse maternal metabolic risk factors.

Why did we explore BMI growth trajectories using both raw BMI values and BMI *z*-scores in this study? Raw BMI values can visually reflect within-child variability over time and depend on a child's level of adiposity,[26] whereas BMI *z*-score trajectories demonstrate how a child's BMI changes over time relative to that of their peers. Regardless of whether raw BMI or BMI *z*-scores, this study identified four distinct trajectories in which the early increase trajectories for both the boys and girls exceeded the overweight threshold curve. Elevated BMI trajectories in childhood are known to be associated with obesity, diabetes and cardiovascular disease in adulthood.[27–30] The 'first 1000 days' of early life has been identified as a specific sensitive window for functional changes during development with increasing risk of disease or dysfunction and a long latency.[7 31] Thus, monitoring the specific trajectories of children may improve chronic disease prevention.

Maternal prepregnancy overweight and an excessive rGWG were found to be risk factors for offspring being included in the early increase trajectory, with maternal prepregnancy BMI having the greatest effect. Our findings were consistent with previous evidence of these associations. Robust evidence from prospective birth cohort studies from Canada,[32] France,[27] Australia[33] and Spain[34] indicates that maternal prepregnancy or early pregnancy obesity/overweight are strongly associated with offspring in the high or ascending trajectory groups. Likewise, mothers with excessive GWG had a greater risk of having a child with an ascending trajectory characterised by a greater birth size followed by an accelerated BMI gain.[34] Additionally, excessive GWG has been shown to be associated with a greater probability of children having a stable high BMI trajectory[35 36] and a greater risk of overweight/obesity in the first two years.[35] Despite the known association between GDM and an increasing/ascending BMI trajectory,[37] our results indicated a slight association between maternal GDM and the early increase trajectory. As reported by a study in the USA, GDM requiring medication treatment was associated with a high and increasing BMI trajectory in offspring, while those not requiring medication treatment exhibited no association.[36] Therefore, future research in this birth cohort is warranted to determine the impact of GDM with or without medication treatment on children's growth trajectories. In addition, we found no statistical association between prepregnancy obesity and offspring growth trajectories, possibly mainly due to the relatively lower prevalence of maternal obesity in Southwest China.

Few studies have evaluated maternal metabolic syndrome and child growth trajectories simultaneously and assessed their joint effects. However, our present study has demonstrated a clear link, indicating that the more adverse maternal metabolic factors a mother has, the greater the likelihood that her child will be classified into the early increase trajectory. For instance, a cohort study conducted in Zhejiang indicated that excessive GWG strengthened the positive correlation between prepregnancy overweight/obesity and rapid offspring growth during early life.[38] Similarly, another Ma'anshan birth cohort study revealed that mothers with gestational metabolic syndrome jointly increased the risk of obesity in all children, and female children had a greater probability of being in the high BMI *z*-score trajectory group.[39] Additionally, two additional studies revealed that adverse maternal metabolic risk factors can jointly increase the risk of having a high BMI trajectory among children and having obesity at 2 and 4 years of age.[40 41] These studies are consistent with our results. Except that this trend was not observed in the stable high trajectory, it might reflect the relatively smaller number of pregnant women in this group with three or more adverse metabolic factors simultaneously. Nevertheless, the early increase trajectory that exceeded the overweight threshold may be of greater public health significance. Thus, our results provide further support that early intervention in patients with these modifiable risk factors, both before and during pregnancy, holds the potential to delay or prevent the development of paediatric obesity.

Table 2 Associations between maternal metabolic risk factors and child body mass index *z*-score trajectory group

	Stable low vs stable average		Stable high vs stable average		Early increase vs stable average	
Variable	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Pregnancy body mass index						
18.5–23.9	1.00 (ref)		1.00 (ref)		1.00 (ref)	
<18.5	1.359 (1.120–1.649)	0.002*	0.777 (0.652–0.926)	0.005*	0.600 (0.450–0.801)	<0.001*
24.0–27.9	0.884 (0.636–1.229)	0.464	1.560 (1.241–1.960)	<0.001*	1.994 (1.480–2.687)	<0.001*
≥28	0.749 (0.379–1.477)	0.403	1.099 (0.684–1.766)	0.696	1.544 (0.839–2.844)	0.163
Rate of gestational weight gain						
Normal	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Insufficient	1.068 (0.702–1.625)	0.759	0.908 (0.622–1.326)	0.618	1.349 (0.787–2.312)	0.276
Excessive	0.907 (0.739–1.113)	0.349	1.200 (1.009–1.427)	0.039*	1.485 (1.131–1.951)	0.004*
Gestational diabetes						
No	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Yes	1.014 (0.775–1.327)	0.919	1.072 (0.863–1.331)	0.532	1.480 (1.109–1.977)	0.008*
Gestational hypertension						
No	1.00(ref)		1.00(ref)		1.00(ref)	
Yes	1.308 (0.832–2.054)	0.245	1.115 (0.755–1.646)	0.585	1.193 (0.686–2.073)	0.532
After adjusting for potential confounders†						
Pregnancy body mass index						
18.5–23.9	1.00 (ref)		1.00 (ref)		1.00 (ref)	
<18.5	1.360 (1.119–1.653)	0.002*	0.762 (0.639–0.910)	0.003*	0.599 (0.449–0.800)	<0.001*
24.0–27.9	0.884 (0.635–1.230)	0.464	1.601 (1.272–2.014)	<0.001*	2.001 (1.482–2.702)	<0.001*
≥28	0.740 (0.374–1.464)	0.387	1.116 (0.693–1.797)	0.652	1.530 (0.828–2.826)	0.175
Rate of gestational weight gain						
Normal	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Insufficient	1.060 (0.697–1.614)	0.785	0.900 (0.616–1.315)	0.586	1.343 (0.783–2.302)	0.284
Excessive	0.902 (0.734–1.107)	0.324	1.189 (0.999–1.416)	0.051	1.496 (1.138–1.966)	0.004*
Gestational diabetes						
No	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Yes	1.026 (0.782–1.346)	0.853	1.102 (0.886–1.372)	0.383	1.470 (1.097–1.970)	0.010*
Gestational hypertension						
No	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Yes	1.304 (0.829–2.049)	0.251	1.127 (0.763–1.666)	0.547	1.192 (0.686–2.073)	0.533

†Adjusted for maternal age, ethnicity, occupational type and educational level.
*P<0.05, statistically significant difference between the groups (tested two-tailed).

The potential mechanisms linking maternal metabolic health factors to offspring growth trajectories could be a complicated process influenced by shared susceptibility genes associated with overweight/obesity and changes in the intrauterine environment, such as oxidative stress, epigenetic modifications and metabolic syndrome.[12] For example, specific variants within introns of the fat mass and obesity-associated gene are associated with body mass and composition phenotypes.[42] Apolipoprotein D, which is critical for lipid regulation, is upregulated by ninefold in the fetuses of mothers with obesity.[43] Moreover, an animal study suggested that pups born to obese mice had significantly larger birth sizes, demonstrating increased cholesterol and body fat and early development of a metabolic syndrome in early life.[44] In addition, mothers with excessive GWG may have greater fat deposition and possibly be in a state of dysmetabolism,[45] which may interact with placental factors, leading to an increased supply of fuels to the fetus.[46] Likewise, offspring exposed to a hyperglycaemic environment are susceptible to the onset of metabolic syndromes.[47] In addition to the physiological aspects, mothers also exert a profound influence on the establishment of their children's eating behaviours and physical activity pattern in early childhood. If a

Table 3 The additive effects of the four maternal metabolic factors on child body mass index *z*-score trajectory group

	Stable slow vs stable average		Stable high vs stable average		Early increase vs stable average	
Variable	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
No risk	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Low risk	0.914 (0.737–1.133)	0.411	1.131 (0.939–1.363)	0.195	1.374 (1.018–1.855)	0.038*
Medium risk	0.935 (0.689–1.269)	0.665	1.788 (1.403–2.278)	<0.001*	2.423 (1.688–3.478)	<0.001*
High risk	0.866 (0.546–1.373)	0.54	1.342 (0.933–1.930)	0.113	2.517 (1.550–4.087)	<0.001*
After adjusting for potential confounders†						
No risk	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Low risk	0.909 (0.733–1.128)	0.388	1.126 (0.934–1.358)	0.212	1.378 (1.021–1.860)	0.036*
Medium risk	0.940 (0.691–1.277)	0.691	1.826 (1.432–2.330)	<0.001*	2.420 (1.683–3.479)	<0.001*
High risk	0.869 (0.547–1.379)	0.551	1.374 (0.954–1.978)	0.088	2.527 (1.554–4.108)	<0.001*

No risk, none of the above four statuses; low risk, one of the four statuses; medium risk, two of the four statuses; high risk, three of the four statuses and above.
†Adjusted for maternal age, ethnicity, occupational type and educational level.
*P<0.05, statistically significant difference between the groups (tested two-tailed).

mother's obesity is primarily attributed to her eating behaviours and sedentary lifestyle, there is a high probability that their children may be more inclined to adopt analogous unhealthy lifestyles.[48]

Our study has several important strengths. The retrospective design with longitudinal birth cohort data and large sample size permitted the collection of repeated BMI measurement data from the children and the evaluation of childhood BMI trajectories. We identified a group trajectory based on the raw BMI values, regardless of sex, that exceeded the overweight threshold. Moreover, we not only assessed the independent effects of adverse maternal metabolic factors on offspring growth trajectories but also explored the additive effects of these factors on offspring growth patterns. However, studies focusing on BMI growth trajectory were mainly from developed countries, and BMI trajectories varied by race and region. Given the paucity of BMI trajectory data in the Chinese population, this study filled the gap in the population of Southwest China and enriched the field. However, there are still several limitations that should be addressed through additional study. First, maternal prepregnancy weights were self-reported, which introduces the possibility of recall bias. Second, mothers and children only come from Chengdu City, and our conclusions might not be representative of the rest of China. Third, trimester-specific weight gain could not be assessed due to data unavailability. Last, we were unable to evaluate residual confounders, such as maternal blood lipids, offspring dietary intake and physical activity levels, all of which are important contributors shaping child growth trajectories, due to the lack of data.

CONCLUSION

Our research suggests that maternal overweight has the greatest association with offspring growth trajectories throughout the first two years of life, followed by a maternal excessive rGWG and GDM, which may be linked to an increased risk of obesity later in life. We further found that the clustering of maternal adverse metabolic factors was associated with a significantly increased risk of children being classified into the early increase BMI trajectory. Consequently, it is crucial to implement effective interventions targeting maternal metabolic risks before and during pregnancy to prevent or delay the onset of childhood obesity. If the intervention window during prepregnancy and pregnancy is missed, it becomes imperative to identify the high-risk population and apply effective hierarchical management, which holds significant potential for controlling childhood obesity.

Author affiliations
[1]Department of Healthcare, Chengdu Women's and Children's Central Hospital, Chengdu, Sichuan, China
[2]Department of Medical Administration, Chengdu Women's and Children's Central Hospital, Chengdu, Sichuan, China
[3]Department of Obstetrics, Chengdu Women's and Children's Central Hospital, Chengdu, Sichuan, China
[4]Department of Women and Children Health, Chengdu Municipal Health Commission, Chengdu, Sichuan, China

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ORCID iD

Ting Lai http://orcid.org/0000-0002-7330-3518

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