Body Mass Index Trajectories in Early Life Is Predictive of Cardiometabolic Risk

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Objective To identify distinct body mass index (BMI) trajectories across the life-course and explore the effects of BMI trajectories on the adult cardiovascular disease outcomes using a dataset with 30 years of follow-up in northern China.

Study design A total of 2839 participants aged 6-18 years whose BMIs were measured 3-6 times during the Hanzhong Adolescent Hypertension Study were included in our analysis. Latent mixture modeling was used to clarify distinct BMI trajectories in longitudinal analyses.

Results Three groups with distinct trajectories in BMI were identified by the latent mixed models: a low-increasing group (n = 1324 [36.64%]), a moderate-increasing group (n = 1178 [16.89%]), and a high-increasing group (n = 337 [39.46%]). Compared with the participants in the low-increasing group, the risk ratios of hypertension, type 2 diabetes mellitus, high-risk triglycerides, and high-risk high-density lipoprotein cholesterol were more than 3.0 in the high-increasing group (all $P < .001$) after being fully adjusted. Increased risks existed in high brachial-ankle pulse wave velocity for the high-increasing group compared with the low-increasing group (RR, 2.75; 95% CI, 1.94-3.91; $P < .001$). Additionally, participants in the moderate-increasing group had a 2.31-fold increased risks of left ventricular hypertrophy (95% CI, 1.25-4.30; $P = .008$).

Conclusions Our study indicates that BMI trajectories from childhood to adulthood vary and that an elevated BMI trajectory in early life is predictive of an increased the risk of developing cardiovascular disease risks. *(J Pediatr 2020;219:31-7)*.

Trial registration ClinicalTrials.gov: NCT02734472.

Overweight and obesity have emerged as significant risk factors that threaten health. By 2030, it is projected that a total of 2.16 billion individuals will be overweight and 1.12 billion will be obese if recent trends continue unabated.[1] Studies have shown that overweight and obesity in youth is strongly associated with the development of cardiovascular disease (CVD) and type 2 diabetes mellitus in adulthood.[2-4]

Body mass index (BMI) is a practical, available, and widely used method to identify overweight and obesity in the population. Previous studies have demonstrated an association between long-term BMI trajectories that reach or persist at high levels and CVD risk factors in adulthood.[3,5] Recent studies have reported predictive values of BMI trajectories for hypertension and subclinical vascular damage in the Chinese population.[6,7] However, a lack of complete serial data in some of these cohorts precludes the accurate and comprehensive description and analysis of the early life BMI trajectories of participants for long-term life-course CVD outcomes in the Chinese population.

To address these gaps, we used the data from participation the Hanzhong Adolescent Hypertension Study, a prospective cohort study, from 1987 to 2017. Our analysis sought to identify distinct BMI trajectories reflecting dynamic development across the life-course and to explore the relationship of BMI trajectories with adult CVD outcomes.

Methods

The Hanzhong Adolescent Hypertension Cohort was an ongoing prospective study that enrolled 4623 participants from 26 rural sites of 3 towns (Qili, Laojun,

BMI	Body mass index	cIMT	Carotid intima-media thickness
CVD	Cardiovascular disease	RR	Risk ratio
ECG	Electrocardiographic	SBP	Systolic blood pressure
HDL	High-density lipoprotein	DBP	Diastolic blood pressure
baPWV	Brachial-ankle pulse wave velocity	TG	Triglycerides
LVH	Left ventricular hypertrophy	LDL	Low-density lipoprotein

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and Shayan) in Hanzhong, Shaanxi, China in March and April 1987. The inclusion criteria in this study were as follows: aged 6-18 years old in 1987; no history of stroke, myocardial infarction, renal failure, or infection disease; and the ability to communicate frequently in Mandarin. We collected data in 6 follow-ups: in 1989, 1992, 1995, 2005, 2013, and 2017. Death, migration, and mental illness mainly contributed to the loss for the 30-year follow-up. There were 2839 participants with at least 3 BMI measurements before 18 years old who were eventually included in the analysis regardless of whether they had CVD measurements in middle age (**Figure 1**, available at www.jpeds.com).

This study followed the principles of the Helsinki Declaration, and was supported and approved by the Ethics Committee of the First Affiliated Hospital of Xi'an Jiaotong University. We obtained written informed consent from each participant and, for those who were younger than age 18 years at baseline, informed consent from a parent/guardian was obtained. ClinicalTrials.gov trial registration number was NCT02734472 (date of registration: 12/04/2016).

The collection methods for anthropometrics and the measurements for biochemical assays, carotid intima-media thickness (cIMT), and brachial-ankle pulse wave velocity (baPWV) are available in the **Appendix** (available at www.jpeds.com). CVD outcomes tracked in this study included hypertension, type 2 diabetes mellitus, high-risk lipid levels, high-risk cIMT, high-risk baPWV, and left ventricular hypertrophy (LVH). In the present study, diabetes was defined as a fasting blood glucose level of 126 mg/dL or greater (7.0 mmol/L) or current treatment for diabetes.[8] Hypertension was defined as systolic blood pressure (SBP) or diastolic blood pressure (DBP) of 140/90 mm Hg or greater or current use of antihypertensive medications.[8] Hyperlipidemia was defined according to any one of the following 3 measures: triglycerides (TG) of 2.26 mmol/L or greater, low-density lipoprotein (LDL) cholesterol of 4.14 mmol/L or greater, and high-density lipoprotein (HDL) cholesterol of 1.04 mmol/L or greater.[3,9] cIMT and baPWV were recognized as markers of subclinical vascular damage.[7] In accordance with guidelines from the joint European Society of Hypertension/European Society of Cardiology, in the present study, we defined patients with high-risk cIMT as those with an asymptomatic IMT of 0.9 mm or greater.[10] Based on the Framingham risk score, a baPWV level of 1400 mm/second corresponds with a moderate risk of cardiovascular events, as well as an increased risk of hypertension onset.[11-13] Therefore, we defined baPWV of 1400 mm/second or greater as a high-risk baPWV level for arterial stiffness. Sokolow-Lyon voltage and Cornell product values were used to assess the occurrence of LVH. Either the Sokolow-Lyon voltage (S_{V1} + $RV_{5/6}$) > 38 mm or the product of QRS duration times the Cornell voltage combination (R_{aVL} + S_{V3}, with 8 mm added in women) >2440 mm/ms were used to identify LVH.[14,15]

A latent mixture model within the STATA Traj (version 14.0; Stata Corp., College Station, TX, USA) command was used to identify the BMI subgroups in this study. Latent mixture modeling represents a flexible approach to investigating population heterogeneity by sorting cases into latent but nonarbitrary subgroups that are more homogeneous, which is an extension of latent variable modeling to occasions when researchers are interested in testing hypotheses about categorical sources of population heterogeneity within a dataset.[16] Latent mixture models assign cases into classes or subgroups, and posterior probabilities, which represent the probability that an individual belongs to each class, are obtained and used to infer the correct class membership.[17] A total of 2839 participants with 3 or more BMI examinations were included in the BMI trajectories analyses. Those with data from only the initial 3 visits data or with only BMI measurements from the last 3 visits were excluded. The mean number of BMI examinations was 5.10 ± 0.89, and 39.67% of participants had 6 BMI measurements. The maximum likelihood method was used to estimate the model parameters and latent mixture modeling assigned each individual to a corresponding group with the greatest posteriori probability. Trajectory shape with a cubic specfication were built first, and then constructed it as quadratic or linear if necessary. The Bayesian information criterion was used to evaluate the best configuration models, and the appropriate average posterior probability (>0.7) with a minimum sample size in each group accounted for 5.0%.

Continuous data were shown as means ± SDs if they were normally distributed and non-normally distributed variables were expressed as the median (IQR). Categorical data were presented as frequency and percentage. If the data met distribution and variance conditions, *t* tests were used to analyze differences between continuous variables for 2-group comparisons, and for 3 or more groups, 1-way ANOVA was used. For other data, the Mann-Whitney *U* test was used for comparing 2 groups and the Kruskal-Wallis test for correlation analysis was determined with the Pearson correlation coefficient or the Spearman. A χ^2 test was used to analyze categorical variables. We further used logistic regression analysis to investigate the association between BMI trajectories and incident CVD outcomes shown as risk ratios (RRs) and their 95% CIs. All statistical analyses were performed using SPSS 16.0 (SPSS, Inc, Chicago, Illinois). A 2-sided *P* value of .05 was used to evaluate statistical significance.

Results

Among 2839 subjects included in the analysis, 1866 individuals had cIMT values and 1975 subjects had baPWV data available in 2017. There were 1634 Sokolow-Lyon voltage values and 1684 Cornell indexes, the markers of LVH, collected from among the 2839 participants.

The 3 BMI trajectory groups were identified with 95% CIs based on predicted trajectory means (**Figure 2**). According to the trend of the trajectory group, we named the 3 groups as follows: low-increasing group (n = 1324 [46.6%]), moderate-increasing group (n = 1178 [41.5%]), and high-

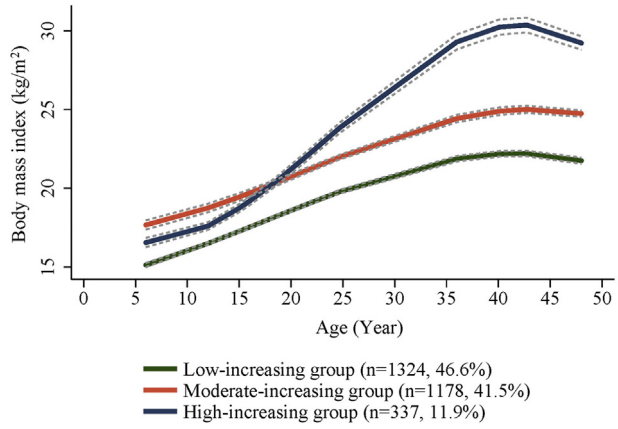

Figure 2. BMI trajectory groups identified from childhood to middle age in the Hanzhong Adolescent Hypertension Cohort: low-increasing group (n = 1324 [46.6%]), moderate-increasing group (n = 1178 [41.5%]), and high-increasing group (n = 337 [11.9%]). Means and SDs of BMI are shown.

increasing group (n = 337 [11.9%]). Participants in moderate-increasing group had higher levels of BMI compared with those in the low-increasing group during the 30-year follow-up. Those in the high-increasing group had relatively moderate initial BMI levels that increased from approximately age 12 years and exceeded BMI levels in the moderate-increasing group at approximately age 18 years (**Figure 2** and **Table I**).

Demographic characteristics and cardiovascular risk factors of participants by BMI trajectory groups were presented in **Table II** (available at www.jpeds.com). There were 1602 males and 1237 females among the population. Significant differences existed in the age, BMI, bust, heart rate, SBP, and DBP in 1987 among BMI trajectory groups ($P < .05$). In 2017, the proportion of education status, current smoking habit, alcohol consumption, and histories of hypertension, diabetes, and hyperlipidemia were significantly different among the BMI trajectory groups ($P < .05$). Levels of total cholesterol, TG, LDL cholesterol, serum creatinine, serum urine acid, and the urinary albumin creatinine ratio increased significantly from the low-increasing group to the high-increasing group ($P < .05$).

Table I. BMI (kg/m^2) levels by age periods in BMI trajectory groups

Trajectory groups	Low-increasing group	Moderate-increasing group	High-increasing group
No. (%)	1324 (46.6)	1178 (41.5)	337 (11.9)
6-10, years	14.3 (13.8-15.0)	15.6 (15.0-16.3)	15.2 (14.5-15.7)
11-15, years	15.6 (14.7-16.6)	17.3 (16.1-18.5)	16.7 (15.7-18.0)
16-20, years	18.3 (17.1-19.3)	19.9 (18.5-21.2)	19.9 (18.7-21.6)
21-25, years	19.4 (18.4-20.3)	21.2 (20.1-22.4)	22.6 (21.0-24.0)
26-30, years	19.3 (18.6-20.0)	21.0 (19.7-22.2)	23.6 (19.5-24.9)
31-35, years	21.9 (20.4-23.4)	25.1 (24.1-26.2)	28.2 (27.2-30.1)
36-40, years	22.0 (20.5-23.7)	24.8 (23.3-26.0)	28.6 (27.4-30.0)
41-45, years	21.7 (20.4-23.3)	24.6 (23.1-26.2)	29.1 (27.8-30.5)
46-50, years	21.5 (20.2-23.3)	24.8 (23.2-26.2)	29.5 (28.3-30.8)

Non-normally distributed variables are expressed as the median (IQR).

First, we compared SBP, DBP, and mean arterial pressure in 2017, among the 3 trajectory groups (**Figure 3**; available at www.jpeds.com). Subjects in the high-increasing group had significantly higher levels of SBP, DBP, and mean arterial pressure compared with the moderate-increasing and low-increasing groups, and subjects in the moderate-increasing group also had significantly higher levels of SBP, DBP and mean arterial pressure compared with the low-increasing group (all $P < .001$).

Significant differences in TG, LDL cholesterol, and HDL cholesterol in 2017 are presented in **Figure 4** (available at www.jpeds.com). The levels of TG and LDL cholesterol were higher and the levels of HDL cholesterol were lower in the high-increasing group compared with the other BMI groups. A similar trend existed between the moderate-increasing and low-increasing groups ($P < .001$).

Participants in the moderate-increasing and high-increasing groups had significantly elevated cIMT and baPWV levels in 2017 compared with the low-increasing group ($P < .001$) (**Figure 5**, A and B; available at www.jpeds.com). The levels of baPWV in the moderate-increasing group were significantly different from those of the low-increasing group ($P = .008$). However, no significant difference in cIMT existed between the moderate-increasing and high-increasing groups ($P = .074$) (**Figure 5**, A).

Because only 5 participants had an elevated Sokolow-Lyon voltage, and all of those five subjects had elevated Cornell indexes, we compared the Cornell products across the BMI trajectory groups (**Figure 5**, C). Compared with the low-increasing group, a significant difference in the Cornell index existed in the moderate-increasing group ($P = .026$) and high-increasing group ($P = .037$), whereas no significant difference in the Cornell index existed between the moderate-increasing group and high-increasing group ($P = .571$).

Table III presents the predictive value of the association of BMI trajectory groups with adult outcomes. After adjusting for sex, age, smoking habits, alcohol consumption, occupation, marital status, and education, participants in the high-increasing group had more than 2 times the odds of having hypertension, type 2 diabetes, high-risk TG, high-risk HDL cholesterol, and high-risk baPWV (all $P < .001$) than those in the low-increasing group. Compared with participants in the low-increasing group, the fully adjusted RRs of hypertension, high-risk TG, and high-risk HDL cholesterol were 2.26 (95% CI, 1.72-2.98), 1.93 (95% CI, 1.41-2.64), and 2.01 (95% CI, 1.56-2.59) in participants in the moderate-increasing group (all $P < .001$). The RR of type 2 diabetes in the moderate-increasing group was 1.89 (95% CI, 1.10-3.24) after adjustment for age and sex compared with the low-increasing group, but the RR was not significant after full adjustment. The subjects in the moderate-increasing group had a 2.31-fold increased risk (95% CI, 1.25-4.30;

Table III. RRs and 95% CIs of the association of BMI trajectories with adult outcomes

Adult outcomes and latent BMI trajectory group	Percentage	Model 1			Model 2		
		RR	95% CI	*P* value	RR	95% CI	*P* value
Hypertension							
Low-increasing group	12.58	1	—	—	1	—	—
Moderate-increasing group	25.48	2.29	1.76-2.97	**<.001**	2.26	1.72-2.98	**<.001**
High-increasing group	37.6	3.95	2.87-5.44	**<.001**	3.95	2.80-5.57	**<.001**
Type 2 diabetes							
Low-increasing group	2.45	1	—	—	1	—	—
Moderate-increasing group	4.85	1.89	1.10-3.24	**.021**	1.53	0.86-2.74	.148
High-increasing group	10.29	4.62	2.60-8.21	**<.001**	4.45	2.41-8.22	**<.001**
High-risk TG							
Low-increasing group	12.44	1	—	—	1	—	—
Moderate-increasing group	19.29	1.72	1.29-2.28	**<.001**	1.93	1.41-2.64	**<.001**
High-increasing group	33.20	3.30	2.35-4.64	**<.001**	3.61	2.49-5.23	**<.001**
High-risk LDL cholesterol							
Low-increasing group	1.08	1	—	—	1	—	—
Moderate-increasing group	1.22	1.56	0.59-4.12	.374	2.07	0.61-7.03	.242
High-increasing group	1.23	1.05	0.28-3.94	.943	2.21	0.49-9.94	.302
High-risk HDL cholesterol							
Low-increasing group	23.80	1	—	—	1	—	—
Moderate-increasing group	36.87	1.98	1.57-2.50	**<.001**	2.01	1.56-2.59	**<.001**
High-increasing group	50.41	3.09	2.27-4.20	**<.001**	3.11	2.21-4.36	**<.001**
High-risk cIMT							
Low-increasing group	3.79	1	—	—	1	—	—
Moderate-increasing group	4.58	0.97	0.58-1.61	.900	1.03	0.61-1.76	.906
High-increasing group	5.00	1.25	0.63-2.50	.522	1.15	0.54-2.45	.718
High-risk baPWV							
Low-increasing group	17.13	1	—	—	1	—	—
Moderate-increasing group	22.77	1.19	0.92-1.53	.187	1.25	0.95-1.65	.117
High-increasing group	33.99	2.34	1.70-3.23	**<.001**	2.75	1.94-3.91	**<.001**
LVH							
Low-increasing group	2.65	1	—	—	1	—	—
Moderate-increasing group	5.33	2.15	1.20-3.84	**.010**	2.31	1.25-4.30	**.008**
High-increasing group	5.07	1.96	0.92-4.18	.081	1.67	0.72-3.84	.231

Model 1 is adjusted for sex and age in 1987; model 2 includes model 1 and is further adjusted for smoke habits, alcohol consumption, occupation, married status, and education. Significant *P* values were presented in bold.

P = .008) of LVH than the low-increasing group. Considering the cIMT values, the RRs of high-risk cIMT were nearly 1 in both the moderate and high-increasing groups, which showed no difference. Detailed outcomes are shown in **Table III**.

The predictive probability of adult CVD outcomes for the sex- and age-adjusted ordinal logistic models are shown in **Figure 6**. Three groups were identified according to the number of CVD outcomes in this study: 0, 1, and 2 or more high-risk outcomes. The probability of participants with 0 high-risk outcomes decreased from 0.79 (low-increasing group) to 0.26 (high-increasing group), and the probability of having more than 2 high-risk outcomes increased from 0.10 (low-increasing group) to 0.71 (high-increasing group).

We further evaluated the relationship between the BMI trajectories and each adult CVD outcome by sex, which was shown in **Table IV** (available at www.jpeds.com). As shown in **Table IV**, similar results of the risks of hypertension, high-risk TG, and a high risk of HDL cholesterol by BMI trajectories existed in males and females. Regarding diabetes mellitus, compared with those in the low-increasing group, males with moderate-increasing BMI had significantly higher risk for diabetes, which was not focused in females with moderate-increasing BMI. Additionally, males in the moderate-increasing and high-increasing group showed significantly higher risks in high-risk baPWV compared with the low-increasing group, which was not shown in females. **Table V** (available at www.jpeds.com) shows the relationship between BMI trajectories and adult CVD outcomes by different baseline age groups. We divided the population into 2 groups as before puberty (aged 4-11 years) and puberty (aged 12-18 years) according to their baseline age. Similar trends existed in comparison between BMI trajectory groups with each CVD outcome in different age groups.

Discussion

Studies have reported that excess adiposity in childhood creates a predisposition to developing adult hypertension.[3,18] In line with an intensifying association between life-course BMI gains and BP, we found that participants in the high-increasing group showed a more than 3-fold increased risk of hypertension compared with those in the low-increasing group, which suggests the importance of early intervention

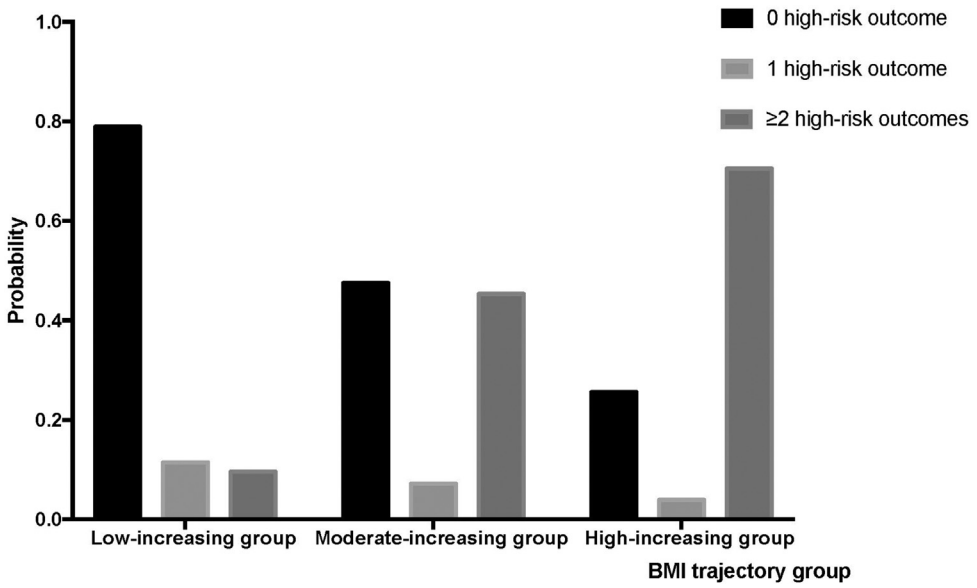

Figure 6. Predictive probability of combined adult CVD outcomes: 0 high-risk outcome (n = 982); 1 high-risk outcome (n = 117); and 2 or more high-risk outcomes (n = 496) according to the logistic regression after adjusting for age and sex.

to address adiposity. In contrast, Li et al found that a steeply increasing BMI was not associated with a detrimental trend in blood pressure in later life in British cohorts.[19] This finding may have been due to improvements in other factors linked to blood pressure, such as smoking.[19] Differences in the statistical methods in used among these studies with limited time points would also be considered when compared with our study. Additionally, differences by ethnic group may also explain this phenomenon.

Evidence has illustrated that an elevated BMI in adolescence, even at a nonobese level, contributes to a high risk for type 2 diabetes mellitus.[20-22] This finding is consistent with our results. Although the participants aged 6-18 years old in the moderate-increasing group had relatively higher BMI levels than those in the other group, the risk for type 2 diabetes mellitus did not increase significantly after being fully adjusted, which may suggest that improving BMI after childhood is beneficial for decreasing the risk of type 2 diabetes mellitus. Tirosh et al demonstrated that the risk of type 2 diabetes mellitus was mainly associated with increased BMI levels rather than the previous high BMI level in childhood, which is similar to our finding.[20]

Obese and overweight adolescents are at an increased risk of having abnormal lipid profiles, including higher TG and LDL cholesterol and a lower HDL cholesterol at maturity than normal-weight individuals.[3,22,23] This is somewhat different from our results, in which no significantly increased risk existed in high-risk LDL cholesterol among the 3 BMI trajectory groups.

Results from previous studies regarding the association between childhood BMI and adult cIMT, have been inconsistent. Hao et al reported that the adverse influence of high BMI on high cIMT begins in childhood, and Buscot claimed that elevated BMI status in early life may alter the arterial structure in ways that are not reversible.[3,5,7] Contrary to those results, Yan et al and Juonala et al reported that obesity in youth is not an independent predictor of cIMT in adulthood and that the association of childhood BMI with adulthood cIMT would be largely attenuated and even become nonsignificant after adjustment.[7,24] This finding is in accordance with our finding that steeper BMI gains might not increase the risk for high-risk cIMT in the later life. An association between elevated BMI and baPWV has been reported in recent studies.[25,26] Regarding the predictive values of BMI trajectory groups for high-risk baPWV, we found that participants in the high-increasing group had more than 2-fold higher risk for high arterial stiffness. Jang-Young Kim et al showed BMI affected PWV in men but not in women, which was consistent with our results.[27] There is controversy in the literature regarding the effects of obesity on arterial stiffness.

The Cornell product has been regarded as the ECG criteria of choice in overweight and obese population, and the Sokolow-Lyon index is considered to be the most specific ECG criteria for diagnosing LVH.[28] In studies of adult blacks and whites, participants with electrocardiographic (ECG)-LVH had significantly higher levels of BMI, total cholesterol, and LDL cholesterol compared with those with no ECG-LVH.[29,30] This finding is consistent with our results that elevated BMI at age 6-18 years was strongly associated with later LVH independent of adult BMI levels. It illustrates the effect of high BMI in childhood (6-18 years old) on the left ventricular structure, a change that may not be reversible. However, the criteria for LVH detection using ECG QRS voltages have been reported to be attenuated by obesity.[31] Further sensitivity and specificity of ECG criteria by distinct BMI trajectory groups in different ethnics groups need to be evaluated.

Some limitations should be mentioned when explaining our findings. First is the ethnic restriction of the study population. The present study enrolled all its participants in northern China, where diets tend to be high in salt. More epidemiologic studies in other ethnicities are needed to replicate our results. The absence of fitness or physical activity data was also an important limitation of this study. Another potential limitation of this study is the enrollment of participants aged 6-18 years. This study, therefore, lacks data on the children before age 6 years, resulting in the absence of data diving adiposity rebound. Finally, we did not evaluate the difference between total body fat and regional fat deposition, which may account for the association of childhood or adolescent obesity with adult disease.

The present study confirmed that distinct BMI trajectories exist from childhood to adulthood and found that trajectories of BMI in childhood were significant predictors of adult CVD outcomes in general. Our results highlight that the cumulative burden of persistent increases in BMI was associated with subsequent increases in CVD risk outcomes and indicate that the control of obesity later in life should be given sufficient attention. ■

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50 Years Ago in *The Journal of Pediatrics*

Diagnosing aortic aneurysms and their causes before they dissect

Strauss RG, McAdams AJ. Dissecting Aneurysm in Childhood. J Pediatr 1970;76:578-84.

The authors describe a 9.5-year-old male child who died suddenly during an exacerbation of wheezing and was found on postmortem examination to have a dissecting aneurysm of the ascending aorta. He had been treated with high dose corticosteroids for 9 months for chronic wheezing. He did not have stigmata of Marfan syndrome. Pathology showed replacement of the aorta elastic tissue with fibrous tissue, without inflammation. They also described 14 other cases from the literature in children younger than 16 years of age. Most cases were male patients in the second decade of life. Twelve of the patients had abnormalities in the aorta, 6 with coarctation and 4 with inflammatory lesions. All these patients died before diagnosis and surgery.

Since this publication, the differential diagnosis of aortic aneurysms has expanded to genetic diseases resulting in defective vascular collagen/connective tissue. In addition to Marfan syndrome (defects in fibrillin 1), the genetic diseases include the vascular type of Ehlers-Danlos syndrome, an autosomal dominant disease in the type III procollagen gene; Loey-Dietz syndrome, an autosomal dominant disease in the receptor of transforming growth factors β1 and 2 gene; Grange syndrome, an autosomal recessive disease in the yin yang 1-associated protein 1 gene and others. Inflammatory conditions such as Takayasu arteritis, a large vessel vasculitis and the third most common primary vasculitis in childhood, can result in aneurysms and dissections. In a series from Toronto, 3 out of 27 (11%) patients presented with large vessel dissection.[1] Infectious disease (syphilis, tuberculosis, and others) can result in aortic aneurysms.

Clues to these diseases include a family history of dissection or rupture of internal organs, other, primarily skeletal and cardiovascular, abnormalities and for Takayasu arteritis hypertension and increased inflammatory markers. Physical examination including listening for bruits, measuring blood pressure in 4 limbs, systematically palpating for pulses, examining for hypermobility, and velvety skin changes can be helpful.

Today, it is possible to diagnosis many of these patients prior to dissection using modern imaging techniques and genetics. Earlier diagnosis can enable lifesaving therapy with β-blockers in early stages of aortic dilation or surgery in more severe cases and anti-inflammatory therapy in patients with vasculitis.

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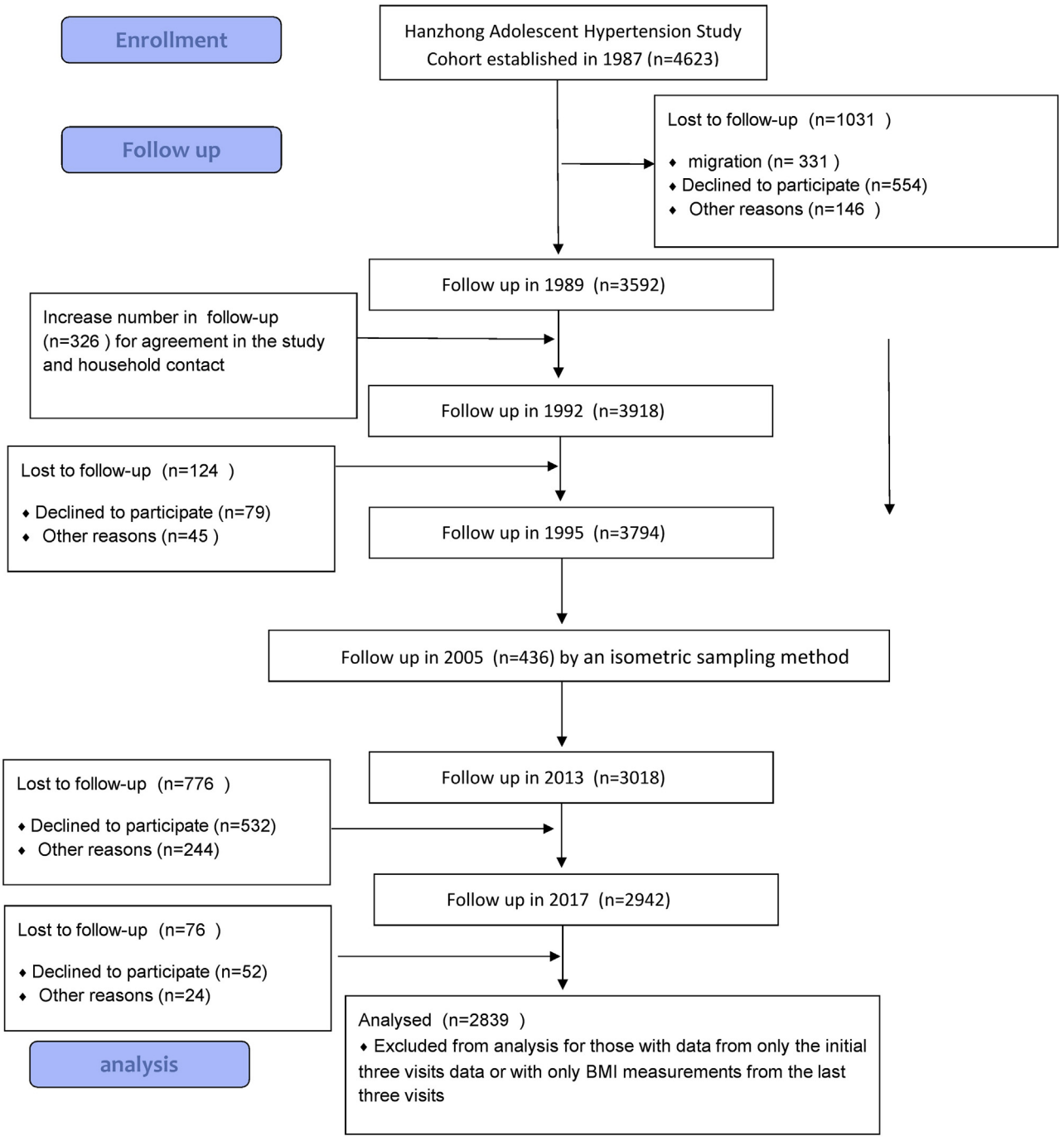

Figure 1. Flow diagram showing the selection of the study population.

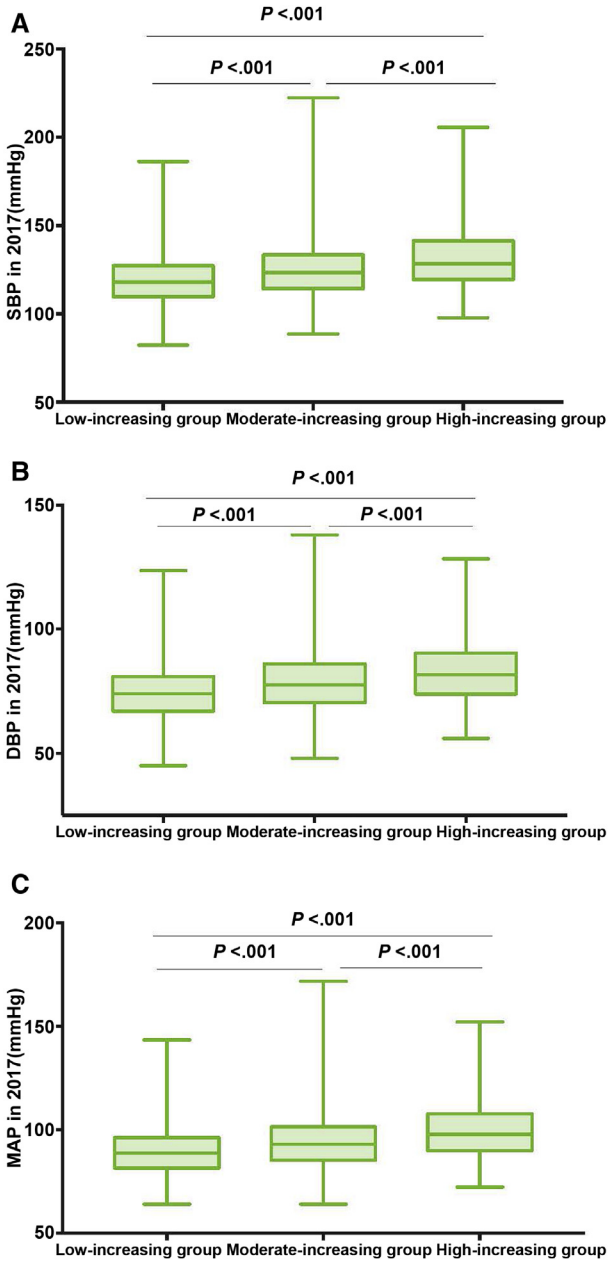

Figure 3. Significant differences in **A,** SBP, **B,** DBP, and **C,** MAP in 2017 among the 3 BMI trajectory groups (n = 2097). Subjects in the high-increasing group had significantly higher levels of SBP, DBP, and MAP compared with the moderate-increasing and low-increasing groups, and subjects in the moderate-increasing group also had significantly higher levels of SBP, DBP, and MAP compared with the low-increasing group ($P < .001$). Means and SDs of blood pressure are shown. *MAP*, mean arterial pressure.

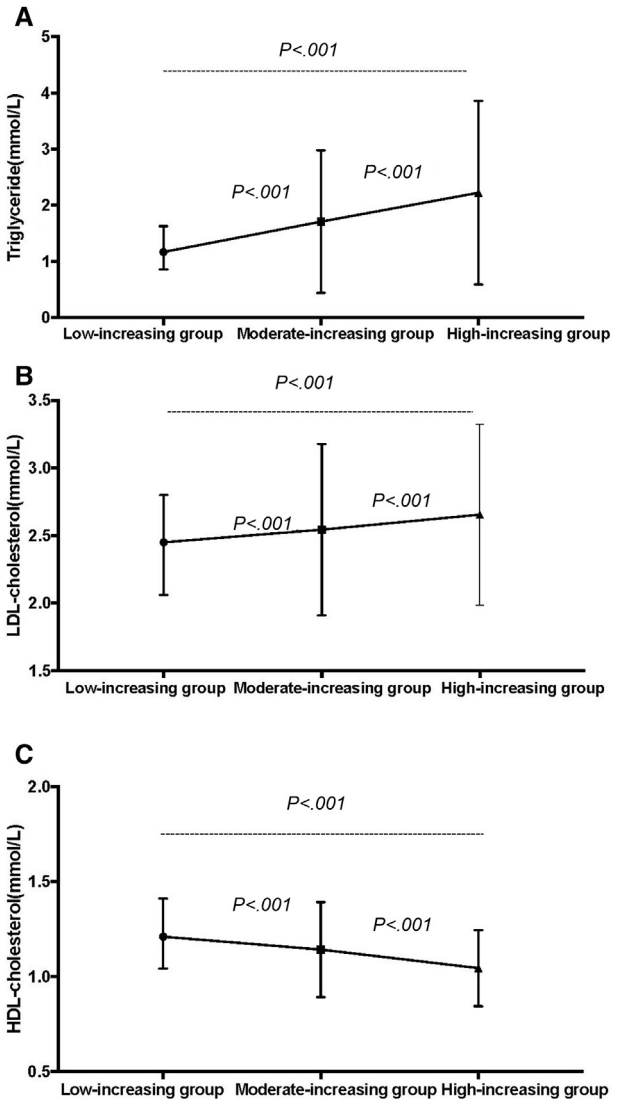

Figure 4. Comparison in **A,** TG, **B,** LDL cholesterol, and **C,** HDL cholesterol in 2017 among the 3 BMI trajectory groups showed significant differences (n = 1899). The levels of TG and LDL cholesterol were notably higher and the levels of HDL cholesterol were markedly lower in the high-increasing group compared with the other BMI groups. A similar trend existed between the moderate-increasing and low-increasing groups ($P < .001$). Medians (IQRs) of values are shown.

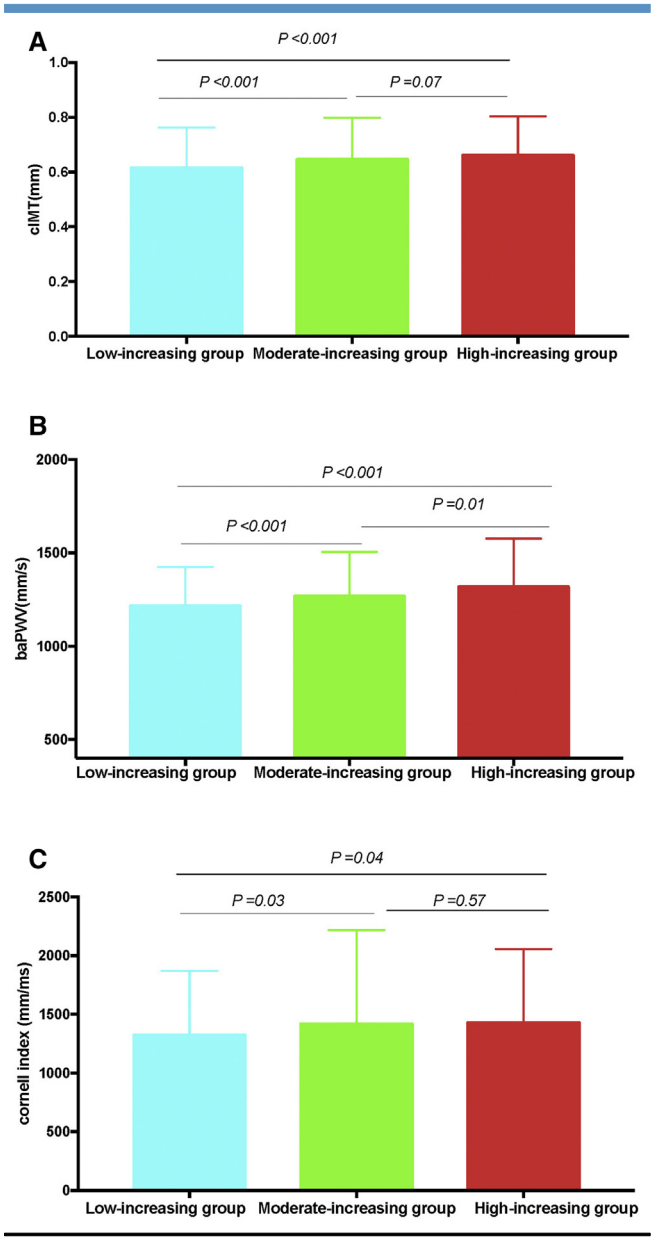

Figure 5. Compared with the low-increasing group, participants had significantly higher levels in **A,** cIMT (n = 1866), **B,** baPWV (n = 1975), and **C,** Cornell index (n = 1684) in 2017 in both moderate-increasing and high-increasing groups ($P < .05$). Compared with the low-increasing group, a significant difference in the Cornell index existed in the moderate-increasing group ($P = .026$) and high-increasing group ($P = .037$), and no significant difference in the Cornell index existed between the moderate-increasing group and high-increasing group ($P = .571$). Medians (IQRs) of values are shown.

Table II. Demographic characteristics and cardiovascular risk factors by the BMI trajectory group

Variables	Total, No.	Low-increasing group	Moderate-increasing group	High-increasing group	*P* value
Sex, %	2839				<.001
Male	1602	732 (55.29)	642 (54.50)	228 (67.66)	
Female	1237	592 (44.71)	536 (45.50)	109 (32.34)	
Age in 1987, years	2839	12.00 (10.00, 15.00)	15.00 (13.00, 16.00)	12.00 (10.00, 15.00)	<.001
BMI in 1987, kg/m^2	2823	15.37 ± 1.63	17.89 ± 2.25	16.88 ± 2.38	<.001
BMI in 1989, kg/m^2	2150	16.16 ± 1.82	18.94 ± 2.25	17.64 ± 2.52	<.001
BMI in 1992, kg/m^2	2488	17.73 ± 2.01	21.05 ± 2.44	19.87 ± 2.98	<.001
BMI in 1995, kg/m^2	2450	19.03 ± 1.60	21.46 ± 1.70	21.75 ± 2.87	<.001
BMI in 2013, kg/m^2	2497	21.66 ± 1.99	24.81 ± 1.79	29.72 ± 2.96	<.001
BMI in 2017, kg/m^2	2088	21.84 ± 1.97	24.90 ± 1.79	29.54 ± 2.40	<.001
Bust in 1987, cm	2834	60.30 ± 8.89	67.41 ± 8.72	63.22 ± 8.48	<.001
HR in 1987, times per min	2838	80.00 (72.00, 84.00)	76.00 (72.00, 84.00)	78.00 (72.00, 84.00)	<.001
HR in 2017, times per min	2097	74.00 (67.00, 82.00)	73.00 (66.00, 79.00)	75.00 (70.00, 82.00)	<.001
SBP in 1987, mm Hg	2839	101.41 ± 11.98	106.73 ± 12.33	103.79 ± 10.04	<.001
DBP in 1987, mm Hg	2838	64.03 ± 9.36	66.10 ± 9.92	64.71 ± 9.22	<.001
SBP in 2017, mm Hg	2097	119.39 ± 14.29	125.75 ± 18.97	131.87 ± 17.53	<.001
DBP in 2017, mm Hg	2097	74.71 ± 12.23	78.73 ± 11.70	83.26 ± 12.48	<.001
WHR in 2017, m	2086	0.90 ± 0.26	0.93 ± 0.08	0.99 ± 0.05	<.001
Occupation, %	2464				.24
Farmer	1005	440 (38.66)	444 (43.40)	121 (39.93)	
Worker	500	234 (20.56)	207 (20.23)	59 (19.47)	
Businessman	192	98 (8.61)	68 (6.65)	26 (8.58)	
Governor	76	29 (2.55)	35 (3.42)	12 (3.96)	
Other	691	337 (29.61)	269 (26.30)	85 (28.05)	
Marital status, %	2555				.22
Married	2451	1116 (95.30)	1026 (96.43)	309 (96.56)	
Divorced	49	28 (2.39)	19 (1.79)	2 (0.63)	
Unmarried or other	55	27 (2.31)	19 (1.79)	9 (2.81)	
Education, %	2497				.010
Primary school or less	187	85 (7.46)	73 (6.99)	29 (9.27)	
Middle school	1543	671 (58.91)	684 (65.45)	188 (60.06)	
High school	550	281 (24.67)	209 (20.00)	60 (19.17)	
College or more	217	102 (8.96)	79 (7.56)	36 (11.50)	
Smoking, %	2098	418 (44.56)	399 (44.98)	145 (53.11)	.035
Drinking, %	2096	252 (26.92)	288 (32.47)	101 (37.00)	.002
Hypertension, %	2098	57 (6.08)	132 (14.88)	61 (22.34)	<.001
Diabetes, %	2098	16 (1.70)	32 (3.61)	17 (6.25)	<.001
Hyperlipidemia, %	2097	41 (4.38)	88 (9.92)	63 (23.08)	<.001
GLU, mmol/L	1898	4.50 (4.24, 4.85)	4.58 (4.29, 4.90)	4.79 (4.42, 5.11)	<.001
TC, mmol/L	1899	4.43 (4.01, 4.95)	4.50 (4.07, 4.99)	4.61 (4.09, 5.23)	.003
TG, mmol/L	1899	1.17 (0.86, 1.63)	1.44 (1.01, 2.03)	1.81 (1.36, 2.54)	<.001
LDL cholesterol, mmol/L	1899	2.45 (2.06, 2.80)	2.51 (2.15, 2.90)	2.59 (2.21, 3.09)	<.001
HDL cholesterol, mmol/L	1899	1.21 (1.04, 1.41)	1.10 (0.97, 1.29)	1.03 (0.90, 1.19)	<.001
Serum uric acid, mmol/L	1900	270.20 (217.80, 320.00)	283.60 (231.20, 338.60)	321.80 (269.05, 373.60)	<.001
Serum creatinine, mmol/L	1900	74.70 (66.00, 85.40)	76.10 (67.60, 86.50)	79.30 (69.55, 88.35)	<.001
eGFR, mL/min per 1.73 m^2	1900	98.05 (87.18, 111.00)	96.29 (86.14, 110.34)	94.23 (86.17, 105.39)	.035
uACR, mg/mmol	1823	0.85 (0.56, 1.44)	1.02 (0.66, 1.75)	1.44 (0.78, 2.81)	<.001
Urine albumin, mg/L	1827	6.50 (3.30, 11.60)	8.20 (4.60, 14.70)	10.25 (4.80, 24.20)	<.001
cIMT, mm	1866	0.60 (0.50, 0.72)	0.65 (0.55, 0.75)	0.65 (0.57, 0.77)	<.001
Sokolow-Lyon voltage, mm	1634	0.93 (0.67, 1.27)	1.00 (0.70, 1.40)	1.15 (0.80, 1.50)	<.001
Cornell product, mm/ms	1684	1282.00 (909.50, 1633.50)	1344.00 (969.00, 1728.00)	1356.00 (968.00, 1782.00)	.030
baPWV, mm/s	1975	1190.50 (1070.00, 1321.50)	1239.50 (1116.50, 1385.75)	1285.00 (1120.00, 1473.00)	<.001

eGFR, estimated glomerular filtration rate; *GLU*, fasting plasma blood glucose; *HR*, heart rate; *MAP*, mean arterial pressure; *TC*, total cholesterol; *uACR*, urinary albumin-to-creatinine ratio; *WHR*, waist-to-hip ratio.

Continuous variables were shown as mean ± SD if normally distributed or median (quartile 1, quartile 3) if non-normally distributed. Categorical variables were expressed as numbers and percentages of subjects. Statistical ANOVA was performed by 1-way ANOVA when normally distributed; otherwise, the Kruskal-Wallis test was used. Differences between groups of categorical variables were compared with χ^2 tests.

Table IV. RRs and 95% CIs of the association of BMI trajectories with adult outcomes by sex

Adult outcomes and latent BMI trajectory group	Male						Female					
	Model 1			Model 2			Model 1			Model 2		
	RR	95%CI	*P* value	RR	95%CI	*P* value	RR	95%CI	*P* value	RR	95%CI	*P* value
Hypertension												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	2.27	1.67-3.08	**<.001**	2.22	1.61-3.08	**<.001**	2.35	1.42-3.87	**.001**	2.17	1.28-3.66	**.004**
High-increasing group	3.93	2.72-5.68	**<.001**	4.09	2.74-6.11	**<.001**	3.63	1.89-6.94	**<.001**	3.16	1.57-6.36	**.001**
Type 2 diabetes												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	2.48	1.23-4.99	**.011**	2.23	1.05-4.73	**.036**	1.21	0.49-2.97	.682	0.78	0.29-2.10	.617
High-increasing group	4.88	2.29-10.39	**<.001**	4.63	2.04-10.50	**<.001**	4.31	1.76-10.55	**.001**	3.43	1.29-9.09	**.013**
High-risk TG												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	1.64	1.16-2.31	**.005**	1.75	1.21-2.54	**.003**	1.91	1.14-3.20	**.014**	2.23	1.24-4.02	**.008**
High-increasing group	3.03	2.03-4.54	**<.001**	3.10	1.99-4.83	**<.001**	3.99	2.12-7.55	**<.001**	4.51	2.24-9.09	**<.001**
High-risk LDL cholesterol												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	1.16	0.36-3.74	.809	1.86	0.38-9.09	.446	3.03	0.48-19.03	.238	2.37	0.33-17.08	.391
High-increasing group	0.79	0.16-3.83	.766	1.22	0.16-9.36	.849	2.37	0.21-26.67	.485	3.42	0.27-43.58	.344
High-risk HDL cholesterol												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	1.81	1.37-2.40	**<.001**	1.80	1.33-2.43	**<.001**	2.44	1.58-3.75	**<.001**	2.57	1.61-4.12	**<.001**
High-increasing group	2.35	1.63-3.83	**<.001**	2.24	1.50-3.36	**<.001**	5.79	3.35-10.03	**<.001**	5.93	3.23-10.88	**<.001**
High cIMT												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	0.91	0.50-1.66	.754	0.96	0.51-1.81	.893	1.16	0.46-2.98	.750	1.26	0.47-3.37	.646
High-increasing group	1.15	0.52-2.55	.730	0.95	0.39-2.35	.914	1.56	0.40-6.07	.522	1.67	0.39-7.07	.489
High baPWV												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	1.40	1.03-1.90	**.034**	1.55	1.10-2.17	**.011**	0.82	0.52-1.30	.400	0.74	0.44-1.24	.251
High-increasing group	2.72	1.86-4.00	**<.001**	3.49	2.27-5.36	**<.001**	1.58	0.85-2.96	.152	1.60	0.81-3.15	.177
High-risk LVH												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	2.19	0.90-5.30	.084	2.13	0.82-5.52	.121	2.13	0.99-4.58	.054	2.27	1.00-5.19	.052
High-increasing group	2.21	0.80-6.05	.125	2.06	0.69-6.15	.197	1.51	0.46-4.91	.495	1.10	0.26-4.60	.890

Model 1 is adjusted for sex and age in 1987; model 2 includes model 1 and is further adjusted for smoke habits, alcohol consumption, occupation, married status, and education.
Significant *P* values were presented in bold.

Table V. RRs and 95% CIs of the association of BMI trajectories with adult outcomes by different age periods

Adult outcomes and latent BMI trajectory group	Prepuberty (aged 4-11 years)						Puberty (aged 12-18 years)					
	Model 1			Model 2			Model 1			Model 2		
	RR	95% CI	*P* value	RR	95% CI	*P* value	RR	95%CI	*P* value	RR	95% CI	*P* value
Hypertension												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	2.36	1.43-3.88	**.001**	1.91	1.09-3.35	**.024**	2.34	1.72-3.18	**<.001**	2.46	1.79-3.39	**<.001**
High-increasing group	2.18	1.28-3.72	**.004**	2.04	1.14-3.65	**.016**	5.40	3.59-8.12	**<.001**	5.69	3.67-8.84	**<.001**
Type 2 diabetes												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	3.42	1.07-10.90	**.038**	2.19	0.49-9.76	.302	1.56	0.87-2.80	.140	1.39	0.75-2.59	.292
High-increasing group	4.06	1.26-13.10	**.019**	4.51	1.24-16.44	**.022**	4.77	2.46-9.25	**<.001**	4.26	2.12-8.55	**<.001**
High-risk TG												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	1.90	1.11-3.23	**.019**	1.84	1.00-3.38	**.050**	1.65	1.18-2.31	**.003**	1.99	1.38-2.87	**<.001**
High-increasing group	3.91	2.33-6.56	**<.001**	3.78	2.10-6.78	**<.001**	2.89	1.83-4.55	**<.001**	3.63	2.22-5.93	**<.001**
High-risk LDL cholesterol												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	2.03	0.45-9.26	.361	3.64	0.47-28.39	.217	0.96	0.30-3.05	.947	1.33	0.33-5.41	.689
High-increasing group	0.77	0.08-7.04	.815	1.83	0.14-24.13	.646	1.27	0.24-6.66	.774	2.50	0.39-15.93	.333
High-risk HDL cholesterol												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	1.94	1.23-3.04	**.004**	1.90	1.14-3.15	**.013**	1.99	1.51-2.61	**<.001**	2.07	1.55-2.77	**<.001**
High-increasing group	2.82	1.76-4.54	**<.001**	3.21	1.88-5.48	**<.001**	3.32	2.21-4.98	**<.001**	3.08	1.99-4.78	**<.001**
High cIMT												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	0.67	0.14-3.20	.611	0.79	0.15-4.15	.781	1.03	0.60-1.77	.916	1.07	0.61-1.89	.815
High-increasing group	0.78	0.16-3.76	.753	0.44	0.05-3.74	.453	1.39	0.64-3.00	.404	1.34	0.59-3.06	.490
High baPWV												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	1.30	0.75-2.27	.350	1.59	0.84-3.01	.153	1.22	0.92-1.63	.167	1.28	0.94-1.75	.121
High-increasing group	2.00	1.16-3.46	**.013**	2.43	1.33-4.43	**.004**	2.52	1.69-3.77	**<.001**	3.02	1.94-4.68	**<.001**
High-risk LVH												
Low-increasing group	1	—	—	1	—	—	1	—	—	1	—	—
Moderate-increasing group	2.91	0.95-8.89	.062	2.91	0.81-10.42	.102	1.80	0.93-3.48	.079	1.89	0.95-3.76	.071
High-increasing group	1.44	0.36-5.77	.610	1.16	0.22-6.09	.860	2.17	0.88-5.38	.094	1.89	0.70-5.09	.209

Model 1 is adjusted for sex and age in 1987; model 2 includes model 1 and is further adjusted for smoke habits, alcohol consumption, occupation, married status, and education.
Significant *P* values were presented in bold.