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Combined effects of weight change trajectories and lifestyle factors on adiposity status at four years of age, a birth cohort study

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Research

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Abstract

Background : Prior studies suggested that rapid weight change in infancy is associated with increased childhood and adulthood weight status. However, the weight change trajectory in early life over time and the extent to which childhood lifestyle behaviors may modify the risk of infant rapid weight change are not completely understood. Our aims were to characterize weight change trajectory early in life and explore its independent/combined effects with childhood lifestyle factors on adiposity outcomes at four years of age.

Methods : In our ongoing birth cohort study, we used nine follow-up time points (birth, 3, 6, 9, 12, 18, 24 months, and 3, 4 years) to calculate the change between two adjacent weight for age z-scores (WAZ-change), and then to define WAZ-change trajectories using group-based trajectory modeling. The independent/combined effects of WAZ-change trajectories with each lifestyle factor (eating behaviors , physical activity, media exposure time and total sleep duration) on childhood adiposity measures were determined using multivariate regression (where applicable).

Results : A total of 84 (38.0%) children had a steady growth trajectory while the other 137 (62.0%) children had an early rapid growth trajectory most notable during the first six months. Compared to children with steady growth, children with early rapid growth had significantly higher adiposity status at four years of age - body mass index (β = 0.93, 95% CI: 0.59, 1.37), waist circumference (β = 1.90, 95% CI: 0.68, 3.12), and subcutaneous fat (β = 2.57, 95% CI: 1.13, 4.01). Moreover, WAZ-change trajectory not only had an independent effect, but also a combined effect with eating behaviors on most adiposity measures.

Conclusions : We have identified two distinct weight change trajectories and described their independent and combined effects with eating behaviors on childhood adiposity measures. Larger samples and a longer period of observation through childhood are needed to replicate our findings.

Background

Over the last 40 years, overweight/obesity has become an epidemic [1]. Childhood weight problems, which can be persistent and are difficult to reverse [2, 3], may predispose children to a myriad of short- and long-term adverse outcomes of physical and mental health [4]. In a cohort of 292827 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 risks of lifelong health problems such as type 2 diabetes [5]. The prevention and reduction in childhood overweight/obesity or even higher than average BMI status would 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 trying to encourage an obese child to lose weight [7]. To address this issue, just as the Commission on Ending Childhood Obesity proposed [8], 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 prevention strategies.

Research already suggests that the path to overweight/obesity is established very early in fetal life and infancy [9]. Infant rapid weight change, commonly being defined as the change of a weight age-and sex-specific z-score (WAZ-change) greater than 0.67 over two time points [10, 11], has been progressively indicated to be positively associated with childhood and adult high BMI values and overweight/obesity [9, 11]. However, the normal growth pattern measured by WAZ-change in early childhood is still unclear. Few studies have illustrated the dynamic WAZ-change over time to determine the exact critical period and characterize different weight trajectories, which may provide guidance for clinicians and public health practitioners in designing early-life interventions targeting specific ages and specific populations. While one recent study identified distinct BMI-change trajectories from birth to age 14 years: “early rising” - excess BMI from 2 years, and “late rising” - excess BMI from 5 years, it did not capture the impact of the growth pattern early in life [12]. Furthermore, most studies only focused on one adiposity indicator (i.e. BMI) [13–16], but neglected the others, such as waist circumference assessing abdominal adiposity, and subcutaneous fat evaluating body fatness.

Strong evidence demonstrates that modifiable lifestyle factors established early in life, especially in the preschool years, are main determinants of the weight status in both child- and adulthood [17–19]. Behaviors, such as eating [20, 21], physical activity [22], media exposure [18, 22] and sleeping [18, 19, 22], are likely to be key influences on the risk of childhood overweight/obesity. However, studies do yield inconsistent results [23, 24]. Meanwhile, the extent to which lifestyle behaviors may modify the risk of rapid infant weight gain is not completely understood, as limited studies have examined their impact [25]. Therefore, from a prevention perspective, insight into the combined effects of rapid infant weight gain and these early lifestyle factors on a child’s overweight/obesity risk is needed.

To address this knowledge gap, our study aimed to 1) characterize different WAZ-change trajectories and the periods of greatest change; 2) explore the independent and combined effects of WAZ-change trajectories with early lifestyle factors on the childhood adiposity status at four years of age.

Methods

Study Subjects and Design

The Shanghai Sleep Birth Cohort Study (SSBC), an ongoing mother-child birth cohort, recruited from the general population aimed to investigate the effects of perinatal and early life environmental and behavioral factors on child growth and development [26]. The recruitment was conducted in an obstetrics clinic at Renji Hospital from May 2012 to July 2013. There were three screening stages based on the predefined inclusion and exclusion criteria (Fig. 1). For the screening steps, we identified 431 candidates - women in late pregnancy carrying a single baby; 262 women with their full-term newborns agreed to participate and attend the pre-scheduled 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, 24 months after birth (± 7 days). Due to lack of motivation, moving away, work schedule and other reasons, 25 participants dropped out during this stage. In the second follow-up stage (n = 237), person-to-person interviews at 3, 4 and 6 years of age (± 1 month) were conducted. The 6-year follow-up has not yet finished, therefore, this study uses the four-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.

Anthropometric measurement

All measurements were done according to standardized protocols by trained research staff. Child weight and length/height were obtained at each visit. Weight was measured using calibrated scales (0–2 years, Seca 335) and electronic personal scale (3–4 years, Seca 877). Recumbent length (0–2 years) using the same calibrated scale as weight and standing height (2–4 years) using a stadiometer (Seca 206) were measured. Weight age-and sex-specific z-score (WAZ) was determined based on least mean square methods using the World Health Organization growth reference [27]. At four years of age, 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 were also measured. We calculated BMI values from the children's weight (kg) being divided by the square of their length/height (cm) and waist-to-height ratio (WHtR) from waist circumference (cm) divided by height (cm). The sum of the triceps and subscapular skinfold thicknesses were used as a measure of subcutaneous fat.

Demographic variables

Demographic information was collected in late pregnancy and at birth. Maternal pre-pregnancy BMI values, gestational weight gain between early and late pregnancy, and paternal BMI values were obtained from the obstetric clinic. We also assessed maternal sleep quality, depression symptoms and anxiety status at the first visit using the Pittsburgh Sleep Quality Index (PSQI) [28], the Center for Epidemiological Survey-Depression Scale (CESD) [29] and the State-Trait Anxiety Index (STAI) [29, 30] respectively.

Childhood lifestyles factors

Infant feeding

Infant feeding method during the first 3 months was categorized as breastfed (entirely or mostly breastfed), bottle fed (entirely or mostly bottle fed), or mixed (equally breastfed and bottle fed), and the latter two were combined as non-breastfed. 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 3-day food diaries, which asked parents/caregivers to list all foods and drinks (including water) the child consumed and 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.

Eating behaviors

At the age of 2 and 4 years, parents reported eating behaviors of the child by using the Children's Eating Behavior Questionnaire (CEBQ) [31], which has been validated in different populations including Chinese [32]. Of the subscales of the CEBQ, we used the following four in our present study: food responsiveness (FR), enjoyment of food (EF), satiety responsiveness (SR) and food fussiness (FF), all of which have 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) [31]. Higher score for FR and EF, with a lower score for SR and FF equate to a greater appetite rating.

Physical activity time

At the age of 3 years, child outdoor playtime as a proxy for physical activity was assessed using a validated survey question [33]. That is, parents reported how much time their child spent playing outdoors per day on a typical weekday and on a typical weekend in the past month. A weighted outdoor playtime was calculated by ((weekday*5 + weekend*2) / 7).

Media exposure

At the age of 2 and 4 years, parents reported the child's media exposure time as the total hours that the child spent per day on media activities, including watching TV or DVDs, using a computer or IPAD and playing with electronic games on a typical weekday and on a typical weekend day in the last month. 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 new media recommendations of the American Academy of Pediatrics (AAP) for children aged 2–5 years [34].

Total sleep duration

At the age of 2 years, child total sleep duration was summed from daytime and nighttime sleep duration, using the Brief Infant Sleep Questionnaire (BISQ) [35]. At the age of 4 years, the Children's ChronoType Questionnaire (CCTQ) [36] was used. Parents were asked 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 weekend were calculated, then a weighted total sleep time was calculated.

Statistical analyses

Maternal and infant characteristics were described with means (95% confident interval, CI) and frequency (percentage), and the differences in characteristics between lost and retained children at 4 years were assessed by t-test and χ2 test for continuous variables and categorical variables, respectively. To address our aims, the main analyses were performed in following steps.

In step 1, to analyze the WAZ-change trajectories, the WAZ-changes were calculated and group-based trajectory modeling (GBTM) was used. We further defined the critical age interval for the most marked changes in the trajectories took place using t-test or ANOVA analysis. We quantified WAZ-change during each age interval as the substraction 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, 11]. The following eight age intervals, i.e. 0–3, 3–6, 6–9, 9–12, 12–18, 18–24, 24–36 and 36–48 months were defined to characterize the WAZ-change trajectories. On average, each child had 4.9 (95% CI: 4.7, 5.2) WAZ-change observations over the first four years, and only children who had completed a minimum of three WAZ-change observations were included. GBTM assesses the average pattern of WAZ-change over time points and assumes that individuals belong to the same underlying population represented by a single growth curve. The best-fitting model was chosen based on 1) largest Bayesian information criteria (BIC) and 2) each trajectory containing at least 5% predicted sample size [37]. Once WAZ-change trajectories were determined, individuals were assigned to the group with the highest posterior probability.

In step 2, estimated WAZ-change trajectory groups, treated as the indicator variable, were related in two separate models to potential exposures and to adiposity outcomes. That is, we examined the predictors of the different WAZ-change trajectories determined in step 1 using t-test and determined their predictive effect on the adiposity outcomes at four years of age using linear regression.

In step 3, we tested the independent and combined effects of different lifestyles with WAZ-change trajectories on each adiposity outcome using multivariate linear regression model. Firstly, if the individual early lifestyle factor (i.e. FR, EF, SR, FF, total sleep duration, outdoor playtime, and media time) had a significant effect on adiposity measures, they were then categorized as dichotomous variables by median levels except for media time whose cut-off was defined as one hour [34]. Secondly, we combined the WAZ-change trajectories and each of the dichotomous lifestyle factors to examine a range of their joint effects on the adiposity outcomes. 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 [38]. Post hoc pairwise comparisons were performed with Bonferroni multiple-comparisons tests. Lastly, the WAZ-change trajectory, each significant lifestyle factor, and their interaction terms as the independent variables were analyzed to clarify whether a synergistic or antagonistic effect on outcomes existed. Notably, the lifestyle factors investigated at 2 and 4 years were averaged as the childhood exposure partly to reduce the number of data points and the odds of chance reporting (e.g. recall bias) [39].

In step 4, the maximum frequency of missing values among the covariates was 35.0% and the missingness was considered as missing at random. 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 set 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 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.

Results

Descriptive Information

In total, 262 mother-child pairs participated, with 221 (84.4%) having at least three WAZ-change datapoints to characterize trajectories, with 209 (79.8%) finishing the 4-year measurement to evaluate childhood adiposity outcomes (Fig. 1). No group differences due to attrition were found at four years old (Table S1). Of the 262 mother-infant pairs with complete data at birth, 50.4% were boys. The majority of women had a college or higher education (91.2%). Maternal age at delivery was 29.47 (95% CI: 29.08, 29.86) years, and child’s birth weight was 3.31 (95% CI: 3.26, 3.36) kg.

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 near but below the zero baseline in subsequent age intervals. The percentage experiencing rapid weight change dropped with a similar trend, from 54.0% over 0–3 and 22.9% over 3–6 months to less than 8% in subsequent age intervals (Table S2). Overall, 63.9% infants had rapid weight gain during the first six months. Over the first four years of life, two distinct trajectories best representing the dynamic WAZ-change were detected using GBTM (Fig. 2). Given the recommended cut-off of the rapid weight change (WAZ-change > + 0.67), two groups can be identified: WAZ-changes being 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 rapid" WAZ-change trajectory.

Age-related trends of children's actual weight in the two groups showed that children with early rapid WAZ-change pattern had significant greater weight compared to children with steady WAZ-change pattern (Fig. S1). Further analyses also indicated a significant difference of the absolute WAZ-change between the two trajectories. The first six months was the critical period, and children with "early rapid" WAZ-change trajectory showed a non-stable weight pattern.

Independent effects

Most of the mother-child characteristics were balanced between steady and early rapid group (Table 1). Compared to the steady group, children in the early rapid group were more likely to have shorter gestational age, shorter birth length and lower birth weight. The early rapid group was also more likely to have a higher EF and a lower FF score, as well as to have less outdoor playtime in early childhood, even after adjusting for confounders.

Table 1
Maternal-child characteristics between the two identified WAZ-change trajectories (non-imputed data).

	All (n = 221)	**Steady** (n = 84)	**Rapid** (n = 137)	t/χ^2	P
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	14.88 (14.34, 15.41)	15.14 (14.21, 16.07)	14.72 (14.06, 15.37)	-0.75	0.452
Maternal PSQI score ≥ 5	114 (58.8)	45 (62.5)	69 (56.6)	0.66	0.417
Maternal SAI score ≥ 41	21 (10.1)	8 (10.3)	13 (10.1)	0.00	0.967
Maternal TAI score ≥ 41	32 (15.5)	14 (18.4)	18 (13.9)	0.77	0.382
Maternal CESD score ≥ 10	108 (50.7)	44 (54.3)	64 (48.5)	0.68	0.408
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

BMI, body mass index; CESD, Epidemiological Survey-Depression Scale; CI, confident interval; EF, enjoyment of food; FF, Food fussiness; FR, food responsiveness; PSQI, Pittsburgh Sleep Quality Index; SAI, State Anxiety Index; SR, satiety responsiveness; TAI, Trait Anxiety Index; WHtR, waist-to-height ratio; WAZ, weight for age- and sex-specific z-score.

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

	All	Steady	Rapid	t/χ^2	P
	(n = 221)	(n = 84)	(n = 137)		
Infancy					
Breastfeeding over the first three months, Yes	81 (37.3)	35 (42.7)	46 (34.1)	1.62	0.204
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

BMI, body mass index; CESD, Epidemiological Survey-Depression Scale; CI, confident interval; EF, enjoyment of food; FF, Food fussiness; FR, food responsiveness; PSQI, Pittsburgh Sleep Quality Index; SAI, State Anxiety Index; SR, satiety responsiveness; TAI, Trait Anxiety Index; WHtR, waist-to-height ratio; WAZ, weight for age- and sex-specific z-score.

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

	All	Steady	Rapid	t/χ^2	P
	(n = 221)	(n = 84)	(n = 137)		
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; CESD, Epidemiological Survey-Depression Scale; CI, confident interval; EF, enjoyment of food; FF, Food fussiness; FR, food responsiveness; PSQI, Pittsburgh Sleep Quality Index; SAI, State Anxiety Index; SR, satiety responsiveness; TAI, Trait Anxiety Index; WHtR, waist-to-height ratio; WAZ, weight for age- and sex-specific z-score.

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

After adjusting for mother-child characteristics, the early rapid group had significantly higher adiposity status (except for WHtR) compared to the steady group, with the regression coefficient being 0.90 (95% CI: 0.37, 1.44) for weight, 0.93 (95% CI: 0.49, 1.37) for BMI, 1.90 (95% CI: 0.68, 3.12) for waist circumference, 1.05 (95% CI: 0.62, 1.48) for biceps circumference, and 2.57 (95% CI: 1.13, 4.01) for subcutaneous fat (Model 1a in Table 2). Meanwhile, scores of FR and EF had positive effects, SR and FF had negative effects on adiposity measures with the exception of WHtR (Model 1b-1e in Table 2). And 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 time and total sleep duration had no significant association on adiposity measures at four years of age (Model 1f-1 h in Table 2).

Table 2

Independent effects of WAZ-change trajectories and childhood lifestyle factors on children's adiposity measures at four years old (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-1 h ζ						
WAZCT	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	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)*

	Weight Ψ	BMI	Waist circumference	WHtR	Biceps circumference	Subcutaneous fat
Model 2b						
WAZCT □	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 □	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 □	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, confident 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- and sex-specific 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 separately, e.g. in Model 1a, we only analyzed WAZCT with adjusting for confounders 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 subscale scores) 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.

[□]Rapid vs steady WAZ-change trajectory.

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

Combined effects

Combined effects were shown in Table 3 and Fig. 3 (post hoc multiple-comparisons tests). Compared to children with steady WAZ-change trajectory and lower FR (the reference group), children with early rapid trajectory and higher FR had significantly higher weight, BMI, waist circumference, biceps circumference and subcutaneous fat values at 4 years old (Model a in Table 3). Compared to children with steady WAZ-change trajectory and lower EF (the reference group), children with early rapid trajectory and higher EF had significantly higher weight, BMI, waist circumference, biceps circumference and subcutaneous fat values at 4 years old, followed by children with early rapid WAZ-change trajectory and lower EF and then children with steady WAZ-change trajectory and higher EF (Model b in Table 3). Compared to children with steady WAZ-change trajectory and higher SR (the reference group), children with early rapid WAZ-change trajectory and lower SR had significantly higher weight, BMI, waist circumference, biceps circumference and subcutaneous fat values at 4 years old, followed by children with early rapid WAZ-change trajectory and higher SR (Model c in Table 3). Compared to children with steady WAZ-change trajectory and higher FF (the reference group), children with early rapid WAZ-change trajectory and lower FF had significantly higher weight, BMI, waist circumference, biceps circumference and subcutaneous fat values at 4 years old, followed by children with early rapid WAZ-change trajectory and higher FF (Model d in Table 3). We did not find an interaction effect of the WAZ-change trajectory and each subscale of eating behaviors on the outcomes at four years old (data not shown).

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 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	0.14 (-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)

BMI, body mass index; CI, confident interval; EF, enjoyment of food; FF, food fussiness; FR, food responsiveness; SR, satiety responsiveness; WHtR, waist-to-height ratio.
ψAdjusted 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 WAZ-change 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.
* $P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

	Weight ψ	BMI	Waist circumference	WHtR	Biceps circumference	Subcutaneous fat
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, 2.3)***	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.

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

ψAdjusted 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 WAZ-change 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.

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

	Weight ψ	BMI	Waist circumference	WHtR	Biceps circumference	Subcutaneous fat
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, confident interval; EF, enjoyment of food; FF, food fussiness; FR, food responsiveness; SR, satiety responsiveness; WHtR, waist-to-height ratio.						
ψAdjusted 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 WAZ-change 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.						
* P < 0.05, **P < 0.01, ***P < 0.001.						

Sensitivity analyses

Our sensitivity analyses found that the results from multiple-imputation and complete-case analyses had limited impact on the results with the exception of the results for the SR score (Table S3-S4 and Fig. S2).

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 life. There are several important findings. Firstly, we found a high percentage of infant with rapid WAZ-change in our full-term birth cohort. Secondly, we identified two WAZ-change groups over 0–4 years, i.e. steady and early rapid trajectories, with the critical window for this change occurring over 0–6 months, especially over 0–3 months. Thirdly, the WAZ-change trajectories and childhood eating behaviors not only had independent but combined effects on adiposity outcomes at the age of four years.

According to the widely used cut-off for a rapid WAZ-change (> + 0.67) between any two measurement points, 54.0% of infants during the first three months and 63.9% during the first six months showed a rapid weight change in our study: this is much higher than other countries, e.g. 22.7% in Japan [41] over 0–3 months, and 13.7%-22.0% in Australia [42, 43], 25.4% in Sweden [44] and 28.0% in Northeast Brazil [45] over 0–6 months. Our study characterized two WAZ-change trajectories over 0–4 years, and more than half of the children (62.0%) exhibited an early rapid growth. This group showed a non-stable growth pattern which would be associated with a higher risk of being overweight/obesity or even metabolic disease in later life [44]. While no study has characterized WAZ-change trajectories in the way that has been done in our study, several studies have illustrated different absolute weight or BMI trajectories [46]. 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 rapid growth trajectories in our study. However, the percentage of early ascending trajectories was lower than our early rapid trajectory [47, 48].

The rapid WAZ-change pattern observed in our study may be attributable to the disparities in infant feeding beliefs, attitudes, knowledge and practices related to cultural perceptions. Chinese families are more likely to consider a fat baby healthy. Consequently, over-nutrition may occur thanks to concomitant use of breast milk and formula, and early consumption of water-based drinks, fruit juice and introduction of solid foods [49, 50]. The postpartum traditions of "zuo yue zi" or "doing the month" in Chinese lactating women may be another reason. During that month, women eat more food and lie in bed for a long time, which might have an impact on their postpartum weight loss, and levels of macronutrients, hormones, cytokines, and other bioactive compounds in the breast milk [51, 52]. All may contribute to the risk of infant rapid growth, especially in the first three or six month.

Many studies explored infant rapid weight change but failed to demonstrate its "exact critical window". That is, either they investigated only one age interval (e.g. 1–3 months [53], 0–6 months [16], 0–1 year [54], 0–2 year [55]) or they reported conflicting evidence regarding the specific critical period. Some reported early infancy [13], some reported later infancy [14] or later life [56], while others indicated both [15]. These discrepancies could be due to differences in length of follow-up, the timing and length of the early-life age intervals, and ethnicity. In the present study, we characterized the dynamic WAZ-change over the first four years and determined two different trajectories, which suggested the first six months were the most critical growth period. 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 picture growth trajectory [12]. The identified patterns of WAZ-change trajectory highlight the key 'change in path', which is particularly relevant in designing early-life interventions to prevent subsequent overweight/obesity by targeting specific populations in specific age intervals.

Extensive research has documented that a larger appetite rating (e.g. greater FR and EF; lower SR and FF) is associated with adiposity in children [20, 21]. The underlying mechanisms may be that the higher FR, the more likely that frequent eating when exposed to food will trigger brain-reward pathways. In addition the lower SR, the more food will be eaten on each eating occasion via a neuroendocrine feedback loop involving hormones secreted in the gut that interact with control centers in the brain [57]. Our study is the first to find that childhood eating behaviors were not only having an independent effect but having a combined effect with WAZ-change trajectories on childhood adiposity measures. Namely, children who had early rapid growth with a larger childhood appetite score were more likely to develop higher adiposity status compared with children showing steady growth with a lower appetite score. The interaction effects of the WAZ-change trajectory and four subscales of eating behaviors were not significant, suggesting that the effects of WAZ-change growth and eating behaviors on adiposity outcomes are additive in the present study. Studies with larger samples and more exact evaluation of appetite are needed to verify our findings.

While eating behaviors have a genetic background [58], they are influenced by environmental factors. A meta-analysis suggested that the critical window for altering eating behaviors might be located after birth, not in the prenatal period [59]. In addition, our findings suggested that it was early rapid weight change, not birth weight, that had a predictive effect on childhood eating behaviors, which was consistent with prior studies. Animal models demonstrated that eating behaviors were altered in low birth weight offspring, especially when low birth weight was followed by postnatal rapid weight change [60]. van Deutekom et al. [61] indicated that there was no association of birth weight with childhood appetite traits and energy intake, but the postnatal rapid weight change altered the appetite regulation. Therefore, in addition to control of the rapid growth in the first six months (especially in the first three months), different strategies may be required to reduce the potential modifying effects of eating behaviors in preschool children, a period where appetite traits are becoming established as many children become autonomous eaters and experience greater socialization of eating [62].

Our findings should be considered within the context of some limitations. Firstly, our sample was 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 within China. Therefore, our findings are likely to reflect what will happen in other developing cities (both in China and around the world) and inform the design of early-life interventions to prevent childhood overweight/obesity in this socioeconomic setting. Secondly, our small sample size and the attrition over time may reduce the power to detect some associations. However, no significant differences were found due to attrition at four years old. In addition, we imputed missing data, and also found no evidence for attrition bias based on the sensitivity analysis (showing nearly identical results from multiple-imputation and complete-case analyses) suggesting a relatively robust results. Thirdly, 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.

Conclusions

Our study identified two weight change patterns, highlighted the first six months as a possible critical growth window, and showed the effect of WAZ-change trajectory and eating behaviors, either alone or in combination, on adiposity measures at four years of age. These findings provide a very valuable model to aid researchers, clinicians and public health practitioners in designing early-life interventions targeting specific ages, specific populations and specific lifestyle behaviors to prevent childhood overweight/obesity. Our cohort is ongoing, and future follow-up on these children would be essential to evaluate whether our observations have long-term repercussions in later childhood or adulthood. And future studies with larger samples, longer time frames and more exact evaluation of lifestyle behaviors in other populations are also needed to verify our findings.

Abbreviations

BMI:body mass index; CI:confident interval; EF:enjoyment of food; FF:food fussiness; FR:food responsiveness; SR:satiety responsiveness; WHtR:waist-to-height ratio; WAZ:weight age-and sex-specific z-score; WAZ-change:the change of a weight age-and sex-specific z-score

Declarations

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Availability of data and materials

Data used for this study were derived from the Shanghai Sleep Birth Cohort Study (SSBC), an ongoing mother-child birth cohort. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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 authors read and approved the final manuscript.

Ethics approval and consent to participate

All participants provided written informed consent, which was renewed before commencing each stage of data collection. The birth cohort protocol was approved by the Shanghai Children's Medical Center Human

Ethics Committee (SCMCIRB-2012033).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests

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Figures

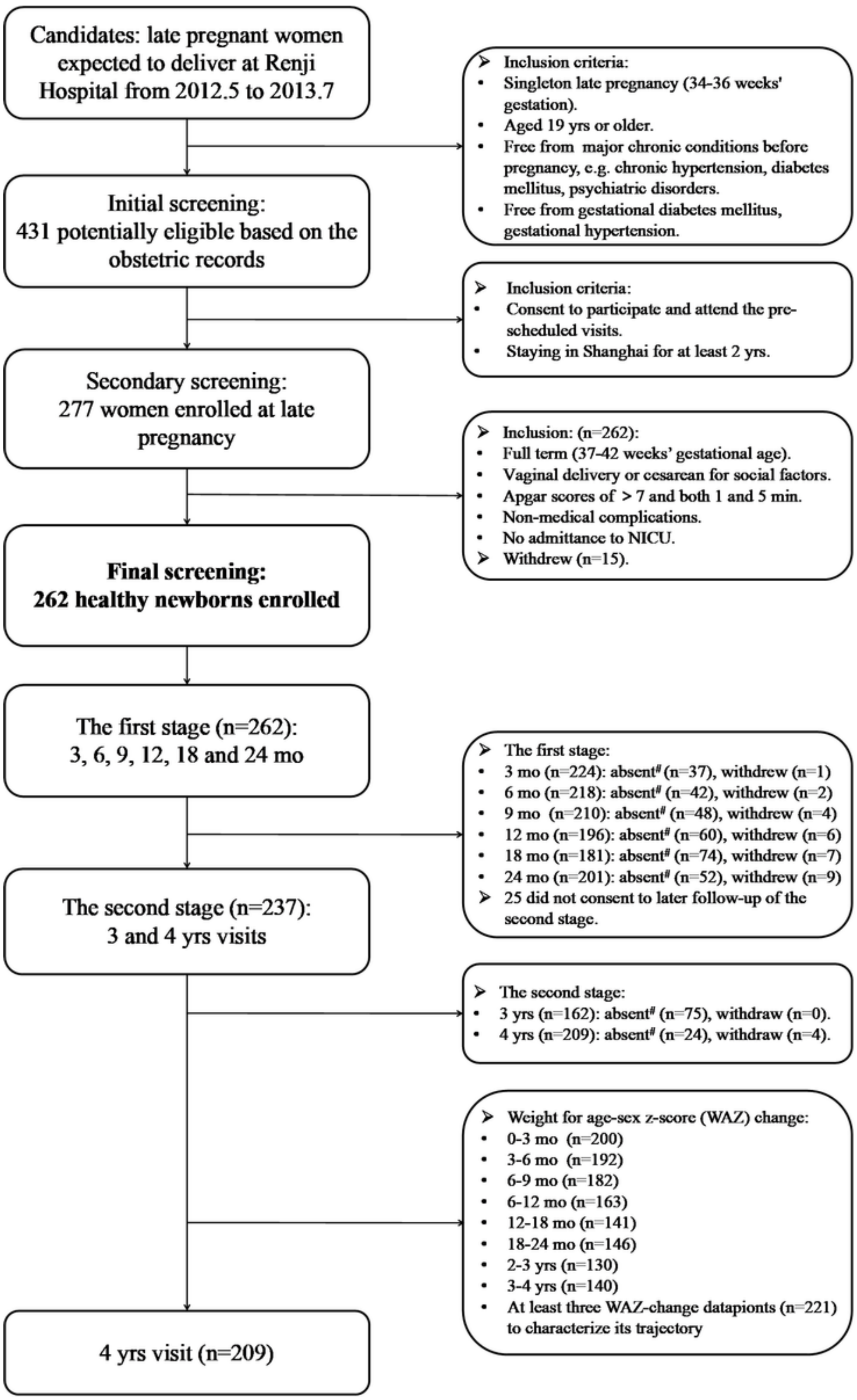

Figure 2

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

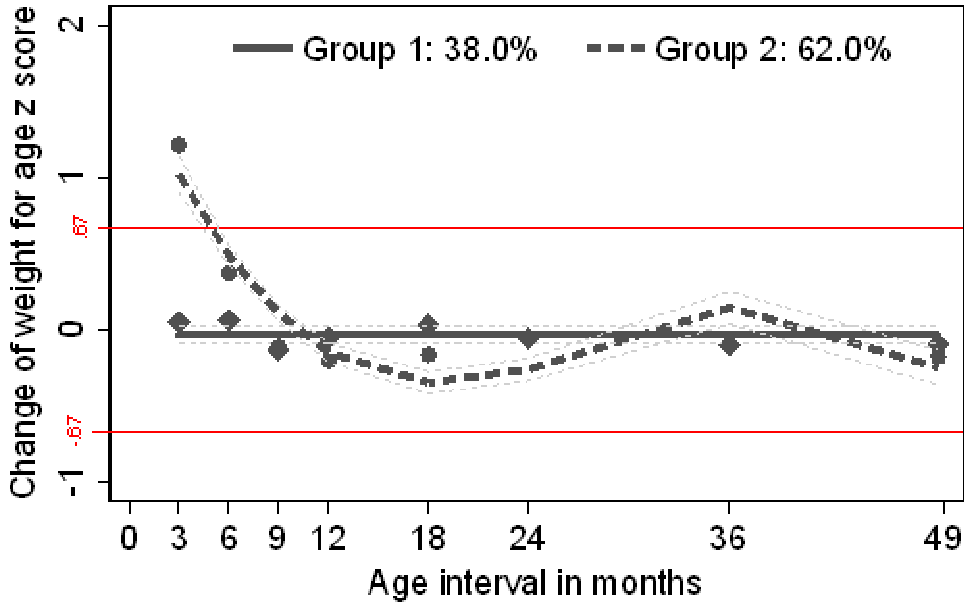

Figure 4

Trajectories of the WAZ-change with 95% confidence intervals across the first four years. Note, WAZ-change indicates the change in weight for age- and sex-specific z-score, and the solid line represents steady WAZ-change (38.0%, n=84), and the dash line represents early rapid WAZ-change (62.0%, n=137).

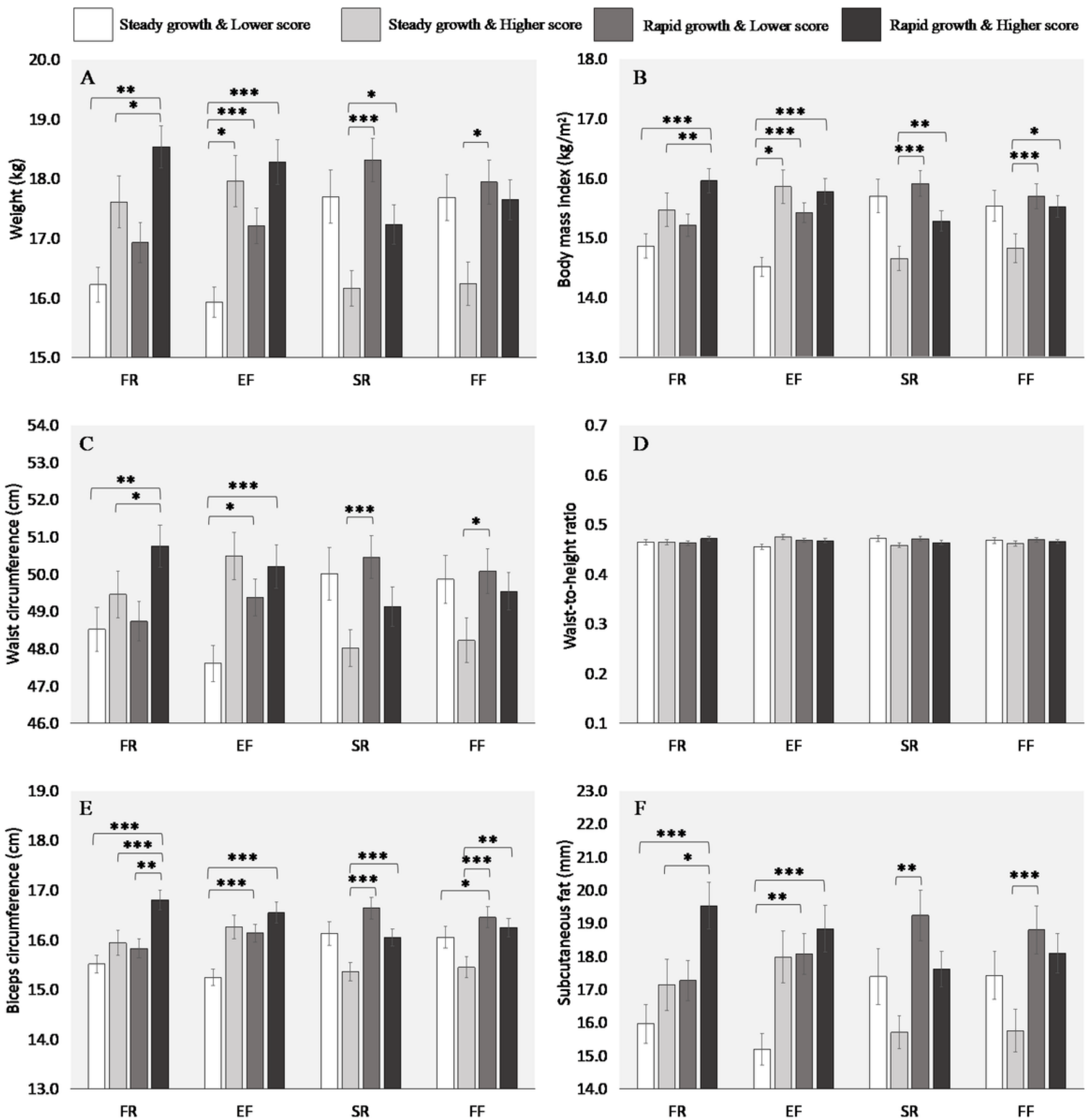

Figure 6

Combined effects of WAZ-change trajectories and four subscales of eating behaviors on children's adiposity measures at four years (imputed data). Note, WAZ-change indicates the change in weight for age- and sex-specific z-score. The X-axis are the combined groups with the two distinct WAZ-change trajectories and the dichotomy variable of four subscales of eating behaviors (FR, EF, SR and FF).

Supplementary Files

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- 5STROBEchecklistcohort.docx
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