Arteriosclerosis, Thrombosis, and Vascular Biology

ORIGINAL RESEARCH

Distinct Body Mass Index Trajectories to Young-Adulthood Obesity and Their Different Cardiometabolic Consequences

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OBJECTIVE: Different body mass index (BMI) trajectories that result in obesity may have diverse health consequences, yet this heterogeneity is poorly understood. We aimed to identify distinct classes of individuals who share similar BMI trajectories and examine associations with cardiometabolic health.

APPROACH AND RESULTS: Using data on 3549 participants in ALSPAC (Avon Longitudinal Study of Parents and Children), a growth mixture model was developed to capture heterogeneity in BMI trajectories between 7.5 and 24.5 years. Differences between identified classes in height growth curves, body composition trajectories, early-life characteristics, and a panel of cardiometabolic health measures at 24.5 years were investigated. The best mixture model had 6 classes. There were 2 normal-weight classes: normal weight (nonlinear; 35% of sample) and normal weight (linear; 21%). Two classes resulted in young-adulthood overweight: normal weight increasing to overweight (18%) and normal weight or overweight (16%). Two classes resulted in young-adulthood obesity: normal weight increasing to obesity (6%) and overweight or obesity (4%). The normal-weight-increasing-to-overweight class had more unfavorable levels of trunk fat, blood pressure, insulin, HDL (high-density lipoprotein) cholesterol, left ventricular mass, and E/e′ ratio compared with the always-normal-weight-or-overweight class, despite the average BMI trajectories for both classes converging at ≈26 kg/m^2 at 24.5 years. Similarly, the normal-weight-increasing-to-obesity class had a worse cardiometabolic profile than the always-overweight-or-obese class.

CONCLUSIONS: Individuals with high and stable BMI across childhood may have lower cardiometabolic disease risk than individuals who do not become overweight or obese until late adolescence.

Key Words: body composition ■ body mass index ■ goals ■ obesity ■ overweight

The number of adults worldwide with obesity increased from ≈100 to 671 million between 1975 and 2016, with an additional 1.3 billion in the overweight range.[1] This epidemic is strongly related to morbidity and mortality rates, particularly due to diseases affecting the circulatory and endocrine systems.[2] Adults with obesity do not, however, form a single homogenous group with the same health profiles, and a substantial part of the heterogeneity is likely explained by different childhood body mass index (BMI) trajectories.[3]

The seminal publication of Abraham et al[4] in 1971 showed that rates of some cardiovascular diseases were the highest among individuals who were overweight in adulthood but below average weight in childhood. Numerous articles have replicated this type of analysis.[5,6] Others have investigated how BMI trajectories and growth traits differ between subgroups of adults with obesity, which are often classified using crude definitions of metabolic health.[7,8] Fewer studies have, however, used growth mixture modeling to identify latent groups or classes of

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Nonstandard Abbreviations and Acronyms

ALSPAC	Avon Longitudinal Study of Parents and Children
BMI	body mass index
CRP	C-reactive protein
HDL	high-density lipoprotein
LDL	low-density lipoprotein

individuals who share similar individual BMI trajectories and then subsequently investigated how adulthood cardiometabolic health measures or events differ between them.[9–11] This is a powerful approach, which does not involve arbitrary categorization, conditioning on an outcome, or imposing linear constraints between growth traits and an outcome. The 2018 *European Heart Journal* article by Buscot et al[9] used data from 2631 individuals in the Cardiovascular Risk in Young Finns Study and is arguably the best published example. Even this article, however, had serious limitations, including the individual BMI trajectories spanning different age ranges for different birth cohorts (eg, 6–37 years if born in 1974; 18–49 years if born in 1962) and multiple categorical outcomes being related to classes with few individuals (eg, n=33). In addition, no previous study has investigated differences in height growth and body composition trajectories between the classes they identified based on serial BMI data. This is fundamentally important to understand and interpret not only the classes but also their associations with outcomes (eg, one class might have high BMI, yet a healthy cardiometabolic profile due to high lean mass).

Using data from the larger and deeply phenotyped ALSPAC (Avon Longitudinal Study of Parents and Children), we aimed to develop a growth mixture model that properly captured heterogeneity in childhood to young-adulthood BMI trajectories. We further aimed to extensively describe each identified latent class (in terms of height growth, body composition trajectories, and early-life characteristics) and quantify between-class differences in young-adulthood cardiometabolic health measures. We hypothesized that there would be 2 distinct groups of individuals who developed young-adulthood obesity and that the more favorable cardiometabolic health profile would be observed in the group of individuals who were consistently heavy across childhood.

Highlights

- It is unclear how cardiometabolic health profiles differ between groups of individuals who share similar childhood to young-adulthood body mass index trajectories.
- This study models heterogeneity in childhood to young-adulthood body mass index trajectories (7.5–24.5 years), using frequent serial data from a large birth cohort, and extensively characterize each identified latent class with respect to cardiometabolic health.
- We found 6 classes and show how height growth curves (7.5 and 17.5 years), body composition trajectories (9.5 and 24.5 years), early-life characteristics, and a comprehensive panel of cardiometabolic health measures (24.5 years) are patterned across the classes.
- Two classes had average trajectories that led to young-adulthood overweight; the class with a high but stable body mass index trajectory (16% of the sample) had more favorable levels of trunk fat, blood pressure, insulin, high-density lipoprotein cholesterol, left ventricular mass, and E/e′ ratio (an indicator of diastolic function) than the class who only transitioned from normal weight to overweight in late adolescence (14% of the sample). A similar pattern of results was found for 2 classes with average trajectories that resulted in obesity.
- Building on the limited evidence base, our results suggest that individuals with high and stable body mass index across childhood may have better cardiometabolic health than individuals who do not become overweight or obese until late adolescence.

MATERIALS AND METHODS

The ALSPAC data are available to scientists on request via the following website, which also provides details and distributions of the study variables: http://www.bristol.ac.uk/alspac/researchers/access/. The statistical code for the analyses in this article has been placed in GitHub—the open-access online repository: https://github.com/tomnorris1988/ALSPAC-BMI-Mixture-model-. Please also see the Major Resources Table in the Data Supplement.

Sample

ALSPAC is a prospective birth cohort study.[12,13] Pregnant women living in the defunct county of Avon in England with an expected delivery date between April 1991 and December 1992 were invited to take part in the study. The total number of pregnancies is 15 454, representing 15 589 fetuses of which 14 901 were alive at 1 year of age. The 688 (ie, 15 589–14 901) who did not survive includes miscarriages and fetal loss/death, as well as (a low incidence of) neonatal death. Follow-up has included parent- and child-completed questionnaires, links to routine data, and clinic attendance at 10 sweeps at target ages of ≈7, 8, 9, 10, 11, 12, 13, 15, 17, and 24 years. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the local research ethics committees (and conformed to the Declaration of Helsinki). Informed consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time. Consent for biological samples has been collected in accordance with the Human Tissue Act (2004). The study website contains

details of all the data that are available through a fully searchable data dictionary and variable search tool: http://www.bristol.ac.uk/alspac/researchers/our-data/.

Individuals were considered eligible for the analysis if they attended the 24-year sweep where cardiometabolic measures were collected, had at least 2 BMI serial BMI measurements between 7 and 24 years, and had some covariate data. Starting with the 4019 individuals who were assessed at the 24-year sweep, 294 did not have any data on potential confounders (other than sex and ethnicity) and a further 176 had <2 serial BMI measurements, after data preparation for mixture modeling (Materials in the Data Supplement). The sample for the present article, therefore, comprised 3549 individuals, of whom >75% had at least 7 BMI measurements. Comparison of this sample to the 24-year sweep cohort (n=4019) and the ALSPAC cohort of children who were alive at 1 year of age (n=14 901) is presented in Table I in the Data Supplement.

Anthropometric and Body Composition Data

Weight and height were measured at all sweeps. Height was measured without shoes to the last complete millimeter using the Harpenden stadiometer (Holtain, Ltd). Weight was measured to the nearest 0.1 kg using the Tanita Body Fat Analyser (model TBF 305). BMI was computed as kilogram per square meter. Whole body, trunk, and peripheral fat and lean masses were derived from dual-energy x-ray absorptiometry scans at target ages 9, 11, 13, 15, 17, and 24 years using a Lunar prodigy densitometer (GE Healthcare, Chicago, IL).

Cardiometabolic Health Data

The 24-year sweep included detailed phenotyping and data collection using REDCap.[14] Resting systolic and diastolic blood pressure was measured, after a 2 minute rest, using an Omron Healthcare (Kyoto, Japan) M6 upper arm blood pressure monitor. The average of 2 or 3 measurements was used. A fasting blood sample was obtained from which cholesterol, HDL (high-density lipoprotein) cholesterol, LDL (low-density lipoprotein) cholesterol, triglycerides, insulin, glucose, and CRP (C-reactive protein) were assayed.

Carotid-femoral pulse wave velocity was assessed using the oscillometric method (Vicorder; Skidmore Medical, Bristol, United Kingdom). Bilateral carotid intima-media thickness was measured using established ultrasound machine techniques with a 13.5-MHz linear array broadband transducer (CardioHealth; Panasonic, Tokyo, Japan).[15] End-diastolic measurements were recorded in the far wall of the right and left common carotid arteries (1 cm proximal to the carotid bifurcation) and were averaged for analysis.

Approximately 1 in 2 participants attending the 24-year clinic sweep were recruited for detailed cardiac phenotyping. An echocardiogram, using a Philips Medical Systems (North Andover, MA) EPIQ 7G Ultrasound System equipped with a X5-1 transducer, was performed using the American Society of Echocardiography protocols.[16] Based on previous literature and to limit multiple comparisons, 5 clinical parameters were computed. Relative wall thickness and left ventricular mass indexed to height in m^3 are principally indicators of cardiac structure. Peak mitral annular velocity in systole measured by pulsed Doppler (s′) is principally an indicator of systolic function. Early/late mitral inflow velocity (E/A ratio) and early mitral inflow velocity/mitral annular early diastolic velocity (E/e′ ratio) are principally indicators of diastolic function.

Potential Confounder Data

Potential confounding variables of the relationship between BMI trajectories and cardiometabolic health measures in adulthood included sex, ethnicity, birth weight, gestational age, gestational hypertension, diabetes in pregnancy, smoking and alcohol consumption during pregnancy, parental age at birth of baby, maternal BMI at 12 weeks of gestation, paternal BMI at 7-year sweep, breastfeeding duration, parental educational qualifications, parental occupation, household income, and a family adversity index.

Statistical Analyses

Using Mplus, a growth mixture model (sexes combined) was developed to identify distinct groups of individuals who had similar BMI trajectories across the 10 sweeps (Figure I in the Data Supplement). The data used in, and diagnostics obtained from, these mixture models are included in Tables II through VI in the Data Supplement and Figure II in the Data Supplement. As a sensitivity analysis, we refitted our final growth mixture model as a multigroup model, in which the growth parameters (ie, intercept, slope, quadratic, and cubic terms) of each trajectory class were allowed to differ by sex. Two figures were produced: one showing the average fitted trajectories (with 95% CIs) between 7.5 and 24.5 years, and the individual observed trajectories, for each class and one showing the average trajectories superimposed on the International Obesity Task Force ranges (averaged across sex) for obesity, overweight, normal weight, and thinness.[17]

To compare the height growth curves for each latent class, we used the Super-Imposition by Translation and Rotation model.[18] Class-specific models were developed and used to plot the average height distance (cm) and velocity (cm/year) curves between 7.5 and 17.5 years for each class, incorporating estimates of age at and magnitude of peak height velocity. Multilevel models were developed to describe how body composition, assessed via dual-energy x-ray absorptiometry, changes over age in each class. A single model was developed for each of the 6 outcomes: whole-body fat and lean masses, trunk fat and lean masses, and peripheral (ie, arms+legs) fat and lean masses. Adjustments for height at each sweep were made. Using the models, we estimated trajectories between 9.5 and 24.5 years, showing how body composition in each of the 5 classes differed compared with a referent class.

Descriptive statistics for each potential confounder, stratified by class, were produced. General linear regression was used to estimate differences in each cardiometabolic health measure between the classes, with adjustment for all potential confounders. The transformation y=100 log(e)× was used for skewed outcomes, and the resulting estimates are symmetrical percentage differences. These analyses were performed using outcome and confounder data that were multiply imputed 100× using chained equations and were weighted by the posterior probabilities of most-likely class membership (using importance weights). The missing data patterns are shown in Tables VII and VIII in the Data Supplement. As

Table 1. Description of the Study Sample

			%Missing
Sex			0
Male	n (%)	1363 (38.4)	
Female	n (%)	2186 (61.6)	
Ethnicity			3.6
White	n (%)	3287 (96.1)	
Non-White	n (%)	134 (3.9)	
Birth weight, g	Mean (SD)	3410 (534)	1.3
Gestational age, wk	Mean (SD)	39.5 (1.8)	0
Gestational hypertension			2.2
No	n (%)	2948 (84.9)	
Yes	n (%)	524 (15.1)	
Diabetes in pregnancy			3.2
No	n (%)	3304 (96.1)	
Yes	n (%)	133 (3.9)	
Mother smoked during the first 3 mo of pregnancy			1.4
No	n (%)	2977 (85.1)	
Yes	n (%)	521 (14.9)	
Mother drank alcohol during the first 3 mo of pregnancy			1.9
No	n (%)	2953 (84.8)	
Yes	n (%)	530 (15.2)	
Mother's age, y	Mean (SD)	29.5 (4.5)	0
Mother's BMI, kg/m^2	Median (IQR)	23.3 (21.5–25.7)	22.3
Mother's highest qualification			2.5
Degree	n (%)	716 (20.7)	
A level	n (%)	1007 (29.1)	
O level	n (%)	1174 (33.9)	
Vocational	n (%)	242 (7.0)	
CSE	n (%)	321 (9.3)	
Partner's age, y	Mean (SD)	31.8 (5.5)	29.9
Partner's BMI, kg/m^2	Median (IQR)	25.2 (23.4–27.4)	52.2
Partner's highest qualification			4.1
Degree	n (%)	914 (26.9)	
A level	n (%)	995 (29.3)	
O level	n (%)	714 (30.0)	
Vocational	n (%)	243 (7.1)	
CSE	n (%)	536 (15.3)	
Partner's (or mother's if partner's missing) occupation			24.0
Higher managerial, administrative, and professional occupations	n (%)	533 (19.8)	
Lower managerial, administrative, and professional occupations	n (%)	942 (34.9)	
Intermediate occupations	n (%)	316 (11.7)	
Small employers and own account workers	n (%)	224 (8.3)	
Lower supervisory and technical occupations	n (%)	319 (11.8)	
Semiroutine occupations	n (%)	191 (7.1)	
Routine occupations	n (%)	171 (6.3)	
Weekly family income, £			19.1
≥400	n (%)	1502 (52.3)	
300–399	n (%)	633 (22.0)	
200–299	n (%)	452 (15.8)	
0–199	n (%)	283 (9.9)	
Family adversity index during pregnancy			1.0
0	n (%)	1748 (49.7)	
1	n (%)	940 (26.7)	
2	n (%)	436 (12.4)	
≥3	n (%)	391 (11.1)	
Family adversity index at 0–2 y of age			1.8
0	n (%)	1125 (32.3)	
1	n (%)	951 (27.3)	
2	n (%)	595 (17.1)	
≥3	n (%)	814 (23.4)	
Family adversity index at 2–4 y of age			5.9
0	n (%)	1475 (44.2)	
1	n (%)	953 (28.5)	
2	n (%)	493 (14.8)	
≥3	n (%)	419 (12.5)	
Breastfeeding duration			6.7
≥6 mo	n (%)	1509 (45.6)	
3–5 mo	n (%)	583 (17.6)	
<3 months	n (%)	684 (20.7)	
Never	n (%)	535 (16.2)	

BMI indicates body mass index; and IQR, interquartile range.

sensitivity analyses, the regression models were rerun 4×. First, stratified by sex; second, not including the weights; third, not including any confounder adjustment; and finally, using a dataset in which only the potential confounders (and not the outcomes) were imputed.

Full details regarding the derivation of echocardiogram outcomes, selection of confounding variables, implementation of the mixture modeling, Super-Imposition by Translation and Rotation analysis, multilevel body composition modeling, and multiple imputation have been published in GitHub (repository URL: https://github.com/tomnorris1988/ALSPAC-BMI-Mixture-model-).

RESULTS

Descriptive statistics of the sample are presented in Tables 1 and 2. Briefly, this is a predominantly White British (96.1%) sample of individuals born with a mean birth weight of 3.4 kg, to relatively well-educated (≈50% of parents educated to A level or beyond) parents from relatively high social classes (>55% fathers in the highest 2, of 7, social class strata). At age 24 years, the average

Table 2. Cardiometabolic Health Data at 24 y of Age

			%Missing
Age, y	Mean (SD)	24.5 (0.8)	0
Height, cm	Mean (SD)	171.3 (9.2)	1.0
Weight, kg	Median (IQR)	70.1 (61.4–81.5)	1.0
BMI, kg/m^2	Median (IQR)	23.7 (21.5–27.0)	1.1
Fat mass, kg	Median (IQR)	20.5 (15.9–27.7)	3.8
Trunk fat mass, kg	Median (IQR)	9.6 (6.9–13.7)	3.8
Peripheral fat mass, kg	Median (IQR)	10.1 (7.9–13.3)	3.8
Lean mass, kg	Median (IQR)	45.0 (39.6–54.4)	3.8
Trunk lean mass, kg	Median (IQR)	21.9 (19.3–25.9)	3.8
Peripheral lean mass, kg	Median (IQR)	20.1 (17.2–25.0)	3.8
SBP, mm Hg	Mean (SD)	116.0 (11.4)	0.6
DBP, mm Hg	Mean (SD)	66.9 (8.0)	0.6
Cholesterol, mmol/L	Mean (SD)	4.43 (0.84)	19.1
HDL-C, mmol/L	Mean (SD)	1.55 (0.42)	19.1
LDL-C, mmol/L	Mean (SD)	2.44 (0.76)	19.1
Triglycerides, mmol/L	Median (IQR)	0.84 (0.65–1.15)	19.1
Insulin, uU/mL	Median (IQR)	7.46 (5.29–10.78)	19.1
Glucose, mmol/L	Median (IQR)	5.26 (4.95–5.60)	19.1
CRP, mg/L	Median (IQR)	0.84 (0.39–2.22)	25.0
PWV, m/s	Mean (SD)	6.31 (1.10)	40.7
cIMT, mm	Mean (SD)	0.46 (0.05)	49.3
Cardiac structure			
LVMI, g/m^3	Mean (SD)	32.5 (7.2)	49.1
Relative wall thickness	Mean (SD)	0.36 (0.06)	48.8
Systolic function			
s′, cm/s	Mean (SD)	9.13 (1.24)	45.2
Diastolic function			
E/A ratio	Mean (SD)	1.98 (0.57)	44.8
E/e′ ratio	Mean (SD)	5.08 (1.03)	47.3

BMI indicates body mass index; cIMT, carotid intima-media thickness; CRP, C-reactive protein; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; LVMI, left ventricular mass indexed to height in m^3; PWV, pulse wave velocity; and SBP, systolic blood pressure.

BMI of the sample was 23.7 kg/m^2 and the average fat mass was 20.5 kg.

Latent BMI Classes

A mixture model with 6 classes and entropy 0.706 provided the best representation of the serial BMI data and the most plausible solution. Figure 1 shows the average fitted and individual observed trajectories for each latent class, while Figure 2 shows the average fitted trajectories against the International Obesity Task Force weight status ranges. The trajectories for the other class solutions (eg, a model with 2 classes) are shown in Figures III through VIII in the Data Supplement. For the chosen 6 class solution:

- Class 5 comprised 35% of the sample and had a nonlinear average trajectory in the normal-weight range, which matches what we would expect due to changes in growth velocity during puberty. This class is referred to as normal weight (nonlinear).
- Class 2 comprised 21% of the sample and had a near-linear average trajectory in the normal-weight range. This class is referred to as normal weight (linear).
- Class 3 comprised 18% of the sample and had an average trajectory that increased from normal weight to overweight. This class is referred to as normal weight increasing to overweight.
- Class 1 comprised 16% of the sample and had an average trajectory that approximated the International Obesity Task Force overweight threshold. This class is referred to as normal weight or overweight.
- Class 6 comprised 6% of the sample and had an average trajectory that increased from normal weight to obesity. This class is referred to as normal weight increasing to obesity.
- Class 4 comprised 4% of the sample and had an average trajectory that approximated the International Obesity Task Force obesity threshold. This class is referred to as overweight or obesity.

As shown in Table IX in the Data Supplement, there was no pattern or relationship between the number of serial measurements a child had and the class they were assigned to. Refitting the growth mixture model as a multigroup model did not provide evidence that the growth parameters characterizing each class' trajectory differed by sex (Table X in the Data Supplement; Figure IX in the Data Supplement).

Height and Body Composition Trajectories

Compared with the normal-weight (nonlinear) class, the 5 other classes were initially taller (on average) but transitioned to being shorter by 17.5 years of age, due to an earlier and lower magnitude of peak height velocity (Figure 3). These differences were most pronounced in the normal-weight-increasing-to-obesity and overweight-or-obesity classes. After accounting for differences in height, we observed large differences in fat mass trajectories between the classes but much smaller differences in lean mass trajectories (Figure 4). The overweight-or-obesity class, for example, was estimated to have 15 to 21 kg more total body fat than the normal-weight (nonlinear) class between 9.5 and 24.5 years but only 2 to 6 kg more lean mass. Figures X and XI in the Data Supplement show similar results for trunk and peripheral body composition measures.

Early-Life Characteristics

The percentage of women in the normal-weight-increasing-to-overweight class, and in the normal-weight-increasing-to-obesity class, was ≈9% higher than in the full sample (Table 3). Conversely, the percentage of men in the normal-weight (nonlinear) class

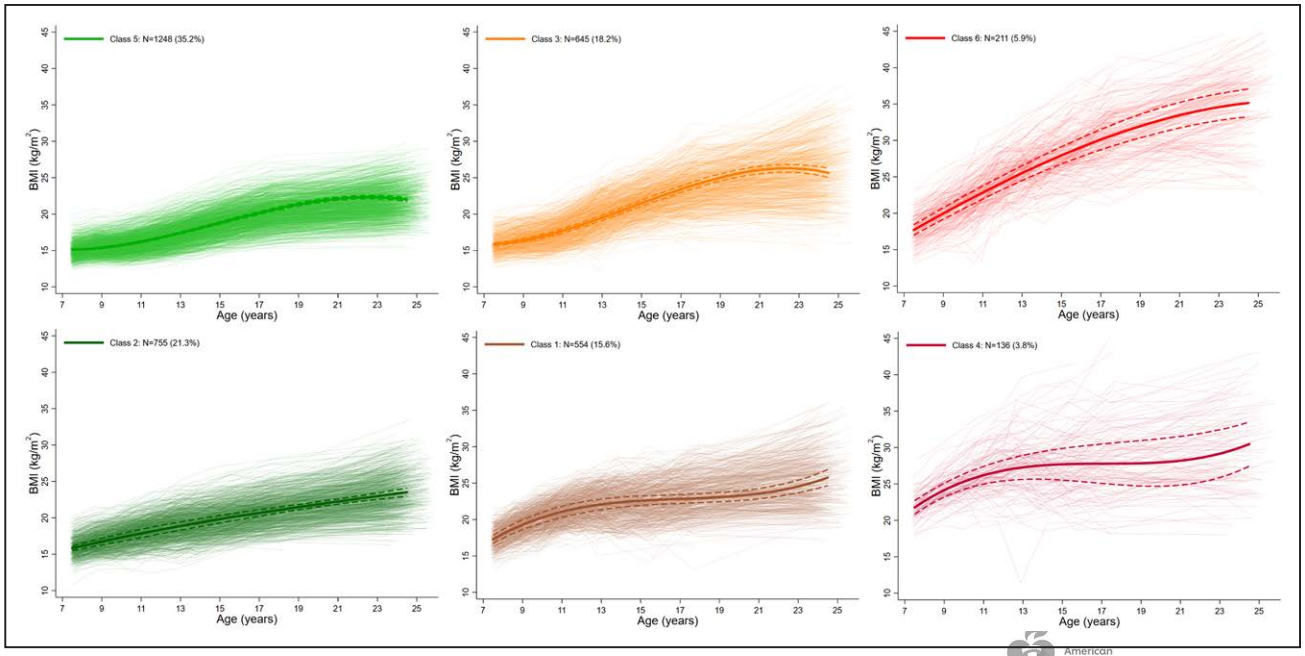

Figure 1. Average fitted trajectories (with 95% CIs) and individual observed trajectories for each class in the final mixture model.
BMI indicates body mass index.

was ≈7% higher than in the full sample. Table 3 also shows a clear, and expected, patterning of estimated levels of potential confounders across the classes. For example, maternal BMI increased across the classes, from 22.8 kg/m^2 in the normal-weight (nonlinear) class to 27.6 kg/m^2 in the normal-weight-increasing-to-obesity class, as did rates of all adverse responses (eg, diabetes in pregnancy, low family income, and never breastfeeding).

Cardiometabolic Outcomes

Estimated differences in each cardiometabolic health measure between the classes are presented in Tables 4

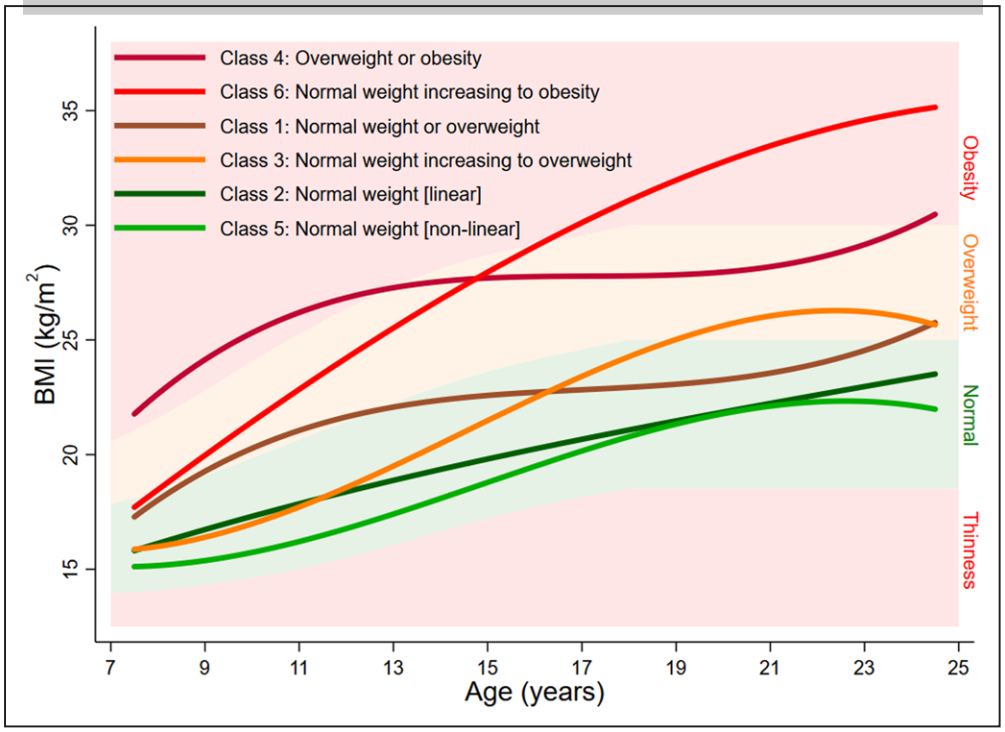

Figure 2. Average fitted trajectories from the final mixture model superimposed on thinness, normal weight, overweight, and obesity ranges (averaged across sex).
BMI indicates body mass index.

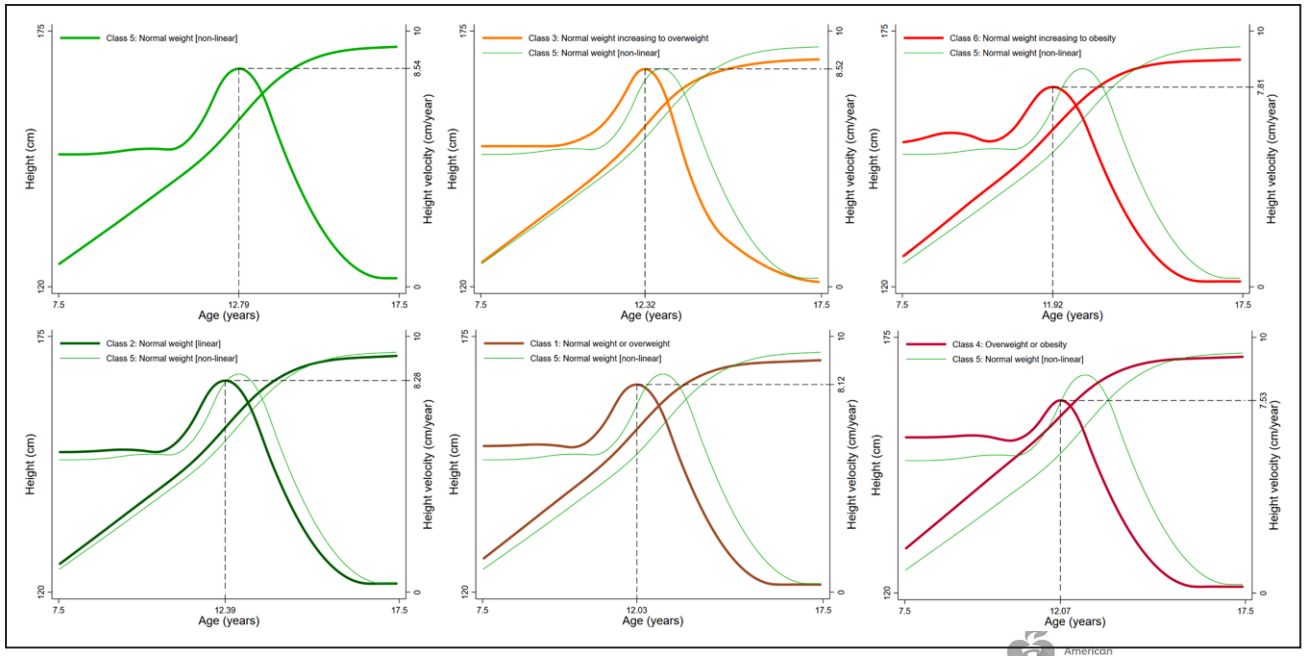

Figure 3. Height distance and velocity growth curves fitted using Super-Imposition by Translation and Rotation.

and 5. The normal-weight (linear) class had 20.6% (95% CI, 17.1–24.1) more trunk fat, and higher blood pressures, left ventricular mass indexed to height in m^3, and insulin, compared with the normal-weight (nonlinear) referent class (Table 4). The normal-weight-or-overweight and normal-weight-increasing-to-overweight classes fared even worse. Despite the average BMI trajectories for these classes converged at ≈26 kg/m^2 at 24.5 years (Figure 2), the normal-weight-increasing-to-overweight class had worse levels of blood pressures, HDL cholesterol, left ventricular mass indexed to height in m^3, E/e′ ratio, trunk fat mass, and insulin compared with the normal-weight-or-overweight class (Table 5). The overweight-or-obesity and normal-weight-increasing-to-obesity classes had worse levels of nearly all health measures compared with the normal-weight (nonlinear) class (Table 4). The normal-weight-increasing-to-obesity class, for example, had 84.4% (72.5–96.2) higher insulin and 110.7% (89.5–131.8) higher CRP. The average BMI trajectory for the normal-weight-increasing-to-obesity class was considerably higher during early adulthood than that for the overweight-or-obesity class (Figure 2), and the former had worse levels of some health measures than the latter (Table 5).

The sensitivity analyses in Tables XI through XV in the Data Supplement show similar patterns of results.

DISCUSSION

This article provides the most detailed investigation in the literature of latent-childhood to young-adulthood BMI trajectory classes and their cardiometabolic

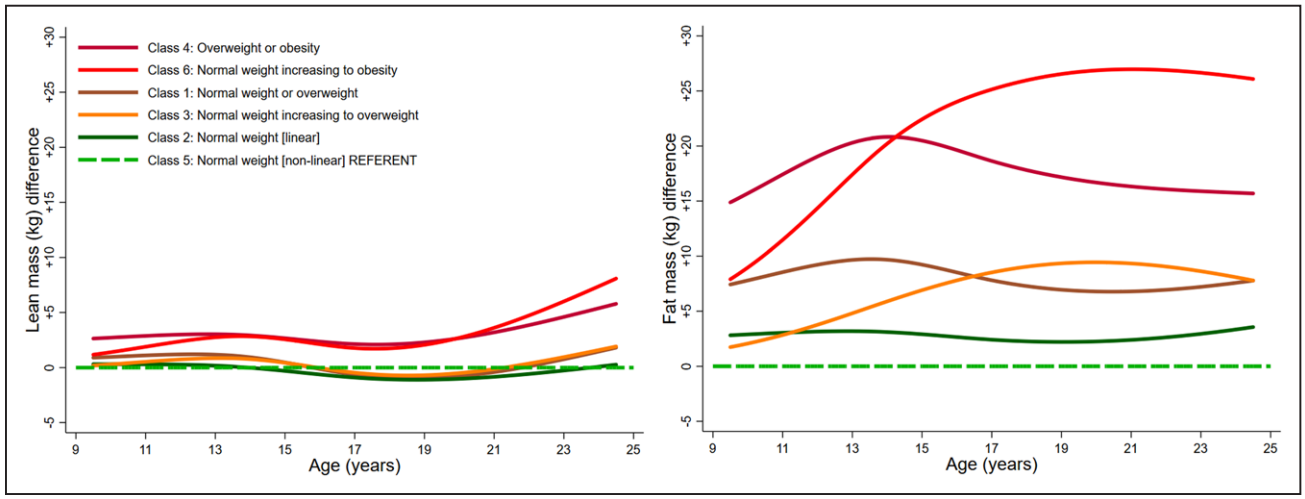

Figure 4. Differences in lean mass and fat mass trajectories, adjusted for height, compared with the normal weight (nonlinear) class.

Table 3. Descriptive Statistics for Each Latent Class

	Class 5	Class 2	Class 1	Class 3	Class 4	Class 6
	Normal weight (nonlinear)	Normal weight (linear)	Normal weight or overweight	Normal weight increasing to overweight	Overweight or obesity	Normal weight increasing to obesity
	Estimates are percentages or mean (95% CI)					
Sex						
Male	45.6 (42.8–48.4)	40.5 (36.9–44.2)	35.3 (31.2–39.4)	29.9 (26.2–33.5)	37.8 (29.4–46.1)	29.5 (23.3–35.8)
Female	54.4 (51.6–57.2)	59.5 (55.8–63.1)	64.7 (60.6–68.8)	70.1 (66.5–73.8)	62.2 (53.9–70.6)	70.5 (64.2–76.7)
Ethnicity						
White	96.1 (95.0–97.2)	96.2 (94.7–97.7)	95.4 (93.5–97.2)	96.7 (95.2–98.1)	96.6 (93.6–99.7)	94.7 (91.6–97.8)
Non-White	3.9 (2.8–5.0)	3.8 (2.3–5.3)	4.6 (2.8–6.5)	3.3 (1.9–4.8)	3.4 (0.3–6.4)	5.3 (2.2–8.4)
Birth weight, g	3364 (3334–3395)	3445 (3409–3482)	3450 (3405–3496)	3367 (3321–3413)	3575 (3483–3668)	3444 (3365–3523)
Gestational age, wk	39.4 (39.3–39.6)	39.5 (39.4–39.7)	39.5 (39.4–39.7)	39.4 (39.2–39.5)	39.7 (39.4–40.0)	39.6 (39.4–39.9)
Gestational hypertension						
No	86.8 (84.9–88.8)	86.0 (83.4–88.6)	85.1 (82.0–88.2)	83.0 (80.0–86.1)	70.6 (62.5–78.6)	80.7 (75.1–86.3)
Yes	13.2 (11.2–15.1)	14.0 (11.4–16.6)	14.9 (11.8–18.0)	17.0 (13.9–20.0)	29.4 (21.4–37.5)	19.3 (13.7–24.9)
Diabetes in pregnancy						
No	96.7 (95.6–97.7)	96.8 (95.5–98.1)	94.8 (92.8–96.8)	95.9 (94.3–97.5)	96.0 (92.5–99.5)	93.0 (89.5–96.6)
Yes	3.3 (2.3–4.4)	3.2 (1.9–4.5)	5.2 (3.2–7.2)	4.1 (2.5–5.7)	4.0 (0.5–7.5)	7.0 (3.4–10.5)
Mother smoked during the first 3 mo of pregnancy						
No	87.3 (85.4–89.2)	87.9 (85.5–90.2)	83.3 (80.1–86.5)	83.5 (80.5–86.4)	82.2 (75.5–88.8)	79.1 (73.4–84.8)
Yes	12.7 (10.8–14.6)	12.1 (9.8–14.5)	16.7 (13.5–19.9)	16.5 (13.6–19.5)	17.8 (11.2–24.5)	20.9 (15.2–26.6)
Mother drank alcohol during the first 3 mo of pregnancy						
No	85.4 (83.4–87.5)	84.6 (81.9–87.2)	84.1 (80.8–87.3)	83.1 (80.1–86.1)	79.6 (72.5–86.7)	89.7 (85.5–94.0)
Yes	14.6 (12.5–16.6)	15.4 (12.8–18.1)	15.9 (12.7–19.2)	16.9 (13.9–19.9)	20.4 (13.3–27.5)	10.3 (6.0–14.5)
Mother's age, y	29.9 (29.6–30.1)	29.8 (29.5–30.1)	29.6 (29.2–30.0)	29.2 (28.9–29.6)	29.3 (28.5–30.1)	28.5 (27.8–29.1)
Mother's BMI, kg/m^2	22.8 (22.6–23.0)	23.3 (23.0–23.5)	24.5 (24.2–24.9)	24.2 (23.9–24.5)	26.9 (26.1–27.9)	27.6 (26.7–28.4)
Mother's highest qualification						
Degree	24.5 (22.1–27.0)	22.1 (19.0–25.2)	16.7 (13.4–19.9)	19.8 (16.6–23.0)	14.0 (7.9–20.1)	13.3 (8.6–18.0)
A level	29.8 (27.2–32.4)	30.8 (27.3–34.2)	33.0 (28.9–37.1)	26.3 (22.7–29.8)	25.8 (18.3–33.4)	22.3 (16.4–28.1)
O level	32.6 (29.9–35.2)	32.4 (29.0–35.9)	34.9 (30.8–39.0)	33.8 (29.9–37.6)	33.8 (25.5–42.0)	39.2 (32.3–46)
Vocational	6.0 (4.6–7.3)	7.2 (5.2–9.1)	6.0 (3.9–8.0)	8.5 (6.2–10.8)	9.7 (4.6–14.9)	9.0 (4.9–13.1)
CSE	7.1 (5.6–8.6)	7.5 (5.7–9.4)	9.5 (6.9–12.1)	11.7 (9.1–14.3)	16.7 (10.1–23.2)	16.3 (11.0–21.5)
Partner's age, y	32.2 (31.8–32.5)	31.9 (31.5–32.4)	32.0 (31.4–32.5)	31.1 (30.7–31.6)	32.1 (30.9–33.4)	31.1 (30.2–32.1)
Partner's BMI, kg/m^2	24.7 (24.5–24.9)	25.4 (25.1–25.7)	26.0 (25.6–26.4)	25.6 (25.2–25.9)	27.0 (26.2–27.9)	27.6 (26.8–28.5)
Partner's highest qualification						
Degree	30.1 (27.5–32.8)	30.4 (27.0–33.8)	22.3 (18.7–26.0)	243 (20.8–27.8)	17.8 (11.1–24.5)	16.8 (11.6–22.0)
A level	28.0 (25.4–30.5)	28.8 (25.4–32.2)	34.7 (30.5–38.9)	28.4 (24.7–32.0)	28.5 (20.6–36.4)	22.0 (16.2–27.8)
O level	19.6 (17.4–21.9)	20.7 (17.7–23.8)	22.0 (18.4–25.6)	21.5 (18.2–24.9)	21.1 (13.8–28.4)	23.6 (17.6–29.6)
Vocational	7.8 (6.2–9.3)	6.4 (4.5–8.2)	4.0 (2.3–5.7)	7.7 (5.5–10.0)	10.5 (5.0–16.0)	13.4 (8.4–18.3)
CSE	14.5 (12.5–16.5)	13.7 (11.2–16.3)	17.0 (13.7–20.3)	18.0 (14.8–21.2)	22.1 (14.7–29.6)	24.2 (18.0–30.3)
Partner's (or mother's if partner's missing) occupation						
Higher managerial, administrative, and professional occupations	20.8 (18.3–23.3)	19.1 (16.0–22.2)	18.2 (14.5–21.8)	16.6 (13.4–19.9)	9.5 (3.8–15.3)	12.8 (7.6–18.0)
Lower managerial, administrative, and professional occupations	34.4 (31.4–37.4)	37.9 (33.8–41.9)	29.0 (24.5–33.4)	30.8 (26.6–34.9)	32.2 (23–41.5)	27.5 (20.3–34.6)
Intermediate occupations	11.4 (9.4–13.4)	11.1 (8.5–13.6)	13.2 (9.8–16.6)	10.8 (8.0–13.7)	8.0 (2.3–13.6)	13.6 (7.8–19.3)
Small employers and own account workers	8.4 (6.6–10.2)	8.1 (5.7–10.4)	9.8 (6.8–12.7)	9.0 (6.2–11.7)	13.1 (5.9–20.3)	11.2 (5.5–16.8)

(*Continued*)

Table 3. Continued

	Class 5	Class 2	Class 1	Class 3	Class 4	Class 6
	Normal weight (nonlinear)	Normal weight (linear)	Normal weight or overweight	Normal weight increasing to overweight	Overweight or obesity	Normal weight increasing to obesity
Lower supervisory and technical occupations	11.4 (9.3–13.5)	10.9 (8.3–13.6)	14.9 (11.4–18.4)	15.5 (12.1–18.8)	13.8 (6.6–21.0)	10.7 (5.5–16.0)
Semiroutine occupations	6.4 (4.8–8.1)	6.4 (4.4–8.5)	10.7 (7.6–13.7)	8.2 (5.6–10.7)	12.1 (5.4–18.9)	11.3 (5.9–16.7)
Routine occupations	7.2 (5.4–8.9)	6.5 (4.3–8.7)	4.3 (2.2–6.5)	9.1 (6.4–11.9)	11.2 (4.7–17.7)	13.0 (7.3–18.7)
Weekly family income, £						
≥400	53.6 (50.5–56.6)	53.9 (49.9–57.8)	47.1 (42.5–51.7)	47.9 (43.7–52.2)	38.4 (29–47.8)	48.2 (40.7–55.6)
300–399	22.5 (19.9–25.2)	21.3 (18.0–24.5)	26.7 (22.6–30.9)	22.0 (18.3–25.7)	23.3 (14.9–31.8)	17.8 (11.9–23.7)
200–299	14.1 (11.9–16.3)	16.8 (13.9–19.8)	17.4 (13.9–21.0)	17.4 (14.0–20.8)	27.3 (18.3–36.2)	14.0 (8.5–19.4)
0–199	9.9 (8.0–11.7)	8.1 (5.9–10.2)	8.8 (6.1–11.4)	12.7 (9.7–15.6)	11.0 (4.9–17.2)	20.1 (13.9–26.2)
Family adversity index during pregnancy						
0	50.8 (48.0–53.6)	52.3 (48.6–56.0)	49.9 (45.6–54.2)	49.4 (45.4–53.4)	44.6 (36.0–53.3)	42.3 (35.5–49.2)
1	27.2 (24.7–29.8)	26.9 (23.6–30.1)	27.8 (23.9–31.6)	25.6 (22.1–29.1)	27.9 (20.0–35.8)	23.2 (17.4–29.1)
2	11.6 (9.8–13.4)	11.6 (9.2–14.0)	12.4 (9.6–15.3)	12.7 (10.1–15.4)	12.2 (6.6–17.9)	15.2 (10.3–20.2)
≥3	10.4 (8.6–12.1)	9.3 (7.1–11.4)	9.9 (7.4–12.5)	12.2 (9.6–14.8)	15.2 (8.9–21.5)	19.2 (13.7–24.8)
Family adversity index at 0–2 y of age						
0	35.4 (32.6–38.1)	31.8 (28.4–35.3)	28.2 (24.3–32.1)	32.3 (28.5–36.1)	30.1 (22.2–38.1)	29.3 (23.0–35.7)
1	27.1 (24.5–29.6)	30.2 (26.8–33.6)	29.4 (25.4–33.3)	25.8 (22.3–29.4)	18.3 (11.6–25.1)	26.1 (19.9–32.3)
2	16.6 (14.5–18.7)	17.5 (14.6–20.3)	16.1 (12.9–19.3)	19.2 (16.0–22.4)	19.8 (12.7–26.9)	15.2 (10.2–20.3)
≥3	21.0 (18.7–23.3)	20.5 (17.6–23.5)	26.4 (22.6–30.2)	22.6 (19.3–26.0)	31.8 (23.6–39.9)	29.4 (23.0–35.7)
Family adversity index at 2–4 y of age						
0	45.0 (42.2–47.9)	46.0 (42.3–49.7)	43.8 (39.4–48.1)	42.0 (38.0–46.1)	39.5 (30.8–48.2)	38.7 (31.8–45.6)
1	30.0 (27.4–32.7)	27.7 (24.3–31.1)	28.5 (24.5–32.4)	29.2 (25.4–32.9)	27.5 (19.5–35.5)	25.6 (19.4–31.7)
2	14.3 (12.3–16.3)	15.6 (12.8–18.3)	13.3 (10.2–16.3)	16.4 (13.3–19.5)	13.1 (6.9–19.4)	15.6 (10.4–20.9)
≥3	10.6 (8.8–12.4)	10.8 (8.4–13.1)	14.5 (11.5–17.5)	12.4 (9.7–15.1)	19.9 (12.7–27.2)	20.1 (14.3–25.8)
Breastfeeding duration						
≥6 mo	48.7 (45.8–51.6)	48.6 (44.8–52.4)	39.5 (35.2–43.8)	43.5 (39.4–47.6)	31.0 (22.8–39.2)	43.2 (36.0–50.3)
3–5 mo	16.1 (13.9–18.2)	18.5 (15.6–21.5)	18.9 (15.5–22.4)	19.0 (15.8–22.2)	19.5 (12.4–26.5)	15.8 (10.4–21.1)
<3 mo	20.9 (18.5–23.3)	18.9 (15.9–21.9)	23.1 (19.4–26.8)	20.3 (16.9–23.6)	35.5 (27.0–44.0)	16.9 (11.4–22.4)
Never	14.4 (12.3–16.4)	14.0 (11.4–16.6)	18.5 (15.0–22.0)	17.3 (14.2–20.4)	14.0 (7.8–20.2)	24.2 (17.8–30.5)

Results estimated using multiply imputed data and weighted by posterior probabilities of most likely class membership. BMI indicates body mass index.

consequences. We found and describe 6 classes in the ALSPAC sample: 2 classes had BMI trajectories that resulted in young-adulthood normal weight, 2 classes had BMI trajectories that resulted in young-adulthood overweight, and 2 classes had BMI trajectories that resulted in young-adulthood obesity. The classes demonstrated remarkable differences in fat mass, but not lean mass, trajectories. Average levels of most cardiometabolic health measures, including echocardiogram measures of heart structure and function, were worse in the classes that led to overweight or obesity. Our key finding, however, is that classes with average BMI trajectories that were high and stable had better cardiometabolic health profiles than classes with average BMI trajectories that demonstrated rapid gain and transitioned in late adolescence from normal weight to overweight or obesity.

A recent systematic review found 14 studies that had used mixture modeling to investigate BMI trajectories from birth onward,[19] and additional articles have considered different age windows in childhood or adulthood.[20–22] In our literature search, only 3 publications had applied growth mixture modeling to capture heterogeneity in age-related BMI trajectories spanning childhood into adulthood and subsequently related the latent classes identified to adulthood cardiometabolic health measures. The studies by Hao et al[10] and Oluwagbemigun et al[11] both had a sample size of only ≈650 individuals and discovered uninformative low, middle, and high BMI trajectory classes. These studies implemented a group-based or latent-class trajectory model, which is a heavily constrained type of mixture model that (unrealistically) assumes no individual variation in growth within each class. This introduces potential problems of meaning and

Table 4. Class Differences in Cardiometabolic Health Measures at 24 y of Age

	Class 5	Class 2			Class 1		
	Normal weight (nonlinear)	Normal weight (linear)			Normal weight or overweight		
			95% CI	*P* value		95% CI	*P* value
		B			B		
Height, cm	…	−0.329	−0.884 to 0.227	0.246	−0.678	−1.293 to −0.063	0.031
SBP, mm Hg	…	1.102	0.222 to 1.982	0.014	0.777	−0.239 to 1.793	0.134
DBP, mm Hg	…	0.936	0.271 to 1.601	0.006	0.903	0.108 to 1.698	0.026
Cholesterol, mmol/L	…	0.054	−0.032 to 0.140	0.219	0.063	−0.034 to 0.160	0.205
HDL-C, mmol/L	…	−0.024	−0.063 to 0.015	0.231	−0.013	−0.058 to 0.033	0.583
LDL-C, mmol/L	…	0.061	−0.017 to 0.140	0.123	0.040	−0.047 to 0.127	0.367
PWV, m/s	…	0.023	−0.099 to 0.145	0.708	0.045	−0.097 to 0.187	0.534
cIMT, mm	…	−0.001	−0.007 to 0.005	0.789	0.004	−0.003 to 0.011	0.246
LVMI, g/m^3	…	1.310	0.519 to 2.100	0.001	2.895	1.968 to 3.821	<0.001
Relative wall thickness	…	0.005	−0.002 to 0.012	0.191	0.013	0.004 to 0.022	0.007
s′, cm/s	…	0.016	−0.139 to 0.171	0.839	−0.164	−0.330 to 0.002	0.053
E/A ratio	…	−0.020	−0.089 to 0.049	0.565	−0.082	−0.162 to −0.003	0.043
E/e′ ratio	…	0.102	−0.022 to 0.226	0.106	−0.014	−0.161 to 0.133	0.855
		s%			s%		
Weight	…	5.4	4.2 to 6.6	<0.001	12.7	11.2 to 14.3	<0.001
BMI	…	5.8	4.7 to 6.9	<0.001	13.5	12.1 to 14.9	<0.001
Fat mass	…	17.4	14.7 to 20.2	<0.001	31.5	28.0 to 35.0	<0.001
Trunk fat mass	…	20.6	17.1 to 24.1	<0.001	36.4	32.1 to 40.8	<0.001
Peripheral fat mass	…	16.1	13.6 to 18.6	<0.001	29.3	26.1 to 32.5	<0.001
Lean mass	…	0.8	−0.3 to 1.9	0.171	4.5	3.1 to 5.8	<0.001
Trunk lean mass	…	0.0	−1.0 to 1.1	0.934	2.8	1.4 to 4.2	<0.001
Peripheral lean mass	…	1.6	0.3 to 2.9	0.018	6.6	5.0 to 8.1	<0.001
Triglycerides	…	2.8	−1.2 to 6.8	0.175	6.7	2.0 to 11.4	0.006
Insulin	…	9.7	4.1 to 15.2	0.001	14–9	7.9 to 21.9	<0.001
Glucose	…	0.5	−0.5 to 1.5	0.348	0.9	−0.3 to 2.1	0.147
CRP	…	10.6	−1.5 to 22.8	0.086	22.4	8.5 to 36.2	0.002

(*Continued*)

utility of the derived classes.[23] The Buscot et al[9] study of 2631 individuals in the Cardiovascular Risk in Young Finns Study presents a stronger analysis but is not without limitations. They also identified 6 classes, but the average BMI trajectories (between 6 and 49 years) were different compared with those presented in the present article, at comparable ages. This must at least partly be due to the different BMI measurement schedules and age ranges. The authors reported that trajectories of worsening or persistent obesity were associated with increased risk of outcomes including type 2 diabetes and hypertension, but these estimates were based on small numbers (eg, 7 individuals had type 2 diabetes in the persistent increasing overweight/obese class).

Over half of our sample demonstrated 1 of the 2 trajectories that persisted in the normal-weight BMI category. Individuals in these normal-weight trajectory classes subsequently displayed, on average, the most optimal cardiometabolic profiles in young adulthood, thus providing further evidence of the benefits associated with the management of a healthy weight in childhood and adolescence. Approximately 6% of our sample belonged to a class with an average trajectory that started in the normal-weight range at 7.5 years but finished in the obesity range at 24.5 years. This class had the highest carotid intima-media thickness, a subclinical marker of atherosclerosis and a surrogate end point for coronary artery disease,[24] the highest left ventricular mass indexed to height in m^3, a risk factor for coronary heart disease and heart failure,[25,26] and the highest E/e′ ratio, a correlate of left ventricular diastolic filling pressure that is related to cardiac events.[27] This class also had 50% higher CRP—an inflammatory marker related to risk of coronary heart disease, stroke, and vascular mortality[28]—than the class whose average BMI trajectory both started and finished in the obesity range. These differences clearly

Table 4. Continued

Class 3			Class 4			Class 6		
Normal weight increasing to overweight			Overweight or obesity			Normal weight increasing to obesity		
	95% CI	*P* value		95% CI	*P* value		95% CI	*P* value
B			B			B		
−0.751	−1.352 to −0.150	0.014	0.028	−1.155 to 1.211	0.963	−0.303	−1.232 to 0.627	0.523
2.186	1.211 to 3.161	<0.001	5.146	3.178 to 7.114	<0.001	6.604	4.801 to 8.408	<0.001
2.043	1.267 to 2.819	<0.001	3.869	2.368 to 5.371	<0.001	7.562	6.031 to 9.092	<0.001
0.038	−0.055 to 0.131	0.419	0.201	0.028 to 0.373	0.023	0.110	−0.047 to 0.267	0.170
−0.124	−0.166 to −0.082	<0.001	−0.072	−0.149 to 0.005	0.065	−0.310	−0.380 to −0.240	<0.001
0.109	0.025 to 0.192	0.011	0.172	0.024 to 0.320	0.023	0.262	0.119 to 0.405	<0.001
0.054	−0.081 to 0.190	0.432	−0.058	−0.310 to 0.195	0.655	0.294	0.056 to 0.531	0.015
0.004	−0.002 to 0.011	0.189	0.008	−0.005 to 0.021	0.240	0.016	0.004 to 0.029	0.012
3.957	3.069 to 4.846	<0.001	5.151	3.212 to 7.090	<0.001	6.306	3.995 to 8.617	<0.001
0.016	0.007 to 0.024	<0.001	0.018	0.002 to 0.035	0.031	0.013	−0.002 to 0.029	0.094
−0.181	−0.354 to −0.008	0.040	−0.267	−0.584 to 0.049	0.098	−0.550	−0.848 to −0.252	<0.001
−0.113	−0.185 to −0.041	0.002	−0.097	−0.248 to 0.054	0.206	−0.048	−0.185 to 0.090	0.493
0.211	0.079 to 0.343	0.002	0.369	0.070 to 0.667	0.016	0.461	0.207 to 0.715	<0.001
s%			s%			s%		
15.2	13.6 to 16.8	<0.001	28.7	24.8 to 32.6	<0.001	42.9	39.9 to 45.8	<0.001
16.1	14.7 to 17.6	<0.001	28.7	25.1 to 32.2	<0.001	43.2	40.4 to 46.0	<0.001
34.7	31.1 to 38.3	<0.001	60.5	52.5 to 68.5	<0.001	84.2	77.4 to 91.1	<0.001
42.5	38.0 to 46.9	<0.001	70.6	61.0 to 80.2	<0.001	98.9	90.7 to 107.2	<0.001
29.7	26.4 to 32.9	<0.001	54.1	46.8 to 61.3	<0.001	74.2	68.1 to 80.3	<0.001
6.1	4.9 to 7.4	<0.001	11.8	9.1 to 14.5	<0.001	15.5	10.8 to 20.1	<0.001
4.4	3.2 to 5.7	<0.001	9.8	7.1 to 12.5	<0.001	12.2	7.0 to 17.3	<0.001
8.4	6.9 to 9.9	<0.001	14.9	11.8 to 18.1	<0.001	20.6	16.3 to 25.0	<0.001
9.5	5.0 to 14.0	<0.001	16.2	6.8 to 25.6	0.001	26.5	18.3 to 34.6	<0.001
24.8	18.4 to 31.2	<0.001	39.0	26.5 to 51.5	<0.001	84.4	72.5 to 96.2	<0.001
1.3	0.2 to 2.4	0.022	0.7	−1.1 to 2.6	0.445	4.4	2.4 to 6.5	<0.001
36.6	23.3 to 49.9	<0.001	60.8	35.6 to 86.0	<0.001	110.7	89.5 to 131.8	<0.001

s% estimates are symmetrical percentage differences. Results estimated using confounder-adjusted regression models applied to multiply imputed data and weighted by posterior probabilities of most likely class membership. BMI indicates body mass index; cIMT, carotid intima-media thickness; CRP, C-reactive protein; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVMI, left ventricular mass indexed to height in m^3; PWV, pulse wave velocity; and SBP, systolic blood pressure.

demonstrate the adverse consequences of rapid adolescent BMI gain. They are also in agreement with a population-based cohort study in Sweden, which reported (relevant to a normal weight group) a higher hazard ratio for cardiovascular mortality in boys who became overweight during puberty (hazard ratio, 2.39) than in boys who were consistently overweight (hazard ratio, 1.85).[29] The reasons why individuals who become obese during adolescence have worse cardiometabolic health prospects than individuals who have been obese for longer since childhood are not well understood. One explanation, supported by work by Sachdev et al,[30] is that adolescent BMI gains are more strongly related (than childhood BMI gains) to increases in visceral adiposity.[30,31] This was observed here, with the normal weight increasing to obesity class having 28% more trunk fat than the overweight or obesity class. Thereafter, it is well known that centrally stored adipose tissue is associated with increases in blood pressure, low-grade inflammation, insulin resistance, and impaired glucose tolerance.[31,32] Alternatively, this may also reflect a greater adulthood lean mass in those who had a high and stable BMI in childhood compared with those who did not become obese until late adolescence, as it has been shown that before adolescence, increases in BMI are driven primarily by increases in fat-free mass.[33]

By modeling height growth curves for each class, we found that the most deleterious classes tended to be taller than their peers initially but transitioned to being shorter than their peers in adulthood, due to an earlier and lower magnitude of peak height velocity. This pattern of growth has been documented before in children with

Table 5. Class Differences in Cardiometabolic Health Measures at 24 y of Age

	Class 1	Class 3			Class 4	Class 6		
	Normal weight or overweight	Normal weight increasing to overweight			Overweight or obesity	Normal weight increasing to obesity		
			95% CI	*P* value			95% CI	*P* value
		B				B		
Height, cm	…	−0.073	−0.759 to 0.613	0.834	…	−0.331	−1.686 to 1.024	0.632
SBP, mm Hg	…	1.409	0.258 to 2.560	0.016	…	1.458	−0.971 to 3.887	0.239
DBP, mm Hg	…	1.140	0.209 to 2.071	0.016	…	3.692	1.709 to 5.676	<0.001
Cholesterol, mmol/L	…	−0.025	−0.130 to 0.081	0.648	…	−0.091	−0.304 to 0.123	0.404
HDL-C, mmol/L	…	−0.111	−0.162 to −0.061	<0.001	…	−0.238	−0.332 to −0.143	<0.001
LDL-C, mmol/L	…	0.069	−0.027 to 0.165	0.161	…	0.090	−0.098 to 0.278	0.348
PWV, m/s	…	0.009	−0.142 to 0.161	0.905	…	0.351	0.021 to 0.681	0.037
cIMT, mm	…	0.000	−0.007 to 0.008	0.916	…	0.008	−0.008 to 0.025	0.321
LVMI, g/m^3	…	1.063	0.034 to 2.092	0.043	…	1.155	−1.505 to 3.815	0.394
Relative wall thickness	…	0.003	−0.008 to 0.013	0.604	…	−0.005	−0.027 to 0.017	0.656
s′, cm/s	…	−0.017	−0.217 to 0.182	0.865	…	−0.283	−0.663 to 0.097	0.144
E/A ratio	…	−0.031	−0.118 to 0.056	0.483	…	0.049	−0.133 to 0.231	0.596
E/e′ ratio	…	0.225	0.073 to 0.376	0.004	…	0.092	−0.275 to 0.459	0.621
		s%				s%		
Weight	…	2.5	0.6 to 4.4	0.009	…	14.2	9.5 to 18.8	<0.001
BMI	…	2.7	0.9 to 4.4	0.003	…	14.5	10.3 to 18.8	<0.001
Fat mass	…	3.2	−1.0 to 7.5	0.132	…	23.7	14.1 to 33.3	<0.001
Trunk fat mass	…	6.0	0.9 to 11.2	0.022	…	28.3	16.8 to 39.8	<0.001
Peripheral fat mass	…	0.4	−3.5 to 4.2	0.853	…	20.1	11.4 to 28.8	<0.001
Lean mass	…	1.7	0.3 to 3.0	0.019	…	3.7	−0.9 to 8.2	0.113
Trunk lean mass	…	1.6	0.3 to 3.0	0.020	…	2.4	−2.5 to 7.2	0.338
Peripheral lean mass	…	1.8	0.2 to 3.5	0.033	…	5.7	1.0 to 10.4	0.017
Triglycerides	…	2.8	−2.6 to 8.2	0.312	…	10.2	−1.3 to 21.7	0.082
Insulin	…	9.8	2.1 to 17.6	0.013	…	45.4	29.5 to 61.3	<0.001
Glucose	…	0.4	−0.9 to 1.7	0.522	…	3.7	1.3 to 6.1	0.003
CRP	…	14.3	−1.4 to 29.9	0.074	…	49.9	20.3 to 79.5	0.001

s% estimates are symmetrical percentage differences. Results estimated using confounder-adjusted regression models applied to multiply imputed data and weighted by posterior probabilities of most likely class membership. BMI indicates body mass index; cIMT, carotid intima-media thickness; CRP, C-reactive protein; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVMI, left ventricular mass indexed to height in m^3; PWV, pulse wave velocity; and SBP, systolic blood pressure.

obesity,[34] and both earlier puberty and shorter adulthood height are related to increased risk of cardiometabolic disease–related morbidity and mortality.[35,36] Relevant to the archetypical normal-weight group, the childhood height advantage was the least pronounced and the final height deficit was the most pronounced, in the two classes with average BMI trajectories that demonstrated rapid gain. This suggests that it might be rapid BMI gain rather than obesity per se which results in earlier puberty and shorter adulthood height.

The ALSPAC cohort is predominantly White British, with low levels of socioeconomic deprivation, which may limit generalizability of the findings. Approximately 25% of the initial ALSPAC cohort participated in the 24-year clinic sweep, and differential selection into our sample may have biased results.[37] A pragmatic decision was made to analyze data from both sexes together, as was done by Buscot et al[9] and others.[19] While there are systematic differences in childhood BMI between boys and girls, this is not a reason to hypothesize that there should be a different number of latent classes for each sex. Further, stratifying analyses by sex would have led to smaller classes and reduced the power of our regression models investigating relationship with cardiometabolic outcomes. However, as sensitivity analyses, we refitted our final growth mixture model as a multigroup mode to investigate whether, in each trajectory class, growth parameters differed between the sexes. We did not find strong evidence to suggest that trajectories differed between the sexes. We also ran sex-specific regression models to investigate whether the relationship between the trajectory classes and cardiometabolic health measures

differed by sex, and we observed similar patterns of results to those observed with sexes combined. In this second step of the analysis, we did not adjust for BMI or height at 24 years because this would have biased the estimates due to conditioning on a mediator. The carotid intima-media thickness, pulse wave velocity, and echocardiogram outcomes had large amounts of missing data, but results were comparable in the main analysis (which accounted for missing data using multiple imputation) and in a sensitivity analysis in which the outcomes were not imputed.

In conclusion, this article demonstrates how the relationship of young-adulthood overweight or obesity with cardiometabolic health is dependent on the process by which a child becomes overweight or obese. Individuals who have high and stable BMI across childhood may have lower cardiometabolic disease risk than individuals who do not become overweight or obese until late adolescence. At a time when the focus of obesity and related-disease prevention is increasingly targeting early childhood, this is an important consideration for researchers, clinicians, and public health officials.

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Disclosures

None.

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