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Associations of early childhood body mass index trajectories with body composition and cardiometabolic markers at age 10 years: the Ethiopian iABC birth cohort study

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Abstract:	Background: Variability in BMI trajectories is associated with body composition and cardiometabolic markers in early childhood, but it is unknown how these associations track to later childhood. Objectives: We aimed to assess associations of BMI trajectories from 0-5 years with body composition and cardiometabolic markers at 10 years. Methods: In the Ethiopian iABC birth cohort, we previously identified 4 distinct BMI

	trajectories from 0-5 years: stable low BMI (19.2%), normal BMI (48.8%), rapid growth to high BMI (17.9%), and slow growth to high BMI (14.1%). At 10 years, we obtained data from 320 children on anthropometry, body composition, abdominal subcutaneous and visceral fat, and cardiometabolic markers. Associations of BMI trajectories and 10-year outcomes were analyzed using multiple linear regression. Results: Compared to children with the normal BMI trajectory, those with rapid growth to high BMI had 1.7 cm (95%CI: 0.1, 3.3) larger waist circumference and slow growth to high had 0.63 kg/m2 (95%CI: 0.09, 1.17) greater fat mass index and 0.19 cm (95%CI: 0.02, 0.37) greater abdominal subcutaneous fat, while stable low BMI had -0.28 kg/m2 (95%CI: -0.59, 0.03) lower fat-free mass at 10 years. Although the confidence bands were wide and included the null value, children with rapid growth to high BMI trajectory had 48.6% (95%CI: -1.4, 123.8) higher C-peptide, and those with slow growth to high BMI had 29.8% (95%CI: -0.8, 69.8) higher insulin and 30.3% (95%CI: -1.1, 71.6) higher HOMA-IR, whereas rapid growth to high BMI had -0.23 mmol/L (95%CI: -0.47, 0.02) lower total cholesterol. The trajectories were not associated with abdominal visceral fat, blood pressure, glucose, and other lipids at 10 years. Conclusions: Children with rapid and slow growth to high BMI trajectories before 5 years showed higher measures of adiposity and higher levels of markers related to glucose metabolism at 10 years.
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Declaration of interests

☐The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Title

Associations of early childhood body mass index trajectories with body composition and cardiometabolic markers at age 10 years: the Ethiopian iABC birth cohort study

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A running title

Data Availability

Data described in the manuscript, code book, and analytic code will be made available upon request pending application and approval.

Abbreviations

ADP, air displacement plethysmograph; BMI, body mass index; FFM, fat-free mass; FFMI, fat-free mass index; FM, fat mass; FMI, fat mass index; HOMA-IR, homeostasis model assessment of insulin resistance; iABC, infant anthropometry and body composition; IWI, international wealth index; LMICs, low- and middle-income countries; WHO, World Health Organization.

Abstract

Background: Variability in ~~We previously reported associations of rapid~~ BMI ~~growth~~ trajectories ~~in early childhood~~ is associated with ~~adiposity~~ body composition and ~~elevated~~ cardiometabolic markers ~~at 5 years~~ in early childhood, but ~~.~~ ~~I~~it is unknown how these associations track ~~through~~ to later childhood~~, particularly in low-income settings~~.

Objectives: ~~T~~We aimed to assess associations of BMI trajectories from 0-5 years with ~~anthropometry,~~ body composition~~, abdominal subcutaneous and visceral fat,~~ ~~-~~and cardiometabolic markers at 10 years.

Methods: In the Ethiopian iABC birth cohort, we previously identified 4 distinct BMI ~~latent class~~ trajectories from 0-5 years ~~among 453 children~~: stable low BMI (19.2%), normal BMI (48.8%), rapid growth ~~catch-up~~ to high BMI (17.9%), and slow growth ~~catch-up~~ to high BMI (14.1%). At 10 years, we obtained data from 320 children on anthropometry, body composition, abdominal subcutaneous and visceral fat, and cardiometabolic markers. Associations of BMI trajectories and 10-year outcomes were analyzed using multiple linear regression.

Results: Compared to children with the normal BMI trajectory, those with rapid growth ~~catch-up~~ to high BMI had 1.7 cm (95%CI: 0.1, 3.3) larger waist circumference and slow growth ~~catch-up~~ to high had 0.63 kg/m^2 (95%CI: 0.09, 1.17) greater fat mass index and 0.19 cm (95%CI: 0.02, 0.37) greater abdominal subcutaneous fat, while stable low BMI had -0.28 kg/m^2 (95%CI: -0.59, 0.03) lower fat-free mass at 10 years. Although the confidence bands were wide and included the null value~~Furthermore~~, children with rapid ~~catch-up~~ growth to high BMI trajectory had 48.6% (95%CI: -1.4, 123.8) higher C-peptide, and those with slow growth ~~catch-up~~ to high BMI had 29.8% (95%CI: -0.8, 69.8) higher insulin and 30.3% (95%CI: -1.1, 71.6) higher HOMA-IR, whereas rapid ~~catch-up~~growth to high BMI had -0.23 mmol/L (95%CI: -0.47, 0.02) lower total cholesterol. The

trajectories were not associated with abdominal visceral fat, blood pressure, glucose, and other lipids at 10 years.

Conclusions: Children with rapid and slow growth ~~catch-up~~ to high BMI trajectories before 5 years showed higher measures of adiposity and higher levels of markers related to glucose metabolism at 10 years.

Keywords: *Body mass index trajectories; latent class trajectory; fat mass; fat-free mass; abdominal subcutaneous fat; visceral fat; cardiometabolic markers.*

Introduction

The increasing prevalence of childhood ~~obesity~~ overweight is a major global health problem (1). Childhood ~~obesity~~ overweight is ~~one of the~~a key risk factor~~s~~ for cardiovascular disease and type 2 diabetes in adulthood (2-4). Several studies from high-income settings have ~~reported associations of~~linked accelerated body mass index (BMI) growth in early childhood ~~(0-5 years)~~ with ~~adiposity~~ overweight and higher ~~concentrations of~~ cardiometabolic risk ~~markers~~ later in life (5-9). However, ~~I~~in middle-income countries, rapid weight and BMI gain in infancy and childhood have been associated with greater lean mass rather than fat mass (FM) in childhood and adulthood (10, 11). ~~BMI is not a measure of body fatness, but it is a measure of weight relative to height (12). Therefore, a faster BMI growth in childhood might indicate faster lean growth, fat growth, or both depending on the child's body composition (12, 13).~~

Most previous studies have assessed BMI ~~at~~ from a single point in time and related it to cardiometabolic risk factors in childhood (14, 15), and cardiometabolic diseases in adulthood (16-18). However, early childhood BMI growth trajectories better predicted later body composition and risk of obesity in childhood than a single-point time BMI measurement (7). In high-income countries, associations of rapid BMI growth ~~trajectories~~ patterns in early life with body composition, adiposity, and cardiometabolic risk track to later childhood or early adulthood (19-24). There is, ~~H~~however, limited evidence on the tracking of body composition, adiposity and cardiometabolic risk ~~information on these associations~~ from low- and middle-income countries (LMICs) ~~is limited~~. Children in many LMICs are also at increasing risk of the double burden of malnutrition, which has been related to later cardiometabolic disease risk (25-27). Therefore, ~~U~~understanding how associations of ~~between rapid~~ BMI growth patterns in early childhood ~~and~~ with body composition, adiposity, and cardiometabolic risk track to later childhood in LMICs is increasingly important to identify those at risk and provide timely interventions.

~~Latent class trajectory modeling identifies subgroups of the study population with distinct growth patterns over time and helps to improve our understanding of relations between growth patterns and health outcomes (28, 29).~~ In the Ethiopian infant anthropometry and body composition (iABC) birth cohort, we previously identified four distinct BMI trajectories from 0-5 years (30). In this cohort, children with high ~~a rapid~~ BMI growth ~~pattern~~ in early childhood had larger body size, higher lean and ~~fat mass~~FM, and concentrations of C-peptide and triglycerides compared to those with an average BMI growth pattern following ~~as compared to~~ the median growth according to the World Health Organization (WHO) child growth standards (30). In this study, we examined associations of ~~the~~ previously ~~identified~~ estimated ~~distinct~~ BMI trajectories from 0-5 years with anthropometry, body composition, abdominal subcutaneous and visceral fat, and cardiometabolic markers at ~~in~~ ~~Ethiopian children~~ age~~d~~ 10 years. We hypothesized that the children with rapid BMI growth in early childhood would have higher FM and concentrations of cardiometabolic markers compared to those with normal BMI growth at10 years. Conversely, we hypothesized that children with slow BMI growth in early childhood would have lower fat-free mass (FFM), levels of adiposity as well as concentrations of cardiometabolic markers related to lipid metabolism.

Methods

The iABC birth cohort, based in Jimma town, Ethiopia, was established in December 2008. Participant selection and recruitment have previously been described in detail (31, 32). Briefly, mothers giving birth in the maternity ward of Jimma University Specialized Hospital, and their newborns were recruited within 48 hours after birth~~.~~ until the estimated sample size was achieved (31). Mother-newborn pairs were eligible based on the following criteria: living in Jimma town,

healthy and term (≥37 weeks of gestation) newborn with a weight of ≥1,500 g, and without any medical complications and congenital malformations. From 0-5 years of age the children were invited for a total of 12 visits (at birth, 1.5, 2.5, 3.5, 4.5, 6 months, 1, 1.5, 2, 3, 4, 5 years). ~~As previously described (30), 4 distinct latent class trajectories were identified from 0-5 years among 453 children.~~ In this study, the previously identified 4 distinct latent class BMI trajectories were used as categorical exposure variables.

We conducted the current follow-up visit from June 2019 to December 2020, when children were 7-12 years old, henceforth referred to as the 10-year follow-up. At the 10-year follow-up, mother/guardian-child pairs were invited for the visit with either a phone call or a home visit by the research team. We informed the mother/guardian-child pairs about the visit and data collection procedures including overnight fast. The trained research team collected the data at Jimma University Clinical and Nutrition Research Center. We studied the following outcomes at the 10-year follow-up: anthropometric measurements (height and waist circumference), body composition (fat mass index [FMI] and fat-free mass index [FFMI]), abdominal fat (subcutaneous and visceral), and cardiometabolic markers including blood pressure (systolic and diastolic), glucose metabolism (glucose, insulin, C-peptide, and homeostatic model assessment of insulin resistance [HOMA-IR]), lipids (total cholesterol, low-density lipoprotein cholesterol [LDL], high-density lipoprotein cholesterol [HDL], and triglycerides).

Anthropometric measurements from birth to 10 years

Weight and length/height were assessed at birth, 1.5, 2.5, 3.5, 4.5, 6 months, 1, 1.5, 2, 3, 4, 5 and 10 years of age. Length from birth up to 2 years was measured in the nearest 0.1 cm in a recumbent position using a Seca 416 Infantometer and height from 2-5 and at 10 years was measured in the standing position using a portable stadiometer (SECA, Hamburg, Germany) to the nearest 0.1 cm.

Waist circumference was assessed in duplicate in standing position to the nearest 0.1 cm using non-stretchable measuring tape midway between the iliac crest and lowest costal margin above umbilicus and the average was used. Weight from birth to 6 months was assessed using an electronic scale attached to a PEA POD, an infant air displacement plethysmograph (ADP) (COSMED, Rome, Italy). Weight from 1 to 3 years was assessed to the nearest 0.1 kg using an electronic UNICEF scale (Seca, Hamburg, Germany), and from 4-5 and at 10 years using the attached electronic scale of the child/adult ADP instrument, the BOD POD. BMI in kg/m^2 was calculated by dividing weight in kilogram (kg) by length/height in meter (m) squared. BMI z-score at 10 years was calculated using the WHO 2007 AnthroPlus R package (version 0.9.0) (33, 34). Stunting was defined as height-for-age z-score <-2, wasting/thinness if BMI-for-age z-score <-2 and overweight/obese if BMI-for-age z-score >1.

Body composition measurement at 10 years

The research nurses calibrated the BOD POD every morning using a cylinder of standard volume before starting the actual body composition assessment. Before the ADP measurement, the child was asked to take off all his/her clothes and were provided tightly fitted underwear pants and a swimming cap to displace accumulated air in the hair (35). ~~Fat mass (~~FM~~)~~ and ~~fat-free mass (~~FFM~~)~~ were calculated using Archimedes principle ~~using~~ of manufacturers' equations (31). FMI and FFMI were calculated as FM (kg) or FFM (kg) divided by height in meters (m) squared (36).

Abdominal fat measurement at 10 years

An experienced radiologist measured abdominal subcutaneous and visceral fat using ultrasound following a standard protocol (37, 38). The measurements were performed in supine position using linear array probe 11MHz for subcutaneous ~~adipose tissue~~fat and convex array probe 3.5MHz for visceral ~~adipose tissue~~fat (GE Logic, Boston, America). The radiologist kept the probe on the upper

median abdomen perpendicular to skin and performed an axial scan in the midpoint between the xiphoid appendix and the navel along the linea alba. Children were instructed to inhale deeply, exhale fully, and then hold their breath for a short period of time while the radiologist adjusted the image for the measurements. Abdominal subcutaneous fat was measured as the depth (cm) from the inner edge of the skin to outer edge of linea alba and visceral fat as the distance (cm) from the peritoneum to the front of lumbar spine.

Blood pressure measurement at 10 years

Research nurses measured blood pressure (in mmHg) using size-appropriate cuffs (Riester, Big Ben round, CE0124) after the child rested sitting for 5 minutes, with arm resting at the chest level. The measurements were performed in duplicate, and the average value used.

Clinical biomarkers assessment at 10 years

An experienced laboratory technician collected overnight-fast intravenous blood sample from the antecubital fossa. Blood glucose concentration was measured in whole blood using the HemoCue Glucose 201 RT System (HemoCue, Ängelholm, Sweden) immediately after collecting blood. Fasting serum was obtained after centrifuging whole blood at 1107 g force (relative centrifugal force) for 10 minutes. The centrifuged samples were divided into a minimum of 3x0.3 mL aliquots and stored at -80°C prior to analysis. The samples were analyzed at Jimma University Specialized Hospital, Clinical Chemistry Unit. Insulin (μU/mL) and C-peptide (ng/mL) concentrations were measured using module e601 of the Cobas 6000 analyzer (Roche Diagnostics International Ltd., Rotkreuz, Switzerland), and concentrations of lipids (total, HDL, and LDL cholesterol, and triglycerides) in mmol/L were determined using module c501 of Cobas 600. We calculated the HOMA-IR as insulin (μU/mL) x glucose (mmoL/L)/22.5 (39).

Covariates

147 An interviewer-administered structured questionnaire was used to obtain information on maternal
148 and child sociodemographic characteristics within 48 hours after delivery including maternal age,
149 highest educational status, and family wealth status. Trained research nurses calculated child
150 gestational age using the Ballard score (40). After obtaining information on household's ownership
151 of certain assets, family economic status was assessed using an International Wealth Index (IWI)
152 (41). Maternal anthropometric measurements were performed within 48 hours of delivery. Maternal
153 height was assessed to the nearest 0.1 cm using a SECA 214 stadiometer (SECA, Hamburg,
154 Germany), and weight was assessed to the nearest 0.1 kg using the scale of the Tanita 418
155 Bioimpedance analyzer (Tanita Corp., US). Breastfeeding status was assessed between 4 and 6
156 months using a structured questionnaire and categorized based on the WHO classification as 1)
157 exclusively breastfed (only breast milk with exception of vitamins, mineral supplements, or
158 medications), 2) predominantly breastfed (breast milk is the predominant source of food, but
159 vitamin and/or mineral supplements, water, and fruit juice are allowed, and 3) partially breastfed
160 (breast milk and solid or semi-solid food) or not breastfed (42).

161 **Statistical analyses**

162 **BMI trajectories in early childhood**

163 As previously described (30), we applied latent class trajectory modeling among 453 children who
164 had at least 3 repeated measurements of weight and length/height from 0-5 years (at birth, 1.5 to 6
165 months, and 1-5 years) (**Supplementary Figure 1**). The figure is already reported (30) and is
166 included in supplementary material for information. Several models with different specifications of
167 BMI as a function of age and number of subgroups (latent classes) were tested. The optimal number
168 of trajectory classes was determined based on Bayesian Information Criterion (BIC), mean posterior
169 probability of class membership (>70% in each class), class sizes (at least 5% of the participants in

each identified trajectory class), and the adequacy of the selected model to address the research question (29, 43, 44). The trajectory classes for males and females were similar (30), so the trajectories were developed for both sexes combined. A 4-class trajectory model specified with natural cubic splines with internal knot points at 3, 6, 24, 48 months and boundary knot points at 0 and 60 months was identified as the best fitting model. The trajectories were stable low BMI (19.2%), normal BMI (48.8%), rapid catch-up to high BMI (17.9%), and slow catch-up to high BMI (14.1%). The terms rapid growth to high BMI and slow growth to high BMI relate to rapid catch-up to high BMI and slow catch-up to high BMI in the previous paper (30), respectively. The patterns of BMI growth changes were mainly observed in the first 24 months, and from 48-month onwards they were almost similar (Supplementary Figure 1).

Descriptive analyses

Maternal and child characteristics are described across the trajectories using mean (standard deviation [SD]) for continuous normally distributed variables, median (interquartile range [IQR]) for skew~~ed~~ variables, and frequencies (n) and percentages (%) for categorical variables. ~~Differences between trajectories were examined by one-way ANOVA F-test for continuous normally distributed variables, Kruskal-Wallis test for continuous skewed variables, Pearson's chi-squared test for categorical variables with expected counts >4 and Fisher's exact test for categorical variables with expected counts ≤4.~~ Significance level was a *P* value <0.05. Data were analyzed using R statistical software version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

Associations of BMI trajectories with the 10-year outcomes

Associations between categorical exposure variables (latent BMI trajectories from 0-5 years) and the continuous outcomes at 10 years were analyzed using multiple linear regression. The normal BMI trajectory which most closely reflected the average pattern in the WHO child growth standards

for BMI and had the highest proportion of children was selected as the reference group for the regression analysis. We tested all models for normal distributions of residuals visually by histogram and Q-Q plots (quantile-quantile plots). We observed a slightly skew~~ed~~ residual distributions for the outcomes including insulin, C-peptide, HOMA-IR, and triglycerides, so these were log-transformed prior to analysis. Models were adjusted for potential confounding variables in models 1-3 to assess whether the effect estimates of the exposure variables changed. All potential confounders included in models 1-3 were identified a priori from the literature (7, 45, 46). In model 4, we further adjusted for body size measurements at the 10-year follow-up (variables on the causal pathway) to assess the effect of the trajectories on the outcomes independently of current body size. Model 1 was adjusted for child's sex and exact age at the 10-year follow-up visit. Model 2 was additionally adjusted for the child's birth order, gestational age at birth, maternal age at delivery, maternal height, maternal highest educational status, and family socioeconomic status (wealth index). Model 3, which is considered as the main model in this study, was further adjusted for birth weight to assess the associations of the BMI trajectories with the outcomes independent of the effect of prenatal growth. In model 4, we adjusted all outcomes for current BMI, except for FFMI which was adjusted for FMI, and waist circumference, FMI, and abdominal subcutaneous and visceral fat which were adjusted for current FFMI. The adjustment of FMI for the FFMI controlled for the fat component of BMI, whereas the adjustment of the adiposity outcomes for the FFMI controlled for the lean component of BMI. Regression analyses were performed as complete case analyses, only children with complete data on all covariates were included in the regression model.

Because FMI is a better capture of fatness than BMI (10, 11), in a sensitivity analysis we adjusted cardiometabolic outcomes for current FMI instead of BMI in model 4. ~~In a sensitivity analysis we adjusted cardiometabolic outcomes for current FMI instead of BMI in model 4.~~ Furthermore, we calculated change in cardiometabolic markers between the 5- and 10-year follow-ups among sample

children with cardiometabolic data. The differences in cardiometabolic markers were calculated by subtracting the value at the 5-year follow-up from the value at the 10-year follow-up. The calculated changes were used as continuous outcome variables in the subsequent regression analysis separately for each cardiometabolic marker. In addition, we evaluated whether the associations between the trajectories and 10-year outcomes were modified by sex by including sex interaction terms in the regression models and observed no significant interactions between the trajectories and sex. Therefore, all the analyses were performed for both sexes combined. In addition to the main adjustments, we further accounted for breastfeeding status at 4-6 months in sensitivity analysis among 272 children having the data. Furthermore, as sensitivity analysis, we performed multiple imputations to impute missing data for children who attended the 10-year follow-up using chained equations (47, 48). The imputation model included all the variables included in the analysis model (49). The imputed datasets were combined using Rubin's rules (50) for the final regression analysis using the 'with' and 'pool' functions in the 'mice' package in R (Version: 3.16.0). We compared the results of the imputed data of 346 children who met the inclusion criteria with the complete case analysis in the final model (model 3). Moreover, we performed sensitivity analysis controlling for multiple testing using Benjamini-Hochberg method in the final model (51).

Ethical consideration.

We obtained ethical clearance from the research ethics review board (RERB) of the College of Public Health and Medical Sciences of Jimma University, Ethiopia (RERB reference number: IHRPHD/333/18) and the ethics committee of the London School of Hygiene and Tropical Medicine (reference number: 15976). Prior to participation, written informed consent for participation was obtained from the mother/guardian of the child. Child assent was also obtained verbally after explaining about the study and data collection procedure in local language. Any child

with serious medical condition was referred to the Pediatric Unit of Jimma University Specialized Hospital for further examination and treatment.

Results

Of 571 children ~~cohort~~enrolled at birth, 355 (62%) attended the 10-year visit. Of the 355 children ~~included in the prospective birth cohort~~, 320 (90%) had exposure variables (BMI trajectories from 0-5 years), ~~children attended the 10-year follow-up~~ and 313 (88%) with complete data on all covariates were included in the regression analysis (**Figure 1**). Children who attended the 10-year follow-up had higher maternal age (24.7 vs 23.6 years; *P*=0.003), birth weight (3.1 vs 3.0 kg; *p*=0.006), and FFM (2.85 vs 2.77 kg/m^2; *P*=0.007) compared to those who did not attend (**Supplementary Table 1)**. There was no difference in maternal characteristics at delivery and child characteristics at birth and in infancy across the 4 trajectories (**Table 1**). Mean (SD) birth weight of the children was 3.1 (0.4) kg and 166 of children (51.9%) were male. Between 4 and 6 months, most children 227 out of 272 (83.5%) were predominantly breastfed (Table 1).

Table 2 describes child anthropometry, body composition, abdominal fat, and cardiometabolic markers at the 10-year follow-up by trajectories. Mean age of the children at the 10-year follow-up was 9.8 (1.0) years. Children in slow growth ~~catch-up~~ to high BMI trajectory had the highest mean BMI z-score (-0.27; *P* <0.001) at 10 years. Based on the WHO growth standards, 27 (8.4%) of the children were stunted, 38 (11.9%) wasted, and 26 (8.1%) overweight/obese at 10 years of age. As expected, children in stable low BMI had the lowest mean waist circumference (54.3 cm), FMI (2.7 kg/m^2), and FFMI (12.1 kg/m^2) compared to the other trajectories (all *P*-values <0.05) (Table 2). **Supplementary Table 2** describes child characteristics for the total sample and based on sex at 10 years.

Associations of BMI trajectories with anthropometry, body composition, and abdominal fat

After adjusting for ~~the~~ potential confounding variables (model 3), children with rapid ~~catch-up~~ growth to high BMI trajectory had 1.7 cm (95% CI: 0.1, 3.3) greater waist circumference compared to those with normal BMI trajectory (**Figure 2 and Supplementary Table 3**). The association remained after further adjusting for current FFMI in model 4. Children with slow growth ~~catch-up~~ to high BMI trajectory had a tendency towards higher waist circumference, whereas those with stable low BMI had a tendency towards lower values compared to those with normal BMI (model 3).

Compared to children with normal BMI trajectory, those with rapid and slow growth ~~catch-up~~ to high BMI trajectories had 0.5 kg/m^2 (95% CI: -0.1, 1.0) and 0.6 kg/m^2 (95% CI: 0.1, 1.2) greater FMI, respectively (model 3). After further adjustment for current FFMI in model 4, the associations remained. Children with stable low BMI had a tendency towards lower FFMI (model 3). At 10 years, children with slow growth ~~catch-up~~ to high BMI trajectory had 0.2 cm (95% CI: 0.0, 0.4) higher abdominal subcutaneous fat compared to those with normal BMI trajectory (model 3), and the association remained after further accounting for current FFMI. None of the trajectories were associated with height or abdominal visceral fat at 10 years (Figure 2 and supplementary Table 3).

Associations of BMI trajectories with cardiometabolic markers

Compared to children with normal BMI, those with slow growth~~catch-up~~ to high BMI trajectory had higher insulin and HOMA-IR and those with rapid growth ~~catch-up~~ to high BMI had higher C-peptide although not significant (model 3). The effect estimates were attenuated after further adjustment for current BMI in model 4 (**Figure 3** and Supplementary Table 3). For example, children with slow growth~~catch-up~~ to high BMI trajectory had 29.8% (95% CI: -0.8, 69.8) higher

insulin and 30.3% (95% CI: -1.1, 71.6) higher HOMA-IR, whereas those with rapid growth~~catch-up~~ to high BMI trajectory had 48.6% (95% CI: -1.4, 123.8) higher C-peptide (model 3).

Children with stable low BMI had a tendency towards a higher insulin concentration compared to those with normal BMI after accounting for current BMI in model 4. Children with rapid growth ~~catch-up~~ to high BMI had a tendency towards lower total cholesterol concentrations, and the effect estimate was increased after adjustment for current BMI in model 4. At 10 years, no evidence for associations were observed between the trajectories and other cardiometabolic markers including blood pressure, glucose, LDL cholesterol, HDL cholesterol, and triglyceride concentrations relative to normal BMI trajectory (Figure 3 and Supplementary Table 3).

After adjusting cardiometabolic markers for current FMI instead of BMI in sensitivity analysis, we only observed minor changes in the associations (**Supplementary Table 4**). In sensitivity analysis of associations between the BMI trajectories and change in cardiometabolic outcomes between the 5- and 10-year follow-ups, children in the rapid growth to high BMI trajectory had lower triglyceride concentrations compared to those in the normal BMI trajectory (**Supplementary Figure 2**). However, none of the trajectories predicted changes in blood pressure or markers of glucose metabolism. In addition, after controlling for breastfeeding status between 4 and 6 months in sensitivity analysis ~~among 272~~in children having the data, children with rapid growth ~~catch-up~~ to high BMI trajectory had greater height compared to those with normal BMI. The associations observed between the trajectories and other outcomes are almost similar to the main results, except for the effect estimates of some cardiometabolic markers were slightly attenuated (**Supplementary Figure ~~32~~**). In additional sensitivity analysis after imputing missing data using multiple imputation, most of the findings observed in the final model were similar to the complete case analysis except for slight increase in effect estimates (**Supplementary Table 5**). Moreover, in sensitivity analysis

after controlling for multiple testing in model 3, none of the observed associations were remained significant (**Supplementary Figure 43**).

Discussion

We assessed associations of previously identified 4-class discrete BMI trajectories from 0-5 years with anthropometry, body composition, abdominal fat, and cardiometabolic markers at 10 years of age. After accounting for potential confounders, children in the slow and rapid growth ~~catch-up~~ to high BMI trajectory had greater waist circumference and FMI and those in the slow growth~~catch-up~~ to high BMI had greater abdominal subcutaneous fat, while those in the stable low BMI had lower FFMI at 10 years of age. Children in the slow growth~~catch-up~~ to high BMI trajectory had higher insulin and HOMA-IR and those in the rapid growth~~catch-up~~ to high BMI had higher C-peptide, whereas those in the rapid growth ~~catch-up~~ to high BMI had lower total cholesterol at 10 years. The trajectories were not associated with abdominal visceral fat, blood pressure, glucose, LDL cholesterol, HDL cholesterol, and triglyceride concentrations at 10 years.

In both this 10-year follow-up and the 5-year follow-up, children with rapid growth ~~catch-up~~ to high BMI trajectory had higher waist circumference (30) suggesting that early childhood central adiposity tracks to later childhood. Children in the rapid growth ~~catch-up~~ trajectory showed deficits in waist circumference compared to either males or females reference data from LMICs (52, 53). This highlights that children in the trajectory may only have larger waist circumstance than those in the normal BMI trajectory, but they might not be at increased risk of central adiposity at 10 years of age. Correspondingly, studies from high income settings assessing group-based BMI trajectories in childhood reported associations of stable high and accelerating BMI trajectories with greater waist

circumference compared to stable low BMI trajectory (6, 54). Similar associations were also reported in adulthood (46).

We found that children in the two ~~catch-up~~high trajectories had higher FMI, whereas those with stable low BMI had lower FMI at both the 5-year and 10-year follow-ups (30). These consistent associations may highlight that those children who experienced high BMI growth patterns in early life are at greater risk of adiposity later in life. For instance, children in the rapid growth to high BMI had 0.5 kg/m^2 higher FMI compared to those in the normal BMI trajectory indicating that being in a rapid BMI trajectory growth is related to FM accumulation later in childhood, which has been consistently linked to cardiometabolic disease risk later in life (2, 55, 56). In addition, the association of stable low BMI trajectory with lower lean mass both at 5 and 10 years indicate that children who had lean mass deficit in early life might not be able to catch-up in FFM later in life (57). At 10-years, males and females in our cohort had lower mean FMI and FFMI compared to the UK reference data (58). Males and females had deficits in FMI of 0.42 and 1.16 kg/m2, respectively, while they had deficits in FFMI of 0.83 and 1.04 kg/m2, respectively. The trajectory with the highest mean FMI and FFMI (slow growth ~~catch-up~~ to high BMI) still showed deficits in both FMI and FFMI compared to either males or females UK reference data, except for FMI, which was slightly higher in the trajectory than males UK reference data (58). Therefore, in this population, children who experienced high BMI in early childhood ~~may not be~~are at increased risk of adiposity in relation to those in the normal BMI trajectory but might not in comparison to other Western populations~~in later childhood~~. ~~However, this relation might change after puberty given that these children are exposed to sedentary lifestyle.~~

In contrast to our current findings, children with rapid growth ~~catch-up~~ to high BMI trajectory had higher FFM at 5 years (30), and the lack of an association at 10 years might be attributed to that children in the rapid growth ~~catch-up~~ to high BMI gained lower lean mass than those in the normal

BMI trajectory from 5 to 10 years. In line with our current findings, studies conducted in high-income countries reported that children with accelerated or stable high BMI trajectory had greater FMI in later childhood or in early adult life (7, 19, 59).

Children with slow growth ~~catch-up~~ to high BMI trajectory had greater abdominal subcutaneous fat at 10 years. Weight gain in early life has been associated with abdominal subcutaneous fat in childhood/adolescent, but the association with visceral fat becomes noticeable later in life (60). Similarly, the lack of association between the trajectories and abdominal visceral fat in our study might be observed after the children accrue visceral fat later in life. At 10 years, children in the trajectory with highest BMI z-score (slow growth ~~catch-up~~ to high BMI) still had mean BMI z-score deficit of -0.27 compared to the WHO growth standards. Although we did not find a study which directly assessed associations of early childhood BMI trajectories with later abdominal subcutaneous fat, studies mainly from high-income settings reported associations between early childhood rapid or stable high BMI trajectory and fatness later in life (7, 61).

We found that children in the slow growth ~~catch-up~~ to high BMI trajectory had higher insulin and HOMA-IR, and those with rapid growth ~~catch-up~~ to high BMI had higher C-peptide after accounting for maternal and child characteristics at birth. These could possibly be explained by variation in adiposity (62). As such, children in the two ~~catch-up~~high BMI trajectories had greater measures of FM and abdominal subcutaneous fat than those in the normal BMI trajectory at 10 years of age. Children in the ~~catch-up~~high BMI trajectories might also have higher concentrations of growth hormone/IGF-1, which is related with increase in insulin concentration and HOMA-IR (63). At the 5-year follow-up of this cohort, only children in the rapid growth ~~catch-up~~ to high BMI, but not those in the slow growth ~~catch-up~~ to high BMI trajectory showed higher insulin, C-peptide, and HOMA-IR.

Children in the slow and rapid growth ~~catch-up~~ to high BMI trajectories had lower median insulin and HOMA-IR, but slightly higher glucose concentrations at 10 years compared to either males or females European reference data (64). Therefore, higher values of insulin, C-peptide, and HOMA-IR observed in the two ~~catch-up~~high trajectories may not suggest impaired glucose metabolism; rather, it only means that those children had higher levels of the markers than the children in the reference trajectory. Correspondingly, studies from high-income countries also showed associations between accelerated/high BMI trajectories and higher insulin and HOMA-IR in adolescents or early adulthood (65, 66).

The mechanism underlying the observed association between rapid ~~catch-up~~ BMI growth in early childhood and lower total cholesterol in later childhood is unclear. In low-income settings, there is limited information whether rapid~~/catch-up~~ growth in early life is related to poor health outcomes or has positive health effects later in life. Therefore, a comparable study from similar settings is warranted to investigate the consistency of our findings. Continued follow-up of the study population will also help to clarify if the observed associations between early childhood BMI trajectories and lipid profiles will continue after puberty. In contrast to the current findings, at 5 years follow-up of this cohort, we found that children in the rapid ~~catch-up~~growth to high BMI had higher triglycerides in relation to those in the normal BMI trajectory (30). The differences in findings at 5 and 10 years with regard to lipid profile could be attributed to that children in this cohort had higher FMI at 5 years (67) but lower values at 10 years of age compared to UK reference data (58). In turn, higher FM accretion is associated with greater cholesterol concentrations in childhood (68). Furthermore, children in our cohort had mean BMI z-score deficit of -0.78 at 10 years compared to the WHO growth reference standards, indicating that these children may not have increased risk of dyslipidemia related to childhood adiposity.

Strengths and limitations

Our study has several strengths. First, a median of 9 repeated measurements of weight and length/height for each child from birth to 5 years was used for the trajectory modelling. Second, we assessed FM and FFM at 10 years using air displacement plethysmography, which is considered a safe, accurate and feasible method for assessing the fat and fat-free components of the body~~body composition~~. Third, we~~the study~~ applied latent class trajectory modeling, a data-~~-~~driven method, and ~~to~~ identifi~~ed~~ed ~~-~~subgroups of children who followed distinct BMI ~~heterogenous~~ growth patterns ~~of BMI trajectories~~ in early childhood. Studies on health implications of early-life growth has conventionally used predetermined cut-offs to categorize growth as low, normal, or accelerated in distinct time intervals (69, 70). While such an approach is straightforward and may require lower longitudinal data density, it inevitably imposes observations into predefined groups in a specific period potentially overlooking the intricate and dynamic trajectories of child growth. It should be noted that latent class trajectory modeling is reducing the longitudinal data dimensionality, and as such these latent patterns should not be considered actual individual growth trajectories, but rather approximations of more complex ones.

~~However, t~~The study also has limitations. First, compared to the 5-year follow-up, we had fewer children in each BMI trajectory class at the 10-year follow-up which could have resulted in false negative results (type 2 error). However, we compared baseline characteristics between the children who attended the 5- and 10-year follow-ups and those who did not attend the 10-year follow-up, and children who attended the follow-ups had a slightly higher mean maternal height and childbirth length (**Supplementary Table 6**). Second, the observed growth patterns are likely a result of unmeasured exposures to other factors related to growth and body composition, and these exposures are most likely the underlaying "causes" of health status later in life. Third, because of the observational nature of the study design, it is not possible to ascertain causal-effect associations and we cannot rule out that the observed associations might be explained by other factors including

maternal BMI before or during pregnancy, or early childhood characteristics such as ~~food intake~~diet and physical activity. Fourth, ~~Third,~~ the children who did not attend the 10-year follow-up may have had different associations between the trajectories and the 10-year outcomes because some differences were observed in the maternal and child characteristics between those who attended and did not (Supplementary Table 1). Finally, children included in this study may not be representative of the general population because the cohort included only healthy and term children from an urban setting.

Conclusions

We have shown that associations of early childhood BMI trajectories with measures of adiposity, body composition, and glucose metabolism track to later childhood. Children with high BMI trajectories showed higher waist circumference, FMI, abdominal subcutaneous fat, and markers of glucose metabolism, whereas those with stable low BMI trajectory showed lower FFMI. However, the associations between the trajectories and lipid profile in childhood are only transient suggesting that in this setting, the risk of dyslipidemia in adult may primarily emerge from adolescence onwards upon accumulation of FM. Continued follow-up of the cohort will help to understand whether those children with stable low and/or high BMI trajectories are at increased risk of cardiometabolic disease in later life

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447 The authors contributions to the paper were: GSA, AA, TG, JCKW, and HF designed the study;
448 BSM, MB, BZ, RA, EK, DY conducted the study; BA, DN, SF, and RW assisted with data
449 interpretation and writing the manuscript; BSM and RW carried out statistical analysis. BSM wrote
450 the paper, and BSM and RW had primary responsibility for the final content. All authors read and
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Legends

Figure 1 Flow diagram of the study participants from birth to the 10-year follow-up.

Figure 2 Associations of BMI trajectories from 0-5 years with anthropometry, body composition, and abdominal fat at 10 years of age. The estimates (95% CI) were derived from multiple linear regression models and represent the mean differences of anthropometric measurements, body composition, and abdominal fat of each trajectory compared to the reference trajectory (normal BMI). We ran four separate models for each outcome variable, and the vertical bars from left to right represent models1, 2, 3, and 4, respectively. Each outcome is presented on the top of the exposure variables (BMI trajectories). Model 1 was adjusted for child's sex and age at 10 years. Model 2 was additionally adjusted for childbirth order, gestational age at birth, maternal age at delivery, maternal height, maternal highest educational status, and family economic status. Model 3 was further adjusted for child's birth weight. In addition to the preceding models, in model 4, we adjusted height for current BMI, waist circumference for fat-free mass index, fat mass index for fat-free mass index, fat-free mass index for fat mass index, and abdominal fat (subcutaneous and visceral) for current fat-free mass index. * = $P \leq 0.05$.

Figure 3 Associations of ~~distinct~~ BMI trajectories from 0-5 years with cardiometabolic markers at 10 years of age. The estimates (95%CI) were derived from multiple linear regression models and represent the mean difference of cardiometabolic markers between each trajectory in relation to the reference trajectory (normal BMI). Skew~~ed~~ variables (insulin, C-peptide, HOMA-IR, and triglycerides) were log-transformed before the regression analyses, and the estimates of these variables were back-transformed and presented as percentage changes. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as insulin (μU/mL) × glucose (mmol/L)/22.5. We ran four separate models for each outcome variable, and the vertical bars from

left to right represent models 1, 2, 3, and 4, respectively. Each outcome is presented on the top of the exposure variables (BMI trajectories). Model 1 was adjusted for child's sex and age at 10 years. Model 2 was additionally adjusted for childbirth order, gestational age at birth, maternal age at delivery, maternal height, maternal highest educational status, and family economic status. Model 3 was further adjusted for child's birth weight. In addition to the preceding models, model 4 was adjusted for BMI at 10-year of age.

Table 1 Maternal and child characteristics according to BMI trajectories from 0-5 years (n = 320)[1]

	Stable low BMI, n=65	Normal BMI, n=153	Rapid ~~catch-~~ ~~up~~growth to~~-~~ high BMI, ~~-~~n=56	Slow ~~catch-~~ ~~up~~growth to high BMI, n=46	~~*P* value~~[2]	Missing, n
Maternal characteristics after delivery						
_Age (years)	25.4 (4.6)	24.6 (4.6)	24.1 (4.5)	24.8 (5.5)	~~0.53~~	1
_Height (cm)	157.4 (5.5)	158.1 (5.9)	157.7 (5.5)	156.5 (6.3)	~~0.42~~	3
_Weight (kg)	54.9 (8.7)	56.8 (9.1)	57.0 (9.7)	58.8 (11.1)	~~0.37~~	82
_Body mass index (kg/m²)	22.3 (3.1)	22.6 (3.2)	23.0 (3.4)	23.8 (3.4)	~~0.26~~	84
_Maternal educational status					~~0.46~~	0
_No school	4 [6.2]	10 [6.5]	1 [1.8]	2 [4.3]		
_Primary school	39 [60.0]	99 [64.7]	31 [55.4]	26 [56.5]		
_Secondary school	10 [15.4]	26 [17.0]	15 [26.8]	13 [28.3]		
_Higher education	12 [18.5]	18 [11.8]	9 [16.1]	5 [10.9]		
_Family socioeconomic status (IWI)	47.0 (16.3)	45.8 (17.0)	48.0 (17.1)	47.4 (17.3)	~~0.83~~	1
Child characteristics at birth						
_Mode of delivery					~~0.68~~	0
_Vaginal delivery	61 [93.8]	145 [94.8]	51 [91.1]	42 [91.3]		
_Caesarean section	4 [6.2]	8 [5.2]	5 [8.9]	4 [8.7]		
_Sex, male	32 [49.2]	79 [51.6]	28 [50.0]	27 [58.7]	~~0.77~~	0
_Gestational age (weeks)	39.1 (0.9)	39.1 (1.0)	39.0 (0.9)	38.8 (0.7)	~~0.38~~	0
_Birth weight (kg)	3.1 (0.4)	3.1 (0.4)	3.0 (0.4)	3.0 (0.5)	~~0.42~~	0
_Length (cm)	49.2 (2.1)	49.4 (1.9)	49.3 (1.8)	49.0 (2.1)	~~0.65~~	0
_Body mass index (kg/m²)	12.7 (1.1)	12.7 (1.1)	12.3 (1.2)	12.6 (1.3)	~~0.20~~	0
_Fat mass (kg)	0.3 (0.2)	0.2 (0.2)	0.2 (0.1)	0.2 (0.2)	~~0.17~~	2
_Fat-free mass (kg)	2.8 (0.3)	2.9 (0.3)	2.8 (0.4)	2.8 (0.4)	~~0.85~~	2
_Fat mass index (kg/m²)	1.0 (0.8)	0.9 (0.6)	0.8 (0.6)	0.9 (0.6)	~~0.17~~	2
_Fat-free mass index (kg/m²)	11.7 (0.8)	11.7 (0.9)	11.6 (1.0)	11.7 (1.0)	~~0.76~~	2
_Birth order					~~0.15~~	2
_First	26 [40.6]	66 [43.4]	35 [62.5]	25 [54.4]		
_Second	18 [28.1]	47 [30.9]	12 [21.4]	9 [19.6]		
_Third and above	20 [31.2]	39 [25.7]	9 [16.1]	12 [26.1]		
_Low birth ~~weight~~[3]weight[2]	4 [6.2]	10 [6.5]	6 [10.7]	6 [13.0]	~~0.41~~	0
_Breastfeeding status at 4–6 months, n (%)					~~0.64~~	48
_Exclusive	3 [5.3]	17 [13.3]	7 [14.9]	3 [7.5]		
_Predominant	51 [89.5]	104 [81.2]	38 [80.8]	34 [85.0]		
_Partial or no	3 [5.3]	7 [5.5]	2 [4.3]	3 [7.5]		

[1]Data are mean (SD) and n [%]. ~~[2] Differences across trajectories were calculated by one-way ANOVA F-test for continuous variables, Pearson's chi-squared test of independence for categorical variables with the expected counts > 4 in all cells and Fisher's exact test of independence for categorical variables with expected count in any cell ≤4. [3]Birth~~ [2]Birth weight <2500 g. IWI, international wealth index.

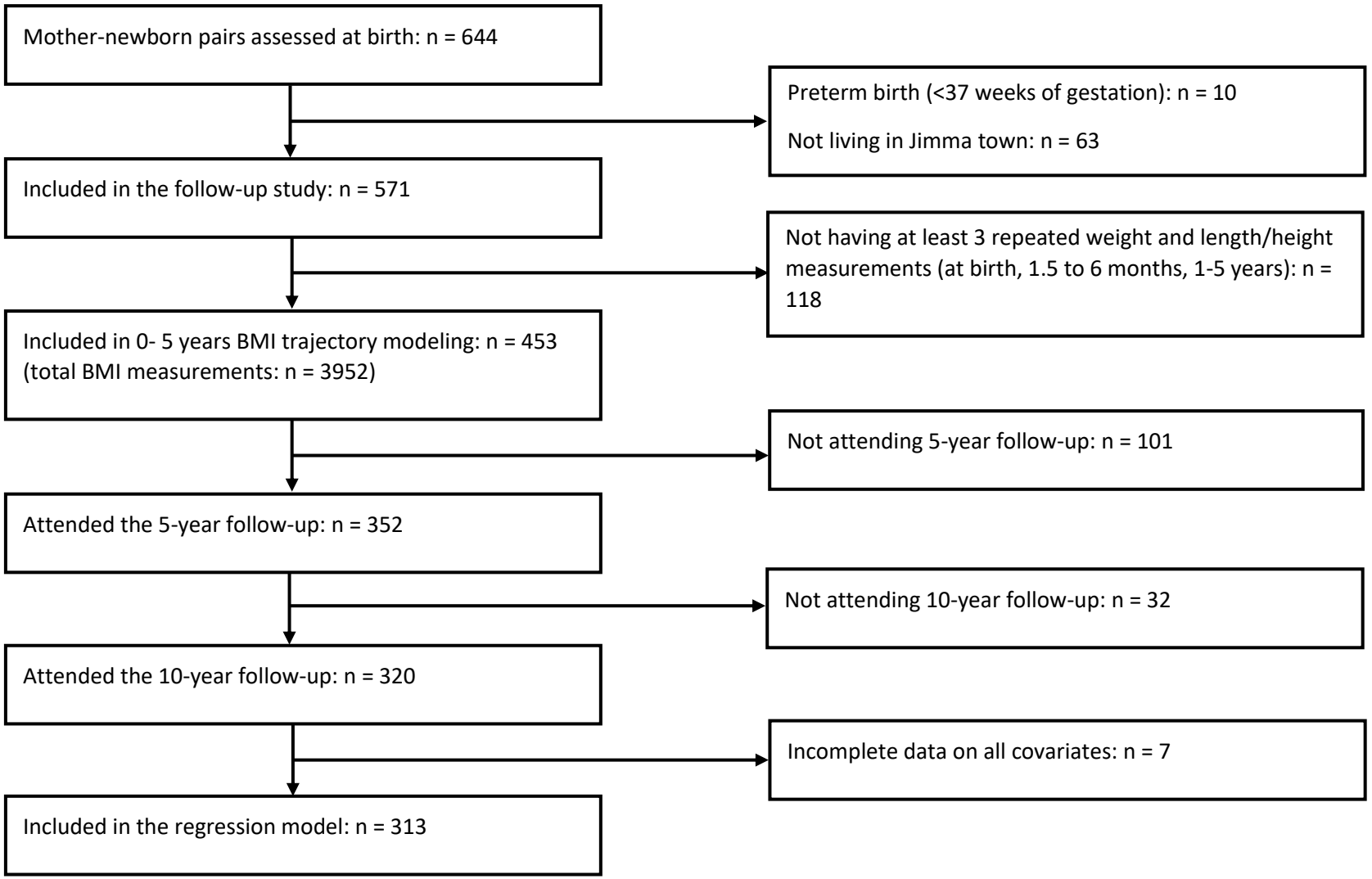
Table 2 Child anthropometry, body composition, abdominal fat, and cardiometabolic markers at 10 years by the trajectories from 0-5 years (n = 320)[1]

	Stable low BMI, n=65	Normal BMI, n=153	Rapid ~~catch up~~growth to high BMI, n=56	Slow ~~catch up~~growth to high BMI, n=46	~~*P* value~~[2]	Missing , n
Age (years)	9.8 (0.9)	9.9 (1.0)	9.5 (1.0)	9.8 (0.9)	~~0.07~~	0
Anthropometry						
_Weight (kg)	25.7 (6.0)	27.3 (5.7)	27.6 (4.5)	28.6 (7.2)	~~0.07~~	0
_Height (cm)	131.4 (7.6)	132.7 (7.7)	132.1 (7.5)	131.6 (8.0)	~~0.65~~	0
_Body mass index (kg/m²)	14.8 (2.4)	15.4 (2.0)	15.8 (1.7)	16.3 (2.5)	~~0.001~~	0
_Height-for-age z-score	-0.85 (0.92)	-0.81 (0.91)	-0.56 (0.85)	-0.85 (0.89)	~~0.23~~	0
_~~Stunted~~[3]Stunted[2]	8 [12.3]	13 [8.5]	2 [3.6]	4 [8.7]	~~0.41~~	0
_BMI-for-age z-score	-1.28 (1.37)	-0.85 (1.02)	-0.44 (0.93)	-0.27 (1.09)	~~<0.001~~	0
_Wasted/~~thinness~~[4]thinness[3]	20 [30.8]	16 [10.5]	1 [1.8]	1 [2.2]	~~<0.001~~	0
_Overweight/~~obese~~[5]obese[4]	5 [7.7]	7 [4.6]	7 [12.5]	7 [15.2]	~~0.06~~	0
_Waist circumference (cm)	54.3 (6.2)	55.9 (5.1)	56.9 (4.7)	57.4 (6.6)	~~0.012~~	0
Body composition						
_Fat mass (kg)	4.8 (3.5)	5.5 (3.3)	6.0 (3.0)	6.5 (4.0)	~~0.049~~	2
_Fat-free mass (kg)	21.0 (3.6)	21.9 (3.3)	21.7 (2.7)	22.0 (3.7)	~~0.23~~	2
_Fat mass index (kg/m²)	2.7 (1.8)	3.0 (1.6)	3.4 (1.6)	3.6 (1.8)	~~0.018~~	2
_Fat-free mass index (kg/m²)	12.1 (1.2)	12.4 (1.1)	12.4 (0.9)	12.6 (1.1)	~~0.043~~	2
Abdominal fat						
_Subcutaneous (cm)	0.6 (0.5)	0.6 (0.5)	0.7 (0.4)	0.9 (0.8)	~~0.016~~	4
_Visceral (cm)	3.9 (0.9)	3.9 (0.9)	3.9 (1.0)	4.1 (0.9)	~~0.40~~	4
Blood pressure						
_Systolic (mmHg)	95.2 (6.5)	95.1 (6.1)	93.9 (7.5)	94.5 (6.1)	~~0.64~~	0
_Diastolic (mmHg)	57.6 (8.4)	58.4 (7.4)	58.3 (7.7)	56.9 (7.2)	~~0.68~~	0
Glucose metabolism						
_Glucose (mmol/L)	5.1 (0.7)	5.2 (0.7)	5.2 (0.6)	5.3 (0.6)	~~0.71~~	5
_Insulin (µU/mL)[6]5	3.8 (2.2-5.8)	3.7 (2.0-5.8)	3.9 (2.3-6.9)	4.0 (2.1-6.5)	~~0.77~~	8
_C-peptide (ng/mL)~~-6~~5	0.3 (0.1-0.7)	0.3 (0.1-0.7)	0.6 (0.1-0.8)	0.4 (0.1-1.0)	~~0.61~~	8
_HOMA-~~IR~~[6]IR[5,7]6	0.9 (0.5-1.3)	0.9 (0.5-1.4)	0.9 (0.5-1.4)	0.8 (0.5-1.6)	~~0.88~~	8
Lipids						
_Total cholestrol (mmol/L)	3.3 (0.8)	3.4 (0.8)	3.2 (0.7)	3.4 (0.7)	~~0.29~~	7
_LDL cholesterol (mmol/L)	1.7 (0.5)	1.7 (0.5)	1.7 (0.5)	1.7 (0.4)	~~0.92~~	7
_HDL cholesterol (mmol/L)	1.0 (0.3)	1.0 (0.3)	1.0 (0.3)	1.0 (0.3)	~~0.90~~	7
_Triglycerides (mmol/L)[6]5	0.8 (0.7-0.9)	0.8 (0.7-1.0)	0.8 (0.6-1.0)	0.8 (0.7-1.0)	~~0.89~~	8

[1]Data are mean (SD), median (IQR), and n [%].-~~[2]Differences across trajectories were calculated by one-way ANOVA F-test for continuous normally distributed variables, Kruskal-Wallis test for continuous skewed variables, Pearson's chi-squared test of independence for~~

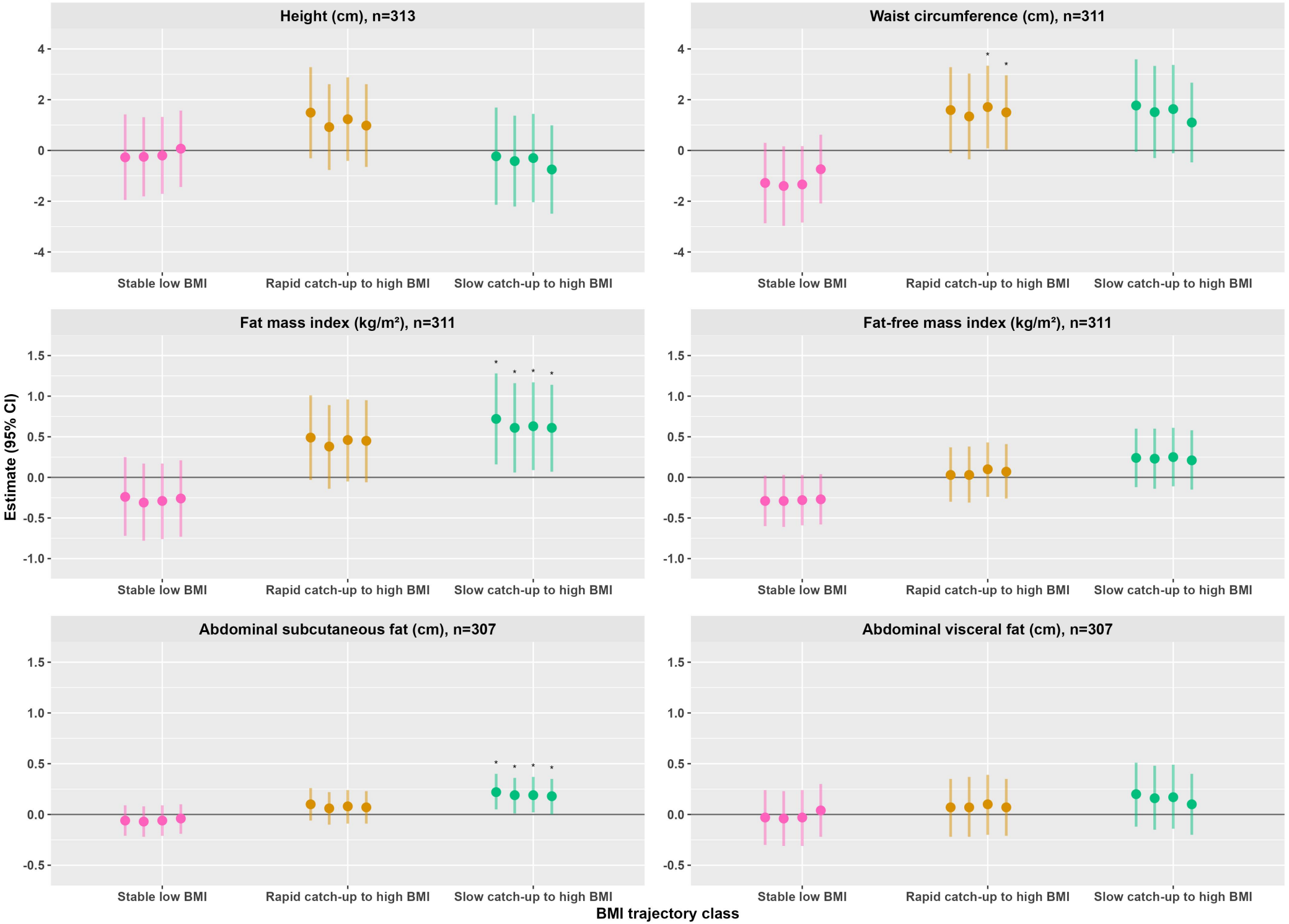
~~categorical variables with the expected counts >4 in all cells and Fisher's exact test of independence for categorical variables with expected count in any cell ≤4.~~ [3]~~Height~~[2]Height-for-age z-score <2. [4]~~BMI~~[3]BMI-for-age z-score <2. [5]~~BMI~~[4]BMI-for-age z-score >1. [6]~~Data~~ [5]Data are median (IQR). [7]~~Homeostasis~~ [6]Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as insulin (μU/mL) × glucose (mmol/L)/22.5.

Figure



Figure

Click here to access/download;Figure;Figure 2.pdf



Figure

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Supplementary material

Title: Associations of early childhood body mass index trajectories with body composition and cardiometabolic markers at age 10 years: the Ethiopian iABC birth cohort study

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Supplementary Table 1 Comparison of maternal and child characteristics between those who attended the 10-year follow-up and those who did not attend[1]

	n	Attended	n	Not attended	*P* value[2]	Missing, n
Maternal characteristics after delivery						
Age (years)	319	24.7 (4.7)	241	23.6 (4.5)	0.003	11
Height (cm)	317	157.7 (5.8)	218	157.5 (5.9)	0.79	36
Weight (kg)	238	56.7 (9.4)	170	55.8 (8.5)	0.28	163
BMI (kg/m²)	236	22.7 (3.3)	170	22.4 (3.0)	0.29	165
Maternal educational status, n (%)	320		245		0.35	6
No school		17 [5.3]		21 [8.6]		
Primary school		195 [60.9]		152 [62.0]		
Secondary school		64 [20.0]		40 [16.3]		
Higher education		44 [13.8]		32 [13.1]		
Family Socioeconomic status (IWI)	319	46.7 (16.8)	239	43.8 (19.6)	0.06	13
Child characteristics						
Mode of delivery, n (%)	320		240		0.42	11
Vaginal delivery		299 [93.4]		219 [91.2]		
Caesarean section		21 [6.6]		21 [8.8]		
Sex, male, n (%)	320	166 [51.9]	251	114 [45.4]	0.15	0
Gestational age (weeks)	320	39.0 (0.9)	251	39.0 (1.0)	0.98	0
Birth weight (kg)	320	3.1 (0.4)	251	3.0 (0.4)	0.006	0
Length (cm)	320	49.3 (2.0)	251	48.9 (2.0)	0.025	0
BMI (kg/m²)	320	12.6 (1.1)	251	12.4 (1.2)	0.027	0
Fat mass (kg)	318	0.2 (0.2)	250	0.2 (0.1)	0.11	3
Fat-free mass (kg)	318	2.85 (0.32)	250	2.77 (0.34)	0.007	3
Fat mass index (kg/m²)	318	0.9 (0.7)	250	0.8 (0.6)	0.15	3
Fat-free mass index (kg/m²)	318	11.7 (0.9)	250	11.6 (1.0)	0.08	3
Child birth order, n (%)	318		239		0.002	14
First		152 [47.8]		149 [62.3]		
Second		86 [27.0]		51 [21.3]		
Third and above		80 [25.2]		39 [16.3]		
Low birth weight, n (%)[3]	320	26 [8.1]	251	33 [13.2]	0.07	0
Breastfeeding status at 4-6 months, n (%)	272		118		0.67	181
Exclusive		30 [11.0]		13 [11.0]		
Predominant		227 [83.5]		101 [85.6]		
Partial or no		15 [5.5]		4 [3.4]		

[1]Data are mean (SD) and n [%]. [2]Differences between children who attended the 10-year follow-up and those did not attend were calculated by one-way ANOVA F-test for continuous variables, Pearson's chi-squared test of independence for categorical variables with expected counts > 4 in all cells, and else Fisher's exact test. [3]Birth weight <2500 g. IWI, International Wealth Index.

Supplementary Table 2 Child anthropometry, body composition, abdominal fat, and cardiometabolic markers at 10 years by sex[1]

	Full sample (n=320)	n	Males	n	Females	Missing, n
Anthropometry						
Weight (kg)	27.2 (5.8)	166	27.2 (6.0)	154	27.4 (5.6)	0
Height (cm)	132.2 (7.7)	166	132.0 (7.6)	154	132.4 (7.8)	0
BMI (kg/m²)	15.5 (2.1)	166	15.4 (2.1)	154	15.5 (2.1)	0
Height z-score	-0.78 (0.90)	166	-0.77 (0.92)	154	-0.80 (0.88)	0
BMI z-score	-0.78 (1.14)	166	-0.82 (1.18)	154	-0.74 (1.09)	0
Waist circumference (cm)	55.9 (5.6)	166	56.3 (5.8)	154	55.5 (5.3)	0
Body composition						
Fat mass (kg)	5.59 (3.43)	165	5.29 (3.40)	153	5.91 (3.45)	2
Fat-free mass (kg)	21.69 (3.32)	165	21.92 (3.51)	153	21.45 (3.10)	2
Fat mass index (kg/m²)	3.12 (1.70)	165	2.95 (1.66)	153	3.30 (1.72)	2
Fat-free mass index (kg/m²)	12.36 (1.08)	165	12.52 (1.09)	153	12.20 (1.04)	2
Abdominal fat						
Subcutaneous fat (cm)	0.7 (0.5)	163	0.6 (0.5)	153	0.7 (0.5)	4
Visceral fat (cm)	3.9 (0.9)	163	4.0 (0.9)	153	3.8 (0.9)	4
Blood pressure						
Systolic (mmHg)	94.8 (6.4)	166	95.0 (6.6)	154	94.6 (6.3)	0
Diastolic (mmHg)	58.0 (7.6)	166	58.0 (7.4)	154	58.0 (7.8)	0
Glucose metabolism						
Glucose (mmol/L)	5.2 (0.7)	163	5.3 (0.6)	152	5.2 (0.7)	5
Insulin (μU/mL) [2]	3.8 (2.1-6.1)	163	3.4 (1.8-5.6)	149	4.3 (3.0-6.2)	8
C-peptide (ng/mL) [2]	0.3 (0.1-0.8)	163	0.3 (0.1-0.8)	149	0.3 (0.1-0.7)	8
HOMA-IR[2,3]	0.9 (0.5-1.4)	163	0.8 (0.4-1.3)	149	1.0 (0.7-1.5)	8
Lipids						
Total cholestrol (mmol/L)	3.3 (0.8)	163	3.3 (0.8)	150	3.4 (0.7)	7
HDL cholesterol (mmol/L)	1.0 (0.3)	163	1.0 (0.3)	150	1.0 (0.3)	7
LDL cholesterol (mmol/L)	1.7 (0.5)	163	1.7 (0.5)	150	1.8 (0.5)	7
Triglycerides (mmol/L)[2]	0.8 (0.7-1.0)	163	0.8 (0.6-0.9)	149	0.8 (0.7-1.1)	8

[1]Data are mean (SD) unless otherwise indicated, [2]median (IQR). [3]Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as insulin (μU/mL) × glucose (mmol/L)/22.5.

Supplementary Table 3 Associations of BMI trajectories from 0-5 years with anthropometry, body composition, abdominal fat, and cardiometabolic risk factors at 10 years of age relative to normal BMI trajectory[1]

	N	Stable low BMI	*P* value	Rapid growth to high BMI	*P* value	Slow growth to high BMI	*P* value
		β(95%CI)		β(95%CI)		β(95%CI)	
Height (cm)							
Model 1	313	-0.27 (-1.95, 1.42)	0.76	1.49 (-0.31, 3.28)	0.10	-0.23 (-2.14, 1.69)	0.82
Model 2	313	-0.25 (-1.81, 1.31)	0.75	0.92 (-0.77, 2.61)	0.29	-0.42 (-2.21, 1.37)	0.64
Model 3	313	-0.20 (-1.71, 1.32)	0.80	1.23 (-0.41, 2.88)	0.14	-0.30 (-2.04, 1.44)	0.73
Model 4	313	0.07 (-1.44, 1.57)	0.93	0.98 (-0.65, 2.61)	0.24	-0.75 (-2.49, 0.99)	0.40
Waist circumference (cm)							
Model 1	311	-1.28 (-2.87, 0.30)	0.11	1.59 (-0.10, 3.28)	0.07	1.77 (-0.05, 3.59)	0.06
Model 2	311	-1.40 (-2.97, 0.16)	0.08	1.34 (-0.35, 3.03)	0.12	1.51 (-0.30, 3.33)	0.10
Model 3	311	-1.34 (-2.84, 0.17)	0.08	1.71 (0.08, 3.34)	0.040	1.63 (-0.11, 3.37)	0.08
Model 4	311	-0.74 (-2.09, 0.62)	0.29	1.50 (0.03, 2.96)	0.045	1.10 (-0.47, 2.67)	0.17
Fat mass index (kg/m²)							
Model 1	311	-0.24 (-0.72, 0.25)	0.34	0.49 (-0.03, 1.01)	0.06	0.72 (0.16, 1.28)	0.012
Model 2	311	-0.31 (-0.78, 0.17)	0.20	0.38 (-0.14, 0.89)	0.15	0.61 (0.06, 1.16)	0.030
Model 3	311	-0.29 (-0.76, 0.17)	0.22	0.46 (-0.05, 0.96)	0.07	0.63 (0.09, 1.17)	0.021
Model 4	311	-0.26 (-0.73, 0.21)	0.27	0.45 (-0.06, 0.95)	0.08	0.61 (0.07, 1.14)	0.028
Fat-free mass index (kg/m²)							
Model 1	311	-0.29 (-0.60, 0.02)	0.07	0.03 (-0.30, 0.37)	0.85	0.24 (-0.12, 0.60)	0.19
Model 2	311	-0.29 (-0.61, 0.03)	0.07	0.03 (-0.31, 0.38)	0.84	0.23 (-0.14, 0.60)	0.23
Model 3	311	-0.28 (-0.59, 0.03)	0.08	0.10 (-0.24, 0.43)	0.57	0.25 (-0.11, 0.61)	0.18
Model 4	311	-0.27 (-0.58, 0.04)	0.09	0.07 (-0.26, 0.41)	0.67	0.21 (-0.15, 0.58)	0.25
Abdominal subcutaneous fat (cm)							
Model 1	307	-0.06 (-0.21, 0.09)	0.46	0.10 (-0.06, 0.26)	0.22	0.22 (0.05, 0.40)	0.013
Model 2	307	-0.07 (-0.22, 0.08)	0.38	0.06 (-0.10, 0.22)	0.48	0.19 (0.01, 0.36)	0.035
Model 3	307	-0.06 (-0.21, 0.09)	0.40	0.08 (-0.09, 0.24)	0.36	0.19 (0.02, 0.37)	0.029
Model 4	307	-0.04 (-0.19, 0.10)	0.56	0.07 (-0.09, 0.23)	0.40	0.18 (0.00, 0.35)	0.047
Abdominal visceral fat (cm)							
Model 1	307	-0.03 (-0.30, 0.24)	0.83	0.07 (-0.22, 0.35)	0.64	0.20 (-0.12, 0.51)	0.22
Model 2	307	-0.04 (-0.31, 0.23)	0.78	0.07 (-0.22, 0.37)	0.63	0.16 (-0.15, 0.48)	0.31
Model 3	307	-0.03 (-0.31, 0.24)	0.80	0.10 (-0.20, 0.39)	0.52	0.17 (-0.14, 0.49)	0.29
Model 4	307	0.04 (-0.22, 0.30)	0.74	0.07 (-0.21, 0.35)	0.62	0.10 (-0.20, 0.40)	0.52
Systolic blood pressure (mmHg)							
Model 1	313	0.27 (-1.50, 2.04)	0.76	-0.30 (-2.19, 1.59)	0.75	-0.56 (-2.58, 1.45)	0.58
Model 2	313	0.36 (-1.43, 2.15)	0.69	-0.24 (-2.18, 1.69)	0.81	-0.58 (-2.64, 1.47)	0.58
Model 3	313	0.39 (-1.40, 2.17)	0.67	-0.09 (-2.03, 1.84)	0.93	-0.53 (-2.58, 1.52)	0.61
Model 4	313	0.47 (-1.32, 2.27)	0.60	-0.18 (-2.12, 1.77)	0.86	-0.67 (-2.75, 1.41)	0.53

Supplementary Table 3 (continued) Associations of BMI trajectories from 0-5 years with anthropometry, body composition, abdominal fat, and cardiometabolic risk factors at 10 years of age relative to normal BMI trajectory[1]

	N	Stable low BMI	*P* value	Rapid growth to high BMI	*P* value	Slow growth to high BMI	*P* value
		β(95%CI)		β(95%CI)		β(95%CI)	
Diastolic blood pressure (mmHg)							
Model 1	313	-0.47 (-2.65, 1.70)	0.67	0.72 (-1.60, 3.04)	0.54	-0.84 (-3.31, 1.63)	0.50
Model 2	313	-0.52 (-2.71, 1.68)	0.64	0.33 (-2.04, 2.70)	0.79	-1.05 (-3.57, 1.47)	0.41
Model 3	313	-0.47 (-2.65, 1.70)	0.67	0.60 (-1.76, 2.96)	0.62	-0.95 (-3.45, 1.55)	0.45
Model 4	313	-0.26 (-2.44, 1.92)	0.82	0.39 (-1.97, 2.76)	0.74	-1.31 (-3.83, 1.22)	0.31
Glucose (mmol/L)							
Model 1	308	-0.12 (-0.31, 0.08)	0.24	-0.03 (-0.23, 0.18)	0.78	0.01 (-0.21, 0.23)	0.93
Model 2	308	-0.10 (-0.29, 0.09)	0.31	-0.01 (-0.22, 0.19)	0.89	0.02 (-0.21, 0.24)	0.87
Model 3	308	-0.10 (-0.29, 0.09)	0.31	-0.02 (-0.23, 0.19)	0.84	0.02 (-0.21, 0.24)	0.89
Model 4	308	-0.11 (-0.31, 0.08)	0.26	-0.01 (-0.22, 0.20)	0.92	0.03 (-0.19, 0.26)	0.77
Insulin (% change)							
Model 1	305	9.6 (-13.1, 38.2)	0.44	16.4 (-9.3, 49.4)	0.23	24.6 (-5.0, 63.4)	0.11
Model 2	305	9.0 (-13.4, 37.2)	0.46	16.6 (-9.2, 49.7)	0.23	28.3 (-2.2, 68.3)	0.07
Model 3	305	9.5 (-12.8, 37.5)	0.44	20.2 (-6.3, 54.1)	0.15	29.8 (-0.8, 69.8)	0.06
Model 4	305	19.7 (-3.0, 47.7)	0.09	9.8 (-12.7, 38.1)	0.42	11.3 (-13.3, 42.9)	0.40
C-peptide (% change)							
Model 1	305	7.2 (-26.4, 56.0)	0.72	36.6 (-8.7, 104.4)	0.13	37.3 (-11.4, 112.7)	0.16
Model 2	305	7.4 (-26.4, 56.7)	0.71	42.7 (-5.4, 115.1)	0.09	43.1 (-8.4, 123.5)	0.11
Model 3	305	8.0 (-25.8, 57.2)	0.69	48.6 (-1.4, 123.8)	0.06	45.4 (-6.6, 126.5)	0.10
Model 4	305	13.1 (-22.3, 64.7)	0.52	41.8 (-5.9, 113.5)	0.09	34.2 (-14.1, 109.8)	0.20
HOMA-IR (% change)							
Model 1	305	7.4 (-15.3, 36.3)	0.55	16.3 (-10.0, 50.1)	0.25	24.7 (-5.6, 64.6)	0.12
Model 2	305	7.3 (-15.2, 35.8)	0.56	16.8 (-9.6, 50.9)	0.23	28.8 (-2.5, 70.0)	0.07
Model 3	305	7.7 (-14.7, 36.0)	0.53	20.2 (-6.8, 55.1)	0.16	30.3 (-1.1, 71.6)	0.06
Model 4	305	17.5 (-5.5, 46.0)	0.15	10.1 (-13.1, 39.6)	0.42	12.1 (-13.4, 45.2)	0.38
Total cholesterol (mmol/L)							
Model 1	306	-0.06 (-0.28, 0.17)	0.61	-0.22 (-0.46, 0.02)	0.08	-0.01 (-0.27, 0.25)	0.93
Model 2	306	-0.10 (-0.32, 0.12)	0.38	-0.22 (-0.47, 0.02)	0.07	-0.02 (-0.29, 0.24)	0.86
Model 3	306	-0.10 (-0.32, 0.12)	0.38	-0.23 (-0.47, 0.02)	0.07	-0.02 (-0.29, 0.24)	0.85
Model 4	306	-0.09 (-0.31, 0.14)	0.44	-0.24 (-0.48, 0.01)	0.06	-0.05 (-0.31, 0.22)	0.74

Supplementary Table 3 (continued) Associations of BMI trajectories from 0-5 years with anthropometry, body composition, abdominal fat, and cardiometabolic risk factors at 10 years of age relative to normal BMI trajectory[1]

	N	Stable low BMI	*P* value	Rapid growth to high BMI	*P* value	Slow growth to high BMI	*P* value
		β(95%CI)		β(95%CI)		β(95%CI)	
LDL cholesterol (mmol/L)							
Model 1	306	-0.07 (-0.21, 0.07)	0.34	-0.03 (-0.18, 0.12)	0.72	-0.04 (-0.20, 0.12)	0.61
Model 2	306	-0.09 (-0.23, 0.05)	0.21	-0.03 (-0.18, 0.12)	0.68	-0.06 (-0.22, 0.10)	0.47
Model 3	306	-0.09 (-0.23, 0.05)	0.21	-0.03 (-0.18, 0.12)	0.70	-0.06 (-0.22, 0.10)	0.48
Model 4	306	-0.08 (-0.22, 0.06)	0.26	-0.04 (-0.19, 0.11)	0.62	-0.07 (-0.24, 0.09)	0.39
HDL cholesterol (mmol/L)							
Model 1	306	-0.02 (-0.11, 0.07)	0.74	-0.03 (-0.13, 0.07)	0.52	-0.03 (-0.13, 0.08)	0.63
Model 2	306	-0.02 (-0.11, 0.07)	0.63	-0.04 (-0.13, 0.06)	0.49	-0.04 (-0.14, 0.07)	0.52
Model 3	306	-0.02 (-0.11, 0.07)	0.64	-0.03 (-0.13, 0.07)	0.56	-0.03 (-0.14, 0.07)	0.54
Model 4	306	-0.03 (-0.12, 0.06)	0.56	-0.02 (-0.12, 0.08)	0.64	-0.02 (-0.13, 0.09)	0.67
Triglycerides (% change)							
Model 1	305	-1.5 (-10.7, 8.7)	0.77	-1.3 (-11.2, 9.6)	0.81	1.8 (-9.2, 14.1)	0.76
Model 2	305	-1.3 (-10.6, 9.0)	0.79	0.6 (-9.7, 12.0)	0.91	3.5 (-8.0, 16.3)	0.57
Model 3	305	-1.3 (-10.6, 9.0)	0.80	0.7 (-9.6, 12.3)	0.89	3.5 (-7.9, 16.4)	0.56
Model 4	305	-0.5 (-10.0, 9.9)	0.92	-0.0 (-10.4, 11.4)	0.99	2.1 (-9.3, 15.0)	0.73

[1]The coefficients (β) and (95 % CI) were derived from multiple linear regression, and represent the mean difference between the reference trajectory (normal BMI) and each trajectory class. [2]Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated as insulin (μU/mL) × glucose (mmol/L)/22.5. Skew variables (insulin, C-peptide, HOMA-IR, and triglycerides) were log-transformed prior to the regression analyses, and the estimates of these variables were back-transformed and presented as percentage changes. Model 1 was adjusted for child's sex and age at 10 years. Model 2 was additionally adjusted for childbirth order, gestational age at birth, maternal age at delivery, maternal height, maternal highest educational status, and parental economic status. Model 3 was further adjusted for child's birth weight. In addition to the preceding models, model 4 was adjusted for current BMI, except for waist circumference which was adjusted for fat-free mass index, fat mass index for fat-free mass index, fat-free mass index for fat mass index, abdominal fat (subcutaneous and visceral) for current fat-free mass index.

Supplementary Table 4 Sensitivity analyses of the associations between BMI trajectories from 0-5 years and cardiometabolic markers at 10 years after adjusting for current FMI instead of BMI in Model 4[1]

	N	Stable low BMI	*P* value	Rapid growth to high BMI	*P* value	Slow growth to high BMI	*P* value
		β (95%CI)		β (95%CI)		β (95%CI)	
Systolic blood pressure (mmHg)	311	0.42 (-1.38, 2.22)	0.65	-0.21 (-2.16, 1.75)	0.84	-0.59 (-2.69, 1.50)	0.58
Diastolic blood pressure (mmHg)	311	-0.42 (-2.57, 1.73)	0.70	0.19 (-2.15, 2.53)	0.87	-1.32 (-3.83, 1.19)	0.30
Glucose (mmol/L)	306	-0.11 (-0.30, 0.09)	0.28	-0.01 (-0.23, 0.20)	0.89	0.04 (-0.19, 0.27)	0.71
Insulin (% change)	303	17.1 (-5.1, 44.5)	0.14	11.9 (-11.1, 40.8)	0.34	13.4 (-11.8, 45.8)	0.33
C-peptide (% change)	303	12.7 (-22.2, 63.2)	0.53	36.9 (-8.7, 105.2)	0.13	33.9 (-14.0, 108.5)	0.20
HOMA-IR (% change)[2]	303	15.1 (-7.4, 43.0)	0.20	12.1 (-11.6, 42.2)	0.34	14.5 (-11.7, 48.5)	0.31
Total cholesterol (mmol/L)	304	-0.09 (-0.32, 0.13)	0.41	-0.24 (-0.49, 0.00)	0.05	-0.04 (-0.31, 0.24)	0.80
LDL cholesterol (mmol/L)	304	-0.08 (-0.22, 0.05)	0.23	-0.05 (-0.20, 0.10)	0.54	-0.07 (-0.23, 0.10)	0.41
HDL cholesterol (mmol/L)	304	-0.02 (-0.11, 0.07)	0.65	-0.04 (-0.14, 0.07)	0.49	-0.04 (-0.15, 0.07)	0.52
Triglycerides (% change)	303	-0.6 (-10.0, 9.8)	0.91	0.7 (-9.7, 12.3)	0.90	2.9 (-8.6, 16.0)	0.64

[1]The coefficients (β) and (95% CI) were derived from multiple linear regression, and represent the mean difference between the reference trajectory (normal BMI) and each trajectory class. [2]Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated as insulin (μU/mL) × glucose (mmol/L)/22.5. Slightly skew variables (insulin, C-peptide, HOMA-IR, and triglycerides) were log-transformed before the regression analyses, and the estimates of these variables were back-transformed and presented as percentage changes. Model 1 was adjusted for child's sex and age at 10 years. Model 2 was additionally adjusted for childbirth order, gestational age at birth, maternal age at delivery, maternal height, maternal highest educational status, and parental economic status (wealth index). Model 3 was further adjusted for child's birth weight. In addition to the preceding models, model 4 was adjusted for fat mass index at the 10-year follow-up.

Supplementary Table 5 Sensitivity analyses of the associations of BMI trajectories from 0-5 years with anthropometry, body composition, abdominal fat, and cardiometabolic markers at 10 years in model 3 (final model) after imputing missing data using multiple imputation[1]

	N	Stable low BMI	*P* value	Rapid growth to high BMI	*P* value	Slow growth to high BMI	*P* value
		β (95%CI)		β (95%CI)		β (95%CI)	
Height (cm)	346	0.09 (-1.57, 1.40)	0.91	1.01 (-0.43, 2.73)	0.23	-0.21 (-1.92, 1.40)	0.81
Waist circumference (cm)	346	-1.14 (-2.68, 0.26)	0.13	1.56 (-0.02, 3.10)	0.06	2.24 (0.76, 4.06)	0.010
Fat mass index (kg/m²)	346	-0.25 (-0.69, 0.20)	0.29	0.41 ((-0.08, 0.91)	0.11	0.83 (0.32, 1.35)	0.003
Fat-free mass index (kg/m²)	346	-0.27 (-0.58, 0.02)	0.08	0.07 (-0.25, 0.41)	0.67	0.39 (0.07, 0.77)	0.034
Abdominal subcutaneous fat (cm)	346	-0.05 (-0.19, 0.09)	0.47	0.06 (-0.10, 0.22)	0.46	0.28 (0.12, 0.45)	0.001
Abdominal visceral fat (cm)	346	-0.03 (0.30, 0.22)	0.85	0.08 (-0.20, 0.35)	0.60	0.26 (-0.03, 0.56)	0.09
Systolic blood pressure (mmHg)	346	0.92 (-0.89, 2.52)	0.31	-0.25 (-2.19, 1.59)	0.80	-0.17 (-2.58, 1.45)	0.87
Diastolic blood pressure (mmHg)	346	-0.31 (-2.65, 1.70)	0.78	0.66 (-1.60, 3.04)	0.56	-1.19 (-3.31, 1.63)	0.33
Glucose (mmol/L)	346	-0.08 (-0.25, 0.11)	0.42	0.02 (-0.18, 0.22)	0.85	0.02 (-0.24, 0.18)	0.85
Insulin (% change)	346	8.3 (-13.5, 33.0)	0.48	19.9 (-4.4, 52.6)	0.15	26.0 (-3.0, 59.6)	0.08
C-peptide (% change)	346	6.9 (-26.4, 56.0)	0.73	47.0 (-1.8, 114)	0.06	37.6 (-4.0, 117)	0.14
HOMA-IR (% change)	346	6.7 (-15.2, 31.2)	0.57	20.5 (-4.1, 54.2)	0.14	26.8 (-2.7, 62.3)	0.08
Total cholesterol (mmol/L)	346	-0.08 (-0.28, 0.17)	0.47	-0.19 (-0.46, 0.02)	0.14	0.05 (-0.27, 0.25)	0.69
LDL cholesterol (mmol/L)	346	-0.08 (-0.21, 0.07)	0.25	-0.03 (-0.18, 0.12)	0.67	-0.02 (-0.20, 0.12)	0.81
HDL cholesterol (mmol/L)	346	-0.02 ((-0.10, 0.07)	0.65	-0.03 (-0.12, 0.07)	0.52	-0.03 (-0.13, 0.06)	0.50
Triglycerides (% change)	346	-1.12 (-10.1, 9.1)	0.82	1.83 (-8.1, 12.8)	0.74	5.18 (-6.3, 16.4)	0.40

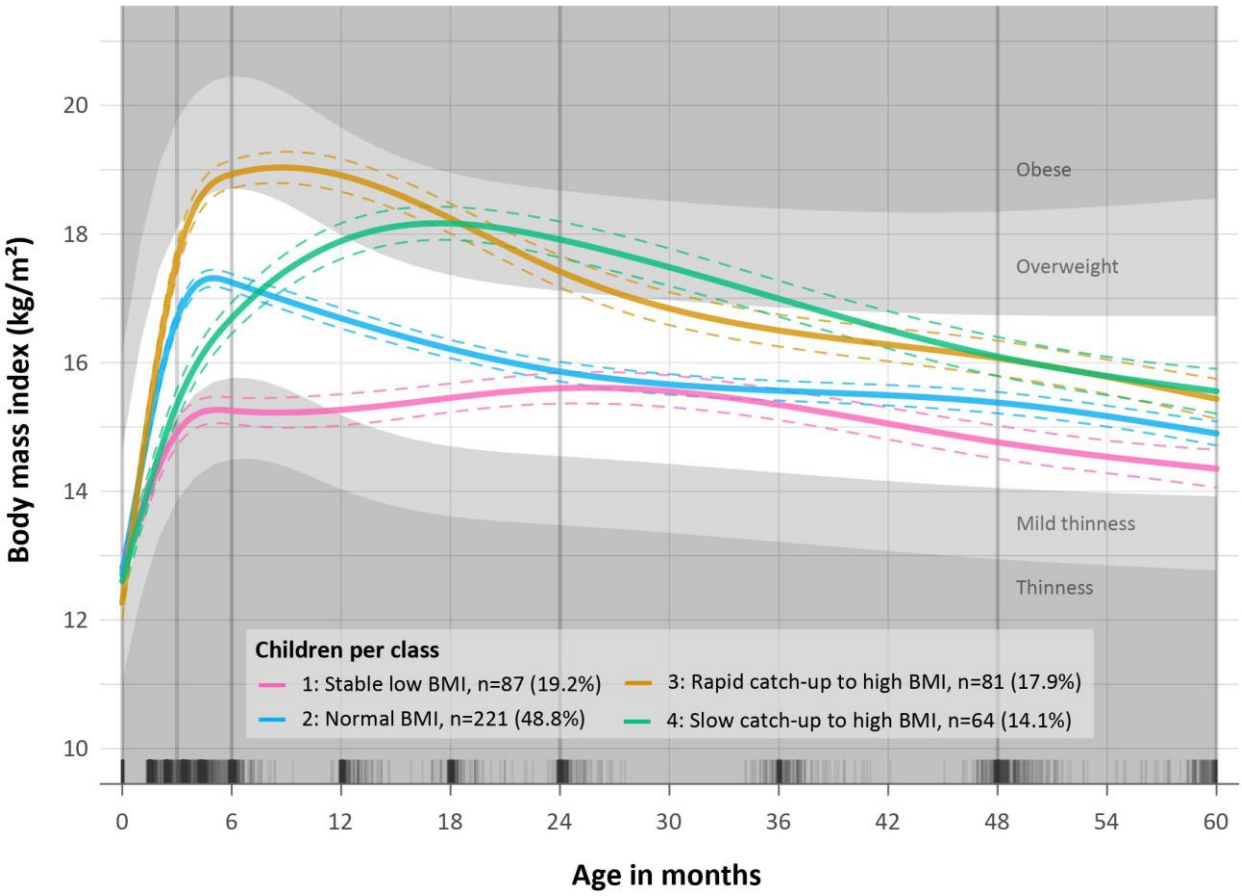
[1]The coefficients (β) and (95% CI) were derived from multiple linear regression after the imputed data sets were combined using Rubin's rules. β (95% CI) represents the mean difference between the reference trajectory (normal BMI) and each trajectory class. [2]Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated as insulin (μU/mL) × glucose (mmol/L)/22.5. Slightly skew variables (insulin, C-peptide, HOMA-IR, and triglycerides) were log-transformed before the regression analyses, and the estimates of these variables were back-transformed and presented as percentage changes. Model 1 was adjusted for the child's sex and age at 10 years. Model 2 was additionally adjusted for childbirth order, gestational age at birth, maternal age at delivery, maternal height, maternal highest educational status, and parental economic status (wealth index). Model 3 was further adjusted for the child's birth weight.

Supplementary Table 6 Comparison of baseline characteristics between children who attended the 5- and 10-year follow-ups and those who only attended the 5-year follow-up (Total sample, n = 352)[1]

	n	Attended	n	Not attended	p-value[2]	Missing, n
Maternal characteristics after delivery						
Age at delivery (years)	286	24.7 (4.8)	66	23.9 (4.6)	0.19	0
Height (cm)	284	157.7 (5.9)	66	156.0 (6.4)	0.048	2
Weight (kg)	218	56.5 (9.5)	52	53.0 (7.5)	0.014	82
Body mass index (kg/m²)	216	22.6 (3.3)	52	21.7 (2.4)	0.052	84
Maternal educational status, n (%)	286		66		0.19	0
No school		16 [5.6]		9 [13.6]		
Primary school		175 [61.2]		37 [56.1]		
Secondary school		57 [19.9]		12 [18.2]		
Higher education		38 [13.3]		8 [12.1]		
Mode of delivery, n (%)	286		64		0.60	2
Vaginal delivery		266 [93.0]		58 [90.6]		
Caesarean section		20 [7.0]		6 [9.4]		
Family socioeconomic status, (IWI)	286	46.3 (16.6)	66	42.5 (18.9)	0.11	0
Child characteristics						
Gestational age (weeks)	286	39.0 (0.9)	66	39.0 (1.1)	0.90	0
Sex, male	286	148 [51.8]	66	29 [43.9]	0.31	0
Birth weight (kg)	286	3.1 (0.4)	66	3.0 (0.4)	0.07	0
Length (cm)	286	49.2 (2.0)	66	48.7 (1.9)	0.049	0
Body mass index (kg/m²)	286	12.6 (1.1)	66	12.4 (1.1)	0.32	0
Fat mass (kg)	284	0.23 (0.17)	66	0.19 (0.15)	0.13	2
Fat-free mass (kg)	284	2.84 (0.32)	66	2.77 (0.32)	0.10	2
Fat mass index (kg/m²)	284	0.92 (0.66)	66	0.79 (0.62)	0.16	2
Fat-free mass index (kg/m²)	284	11.68 (0.90)	66	11.65 (0.85)	0.75	2
Birth order, n (%)	284		62		0.34	6
First		136 [47.9]		35 [56.5]		
Second		79 [27.])		12 [19.4]		
Third and above		69 [24.3]		15 [24.2]		
Low birth weight, n (%)[3]	286	25 [8.7]	66	8 [12.1]	0.54	0
Breastfeeding	251		57		0.40	44
Exclusive		29 [11.6]		3 [5.3]		
Predominant		208 [82.9]		51 [89.5]		
Partial or no		14 [5.6]		3 [5.3]		

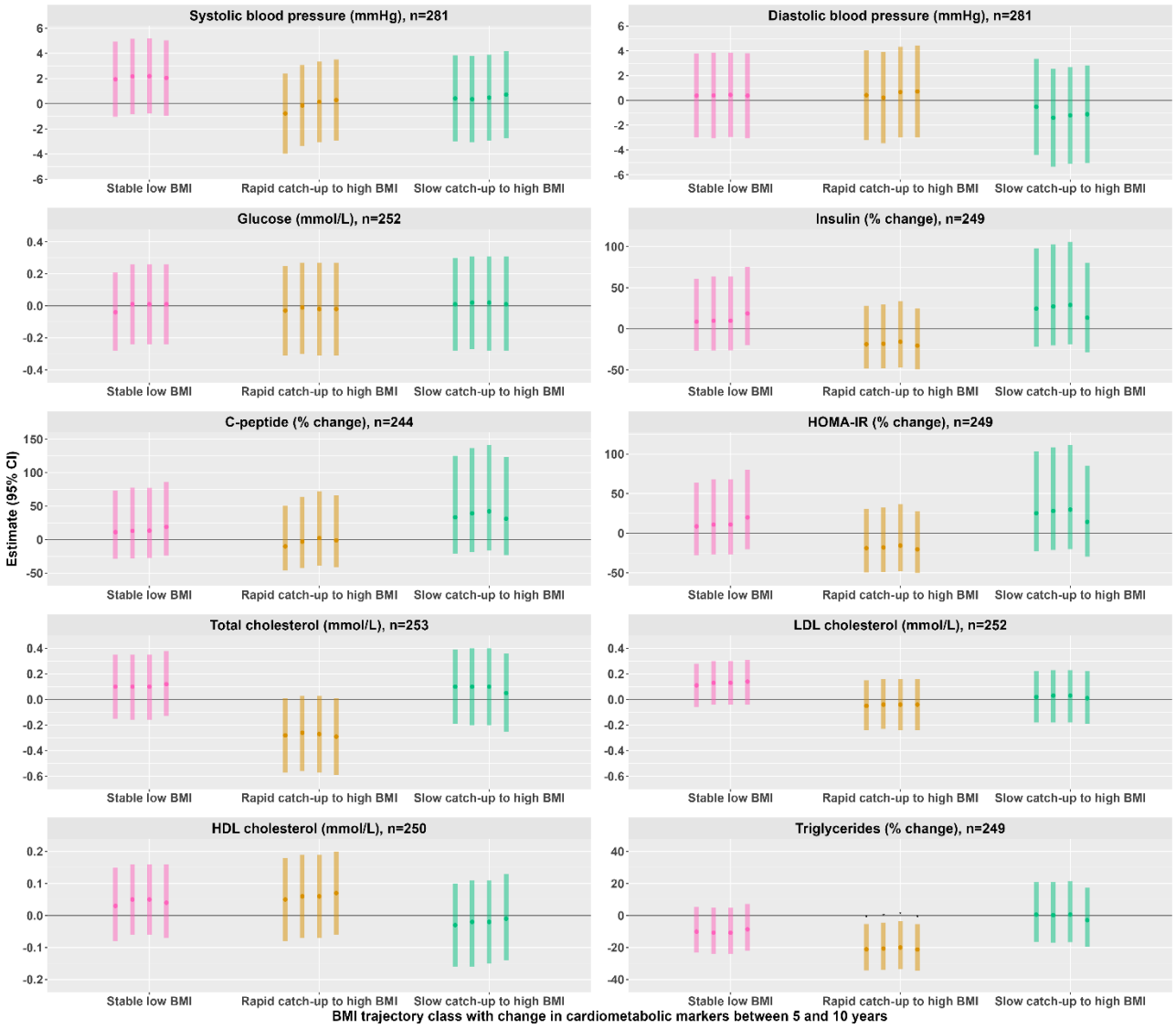
[1]Data are mean (SD) and n [%]. [2]Differences between children who attended the 5- and 10-year follow-ups and those who only attended the 5-year follow-up were calculated by one-way ANOVA for continuous variables, Pearson's chi-squared test of independence for categorical variables with expected counts > 4 in all cells, and else Fisher's exact test. [3]Birth weight <2500 g. IWI, International Wealth Index.

Supplementary Figure 1



Supplementary Figure 1 Distinct BMI trajectory classes from birth to 60 months derived from latent class trajectory modeling [reproduced from (Wibaek et al., 2019) with permission]. The identified trajectories represent individual class average BMI as a function of age in months. The shaded area represents BMI for age in reference to the median WHO growth standard populations. Normal BMI (white) is defined as a BMI z-score (–1 to +1 SD), mild thinness (light gray) ≥−2 to <−1 SD, thinness (gray) <−2 SD, overweight (light gray) >1 to ≤2 SD, and obese (gray) >2 SD above the WHO median. The dashed lines with similar colors for each mean BMI trajectory represent 95% CI, and the rug plot along the x-axis shows the density of BMI observations.

Supplementary Figure 2

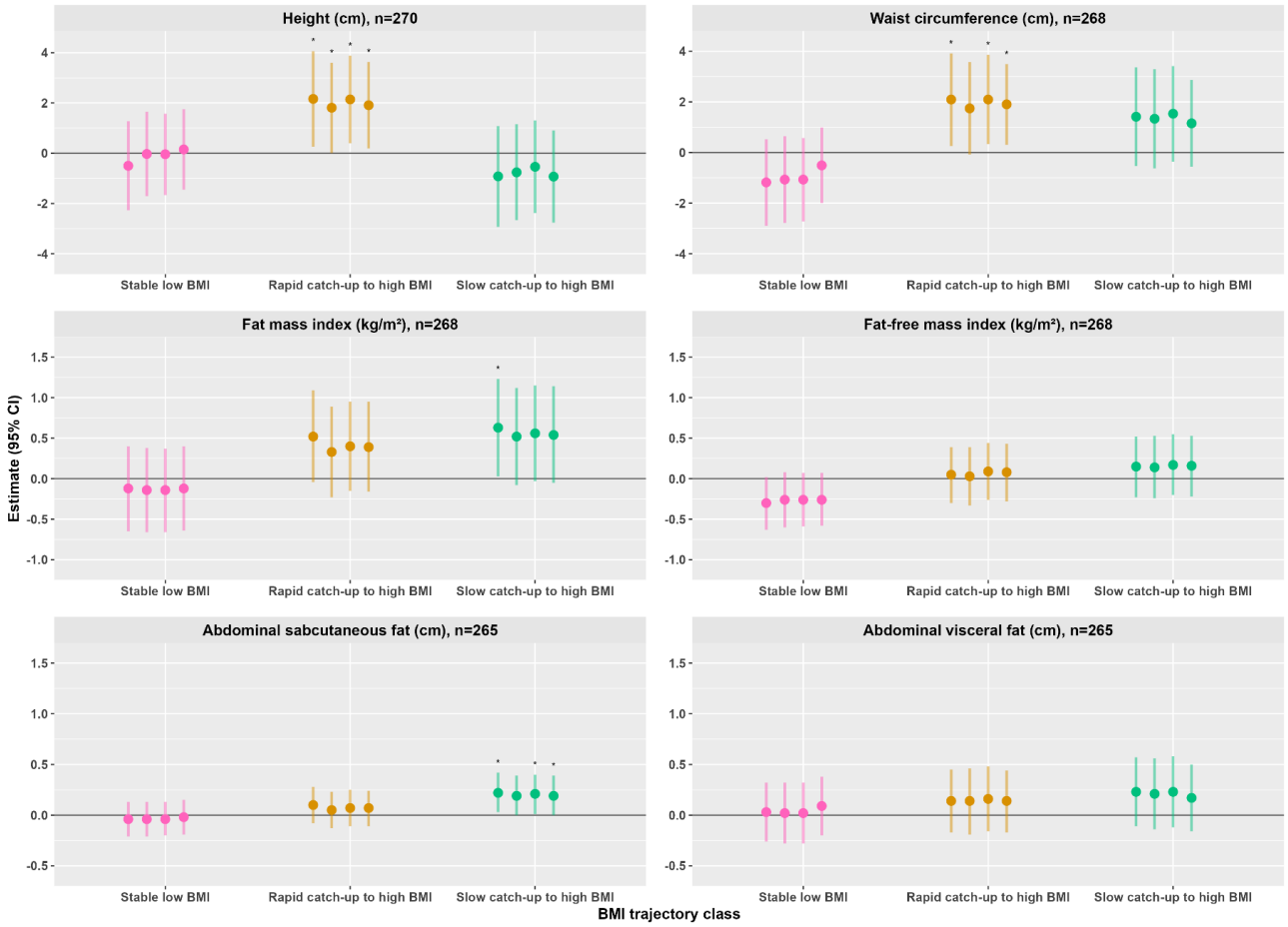


Supplementary Figure 2 Sensitivity analysis of associations of BMI trajectories from 0-5 years with change in cardiometabolic marker between the 5- and 10-year follow-up. Change in cardiometabolic marker was calculated as the difference between measurements at 10-year follow-up and 5-year follow-up. The estimates (β) and (95 % CI) were derived from multiple linear regression, and represent the mean difference between the reference trajectory (normal BMI) and each trajectory class. The vertical bars from left to right represent models 1 to 4 and each outcome is presented on the top of the exposure variables (BMI trajectories). [2]Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated as insulin (μU/mL) × glucose (mmol/L)/22.5. Slightly skew variables (insulin, C-peptide, HOMA-

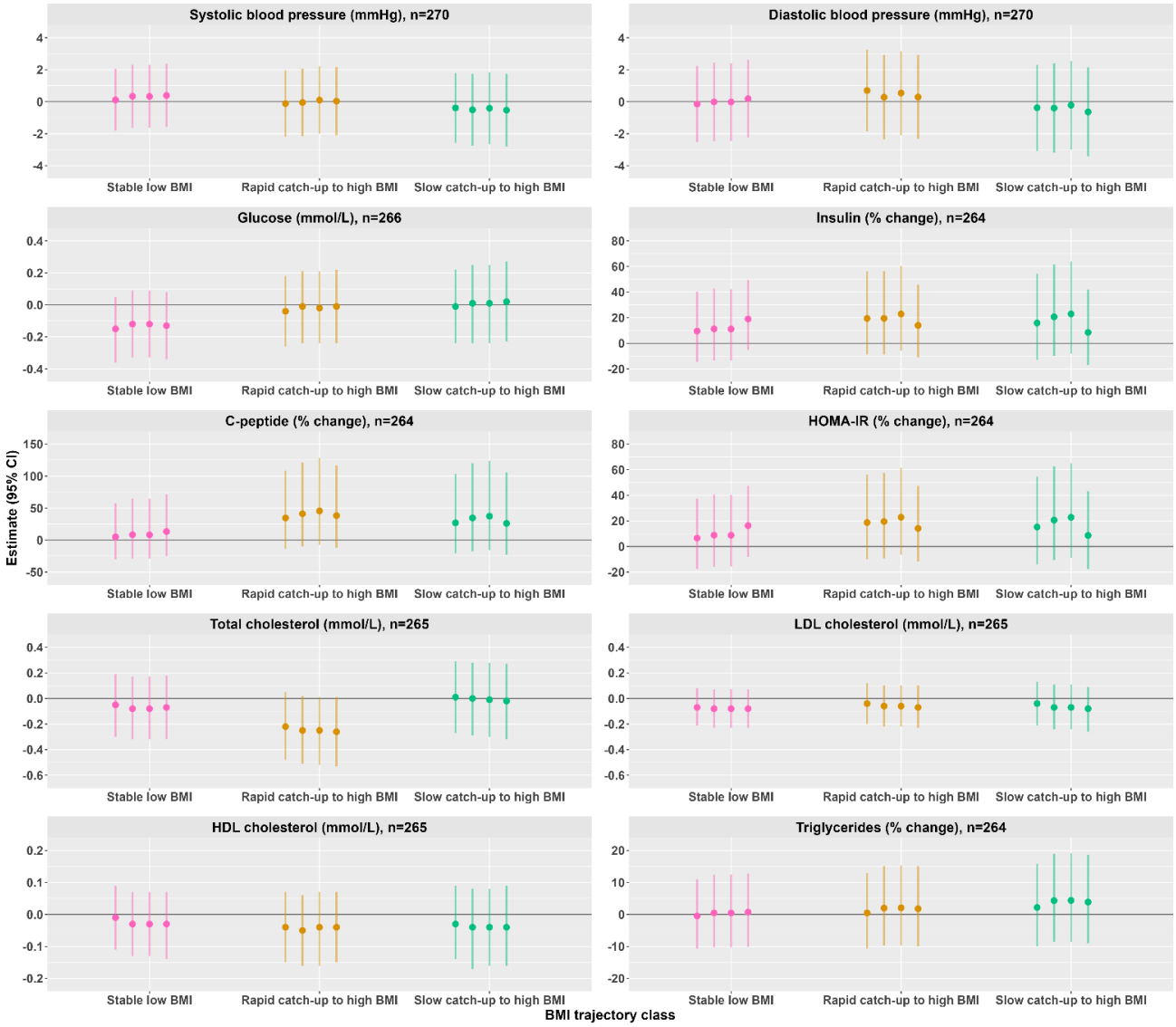
IR, and triglycerides) were log-transformed before the regression analyses, and the estimates of these variables were back-transformed and presented as percentage changes. We ran four separate models for each outcome variable, and the vertical bars from left to right represent models 1, 2, 3, and 4, respectively. Each outcome variable is presented on the top of exposure variables (BMI trajectories). Model 1 was adjusted for the child's sex and age at 10 years. Model 2 was additionally adjusted for childbirth order, gestational age at birth, maternal age at delivery, maternal height, maternal highest educational status, and parental economic status. Model 3 was further adjusted for the child's birth weight. In addition to the preceding models, model 4 was adjusted for current BMI, except for waist circumference which was adjusted for fat-free mass index, fat mass index for fat-free mass index, fat-free mass index for fat mass index, abdominal fat (subcutaneous and visceral) for current fat-free mass index.

Supplementary Figure 3

A)



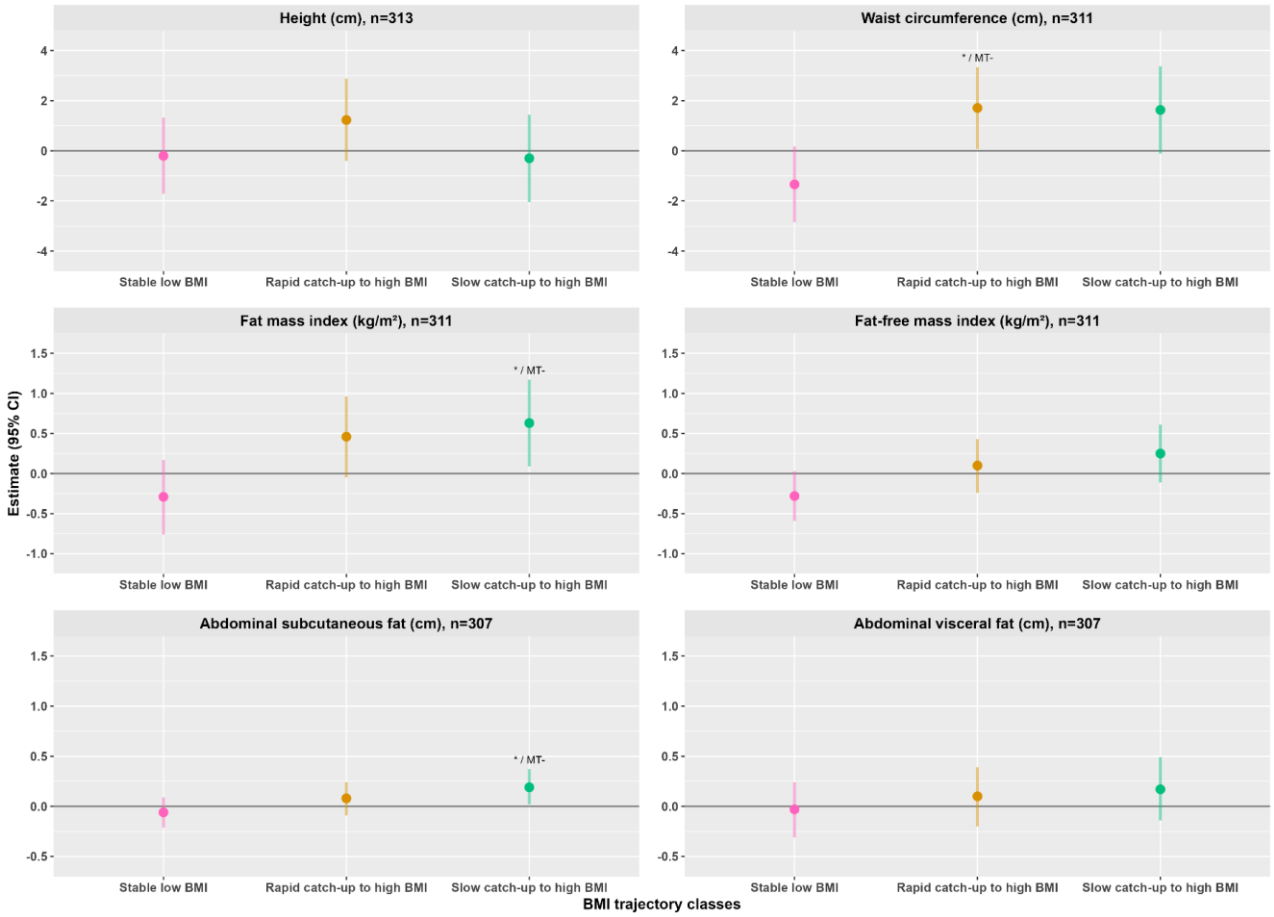
B)



Supplementary Figure 3 Shows a sensitivity analysis of associations between BMI trajectories from 0-5 years with anthropometry, body composition, and abdominal fat (panel A), and with cardiometabolic markers (panel B) after further adjusting for breastfeeding among 270 children having breastfeeding data at 4-6 months. The estimates (β) and (95 % CI) were derived from multiple linear regression, and represent the mean difference between the reference trajectory (normal BMI) and each trajectory class. [2]Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated as insulin (μU/mL) × glucose (mmol/L)/22.5. Slightly skew variables (insulin, C-peptide, HOMA-IR, and triglycerides) were log-transformed before the regression analyses, and the estimates of these variables were back-transformed and presented as percentage changes. We ran four separate models for each outcome variable, and the vertical bars from left to right represent models 1, 2, 3, and 4, respectively. Each outcome variable is presented on the top of exposure variables (BMI trajectories). Model 1 was adjusted for child's sex and age at 10 years.

Model 2 was additionally adjusted for childbirth order, gestational age at birth, maternal age at delivery, maternal height, maternal highest educational status, and parental economic status. Model 3 was further adjusted for child's birth weight. In addition to the preceding models, model 4 was adjusted for current BMI, except for waist circumference which was adjusted for fat-free mass index, fat mass index for fat-free mass index, fat-free mass index for fat mass index, abdominal fat (subcutaneous and visceral) for current fat-free mass index.

Supplementary Figure 4



Supplementary Figure 4 Sensitivity analysis of associations between BMI trajectories from 0-5 years and 10-year outcomes (anthropometry, body composition, abdominal fat, and cardiometabolic markers) after accounting for multiple testing in the final model (model 3). We adjusted significant associations, $P \leq 0.05$ for multiple testing using the Benjamin-Hochberg method. The significant stars (* $P \leq 0.05$) before the forward slash show significance levels before Benjamin-Hochberg adjustment, and the designated "MT+" indicates the remained significance, whereas "MT-" shows that no significance is left after the adjustment. The estimates (β) and (95% CI) were derived from multiple linear regression, and represent the mean difference between the reference trajectory (normal BMI) and each trajectory. Each outcome variable is presented on the top of the exposure variables (BMI trajectories), and the vertical bar stands for the 95% CI of each outcome from model 3. The final model (model 3) was adjusted for child's sex, age at 10 years, childbirth order, gestational age at birth, maternal age at delivery, maternal height, maternal highest educational status, parental economic status at delivery, and child's birth weight. Each outcome variable is presented on top of the exposure variables (BMI trajectories).

Reference

WIBAEK, R., VISTISEN, D., GIRMA, T., ADMASSU, B., ABERA, M., ABDISSA, A., MUDIE, K., KÆSTEL, P., JØRGENSEN, M. E., WELLS, J. C. K., MICHAELSEN, K. F., FRIIS, H. & ANDERSEN, G. S. 2019. Body mass index trajectories in early childhood in relation to cardiometabolic risk profile and body composition at 5 years of age. *Am J Clin Nutr,* 110**,** 1175-1185.