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Qingmin Lin[1,2,3], Yanrui Jiang[1,2,3], Guanghai Wang[1,2,3], Wanqi Sun[1,2,3], Shumei Dong[1,2,3], Yujiao Deng[1,2,3], Min Meng[1,2,3], Qi Zhu[1,2,3], Hao Mei[2,4], Yingchun Zhou[5], Jun Zhang[3,6], Peter E. Clayton[7], Karen Spruyt[1,8], Fan Jiang[1,2,3#]

Qingmin Lin: qml2014@sjtu.edu.cn; Yanrui Jiang: yanrui1027@126.com; Guanghai Wang: wang-guanghai@163.com; Wanqi Sun: yiyunsays@hotmail.com; Shumei Dong: shumeidong1217@163.com; Yujiao Deng: yujiaodeng@126.com; Min Meng: mengmin0219@163.com; Qi Zhu: zhu_qi_yuland@163.com; Hao Mei: meihao@uw.edu; Yingchun Zhou: yczhou@stat.ecnu.edu.cn; Jun Zhang: junjimzhang@sina.com; Peter E. Clayton: peter.clayton@manchester.ac.uk; Karen Spruyt: spruytsleep@gmail.com; Fan Jiang: fanjiang@shsmu.edu.cn

Affiliations:

[1]Department of Developmental and Behavioral Pediatrics, Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200127, China.

[2]Pediatric Translational Medicine Institution, Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200127, China.

[3]MOE-Shanghai Key Laboratory of Children's Environmental Health, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200092, China.

[4]Department of Data Science, School of Population Health, University of Mississippi Medical Center, Jackson, MS 39216, USA.

[5]KLATASDS-MOE, School of Statistics, East China Normal University, Shanghai 200062, China.

[6]School of Public Health, Shanghai Jiao Tong University, Shanghai 200025, China.

[7]Division of Developmental Biology and Medicine, Faculty of Biology, Medicine and Health,

University of Manchester and Manchester Academic Health Science Centre, Manchester M13 9PL, United Kingdom.

[8]INSERM, University Claude Bernard, School of Medicine, Lyon, France.

[#]**Corresponding Author:** Fan Jiang, Department of Developmental and Behavioral Pediatrics, Pediatric Translational Medicine Institution, Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine, 1678 Dongfang Rd. Shanghai 200127, China. Tel: 86-21-38626012; Fax: 86-21-58706129; fanjiang@shsmu.edu.cn

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Abbreviations

BMI: body mass index;

CI: confidence interval;

EF: enjoyment of food;

FF: food fussiness;

FR: food responsiveness;

SR: satiety responsiveness;

WHtR: waist-to-height ratio;

WAZ: weight-for-age z-score;

WAZ-change: the change of weight-for-age z-score

1. Introduction

Over the last 40 years, overweight/obesity has become an epidemic[1]. When excess weight is accrued in early life , it can be persistent and is difficult to reverse[2], predisposing children to a myriad of short- and long-term adverse physical and mental health outcomes[3,4]. In a cohort of 292,827 individuals, it was demonstrated that above average body mass index (BMI) in childhood, even at levels far below current overweight/obesity classifications, was associated with increased risk of lifelong health problems such as type 2 diabetes[5]. The prevention and reduction of childhood overweight/obesity or even higher BMI level than average may thus have the potential to realize substantial health benefits[6]. Strategies to maintain the weight of a growing child are likely to be much easier than encouraging a child with obesity to lose weight[7]. Therefore, identifying the critical periods and the risk factors for the occurrence and development of overweight/obesity early in life is the first and most important step for formulating preventive strategies.

Research suggests that the path to overweight/obesity is established very early in life[8]. Two systematic reviews (including one meta-analysis) have demonstrated that rapid weight change in infancy, commonly defined as a change of weight-for-age z-score (WAZ-change) greater than 0.67 over two time points, is associated with later life excessive body weight[9,10]. As several studies only investigated one infancy WAZ-change (e.g. between 0-6 months[11], 0-1 year, and 0-2 years[10]), it was not possible to determine the "exact critical age window" in which the greatest WAZ-change occurred. Furthermore, a recent study identified distinct BMI-change trajectories from birth to age 14 years old that can provide guidance to design interventions targeting specific populations and specific ages, however, it did not capture the growth patterns in early life[12]. Whether a range of WAZ-change trajectories may exist in early childhood also remains unclear. In the current study we planned to determine more precisely early life WAZ-changes by measuring children at frequent intervals over the first four years.

While genes are known to be robust predictors, evidence demonstrates that lifestyle behaviors established in early childhood life are the main modifiable factors of the weight status[8]. Lifestyles, such as eating behavior, physical activity, media exposure and sleeping, are likely to be key factors influencing the risk of childhood overweight/obesity. However, both observational and interventional studies have reported inconsistent results[13-20]. Furthermore, two reviews proposed that the combination of obesity-associated risk factors (e.g. low physical activity, more sedentary time, and poor sleep) may have an effect in a way that differs from their impacts when studied in isolation[21,22]. Similarly, synergistic effects of rapid WAZ-change and risk lifestyle behaviors (e.g. higher eating appetite, lower physical activity, more media exposure and shorter sleep duration) on childhood adiposity in early life have not been characterized, because they were most often studied independently[12,15-17,23]. Therefore, from a prevention perspective, insight into the combined effects of rapid weight gain and early childhood lifestyle factors on risk of childhood overweight/obesity is required.

Therefore, we used a birth cohort with nine follow-up time points (at birth, 3, 6, 9, 12, 18, 24, 36, and 48 months) to characterize WAZ-change trajectories, to determine the periods with the greatest WAZ-change, and to investigate independent and combined effects of WAZ-change trajectories with early lifestyle factors on children's adiposity indicators at age of 4 years old. Based on our prior clinical observations, we hypothesized that WAZ-change trajectories in early life could be categorized into distinct patters, such as steady WAZ-change or early infancy rapid WAZ-change trajectory, and the greatest WAZ-change could be occurred very earlier as compared to later life in the first four years. We also hypothesized that distinct growth patterns not only have an independent influence, but also an interactive effect with childhood lifestyle factors on obesity status. For example, individuals with early infancy rapid growth trajectory combined with unhealthy behaviors (i.e. higher appetite, lower physical activity, more media exposure and shorter sleep duration) may have a much higher risk of obesity conditions in later life when compared with those with steady growth pattern and without lifestyle risk factors.

2. Methods

2.1. Participants

The Shanghai Sleep Birth Cohort Study (SSBCS), an ongoing mother-child birth cohort recruited from the general population, aims to investigate the effects of perinatal and early life environmental and behavioral factors on child growth and development. Detailed information has been described previously[24]. Briefly, the recruitment was conducted at the Obstetric Clinic of Renji Hospital (Shanghai, China), which is adjacent to our unit, from May 2012 to July 2013. There were three screening stages based on the predefined inclusion and exclusion criteria (**Figure 1**). For the screening steps, all the pregnant women who met the inclusion criteria were approached by our research team and 431 candidates (i.e. women in late pregnancy carrying a single baby) were identified. Finally, 262 women with full-term newborns agreed to participate and attend the scheduled follow-up visits in our study. In the first follow-up stage (n = 262), we carried out a person-to-person interview at 9 time points, namely late pregnancy, birth within 3 days, 42 days' postpartum (± 3 days), and 3, 6, 9, 12, 18, and 24 months after birth (± 7 days). Due to losing interest for further follow-up, moving away, busy work schedule and other reasons, 25 participants dropped out in this stage. In the second follow-up stage (n = 237), person-to-person interviews at age of 36, 48 and 72 months (± 1 month) were conducted. The 6-year follow-up has not yet completed; therefore, the current study used the 4-year data.

The birth cohort protocol was approved by the Shanghai Children's Medical Center Human Ethics Committee (SCMCIRB-2012033). All participants provided written informed consent, which was renewed before commencing each stage of data collection. All families received ¥50 in remuneration at each follow-up visit.

2.2. Measures

2.2.1 Anthropometric measurement—All measurements were undertaken according to standardized protocols by trained research staff. Child weight and length/height were obtained with light clothes and without shoes at each visit. Weight was measured using calibrated scales (0-2 years, Seca 335) and electronic personal scales (3-4 years, Seca 877). Recumbent length (0-2 years) was measured on the same calibrated scale as used for weight and standing height (2-4 years) was measured using a stadiometer (Seca 206). Weight-for-age z-score (WAZ) was determined using the least mean square method according to the World Health Organization growth reference[25]. At the age of 4 years old, the following measurements without clothes were taken: child waist circumference using the Ergonomic circumference measuring tape (Seca 201), biceps circumference using the Heochstmass measuring tape, triceps and subscapular skinfold thicknesses using the Harpenden skinfold caliper. We calculated BMI value from weight being divided by the square of height, computed waist-to-height ratio (WHtR) from waist circumference divided by height and summed the triceps and subscapular skinfold thicknesses as a measure of subcutaneous fat for children at age 4 years.

2.2.2 Eating behaviors—At the age of 2 and 4 years old, parents reported child eating behaviors using the Children's Eating Behavior Questionnaire (CEBQ)[26], which has been validated in different populations including Chinese[27]. The original CEBQ is a 35-item measure constructed in UK children designed to assess 8 dimensions[26]. Considering its applicability (sensitive to cultural disparities) to Chinese population[28], perhaps difficulty in identifying negative moods in early childhood and the lack of correspondence between questionnaire and laboratory food intake measures for emotional eating[29], we only used the following four dimensions in the present study: food responsiveness (FR), to assess responsiveness to external food cues; enjoyment of food (EF), to investigate the child's general appetite; satiety responsiveness (SR), to evaluate the sensitivity to internal satiety cues; and food fussiness (FF), to assess a common eating behavior with limited variety or quantity of foods. The four subscales that we selected had good test-retest reliability (Coefficients (r) = 0.83, 0.87, 0.85 and 0.87 respectively) and high internal consistency (Cronbach's α = 0.82, 0.91, 0.83 and 0.91 respectively)[26]. A higher score for FR and EF, as well as a lower score for SR and FF equate to a greater appetite rating.

2.2.3 Physical activity time—At the age of 3 years old, child's outdoor playtime, as a proxy for physical activity, was assessed using a validated survey question[30]. That is, parents reported how much time their child spent on playing outdoors per day on a typical weekday and on a typical weekend in the past month. A weighted outdoor playtime per day was calculated by ((hours/weekday*5 + hours/weekend*2) / 7).

2.2.4 Media exposure time—At the age of 2 and 4 years old, parents reported the child's media exposure time including watching TV or DVDs, using a computer or IPAD, as well as playing with electronic games on a typical weekday and on a typical weekend day in the last month. Total media exposure time was summed and a weighted average was calculated using the same function as physical activity time at each age. We also categorized media exposure time into < 1 and ≥ 1 hour/day based on the media recommendations of the American Academy of Pediatrics (AAP) for children who aged 2-5 years old.

2.2.5 Total sleep duration—At the age of 2 years old, child's total sleep duration was summed from daytime and nighttime sleep duration using the Brief Infant Sleep Questionnaire (BISQ)[31]. At the age of 4 years old, the Children's ChronoType Questionnaire (CCTQ)[32] was utilized. Parents were asked about their child's bedtime and wake-up time as well as their daytime sleep on a typical weekday and on a typical weekend day in the last month. Both nighttime sleep on weekdays and weekends were calculated, then a weighted total sleep time was calculated.

2.2.6 Other variables—Demographic data reported by mothers were collected in late pregnancy and at birth. Maternal pre-pregnancy BMI, total gestational weight gain between pre-pregnancy and the last clinically recorded weight within two weeks after delivery, and paternal BMI values were obtained from the Obstetric Clinic. We also assessed maternal sleep quality, depressive symptom and anxiety status at the first visit using the Pittsburgh Sleep Quality Index[33], the Center for Epidemiological Survey-Depression Scale[34] and the State-Trait Anxiety Index[35], respectively, all of which are standardized questionnaires and are widely used in China. Details can be found in our previous articles[24,36]. On each postnatal follow-up (until 24 months' postpartum), the mothers were asked to report the feeding method (exclusive breastfeeding, mixed feeding, or bottle feeding). Infant feeding method during the first 3 months was categorized as exclusive breastfeeding and non-exclusive breastfeeding (mixed feeding and bottle feeding). Breastfeeding duration (weaning time) was categorized as <6 months, 6 to 12 months or ≥12 months. Infant dietary intake was assessed at 6 months using a 3-day food diary, which asked parents/caregivers to list all foods and drinks (including water) that the child consumed and to record the time, content and quantity of each meal. Electronic kitchen scales (CAMRY- EK3550-31P, Beijing, China) and precise instructions were provided to assist parents in quantifying their child's food intake. Total energy, protein, fat, and carbohydrate intake were estimated by research staff using the China Food Composition Tables.

2.3. Statistical analysis

Maternal and infant characteristics were presented as mean (95% confidence interval, CI) or frequency (percentage), and differences in characteristics between lost and retained children when aged 4 years old were assessed by the t-test and $\chi 2$ test, for continuous variables and categorical variables, respectively. To address our aims, the statistical analyses were performed in the following steps.

In step 1, to identify the WAZ-change trajectories, the WAZ-changes were calculated and group-based trajectory modeling (GBTM) was used[37]. We quantified WAZ-changes during each age interval as the subtraction between adjacent measurement points with positive differences representing WAZ gain and negative differences representing WAZ loss, and defined WAZ-change ≥ +0.67 over two time points as rapid change[10]. The following eight time intervals, i.e. 0-3, 3-6, 6-9, 9-12, 12-18, 18-24, 24-36, and 36-48 months were used to characterize the WAZ-change trajectories. On average, each child had 4.9 (95% CI: 4.7, 5.2) WAZ-change observations, and only children with a minimum of three observations were included. The GBTM assesses the average pattern of WAZ-change over time and assumes that individuals belong to the same underlying population represented by a single growth curve. The best-fitting model was chosen based on the largest Bayesian information criterion and each trajectory included at least 5% of the sample size.

In step 2, we tested the independent and combined effects of WAZ-change trajectories and different lifestyles on each adiposity outcome using a multivariate linear regression model, controlling for multiple baseline factors (family income, gestational age of the child at delivery, maternal pre-pregnancy BMI, paternal BMI, newborn weight over the first three days, sex and energy intake at six months) Firstly, we assessed the effects of WAZ-change trajectories and each lifestyle factor (i.e. FR, EF, SR, FF, outdoor playtime, media exposure time and total sleep duration) on adiposity measures solitarily. Secondly, both WAZ-change trajectories and lifestyle factors that had a significant effect on adiposity measures, were imported into the same model to test their independent effects on adiposity indicators. Thirdly, to aid clinical interpretation, lifestyle factors that had an independent effect on adiposity measures were then categorized as dichotomous variables by median levels, except for media exposure time whose cut-off value was defined as one hour[13]. As, only four eating behaviors had significant effects on adiposity measures, they were dichotomized and put into the next combined analyses. Fourthly, we combined the WAZ-change trajectories and each of these four dichotomous eating behaviors to examine a range of joint effects on the adiposity outcomes[38]. Children with lower risk factors of overweight/obesity were used as the reference group in the analyses, e.g. steady growth pattern and lower FR score, or steady growth pattern and higher SR score. Post-hoc pairwise comparisons were performed with Bonferroni multiple comparison test. Notably, the lifestyle factors investigated at the age of 2 and 4 years old were averaged as the childhood exposure during this period and to reduce the number of variables in further multivariate regression models, as had been done in a previous study[39].

In step 3, to avoid loss of statistical power due to missing data, we performed a multiple imputation using chained equations (MICE) with 100 imputed data sets and 1,000 burn-ins for each dataset to estimate the missing values[40]. To test whether substantial differences existed due to imputation, we compared the results before and after the data imputation.

All analyses were performed by using the Stata SE 15.0 software (Stata Corp, College Station, TX, USA), and the statistical significance was set at a 2-sided P value less than 0.05.

3. Results

3.1. Descriptive information

Overall, 262 mother-child pairs participated, with 221 (84.4%) cases having at least three WAZ-change data points to characterize trajectories, and 209 (79.8%) cases finishing the 4-year measurement to evaluate childhood adiposity outcomes (**Figure 1**). No significant differences due to attrition were found at the age of 4 years (**Table 1)**. Of the 262 mother-infant pairs with complete data at birth, 50.4% were boys. The majority of women had a college or higher level of education (91.2%). Maternal age at delivery was 29.5 (95% CI: 29.1, 29.9) years old, and child's birth weight was 3.31 (95% CI: 3.26, 3.36) kg.

3.2. WAZ-change trajectories

Mean WAZ-change decreased from 0.80 (95% CI: 0.67, 0.93) over 0-3 months and 0.26 (95% CI: 0.19, 0.34) over 3-6 months to just below the zero baseline in subsequent age intervals. The percentage of cases experiencing rapid weight change dropped with a similar trend, from

54.0% over 0-3 months and 22.9% over 3-6 months to less than 8% in subsequent age intervals (**Table S1**).

Over the first four years of life, two distinct trajectories that best represent the dynamic WAZ-changes were detected using GBTM (**Figure 2**). Given the recommended cut-off value of the rapid weight change (WAZ-change > +0.67), two groups were identified: WAZ-changes near to zero at all age intervals (group 1, N = 84, 38.0%); and a rapid WAZ-change over 0-3 months, while fluctuating near zero afterwards (group 2, N = 137; 62.0%). Therefore, we defined group 1 as "steady" and group 2 as "early infancy" rapid WAZ-change trajectory.

Further analyses also indicated a significant difference in the absolute WAZ-change and weight increment (kg) between the two trajectories (**Table S1**). The first 6 months, in particular the first 3 months with the largest WAZ-change, was the critical period, and children with "early infancy" rapid WAZ-change trajectory showed a non-stable weight pattern.

3.3. Independent effects

Most of the mother-child characteristics were similar between steady and early infancy rapid groups (**Table S2**). However, children in the early infancy rapid group were more likely to have shorter gestational age, shorter birth length and lower birth weight. The early infancy rapid group was also more likely to have higher EF and lower FF scores, in addition to having less outdoor playtime in early childhood, even after adjusting for confounders.

After adjusting for mother-child characteristics, the early infancy rapid group had significantly higher adiposity status (except for WHtR) compared with the steady group, with the regression coefficient of 0.90 (95% CI: 0.37, 1.44) kg for weight, 0.93 (95% CI: 0.49, 1.37) kg/m^2 for BMI, 1.90 (95% CI: 0.68, 3.12) cm for waist circumference, 1.05 (95% CI: 0.62, 1.48) cm for biceps circumference, and 2.57 (95% CI: 1.13, 4.01) mm for subcutaneous fat (**Model 1a in Table 2**). Meanwhile, scores of FR and EF had positive effects, and, SR and FF had negative effects on adiposity measures with the exception of WHtR (**Model 1b-1e in Table 2**). Further analyses showed that either the WAZ-change trajectory or four eating subscale scores independently had significant associations on adiposity measures except for WHtR (**Model 2a-2d in Table 2**). However, the other lifestyle factors, such as outdoor playtime, media exposure time and total sleep duration had no significant association with adiposity measures **(Model 1f-1h in Table 2)**.

3.4. Combined effects

Combined effects were shown in **Table 3** and **Figure 3** (post-hoc multiple comparison test).

While we did not find statistically interactive effect of growth trajectory and each eating behavior (**Table S3**), we did find significantly combined effects of the WAZ-change trajectory with three in four subscales of eating behaviors alone on the majority of childhood adiposity outcomes (except for WHtR) at the age of 4 years, all of which were in the absence of independent effects from early infancy rapid trajectory and eating behaviors. Specifically, compared to children with steady WAZ-change trajectory and lower appetite score (the reference group), children with early infancy rapid trajectory and larger appetite rating (i.e. higher FR score, lower SR and FF score) had significantly more waist circumference and subcutaneous fat, children with early infancy rapid trajectory and higher FR or lower FF score had obliviously more weight, additionally, children with early infancy rapid trajectory and higher FR score had apparently more BMI and subcutaneous fat.

3.5. Sensitivity analysis

Our sensitivity analysis found that the results of multiple-imputation had limited effect on the results of complete-case analysis with the exception of the results for the SR score (**Table S4-S6 and Figure S1**).

4. Discussion

To the best of our knowledge, no studies have characterized different trajectories of WAZ-change among full-term children and determined their combined effects with lifestyle factors on adiposity outcomes in early childhood life. There are several important findings. We found (1) a high percentage of infants with rapid growth in our cohort, (2) characterized two distinct WAZ-change trajectories from birth to 4 years - one was a steady trajectory and the other an early infancy rapid WAZ-change trajectory - with the critical window for this change occurring over 0-6 months, especially with the greatest change over 0-3 months, and (3) identified significant independent and combined effects of WAZ-change trajectories and eating behaviors on childhood adiposity markers at age 4 years, indicating that both early growth and appetite have impacts that manifest in later childhood .

According to the widely used cut-off for a rapid WAZ-change (> +0.67) between any two measurement points, 54% of infants during the first three months and 64% during the first six months showed rapid growth in our study, which was a much higher percentage than that reported from other countries, e.g. 19% in Japan[41] and 30% in the USA[42] over 0-4 months, and 22% in Australia[43], 24% in Spain[44], 28% in Northeast Brazil[45] over 0-6 months. The present study characterized two WAZ-change trajectories from birth to 4 years: only 38% of children had a steady WAZ-change growth pattern, and the remainder of the children exhibiting an early infancy rapid growth with the weight increment in 0-3 months interval at the 85th percentile (boys) or the 95th percentile (girls) according to the WHO standard[46]. While a limited number of studies have characterized WAZ-change trajectories in the same way as the present study, several studies have identified different absolute weight or BMI trajectories[47]. Most reported a combination of stable (low, medium or high) and ascending (early or later) trajectories over time, which might be somewhat clinically similar to the steady and early infancy rapid growth trajectories in the current research. However, the percentages with an early ascending trajectory in other studies were lower than that presented in this study.

Children with early infancy rapid growth in our cohort were more likely to have a lower birth weight, which is in line with findings of a previous study[8], and is likely to be related in part to a significantly shorter pregnancy (albeit only a few days). However, all participants in the current study were normal pregnant women with healthy full-term neonates, 97.6% of children were appropriate for gestational age (post hoc analysis), and no significant difference in the method of delivery was found between the two growth trajectories. Future larger cohort studies should be conducted to confirm our findings. As for the postnatal factors, the rapid WAZ-change pattern may be attributable to the disparities in parents' feeding beliefs, attitudes, knowledge or practices related to cultural perceptions. Chinese families are more likely to consider a baby with more weight to be healthy. Consequently, over-nutrition combined with early consumption of formula, water-based drinks, fruit juice and introduction of complementary foods will be much more likely to occur[48,49].

Several studies have explored rapid infant weight change, but failed to demonstrate its "exact critical age window". That is, they either investigated only one age interval[10,11] or reported conflicting evidence regarding the specific critical period. Some reported early infancy[50], some reported later infancy[51] or later life[52], while others indicated both[53]. These discrepancies could be due to differences in length of follow-up, age intervals, or ethnicity. Characterizing distinct WAZ-change trajectories not only can precisely illustrate the dynamic weight changes in size over time, but also can determine the critical rapid growth window over the whole growth picture[47]. In our four-year birth cohort study with nine follow-up visits, we identified two different WAZ-change trajectories, which suggested that the first six months, particularly the first three months, was the most critical growth period. One study showed that infants with rapid weight change over the first one month tended to continue to exhibit rapid growth in the following months[54]. The two distinct growth patterns from our data are particularly useful for clinicians and health professionals to design early-life interventions by targeting infants with rapid weight gain in the first few months.

The current study suggested that it is the eating behavior, not the other lifestyle factors tested (i.e. outdoor playtime, media exposure time and total sleep duration) in early childhood, that significantly predicted later adiposity status. Previous research has found that a larger appetite rating (e.g. greater FR and EF scores; lower SR and FF scores) was associated with adiposity in children[55,56]. The underlying mechanisms may be related to the higher FR, leading to more frequent eating when exposed to food that triggers brain-reward pathways; and to the lower SR, leading to more food being eaten on each eating occasion again related to a neuroendocrine feedback loop[57]. One prior study also observed that a higher FR score was correlated to a greater energy intake. In addition a higher EF score was associated with a greater energy intake and more food eaten without hunger, while children with a higher SR score had a lower energy intake, a smaller food intake without hunger and a better average caloric compensation[58].

In the present study, we observed a significantly joined effect between growth trajectory and each eating behavior on most of adiposity indicators. Our study extends the current literature, in which WAZ-change trajectories not only have an independent effect, but also a biologically combined impact with children's eating behaviors (such as FR, SR and FF) on childhood adiposity measures, which suggested a synergistic effect between them in early childhood. Thus, children who had an early infancy rapid growth with a larger appetite score were more likely to develop a higher adiposity status compared with children showing steady growth with a lower appetite score. Some studies have indicated that higher weight gain and weight status in early life can positively predict subsequent energy intake, FR and EF, as well as negatively predicting later SR[59,60]. Previous studies also have demonstrated that a larger appetite would facilitate early rapid weight gain[61,62]. The interactive influence between them was more likely to exacerbate the occurrence and development of childhood and adulthood overweight/obesity. If not treated proactively, they can persist and are not easy to improve by themselves. Therefore, control of rapid growth in the first three to six months of life, followed by strategies to reduce the potential modifying effects of eating behaviors in preschool children[63], in a period when appetite traits are becoming established as many children become autonomous eaters and experience greater socialization of eating[64,65], are required.

While eating behaviors have a genetic background[66], they are also influenced by environmental factors. Studies have suggested that the critical window for altering eating behaviors might occur after birth[62], and parental feeding practices are potentially a good behavior to target early in life[67,68]. Sustaining exclusive breastfeeding and delaying complementary feeding until 6 months can not only promote maternal feeding styles with less controlling and more responsive to infant cues of hunger and satiety, but also can modify infants' self-regulation of energy intake and SR[61,69]. While early children characterized of rejection of new foods and increased autonomy and self-regulation abilities, parents can also play a critical role in shaping their children's eating behaviors by avoiding maladaptive feeding strategies such as pressure to eat, using food as a reward and unhealthy food habits[64,65,68].

Our findings should be considered in the context of potential limitations. Firstly, our samples were from Shanghai, a relatively socioeconomically advantaged city in China. The majority of parents were university educated and had family incomes at or above the national average. Hence, the findings might not be generalizable to the national population. However, Shanghai is representative of most of the cities that have evolved from developing to developed status. Therefore, our findings are likely to reflect what will happen in other developing cities and can assist clinicians designing early-life interventions in this socioeconomic setting. Samples with a wider range of socioeconomic status should be collected in the future work. Secondly, our small sample size and the attrition over time may reduce the power to detect some associations. However, no significant differences in maternal or child characteristics at the age of 4 years were found in those who stayed in the cohort versus those that did not; additionally, we did not find attrition bias based on the results of sensitivity analyses (nearly identical results between multiple-imputation and complete-case analyses) suggesting a relatively robust result. Thirdly, parent-reported behavioral data may be subject to recall bias. Objective measurements should be collected in the future studies. Fourthly, we did not obtain children's caloric intake in other periods except for 6 months. The caloric intake in other periods should be also assessed in the future research to identify differences between the two WAZ-change growth patterns. Fifthly, the multiple comparisons performed in our study could increase the type I errors. Finally, given its observational nature, we cannot claim the causality and cannot exclude the possibility that our results may be influenced by residual and unmeasured or unknown confounding factors.

5. Conclusions

Our study has identified two distinct weight change trajectories, highlighted the first six months, particularly the first three months, as a possible critical growth window, and showed a significant effect of weight change trajectory and eating behaviors (e.g. FR, SR and FF), either alone or in combination, on the majority of adiposity measures at the age of 4 years. These findings extend the current literature and provide a potentially valuable model to aid clinicians and health professionals in designing early-life interventions targeting specific populations, specific ages and specific lifestyle behaviors to prevent childhood overweight/obesity. Our cohort is ongoing, and future follow-up on these children will be essential to indicate whether our observations may have long-term repercussions. Further studies with larger sample size, longer timeframes, and more exact evaluation of lifestyle behaviors in different populations are needed to verify our findings.

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Authors' Contributions

Ms. Lin designed the study, analyzed and interpreted the data, drafted the initial manuscript as well as all subsequent drafts, and reviewed and revised the manuscript. Ms. Jiang and Mr. Wang designed the study, and critically reviewed and revised the manuscript. Ms. Sun, Dong, Deng, Meng and Zhu designed the study, managed participant recruitment and data collection, and critically reviewed the manuscript. Dr. Mei, Zhou, Zhang, and Clayton conceptualized and designed the study, provided guidance on the statistical analyses, and critically reviewed the manuscript. Dr. Spruyt designed the study, provided guidance on the statistical analyses, interpreted the data, and critically reviewed and revised the manuscript. Dr. Jiang conceptualized and designed the study, provided guidance on the statistical analyses, interpreted the data, and critically reviewed and revised the manuscript. All the authors read and approved the final manuscript.

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Table 1 Maternal-child characteristics between retained and lost children at four years (non-imputed data).

	All (n=262)	Retained (n=209)	Lost (n=53)	t/χ^2	*P* value
Maternal (pregnancy)					
Highest parents education				1.22	0.544
High school or lower	23 (8.8)	18 (8.6)	5 (9.4)		
College or higher	239 (91.2)	190 (91.4)	48 (90.6)		
Maternal age at birth, year	29.47 (29.08, 29.86)	29.70 (29.24, 30.15)	28.71 (27.95, 29.47)	-2.00	0.046
Gestational age, week	39.65 (39.53, 39.77)	39.63 (39.49, 39.77)	39.71 (39.47, 39.96)	-0.10	0.922
Pre-pregnancy BMI, kg/m^2	20.61 (20.30, 20.93)	20.72 (20.34, 21.10)	20.25 (19.72, 20.78)	-0.89	0.377
Paternal BMI, kg/m^2	24.37 (23.86, 24.88)	24.55 (23.93, 25.17)	23.77 (22.95, 24.59)	-1.58	0.116
Gestational weight gain, kg	16.28 (15.75, 16.81)	16.11 (15.49, 16.73)	16.96 (15.97, 17.94)	-1.26	0.208
Maternal sleep quality	96 (40.7)	80 (42.1)	16 (34.8)	0.82	0.364
Maternal state anxiety	20 (8.2)	15 (7.7)	5 (10.2)	0.32	0.574
Maternal trait anxiety	29 (12.0)	22 (11.3)	7 (14.6)	0.38	0.536
Maternal depression	30 (12.0)	22 (11.0)	8 (16.0)	0.97	0.324
Newborn					
Male	132 (50.4)	105 (50.2)	27 (50.9)	0.01	0.927
Vaginal delivery	100 (39.4)	78 (38.6)	22 (42.3)	0.24	0.627
Birth order 1	237 (92.9)	188 (93.1)	49 (92.5)	0.02	0.537
Birth season				3.24	0.356
Spring, Mar to May	57 (21.8)	44 (21.1)	13 (24.5)		
Summer, Jun to Aug	88 (33.6)	66 (31.6)	22 (41.5)		
Fall, Sep to Nov	49 (18.7)	42 (20.1)	7 (13.2)		
Winter, Dec to Feb	68 (26.0)	57 (27.3)	11 (20.8)		
Birth length, cm	49.96 (49.77, 50.15)	49.93 (49.71, 50.16)	50.06 (49.69, 50.43)	-1.07	0.291
Birth weight, kg	3.31 (3.26, 3.36)	3.31 (3.25, 3.37)	3.31 (3.23, 3.40)	-0.58	0.563
Birth BMI, kg/m^2	13.22 (13.08, 13.37)	13.24 (13.07, 13.41)	13.17 (12.93, 13.41)	0.02	0.986

BMI = body mass index; CI = confidence interval.

Table 2 Independent effects of WAZ-change trajectories and childhood lifestyle factors on children's adiposity measures at four years old (imputed data).

	Weight ᴪ	BMI	Waist circumference	WHtR	Biceps circumference	Subcutaneous fat
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Model 1a-1h ζ						
WAZCT ǂ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**0.90 (0.37, 1.44)****	**0.93 (0.49, 1.37)*****	**1.90 (0.68, 3.12)****	0.01 (0.00, 0.02)	**1.05 (0.62, 1.48)*****	**2.57 (1.13, 4.01)****
FR	**0.46 (0.09, 0.83)***	**0.52 (0.22, 0.83)****	**1.03 (0.22, 1.85)***	0.00 (0.00, 0.01)	**0.54 (0.25, 0.83)*****	**1.41 (0.47, 2.36)****
EF	**0.71 (0.36, 1.06)*****	**0.72 (0.44, 1.00)*****	**1.65 (0.88, 2.42)*****	**0.01 (0.00, 0.02)***	**0.69 (0.41, 0.96)*****	**1.79 (0.87, 2.71)*****
SR	**-0.65 (-1.09, -0.21)****	**-0.69 (-1.05, -0.33)*****	**-1.63 (-2.58, -0.69)****	**-0.01 (-0.02, 0.00)***	**-0.60 (-0.95, -0.26)****	-0.90 (-2.09, 0.29)
FF	**-0.51 (-0.92, -0.09)***	**-0.56 (-0.90, -0.21)****	**-1.19 (-2.12, -0.25)***	0.00 (-0.01, 0.00)	**-0.58 (-0.91, -0.25)****	**-1.41 (-2.53, -0.28)***
Outdoor playtime	0.03 (-0.08, 0.15)	0.01 (-0.09, 0.10)	-0.15 (-0.42, 0.13)	0.00 (0.00, 0.00)	-0.01 (-0.11, 0.09)	0.09 (-0.23, 0.40)
Media time	0.11 (-0.15, 0.37)	0.10 (-0.12, 0.33)	0.28 (-0.34, 0.90)	0.00 (0.00, 0.01)	**0.26 (0.03, 0.49)***	0.31 (-0.43, 1.06)
Total sleep time	0.24 (-0.10, 0.58)	0.22 (-0.07, 0.52)	0.60 (-0.19, 1.40)	0.01 (0.00, 0.01)	0.19 (-0.10, 0.49)	0.76 (-0.20, 1.71)
Model 2 ξ						
Model 2a						
WAZCT ǂ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**0.83 (0.30, 1.36)****	**0.82 (0.38, 1.26)*****	**1.70 (0.47, 2.92)****	0.01 (0.00, 0.02)	**0.92 (0.50, 1.35)*****	**2.25 (0.81, 3.69)****
FR	**0.41 (0.04, 0.78)***	**0.44 (0.14, 0.74)****	**0.88 (0.05, 1.70)***	0.00 (0.00, 0.01)	**0.44 (0.16, 0.72)****	**1.20 (0.24, 2.15)***
Model 2b						
WAZCT ǂ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**0.72 (0.19, 1.24)****	**0.69 (0.25, 1.12)****	**1.37 (0.15, 2.59)***	0.01 (-0.01, 0.02)	**0.81 (0.39, 1.23)*****	**1.96 (0.52, 3.41)****
EF	**0.64 (0.29, 1.00)*****	**0.64 (0.35, 0.92)*****	**1.45 (0.66, 2.25)*****	0.01 (0.00, 0.01)	**0.60 (0.33, 0.87)*****	**1.58 (0.64, 2.53)****
Model 2c						
WAZCT ǂ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**0.81 (0.28, 1.33)****	**0.79 (0.35, 1.23)*****	**1.58 (0.37, 2.79)***	0.01 (0.00, 0.02)	**0.92 (0.49, 1.34)*****	**2.39 (0.93, 3.85)****
SR	**-0.60 (-1.05, -0.15)***	**-0.62 (-0.99, -0.25)****	**-1.50 (-2.47, -0.53)****	-0.01 (-0.02, 0.00)	**-0.53 (-0.87, -0.19)****	-0.76 (-1.98, 0.45)
Model 2d						
WAZCT ǂ						

Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**0.79 (0.25, 1.33)****	**0.78 (0.33, 1.23)****	**1.62 (0.37, 2.86)***	0.01 (0.00, 0.02)	**0.89 (0.45, 1.32)*****	**2.21 (0.74, 3.69)****
FF	**-0.44 (-0.87, -0.01)***	**-0.46 (-0.82, -0.11)***	-0.97 (-1.94, -0.01)	0.00 (-0.01, 0.01)	**-0.48 (-0.81, -0.15)****	-1.13 (-2.29, 0.03)

BMI = body mass index; CI = confidence interval; EF = enjoyment of food; FF = food fussiness; FR = food responsiveness; SR = satiety responsiveness; WHtR = waist-to-height ratio; WAZCT = WAZ-change trajectories, i.e. trajectory for change of weight-for-age z-score.

[ψ]Adjusted child's height at four years old.

[ζ]Examined the effect of WAZ-change trajectory and each interested lifestyle factor on each adiposity measure with adjusting for baseline family income, gestational age of the child at delivery, maternal pre-pregnancy BMI, paternal BMI, newborn weight at the first three days, sex and energy intake at six months. Note, each lifestyle factor was analyzed solitarily, e.g. in Model 1a, we only analyzed WAZ-change trajectory and in Model 1b only analyzed food responsiveness (FR) with adjusting for confounders.

[ξ]Tested the independent effect of WAZ-change trajectory and each childhood lifestyle factors (i.e. four eating behaviors) which reached statistic significance in model 1, with adjusting for characteristic confounding factors the same as Model 1. Note, four subscales of eating behaviors were analyzed separately, e.g. in Model 2a, both WAZ-change trajectories and food responsiveness (FR) were included in the model to test their independent effects on adiposity indicators.

[ǂ]Early infancy rapid vs steady WAZ-change trajectory.

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Table 3 Combined effects of WAZ-change trajectories and four subscales of eating behaviors on children's adiposity measures at four years old (imputed data).

	Weight ᴪ	BMI	Waist circumference	WHtR	Biceps circumference	Subcutaneous fat
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Model a ζ,1						
Steady & lower FR	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Steady & higher FR	0.14 (-0.70, 0.98)	0.24 (-0.47, 0.94)	0.18 (-1.77, 2.12)	-0.01 (-0.02, 0.01)	0.18 (-0.49, 0.85)	0.96 (-1.28, 3.20)
Rapid & lower FR	0.62 (-0.11, 1.35)	0.64 (0.02, 1.25)	0.94 (-0.75, 2.63)	0.00 (-0.01, 0.02)	0.59 (0.00, 1.18)	1.56 (-0.41, 3.54)
Rapid & higher FR	**1.24 (0.51, 1.97)****	**1.31 (0.73, 1.90)****	**2.76 (1.15, 4.36)****	0.01 (0.00, 0.02)	**1.49 (0.93, 2.05)*****	**3.99 (2.09, 5.89)*****
Model b ζ,1						
Steady & lower EF	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Steady & higher EF	**1.13 (0.32, 1.95)***	**1.08 (0.40, 1.77)***	2.30 (0.41, 4.19)	0.02 (0.00, 0.03)	0.83 (0.16, 1.49)	2.48 (0.28, 4.68)
Rapid & lower EF	**1.30 (0.58, 2.02)****	**1.25 (0.64, 1.85)****	**2.63 (0.94, 4.32)***	0.02 (0.00, 0.03)	**1.21 (0.61, 1.81)*****	**3.32 (1.32, 5.32)****
Rapid & higher EF	**1.43 (0.74, 2.12)****	**1.46 (0.90, 2.01)****	**3.02 (1.47, 4.57)*****	0.01 (0.00, 0.03)	**1.48 (0.94, 2.03)*****	**3.73 (1.89, 5.57)*****
Model c ζ,1						
Steady & lower SR	1.04 (0.17, 1.91)	0.98 (0.25, 1.71)	1.82 (-0.11, 3.75)	0.01 (0.00, 0.03)	0.71 (0.03, 1.40)	1.44 (-0.83, 3.71)
Steady & higher SR	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid & lower SR	**1.60 (0.89, 2.30)*****	**1.59 (1.01, 2.17)*****	**3.18 (1.57, 4.78)*****	0.02 (0.00, 0.03)	**1.55 (0.99, 2.12)*****	**3.75 (1.83, 5.67)*****
Rapid & higher SR	**1.06 (0.33, 1.78)***	**1.04 (0.44, 1.65)****	2.09 (0.43, 3.75)	0.01 (0.00, 0.03)	**1.07 (0.49, 1.66)*****	2.44 (0.47, 4.41)
Model d ζ,1						
Steady & lower FF	0.33 (-0.57, 1.24)	0.48 (-0.28, 1.23)	0.95 (-1.07, 2.97)	0.00 (-0.02, 0.02)	0.47 (-0.23, 1.17)	1.36 (-0.95, 3.66)
Steady & higher FF	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid & lower FF	**1.16 (0.43, 1.90)***	**1.24 (0.64, 1.83)*****	**2.62 (1.00, 4.24)***	0.01 (0.00, 0.03)	**1.36 (0.79, 1.93)*****	**3.51 (1.58, 5.43)*****
Rapid & higher FF	0.88 (0.12, 1.64)	**0.98 (0.35, 1.61)***	1.91 (0.17, 3.64)	0.01 (-0.01, 0.02)	**1.06 (0.46, 1.66)****	2.62 (0.59, 4.65)

BMI = body mass index; CI = confidence interval; EF = enjoyment of food; FF = food fussiness; FR = food responsiveness; SR = satiety responsiveness; WHtR = waist-to-height ratio.

ᴪAdjusted child's height at four years old.

ζAdjusted for baseline family income, gestational age of the child at delivery, maternal pre-pregnancy BMI, paternal BMI, newborn weight at the first three days, sex and energy intake at six months.

[1]The reference group was children with steady growth trajectory and lower food responsiveness score (model a), lower enjoyment of food score (model b), higher satiety responsiveness score (model c) or higher food fussiness score (model d), which were more likely to have a lower risk of overweight/obesity. Low eating behavior scores present the values less than the median levels of each subscale and the high scores present the values more than the median levels of each subscale.

* $P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

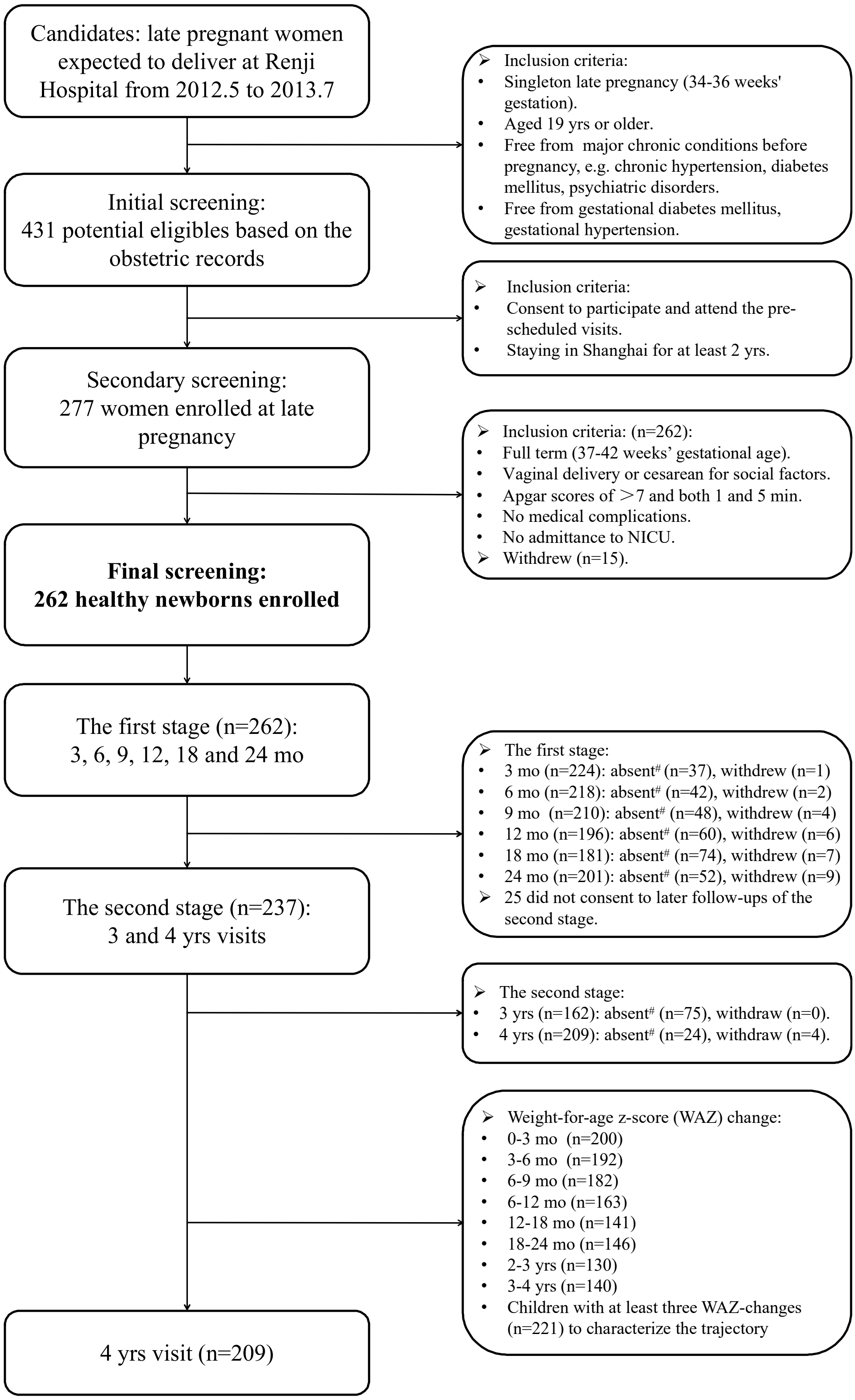

Figure 1. Flow chart of the study participants. #includes non follow-up children and follow-up children with exceeding our critical following-age-window.

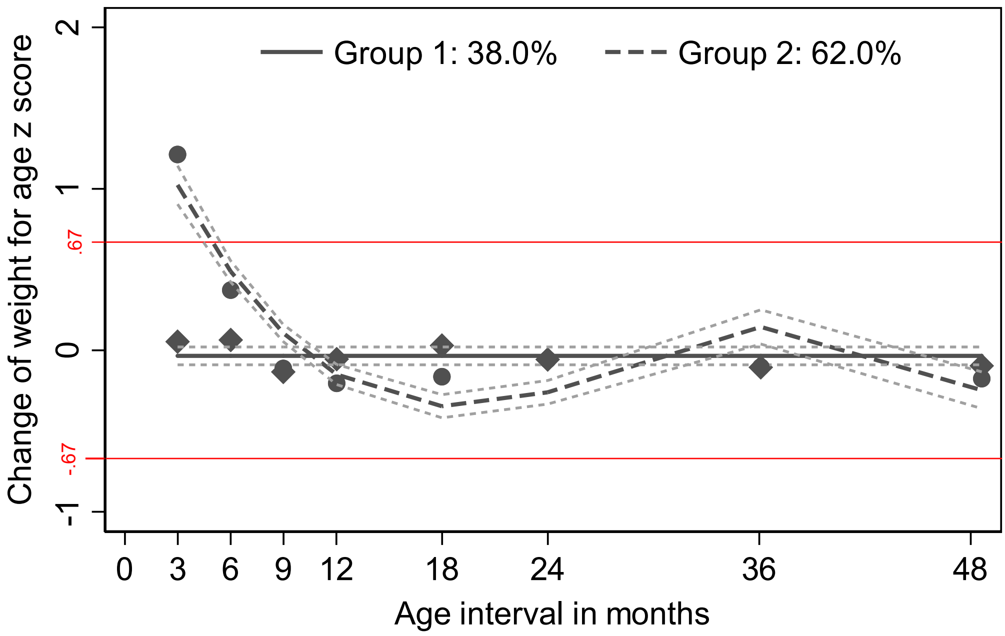

Figure 2. WAZ-change trajectories with 95% confidence intervals across the first four years.

Note, WAZ-change indicates the change in weight-for-age z-score; the solid line represents steady WAZ-change (38.0%, n=84), and the dash line represents early infancy rapid WAZ-change (62.0%, n=137). The vertical axis indicates the absolute WAZ-change from the first age point to the second age point with positive values representing WAZ gain and negative values representing WAZ loss, and the +0.67 cut-off means rapid WAZ-change. The horizontal axis indicates the second age point of each WAZ-change month interval, e.g. three-month is the second age point of 0-3 month interval, six-month is the second age point of 3-6 months interval.

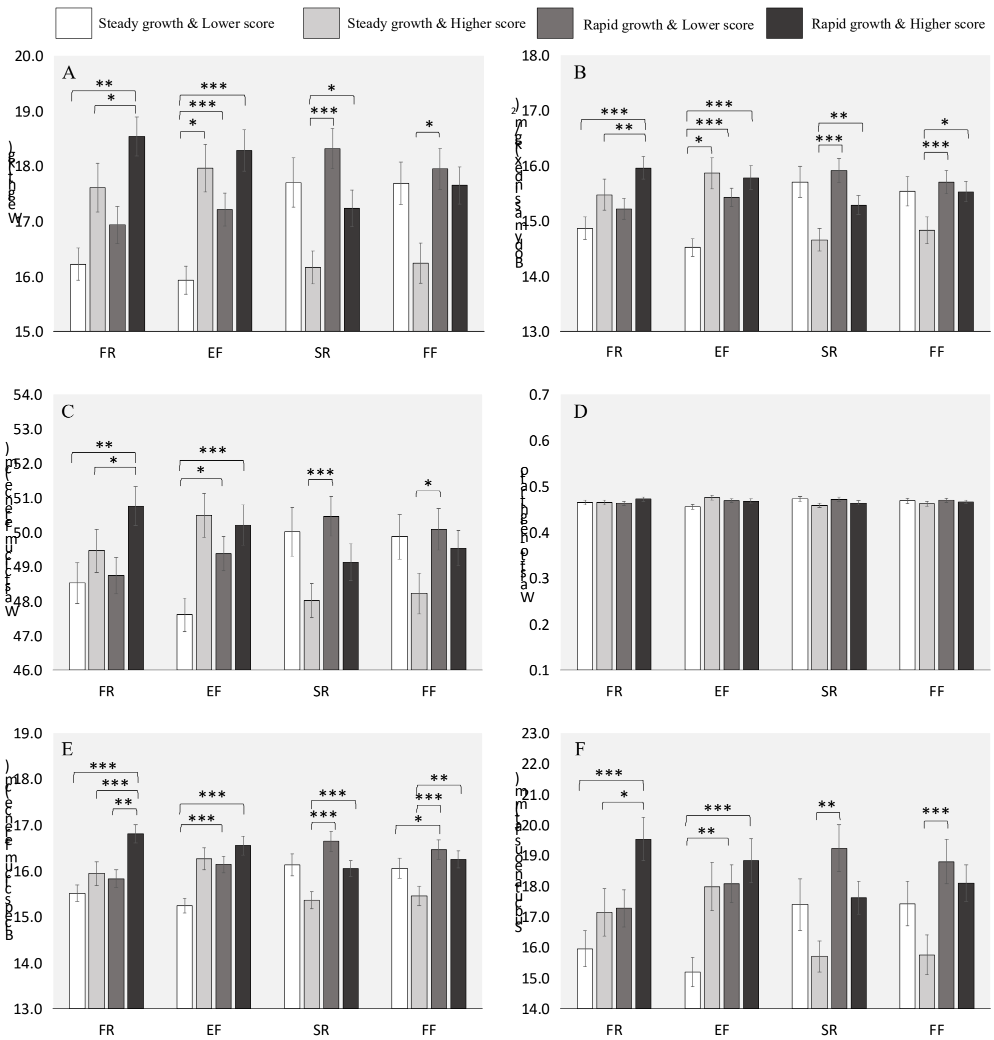

Figure 3. Combined effects of WAZ-change trajectories and four subscales of eating behaviors on children's adiposity measures at four years (imputed data).

Note, EF indicates enjoyment of food; FF indicates food fussiness; FR indicates food responsiveness; SR indicates satiety responsiveness. Low scores present the values less than the median levels of each subscale and the high scores present the values more than the median levels of each subscale.

The Y-axes are: A, weight (kg); B, body mass index (kg/m^2); C, waist circumference (cm); D, waist-to-height ratio; E, biceps circumference (cm); F, subcutaneous fat (mm) respectively. The X-axes are the combined groups with the two distinct WAZ-change trajectories and the dichotomy variable of four subscales for eating behaviors (FR, EF, SR and FF). The white bars indicate children with steady growth trajectory and lower score of the four eating behaviors, the very light black bars indicate children with steady growth trajectory and higher score of the four eating behaviors, the moderate black bars indicate children with early infancy rapid growth trajectory and lower score of the four eating behaviors, and the dark black bars indicate children with early infancy rapid growth trajectory and higher score of the four eating behaviors. Note, EF indicates enjoyment of food; FF indicates food fussiness; FR indicates food responsiveness; SR indicates satiety responsiveness. Low scores present the values less than the median levels of each subscale and the high scores present the values more than the median levels of each subscale.

Error bars represent mean ± s.e.m.

* $P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Table S1 Absolute WAZ-change and weight increment of the steady and early infancy rapid growth trajectory groups in each age interval (non-imputed data).

Age interval	WAZ-change ≥0.67 n (%)	Absolute WAZ-change				Weight increment (kg)			
		Total (n=221)	Steady (n=84)	Early infancy rapid (n=137)	*P* value	Total (n=221)	Steady (n=84)	Early infancy rapid (n=137)	*P* value
0-3 mo	108 (54.0)	0.80 (0.67, 0.93)	0.00 (-0.13, 0.13)	1.27 (1.14, 1.40)	**< 0.001**	3.37 (3.27, 3.46)	2.89 (2.78, 3.01)	3.65 (3.55, 3.76)	**< 0.001**
3-6 mo	44 (22.9)	0.26 (0.19, 0.34)	0.01 (-0.10, 0.12)	0.40 (0.31, 0.49)	**< 0.001**	1.77 (1.69, 1.84)	1.49 (1.40, 1.57)	1.92 (1.83, 2.02)	**< 0.001**
6-9 mo	9 (5.0)	-0.12 (-0.19, -0.05)	-0.16 (-0.29, -0.03)	-0.10 (-0.18, -0.02)	0.412	1.00 (0.93, 1.07)	0.90 (0.79, 1.01)	1.06 (0.98, 1.14)	**0.025**
9-12 mo	6 (3.7)	-0.15 (-0.22, -0.08)	-0.05 (-0.15, 0.06)	-0.21 (-0.30, -0.12)	**0.025**	0.71 (0.63, 0.78)	0.78 (0.66, 0.89)	0.66 (0.57, 0.76)	0.129
12-18 mo	10 (7.1)	-0.09 (-0.17, -0.01)	0.10 (-0.03, 0.23)	-0.21 (-0.31, -0.11)	**< 0.001**	1.32 (1.21, 1.42)	1.48 (1.31, 1.65)	1.22 (1.08, 1.35)	**0.016**
18-24 mo	7 (4.8)	-0.06 (-0.13, 0.01)	-0.06 (-0.17, 0.05)	-0.05 (-0.15, 0.04)	0.896	1.27 (1.17, 1.38)	1.18 (1.03, 1.32)	1.32 (1.18, 1.47)	0.193
2-3 yrs	5 (3.9)	-0.10 (-0.18, -0.03)	-0.13 (-0.22, -0.04)	-0.09 (-0.20, 0.03)	0.602	2.39 (2.22, 2.56)	2.11 (1.97, 2.25)	2.56 (2.31, 2.82)	**0.010**
3-4 yrs	4 (2.9)	-0.15 (-0.21, -0.08)	-0.06 (-0.16, 0.04)	-0.20 (-0.29, -0.11)	**0.042**	2.19 (2.04, 2.35)	2.24 (2.03, 2.46)	2.16 (1.94, 2.37)	0.597

Note, WAZ-change, change of weight-for-age z-score between adjacent measurement points with positive differences representing WAZ gain and negative differences representing WAZ loss.

Table S2 Maternal-child characteristics between the two identified growth trajectories (non-imputed data).

	All (n=221)	Steady (n=84)	Rapid (n=137)	t/χ^2	*P* value
Demographic Factors					
Highest parents education				0.69	0.709
High school or lower	11 (5.0)	3 (3.6)	8 (5.8)		
College or higher	210 (95.0)	81 (96.4)	129 (94.2)		
Maternal age at birth, year	29.47 (29.04, 29.90)	29.60 (28.81, 30.39)	29.39 (28.88, 29.90)	-0.47	0.642
Gestational age, week	39.59 (39.46, 39.73)	39.89 (39.70, 40.09)	39.41 (39.24, 39.58)	-3.66	**< 0.001**
Pre-pregnancy BMI, kg/m^2	20.60 (20.25, 20.95)	20.78 (20.13, 21.42)	20.49 (20.08, 20.90)	-0.78	0.436
Paternal BMI, kg/m^2	24.52 (23.95, 25.10)	24.92 (24.22, 25.63)	24.28 (23.45, 25.10)	-1.07	0.284
Gestational weight gain, kg	16.16 (15.58, 16.74)	16.50 (15.50, 17.50)	15.95 (15.24, 16.67)	-0.90	0.368
Maternal sleep quality	85 (42.1)	30 (39.5)	55 (43.7)	0.34	0.560
Maternal state anxiety	18 (8.7)	7 (9.0)	11 (8.5)	0.01	0.912
Maternal trait anxiety	28 (13.6)	12 (15.8)	16 (12.3)	0.50	0.482
Maternal depression	27 (12.7)	9 (11.1)	18 (13.6)	0.29	0.591
Newborn					
Male	113 (51.1)	45 (53.6)	68 (49.6)	0.32	0.570
Vaginal delivery	85 (39.7)	28 (35.4)	57 (42.2)	0.96	0.328
Birth length, cm	49.92 (49.7, 50.13)	50.28 (49.92, 50.63)	49.69 (49.43, 49.95)	-2.68	**0.008**
Birth weight, kg	3.30 (3.25, 3.35)	3.48 (3.40, 3.56)	3.19 (3.13, 3.25)	-5.64	**< 0.001**
Birth BMI, kg/m^2	13.22 (13.06, 13.37)	13.74 (13.49, 14.00)	12.89 (12.71, 13.06)	-5.67	**< 0.001**
Infancy					
Exclusive breastfeeding over the first three months, Yes	88 (40.2)	37 (45.1)	51 (37.2)	1.33	0.249
Weaning time				1.23	0.268
<6 months	94 (43.1)	39 (46.4)	55 (41.0)		
6-12 months	71 (32.6)	29 (34.5)	42 (31.3)		
≥12months	47 (29.2)	20 (34.5)	27 (26.2)		
Total energy intake at 6 months, kcal/day	580.26 (558.45, 602.07)	573.78 (541.8, 605.77)	584.14 (554.68, 613.60)	0.45	0.652
Lifestyle in childhood					
Eating behaviors [a]					
FR, unit	2.76 (2.64, 2.89)	2.67 (2.48, 2.86)	2.83 (2.66, 2.99)	1.25	0.215
EF, unit	3.59 (3.47, 3.71)	3.43 (3.23, 3.64)	3.70 (3.55, 3.85)	2.16	**0.033**
SR, unit	2.66 (2.56, 2.76)	2.73 (2.57, 2.89)	2.61 (2.48, 2.74)	-1.18	0.240
FF, unit	2.67 (2.56, 2.78)	2.80 (2.65, 2.96)	2.58 (2.43, 2.73)	-2.03	**0.044**
Outdoor playtime, hour/day	3.94 (3.63, 4.25)	4.41 (3.84, 4.97)	3.63 (3.28, 3.99)	-2.42	**0.016**
Media time, hour/day [a]	1.40 (1.25, 1.54)	1.34 (1.07, 1.60)	1.43 (1.24, 1.61)	0.57	0.572
Total sleep time, hour/day [a]	11.98 (11.88, 12.08)	11.95 (11.80, 12.11)	11.99 (11.85, 12.14)	0.37	0.711
Adiposity outcomes at 4 years					
Height, cm	106.09 (105.51, 106.67)	105.38 (104.51, 106.25)	106.58 (105.81, 107.35)	2.02	**0.045**
Weight, kg	17.42 (17.06, 17.78)	16.82 (16.32, 17.33)	17.83 (17.34, 18.31)	2.77	**0.006**
BMI, kg/m^2	15.42 (15.21, 15.63)	15.11 (14.78, 15.43)	15.63 (15.36, 15.91)	2.44	**0.016**
Waist circumference, cm	49.44 (48.88, 50.00)	48.86 (48.06, 49.66)	49.85 (49.08, 50.61)	1.72	0.087
WHtR, unit	0.47 (0.46, 0.47)	0.46 (0.46, 0.47)	0.47 (0.46, 0.47)	0.78	0.438
Biceps circumference, cm	16.1 (15.90, 16.31)	15.70 (15.42, 15.99)	16.38 (16.10, 16.66)	3.28	**0.001**
Subcutaneous fat, mm	17.71 (17.04, 18.38)	16.50 (15.59, 17.41)	18.54 (17.62, 19.46)	3.02	**0.003**

BMI = body mass index; CI = confidence interval; EF = enjoyment of food; FF = Food fussiness; FR = food responsiveness; SR = satiety responsiveness; WHtR = waist-to-height ratio; WAZ = weight-for-age z-score.

[a]Average values of lifestyle factors assessed at two and four years old.

Table S3 Interactive effects of WAZ-change trajectories and four subscales of eating behaviors on children's adiposity measures at four years (imputed data).

	Weight ψ	BMI	Waist circumference	WHtR	Biceps circumference	Subcutaneous fat
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Model 1a						
WAZCT ǂ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	0.55 (-0.18, 1.27)	0.56 (-0.04, 1.17)	0.82 (-0.84, 2.48)	0 (-0.01, 0.02)	0.51 (-0.07, 1.09)	1.47 (-0.47, 3.41)
FR ζ						
Low	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High	0.25 (-0.57, 1.07)	0.33 (-0.36, 1.01)	0.31 (-1.57, 2.20)	0 (-0.02, 0.01)	0.23 (-0.42, 0.88)	1.17 (-1.00, 3.34)
WAZCT*FR	0.48 (-0.54, 1.50)	0.43 (-0.43, 1.29)	1.66 (-0.70, 4.02)	0.01 (-0.01, 0.04)	0.73 (-0.09, 1.54)	1.37 (-1.40, 4.13)
Model 1b						
WAZCT ǂ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**1.25 (0.54, 1.96)****	**1.18 (0.59, 1.77)*****	**2.52 (0.87, 4.16)****	**0.02 (0, 0.03)***	**1.12 (0.54, 1.70)*****	**3.26 (1.31, 5.21)****
EF ζ						
Low	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High	**1.20 (0.41, 1.99)****	**1.13 (0.47, 1.79)****	**2.35 (0.53, 4.17)***	**0.02 (0, 0.03)***	**0.84 (0.20, 1.49)***	**2.72 (0.60, 4.84)***
WAZCT*FR	-0.98 (-1.99, 0.03)	**-0.86 (-1.71, -0.02)***	-1.83 (-4.17, 0.52)	-0.02 (-0.04, 0)	-0.52 (-1.36, 0.31)	-2.16 (-4.95, 0.64)
Model 1c						
WAZCT ǂ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	0.56 (-0.21, 1.32)	0.58 (-0.06, 1.22)	1.29 (-0.43, 3.01)	0 (-0.01, 0.02)	**0.82 (0.21, 1.43)****	**2.35 (0.28, 4.41)***
SR ζ						
Low	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High	**-1.01 (-1.86, -0.17)***	**-0.94 (-1.65, -0.24)****	**-1.88 (-3.73, -0.02)***	-0.01 (-0.03, 0)	-0.64 (-1.31, 0.03)	-1.32 (-3.51, 0.88)
WAZCT*FR	0.41 (-0.64, 1.46)	0.35 (-0.54, 1.24)	0.69 (-1.65, 3.04)	0.01 (-0.01, 0.03)	0.12 (-0.73, 0.95)	-0.14 (-2.96, 2.68)
Model 1d						
WAZCT ǂ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**0.79 (0.03, 1.56)***	**0.71 (0.06, 1.36)***	1.56 (-0.19, 3.31)	0.01 (-0.01, 0.03)	**0.86 (0.24, 1.47)****	**2.14 (0.09, 4.19)***
FF ζ						
Low	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High	-0.35 (-1.23, 0.53)	-0.47 (-1.20, 0.27)	-1.05 (-3.00, 0.91)	0 (-0.02, 0.02)	-0.41 (-1.09, 0.27)	-1.28 (-3.52, 0.96)

WAZCT*FR	0.03 (-1.05, 1.11)	0.18 (-0.73, 1.10)	0.27 (-2.19, 2.72)	0 (-0.02, 0.02)	0.08 (-0.78, 0.93)	0.27 (-2.59, 3.13)

BMI = body mass index; CI = confidence interval; EF = enjoyment of food; FF = food fussiness; FR = food responsiveness; SR = satiety responsiveness; WHtR = waist-to-height ratio; WAZCT = WAZ-change trajectories, i.e. trajectory for change of weight-for-age z-score.

[ψ]Adjusted children's height at four years old.

[ζ]Low scores present the values less than the median levels of each subscale and the high scores present the values more than the median levels of each subscale.

Note, all models were adjusted for baseline family income, gestational age of the child at delivery, maternal pre-pregnancy BMI, paternal BMI, newborn weight at the first three days, sex and energy intake at six months.

* $P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Table S4 Independent effects of WAZ-change trajectories and childhood lifestyle factors on children's adiposity measures at four years (non imputed data).

	Weight ψ	BMI	Waist circumference	WHtR	Biceps circumference	Subcutaneous fat
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Model 1a-1h ζ						
WAZCT ǂ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**0.86 (0.30, 1.43)****	**0.89 (0.42, 1.35)*****	**2.07 (0.81, 3.33)****	0.01 (0.02, 0.15)	**1.00 (0.56, 1.44)*****	**2.16 (0.62, 3.7)****
FR	**0.63 (0.27, 0.99)****	**0.63 (0.32, 0.93)*****	**1.59 (0.74, 2.44)*****	0.01 (0.02, 0.19)	**0.67 (0.35, 0.99)*****	**1.56 (0.46, 2.65)****
EF	**0.59 (0.24, 0.93)*****	**0.57 (0.28, 0.86)*****	**1.35 (0.53, 2.17)****	0.01 (0.01, 0.15)	**0.50 (0.19, 0.81)****	**1.39 (0.34, 2.45)***
SR	-0.30 (-0.73, 0.13)	-0.34 (-0.71, 0.03)	-0.73 (-1.79, 0.32)	0.00 (0.01, 0.00)	-0.30 (-0.69, 0.10)	0.04 (-1.32, 1.4)
FF	**-0.42 (-0.82, -0.02)***	**-0.45 (-0.79, -0.11)***	-0.79 (-1.76, 0.18)	0.00 (0.01, -0.03)	-0.35 (-0.72, 0.02)	-1.12 (-2.34, 0.11)
Outdoor playtime	0.03 (-0.09, 0.15)	0.00 (-0.10, 0.11)	-0.15 (-0.42, 0.12)	0.00 (0.00, -0.04)	-0.02 (-0.12, 0.08)	0.09 (-0.25, 0.43)
Media time	0.07 (-0.28, 0.42)	0.09 (-0.22, 0.39)	0.33 (-0.49, 1.14)	0.00 (0.01, 0.01)	**0.31 (0.01, 0.60)***	0.4 (-0.61, 1.42)
Total sleep time	0.3 (-0.05, 0.66)	0.28 (-0.04, 0.59)	**0.85 (0.01, 1.69)***	0.01 (0.01, 0.16)	0.24 (-0.07, 0.55)	0.97 (-0.05, 1.98)
Model 2 ξ						
Model 2a						
WAZCT ǂ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**0.81 (0.25, 1.36)****	**0.76 (0.29, 1.23)****	**1.64 (0.31, 2.98)***	0.01 (0.02, 0.15)	**0.83 (0.34, 1.32)****	**2.36 (0.67, 4.05)****
FR	**0.59 (0.23, 0.95)****	**0.56 (0.26, 0.86)*****	**1.46 (0.61, 2.32)****	0.01 (0.02, 0.18)	**0.58 (0.27, 0.89)*****	**1.35 (0.27, 2.42)***
Model 2b						
WAZCT ǂ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**0.73 (0.18, 1.28)***	**0.67 (0.20, 1.14)****	1.36 (-0.01, 2.73)	0.01 (0.02, 0.13)	**0.76 (0.26, 1.25)****	**2.13 (0.43, 3.83)***
EF	**0.55 (0.19, 0.90)****	**0.51 (0.22, 0.80)****	**1.20 (0.35, 2.06)****	0.00 (0.01, 0.11)	**0.46 (0.15, 0.77)****	**1.24 (0.18, 2.29)***
Model 2c						
WAZCT ǂ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**0.89 (0.33, 1.45)****	**0.82 (0.35, 1.30)****	**1.73 (0.32, 3.14)***	0.01 (0.02, 0.16)	**0.89 (0.39, 1.40)****	**2.61 (0.85, 4.37)****
SR	-0.32 (-0.76, 0.12)	-0.34 (-0.70, 0.03)	-0.72 (-1.8, 0.35)	0.00 (0.01, 0.02)	-0.31 (-0.70, 0.08)	-0.05 (-1.4, 1.3)
Model 2d						
WAZCT ǂ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**0.80 (0.22, 1.37)****	**0.75 (0.26, 1.24)****	**1.54 (0.13, 2.96)***	0.01 (0.02, 0.16)	**0.82 (0.31, 1.33)****	**2.3 (0.58, 4.02)****

FF	-0.36 (-0.78, 0.05)	**-0.39 (-0.74, -0.04)***	-0.64 (-1.65, 0.36)	0.00 (0.01, 0.00)	-0.30 (-0.66, 0.07)	-0.91 (-2.14, 0.32)

BMI = body mass index; CI = confidence interval; EF = enjoyment of food; FF = food fussiness; FR = food responsiveness; SR = satiety responsiveness; WHtR = waist-to-height ratio; WAZCT = WAZ-change trajectories, i.e. trajectory for change of weight-for-age z-score.

$^{\psi}$Adjusted children's height at four years old.

$^{\zeta}$Examined the effect of WAZ-change trajectory and each interested lifestyle factor on each adiposity outcome with adjusting for baseline family income, gestational age of the child at delivery, maternal pre-pregnancy BMI, paternal BMI, newborn weight at the first three days, sex and energy intake at six months. Note, each lifestyle factor was analyzed solitarily, e.g. in Model 1a, we only analyzed WAZ-change trajectory with adjusting for confounders and in Model 1b only analyzed food responsiveness (FR) with adjusting for confounders.

$^{\xi}$ Tested the independent effect of WAZ-change trajectory and each childhood lifestyle factors (i.e. four eating behaviors) which reached statistic significance in model 1, with adjusting for characteristic confounding factors same as Model 1. Note, four subscales of eating behaviors were analyzed separately, e.g. in Model 2a, both WAZ-change trajectories and food responsiveness (FR) were included in the model to test their independent effects on adiposity indicators.

ǂ Early infancy rapid vs steady WAZ-change trajectory.

* $P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Table S5 Combined effects of WAZ-change trajectories and four subscales of eating behaviors on children's adiposity measures at four years (non imputed data).

	Weight ψ	BMI	Waist circumference	WHtR	Biceps circumference	Subcutaneous fat
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Model a ζ,1						
Steady & lower FR	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Steady & higher FR	0.13 (-0.71, 0.96)	0.14 (-0.57, 0.86)	0.23 (-1.78, 2.24)	-0.01 (-0.03, 0.01)	-0.09 (-0.80, 0.63)	-0.04 (-2.45, 2.38)
Rapid & lower FR	0.61 (-0.14, 1.36)	0.57 (-0.07, 1.22)	0.93 (-0.87, 2.74)	0.00 (-0.02, 0.02)	0.37 (-0.28, 1.01)	1.00 (-1.17, 3.17)
Rapid & higher FR	**1.30 (0.51, 2.09)****	**1.29 (0.64, 1.94)****	**3.14 (1.31, 4.97)****	0.01 (0.00, 0.03)	**1.46 (0.81, 2.11)*****	**4.34 (2.12, 6.57)****
Model b ζ,1						
Steady & lower EF	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Steady & higher EF	0.73 (-0.11, 1.56)	0.66 (-0.06, 1.38)	1.94 (-0.12, 4.00)	0.01 (-0.01, 0.03)	0.48 (-0.27, 1.23)	1.82 (-0.73, 4.36)
Rapid & lower EF	0.93 (0.24, 1.62)	**0.88 (0.28, 1.47)***	1.90 (0.19, 3.60)	0.01 (0.00, 0.03)	**0.86 (0.23, 1.48)***	2.73 (0.63, 4.84)
Rapid & higher EF	**1.34 (0.61, 2.07)****	**1.26 (0.65, 1.87)*****	**2.96 (1.22, 4.70)****	0.01 (0.00, 0.03)	**1.30 (0.66, 1.94)****	**3.55 (1.38, 5.72)****
Model c ζ,1						
Steady & lower SR	0.72 (-0.08, 1.53)	0.67 (-0.02, 1.36)	0.88 (-1.19, 2.95)	0.00 (-0.02, 0.02)	0.53 (-0.21, 1.28)	0.58 (-1.97, 3.13)
Steady & higher SR	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid & lower SR	**1.46 (0.71, 2.21)****	**1.38 (0.75, 2.02)*****	**2.60 (0.70, 4.50)***	0.01 (0.00, 0.03)	**1.28 (0.60, 1.96)****	**3.48 (1.12, 5.83)***
Rapid & higher SR	**1.04 (0.31, 1.76)***	**0.95 (0.33, 1.57)***	1.84 (-0.01, 3.69)	0.01 (-0.01, 0.03)	**1.05 (0.39, 1.72)***	2.37 (0.09, 4.64)
Model d ζ,1						
Steady & lower FF	0.72 (-0.12, 1.56)	0.78 (0.08, 1.48)	1.89 (-0.12, 3.89)	0.01 (-0.01, 0.02)	0.69 (-0.04, 1.42)	2.38 (-0.04, 4.80)
Steady & higher FF	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid & lower FF	**1.17 (0.42, 1.91)***	**1.17 (0.55, 1.79)****	2.29 (0.52, 4.06)	0.01 (-0.01, 0.03)	**1.14 (0.50, 1.79)****	**3.70 (1.53, 5.86)****
Rapid & higher FF	**1.24 (0.45, 2.04)***	**1.19 (0.53, 1.86)****	**2.80 (0.90, 4.70)***	0.01 (0.00, 0.03)	**1.25 (0.56, 1.95)****	**3.32 (1.02, 5.62)***

BMI = body mass index; CI = confidence interval; EF = enjoyment of food; FF = food fussiness; FR = food responsiveness; SR = satiety responsiveness; WHtR = waist-to-height ratio.

ψAdjusted children's height at four years old.

ζAdjusted for baseline family income, gestational age of the child at delivery, maternal pre-pregnancy BMI, paternal BMI, newborn weight at the first three days, sex and energy intake at six months.

[1]The reference group was children with steady growth trajectory and lower food responsiveness score (model a), lower enjoyment of food score (model b), higher satiety responsiveness score (model c) or higher food fussiness score (model d), which were more likely to have a lower risk of overweight/obesity. Low eating behavior scores present the values less than the median levels of each subscale and the high scores present the values more than the median levels of each subscale.

* $P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Table S6 Interactive effects of WAZ-change trajectories and four subscales of eating behaviors on children's adiposity measures at four years (non imputed data).

	Weight ᴪ	BMI	Waist circumference	WHtR	Biceps circumference	Subcutaneous fat
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Model 1a						
WAZCT ᵻ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	0.55 (-0.18, 1.29)	0.52 (-0.10, 1.15)	0.89 (-0.85, 2.63)	0 (-0.02, 0.02)	0.29 (-0.34, 0.93)	1.03 (-1.11, 3.18)
FR ζ						
Low	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High	0.23 (-0.58, 1.03)	0.24 (-0.45, 0.92)	0.33 (-1.57, 2.22)	-0.01 (-0.02, 0.01)	-0.03 (-0.72, 0.66)	0.16 (-2.17, 2.50)
WAZCT*FR	0.55 (-0.50, 1.60)	0.54 (-0.37, 1.45)	1.97 (-0.54, 4.48)	0.02 (0, 0.04)	**1.17 (0.25, 2.08)***	**3.25 (0.14, 6.35)***
Model 1b						
WAZCT ᵻ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**0.91 (0.25, 1.58)****	**0.85 (0.27, 1.42)****	**1.89 (0.28, 3.50)***	0.01 (0, 0.03)	**0.8 (0.20, 1.39)****	**2.92 (0.89, 4.95)****
EF ζ						
Low	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High	**0.82 (0.03, 1.61)***	**0.74 (0.06, 1.42)***	**1.94 (0.03, 3.86)***	0.01 (-0.01, 0.03)	0.54 (-0.17, 1.25)	2.20 (-0.21, 4.62)
WAZCT*FR	-0.32 (-1.34, 0.70)	-0.29 (-1.18, 0.59)	-0.78 (-3.27, 1.72)	-0.01 (-0.03, 0.02)	-0.04 (-0.97, 0.88)	-1.29 (-4.44, 1.87)
Model 1c						
WAZCT ᵻ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	**0.81 (0.04, 1.59)***	**0.77 (0.10, 1.44)***	1.79 (-0.17, 3.75)	0.01 (-0.01, 0.03)	**0.8 (0.07, 1.52)***	**3.21 (0.72, 5.69)***
SR ζ						
Low	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High	-0.64 (-1.41, 0.13)	-0.58 (-1.24, 0.09)	-0.89 (-2.83, 1.06)	0 (-0.02, 0.02)	-0.41 (-1.13, 0.30)	-0.41 (-2.86, 2.04)
WAZCT*FR	0.12 (-0.89, 1.13)	0.07 (-0.80, 0.95)	-0.02 (-2.58, 2.54)	0 (-0.03, 0.02)	0.09 (-0.85, 1.03)	-0.97 (-4.20, 2.25)
Model 1d						
WAZCT ᵻ						
Steady	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Rapid	0.48 (-0.30, 1.26)	0.41 (-0.26, 1.09)	0.48 (-1.40, 2.36)	0.01 (-0.01, 0.02)	0.47 (-0.23, 1.17)	1.54 (-0.81, 3.89)
FF ζ						
Low	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High	-0.66 (-1.47, 0.16)	**-0.70 (-1.38, -0.02)***	-1.84 (-3.75, 0.07)	0 (-0.02, 0.01)	-0.58 (-1.29, 0.13)	-2.20 (-4.57, 0.17)

WAZCT*FR	0.63 (-0.45, 1.71)	0.64 (-0.28, 1.55)	2.16 (-0.39, 4.72)	0.01 (-0.02, 0.03)	0.62 (-0.33, 1.57)	1.66 (-1.53, 4.85)

BMI = body mass index; CI = confidence interval; EF = enjoyment of food; FF = food fussiness; FR = food responsiveness; SR = satiety responsiveness; WHtR = waist-to-height ratio; WAZCT = WAZ-change trajectories, i.e. trajectory for change of weight-for-age z-score.

$^{\psi}$Adjusted children's height at four years old.

$^{\zeta}$Low scores present the values less than the median levels of each subscale and the high scores present the values more than the median levels of each subscale.

Note, all models were adjusted for baseline family income, gestational age of the child at delivery, maternal pre-pregnancy BMI, paternal BMI, newborn weight at the first three days, sex and energy intake at six months.

* $P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

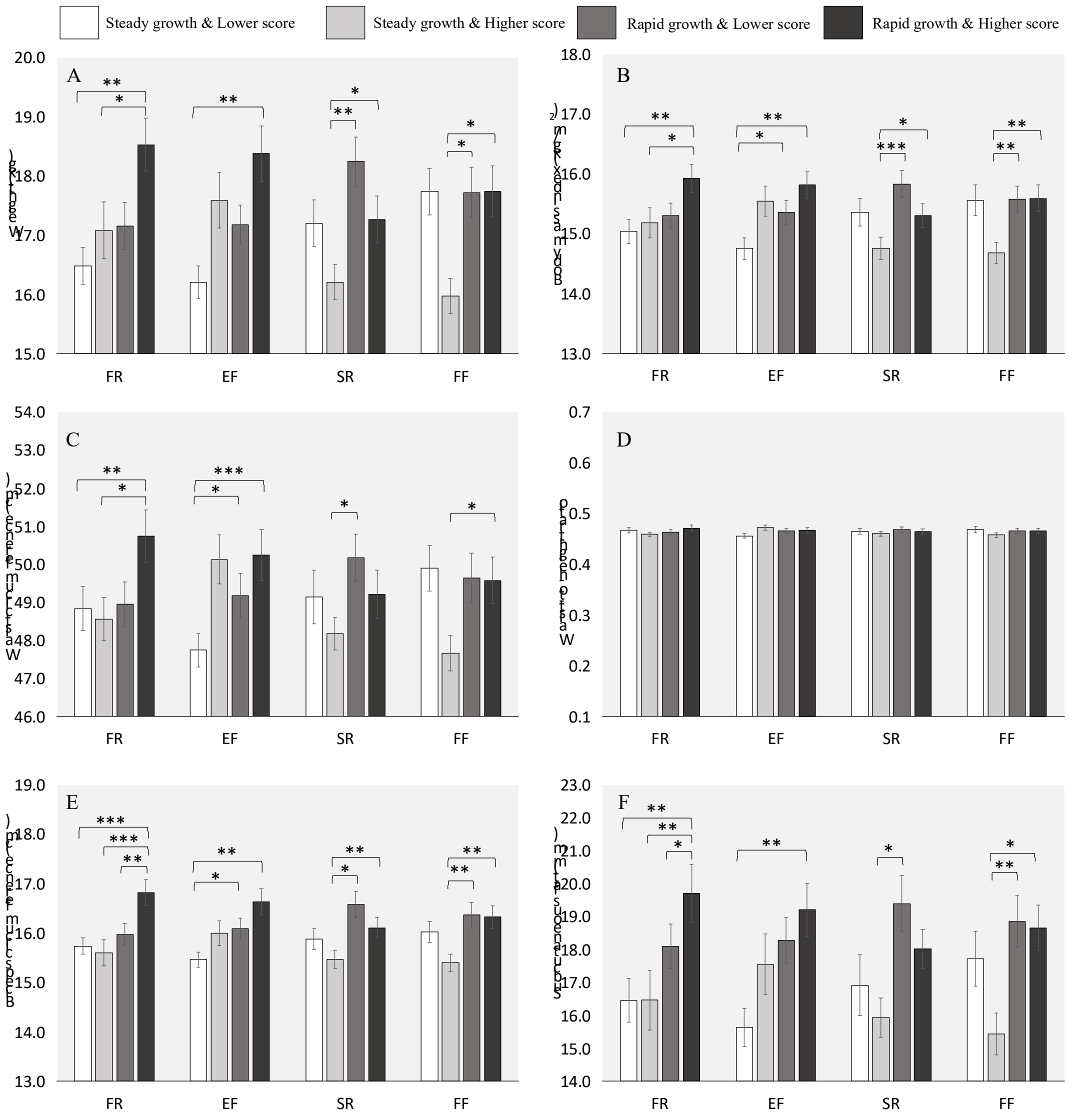

Figure S1 Combined effects of WAZ-change trajectories and four subscales of eating behaviors on children's adiposity measures at four years (non imputed data).

Note, EF indicates enjoyment of food; FF indicates food fussiness; FR indicates food responsiveness; SR indicates satiety responsiveness. Low scores present the values less than the median levels of each subscale and the high scores present the values more than the median levels of each subscale.

The Y-axes are: A, weight (kg); B, body mass index (kg/m^2); C, waist circumference (cm); D, waist-to-height ratio; E, biceps circumference (cm); F, subcutaneous fat (mm) respectively. The X-axes are the combined groups with the two distinct WAZ-change trajectories and the dichotomy variable of four subscales for eating behaviors (FR, EF, SR and FF). The white bars indicate children with steady growth trajectory and lower score of the four eating behaviors, the very light black bars indicate children with steady growth trajectory and higher score of the four eating behaviors, the moderate black bars indicate children with early infancy rapid growth trajectory and lower score of the four eating behaviors, and the dark black bars indicate children with early infancy rapid growth trajectory and higher score of the four eating behaviors. Note, EF indicates enjoyment of food; FF indicates food fussiness; FR indicates food responsiveness; SR indicates satiety responsiveness. Low scores present the values less than the median levels of each subscale and the high scores present the values more than the median levels of each subscale.

Error bars represent mean ± s.e.m.

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.