Body Mass Index Trajectories in Adolescence And Incident Metabolic Syndrome in Early Adulthood

Ming Ying (2365912989@qq.com)
Guangdong Provincial People\'s Hospital: Guangdong Provincial People's Hospital
https://orcid.org/0000-0003-1680-9480

Xiangming Hu
Guangdong Provincial People\'s Hospital: Guangdong Provincial People's Hospital

Qiang Li
Guangdong Provincial People\'s Hospital: Guangdong Provincial People's Hospital

Zhujun Chen
Guangdong Provincial People\'s Hospital: Guangdong Provincial People's Hospital

Yingling Zhou
Guangdong Provincial People\'s Hospital: Guangdong Provincial People's Hospital

Research Article

Keywords: Body Mass Index Trajectory, Metabolic Syndrome, Cohort Study

Posted Date: October 28th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1015828/v1

Abstract

Background: The incidence of metabolic syndrome (MetS) is increasing each year, and MetS is closely related to cardiovascular diseases. Body mass index (BMI) has been widely used to measure obesity, and the relationship between MetS and BMI has been widely reported. However, the relationship between the trajectory of BMI and MetS is still unclear.

Methods: Six waves of the cross-sectional China Health and Nutrition Survey (CHNS) were completed in nine provinces in China from 1993 to 2009, with more than 12,000 participants. We enrolled individuals who were aged 10 to 20 years in 1993, and 554 participants were finally included in our study. A latent class growth mixed model was used to identify different BMI trajectory patterns based on the BMI value measured at each follow-up. Participants completed blood tests and a physical examination in 2009 to allow for the diagnosis of MetS. The primary aim was to explore the relationship between different BMI trajectories and the incidence of MetS through logistic regression, adjusting for baseline age, sex, BMI, waist circumference, residence, educational background, smoking status, alcohol consumption, and nutritional intake.

Result: During a follow-up of 16 years, 61 (11.01%) participants developed MetS. In multivariate-adjusted models, different BMI trajectories were significantly associated with the occurrence of MetS in early adulthood. Childhood or adolescents with a low-high BMI trajectory or a high-high BMI trajectory showed a significantly higher risk of MetS in early adulthood than those with a low-low trajectory (low-high: OR=3.40, 95% CI: 1.14-10.13, P <0.05; high-high: OR=5.81, 95% CI: 1.63-20.69, P <0.05).

Conclusion: Our study identified three BMI trajectories from adolescence through 16 years of follow-up and found that in addition to baseline BMI, BMI trajectories were also an independent risk factor for incident MetS in early adulthood.

Introduction

Metabolic syndrome (MetS), a common metabolic disorder syndrome, occurs in between 20% and 45% of the population, and its incidence has increased substantially in children and adolescents in developed countries [1]. A previous study found that MetS is associated with an increased risk of coronary artery disease (CAD), cerebrovascular disease, and all-cause mortality [2]. In fact, these diseases occur in late adulthood and have certain correlations with metabolic risk factors present in childhood or adolescence that are overlooked [3, 4]. Obesity contributes directly to metabolic disorders and thus leads to MetS, especially among childhood and adolescence in the growth development period [5]. However, in childhood or adolescence, the prevention of obesity does not always receive as much attention as that in adults.

As an anthropometric indicator of growth, body mass index (BMI) has been used to measure obesity, and its relationship with MetS has been widely reported [4, 6]. Children or adolescents with a higher BMI have a high risk of being overweight or obese in adulthood [7]. In addition to the absolute level of BMI,

increasing evidence indicates that in a specific life stage, such as childhood or adolescence, the longitudinal BMI growth trajectory also has an adverse effect on the development of disease [8]. Liu et al. found that adolescents with a high baseline BMI and a large change in the absolute value of BMI had the highest risk of MetS, but the relationship between the trajectory of BMI and MetS is still unclear [9].To address this problem, we used data from the China Health and Nutrition Survey (CHNS) that included inhabitants whose BMI was measured from childhood to early adulthood to identify different associations of BMI trajectory with incident MetS.

Methods

Study population

This study used data from CHNS, an ongoing population-based cohort study carried out by the national and local government of China. From 1993 to 2009, six waves of cross-sectional surveys were completed in nine provinces (Liaoning, Jiangsu, Henan, Hunan, Guizhou, Heilongjiang, Shandong, Hubei and Guangxi) using a multistage, random-clustering process, with more than 12,000 participants enrolled. The study takes into account Chinese geographic distribution, economic development level and public health resources, and the sample can be considered to provide a representative data set reflecting ordinary Chinese adolescents. The survey collects comprehensive demographic data, including gender, age, education level, dietary and nutritional status, health behavior and clinical data. Each participant signed an informed consent form, and the relevant information related to this study has been published elsewhere [10].

The study staff conducted face-to-face interviews with participants in 1997, 2000, 2004, 2006 and 2009 to measure height and weight to calculate BMI. In 2009, 9549 fasting blood samples of participants were collected by study staff. We excluded individuals who were either aged < 10 years or > 20 years (n = 8,484) in 1993, pregnant women (n = 24), people without fasting blood glucose (FBG) or glycosylated hemoglobin (HbA1c) information and people whose waist circumference and hip circumference measurements were conducted less than 3 times of follow-up visits (n = 447) **(Figure 1)**.

Measurement and definition

BMI was calculated as weight (kg) divided by height squared (m^2). Blood collection and examination were done by professional study staff. All subjects provided 12 mL of blood (in three 4-mL test tubes) after an overnight fast. The levels of high-density lipoprotein cholesterol (HDL-c), total cholesterol (TC), and FBG were assessed using a Hitachi 7,600 machine (Randox, Crumlin, UK; Kyowa, Tokyo, Japan). HbA1c was measured using an HLC-723 G7/D10/PDQ A1c Automated Glycohemoglobin Analyzer (Tosoh Bioscience LLC, Osaka, Japan; Bio-Rad Laboratories, Hercules, CA, USA; Primus Electronics, Morris, IL, USA). Intakes of total energy, carbohydrates, fat and protein were all calculated from participants' average 3-day dietary intake data obtained by questionnaire. Trained health workers or nurses measured subjects' right arm blood pressure following a standardized procedure using a regularly calibrated

mercury sphygmomanometer with a suitable cuff size. Systolic blood pressure (SBP) at the first appearance of pulse sound (Korotkoff stage 1) and diastolic blood pressure (DBP) at disappearance of the pulse sound (Korotkoff stage 5) were recorded. SBP and DBP measurements were repeated 3 times, and the mean value was taken to reduce the influence of measurement error. Height, weight were measured while the subjects were wearing light clothing and no shoes. Waist circumference was measured with tape located at the level of the umbilicus when the participants stood normally with their feet 25-30 cm apart and at the end of the expiratory phase. Educational level and history of hypertension were obtained through self-report. Smoking was defined as previous smoking. Alcohol consumption was defined as drinking alcohol > 3 times/week.

Outcome

MetS was diagnosed in 2009 according to the International Diabetes Federation criteria [11], which defined as central obesity (waist ≥ 90 cm in men or ≥ 80 cm in women) plus any two of the following: 1) elevated TGs (> 1.7 mmol/L) or specific treatment for TG abnormality; 2) reduced HDL cholesterol (in men < 1.0 mmol/L and in women < 1.3 mmol/L) or specific treatment for TG abnormality; 3) elevated blood pressure (SBP ≥ 130 mm Hg or DBP ≥ 85 mmHg) or treatment of previously diagnosed hypertension; and 4) elevated fasting plasma glucose (FBG ≥ 5.6 mmol/L) or previously diagnosed type 2 diabetes).

Statistical analysis

For continuous variables, Student's t test (for normally distributed variables) /Mann-Whitney U test (for variables with a skewed distribution) and analysis of variance (for normally distributed variables)/Kruskal-Wallis H (for variables with a skewed distribution) were used to detect differences between groups. For categorical variables, the chi-square test/Fisher's exact test was used to detect differences between groups. We explored the relationship between different BMI development trajectories and incident MetS through logistic regression to calculate the odds ratios (ORs) with 95% confidence intervals (CIs), and the effects of age, sex, BMI, waist circumference, residence, education background, smoking status, alcohol consumption, and nutritional intake were adjusted according to different models.

A latent class growth mixed model (LCGMM) [12]was used to identify different trajectory patterns of BMI since it can take into account random individual variation and within-group variance. Based on the BMI measured three times or more by the participants, a growth model was established according to the measurements over time, while sex was taken as a covariate. Multiple LCGMMs were analyzed with different trajectories to obtain linear and nonlinear model parameters. The model selection criterion was based on the Bayesian information criterion, Vuong-Lo-Mendell-Rubin likelihood ratio test, efficiency of classification and posterior probabilities. After that, the estimated slope and variance in different trajectory classifications were obtained. $P < 0.05$ (two-sided) indicated statistical significance. All of the analyses were performed with Mplus 8, Stata 15.0 and R (version 3.6.1).

Results

Participant characteristics

Of the 554 people without diabetes at baseline, 61 (11.0%) developed MetS during the 16-year follow-up. The baseline characteristics of the individuals and their follow-up characteristics as adults are shown in Table 1. People with MetS were older and had higher BMI and waist circumference. Concerning blood tests, patients with MetS were more likely to have abnormalities in blood lipids and blood sugar. Sex, residence, smoking and alcohol consumption were not significantly different between the two groups.

Table 1
Baseline characteristics by incident MetS at follow-up.

	Non-MetS **n=493**	**MetS** **n=61**	**P-value**
Age, year	31.9 ± 3.2	33.4 ± 2.7	<0.001
Female	227 (46.0%)	26 (42.6%)	0.613
Urban residence	162 (32.9%)	21 (34.4%)	0.806
Waist, mm	77.2 ± 8.6	94.8 ± 6.5	<0.001
BMI	22.0 ± 2.9	28.0 ± 2.7	<0.001
Total cholesterol, mmol/L*	4.4 ± 0.9	4.9 ±1.0	<0.001
HDL-C, mmol/L*	1.4 ± 0.4	1.0 ± 0.2	<0.001
Glucose, mmol/L*	4.9 ± 0.6	5.8 ± 1.9	<0.001
Smoking	164 (33.27%)	23 (37.70%)	0.489
Alcohol consumption	235 (47.67%)	37 (60.66%)	0.056
Notes: Data are expressed as mean ± SD or median (Q1–Q3) or N (%). BMI, body mass index; HDL-C: high-density lipoprotein cholesterol. Smoking was defined as previous smoking. Alcohol consumption was defined as drinking alcohol > 3 times/week			
*Data was shown after interpolation by mean.			

Trajectory analysis

According to the model selection criteria mentioned above, we modeled the BMI change tendency of each individual, compared the parameters of different class models (**Supplementary Table 1**) and finally chose a three-class model as the best fit. We numbered them Class 1 (low-low), Class 2 (low-high), and Class 3 (high-high). Estimated and observed mean values of BMI are presented in **Supplementary Figure 1**. The estimated parameters of each model, including slope, intercept, quadratic parameters, and the incidence

of MetS, are listed in Table 2. Except for the quadratic parameters in Class 2, the other three latent-variable parameters of the model were all positively correlated with MetS risk.

Table 2
Estimated mean of slope, intercept, and quadratic parameters for each class, and the incidence of MetS.

Classes	Slope, *P*	Intercept, *P*	Quadratic, *P*	Incidence of MetS
1	1.433, < 0.001	18.477, < 0.001	-0.176, < 0.001	10/438
2	1.447, 0.001	18.959, < 0.001	0.021, 0.791	22/66
3	2.454, < 0.001	23.314, < 0.001	-0.299, < 0.001	29/50

Effects of BMI trajectory on the risk of MetS

Figure 2 illustrates the longitudinal trajectory of the BMIs of adolescents aged 10–20 years with a low-low trajectory (Class 1, 79.1%, n = 438), a low-high trajectory (Class 2, 11.9%, n = 66), and a high-high trajectory (Class 3, 9.0%, n = 50). Class 1 shows a steady growth trend, while Class 2 shows a rapid growth pattern with a low baseline value. Class 3 presented a steady growth pattern with a high baseline value. By 2009, the BMI values of Class 2 and Class 3 were close. At an early age, BMI increased faster (positive slope) in all three classes. In early adolescence, classes 1 and 3 tended to be stable, while class 2 continued to increase faster.

Participants were also grouped according to changes in BMI (Table 3). We discovered that participants in Class 3 were inclined to have higher BMI, waist circumference, blood lipids and blood sugar at follow-up. Moreover, the change in BMI showed a significant difference between the sexes. The BMI of Class 2 increased faster in both men and women. However, in Class 3, it seems that the rapid increase in early youth was attributed to males (**Supplementary Figure 2**).

Table 3
Baseline characteristics by different classes at follow-up.

BMI trajectory	1 n = 438	2 n = 66	3 n = 50	P-value
Age, year	32.0 ± 3.2	31.7 ± 3.2	33.1 ± 2.4	0.051
Female, (%)	214 (48.9%)	14 (21.2%)	25 (50.0%)	<0.001
Waist, cm	75.8 ± 7.7	75.8 ± 7.7	93.4 ± 6.8	<0.001
BMI, kg/M^2	21.3 ± 2.1	27.4 ± 1.9	28.4 ± 2.5	<0.001
Urban resident	141 (32.2%)	25 (37.9%)	17 (34.0%)	0.650
Average energy intake, kcal/day†	2090.4 (1752.0-2574.9)	2453.6 (1954.3-2836.0)	2226.1 (1851.6-2800.7)	0.007
Average carbohydrate intake, g/day†	295.1 (235.8-375.8)	335.4 (310.7-397.0)	291.1 (241.5-342.2)	0.015
Average fat intake, g/day†	68.9 (50.1-92.9)	80.0 (53.6-105.5)	79.57 (65.2-103.6)	0.006
Average protein intake, g/day†	65.2 (53.0-80.6)	72.1 (62.0-92.3)	69.1 (52.6-97.3)	0.020
Total cholesterol, mmol/L*	4.4 ± 0.9	4.8 ± 1.0	4.8 ± 0.9	<0.001
HDL-C, mmol/L*	1.4 ± 0.4	1.1 ± 0.2	1.2 ± 0.3	<0.001
Glucose, mmol/L*	4.9 ± 0.6	5.3 ± 0.8	5.8 ± 2.1	<0.001
Level of education				0.908
None	19 (4.3%)	2 (3.0%)	2 (4.0%)	
Grad from primary	61 (13.9%)	9 (13.6%)	8 (16.0%)	
Lower middle school degree	218 (49.8%)	33 (50.0%)	23 (46.0%)	
Upper middle school degree	45 (10.3%)	9 (13.6%)	9 (18.0%)	
Technical or vocational degree	58 (13.2%)	7 (10.6%)	6 (12.0%)	
University or college degree	37 (8.4%)	6 (9.1%)	2 (4.0%)	
Smoking, (%)	147 (33.6%)	25 (37.9%)	15 (30.0%)	0.662
Alcohol consumption, (%)	202 (46.1%)	43 (65.1%)	27 (54.0%)	0.012
†Data was shown after interpolation by median.				
*Data was shown after interpolation by mean.				

BMI trajectory	1 n = 438	2 n = 66	3 n = 50	P-value
MetS	10 (2.3%)	22 (33.3%)	29 (58.0%)	<0.001
†Data was shown after interpolation by median.				
*Data was shown after interpolation by mean.				

The results of the multivariate logistic regression model showed that different trajectory patterns were associated with the occurrence of MetS in adolescents after adjustment for variables (Figure 3). In the fully adjusted models, participants in Class 2 and Class 3 had a significantly higher risk of MetS than Class 1 participants (Class 2: OR=3.40, 95% CI: 1.14-10.13, P < 0.05; Class 3: OR=5.81, 95% CI: 1.63-20.69, P < 0.05).

Discussion

Our study identified three types of BMI trajectories, and the risks of incident MetS were different according to these trajectories. We found that continuously increasing BMI was related to an increased risk of MetS after adolescents grew up and that the rapid increase in BMI in adolescents was attributed more to males than females in China. In our study, individuals with a low-high BMI trajectory had a 3.4-times higher risk of MetS in early adulthood than those with a low-low trajectory. Individuals with a high-high BMI trajectory had a 5.8-times higher risk of MetS in early adulthood than those with a low-low trajectory. Regardless of the initial BMI level, a change in BMI is an independent risk factor for MetS. To our knowledge, this study is the first to investigate the relationship between BMI trajectory and MetS in childhood or adolescence.

In a study enrolling 23,993 individuals, Ofer et al. found that normal BMI had a very high negative predictive value for MetS and pointed out that BMI equal to 27 was the ideal value for the identification of MetS in the entire cohort [13]. Stolzman et al. discovered that adolescents with higher BMI demonstrated a greater incidence MetS than those with normal BMI [14]. Childhood adiposity is a good predictor of MetS in adulthood, especially in those with rapid growth of adipose tissue [15]. Although BMI as an indicator of adiposity is closely related to the occurrence and development of MetS, a one-time measurement does not represent changes in BMI over time. Another study including 5317 university graduates with a median follow-up time of 6.1 years discovered that weight gain from childhood to adolescence/young adulthood increased the chance of incident MetS in adulthood. This study focused on the effect of changes in body weight on the occurrence of MetS, and the results were also consistent with our findings. However, there were some deficiencies that may cause controversy. First, the research used participant body images at age 5 years and 20 years to estimate the change in BMI, which may have led to inaccurate information on the change in BMI. Second, the study was conducted using a questionnaire, and the conclusion of the study was greatly affected by selection bias.

Liu et al. conducted a similar study among 93 students aged between 18 and 22 years in Liaoning Province. The participants were divided into four study groups according to the baseline level of BMI and change in BMI values. They found that both baseline BMI and BMI changes were predictive of MetS in early adulthood and that adolescents with a baseline BMI > 23.47 kg/m^2 or a change in BMI > 1.95 kg/m^2 were at increased risk of MetS in adulthood. Our study also focused on adolescents, but we fit the BMI trajectory based on the longitudinal study design with six cross-sectional surveys conducted in nine provinces involving 554 adolescents, which better classified different classes for screening those with a high risk of MetS. The result was also independent of people's demographic characteristics, such as age, sex, BMI and education level. The change in BMI represents the accumulation of adiposity, which can better reflect the degree of individual exposure to obesity over time.

Currently, the mechanism of the association between changes in BMI and MetS is not entirely clear. Body fat content and the distribution of fat are considered important indicators of health risk [16]. It has been reported that the central accumulation of body fat is associated with insulin resistance (IR) [17]. IR occurs when insulin action on glucose uptake, suppression of adipose tissue lipolysis and vasodilatation are impaired [18]. Studies in mice have demonstrated that Akt inactivation and Foxo1 activation following the suppression of IRS1 and IRS2 play fundamental roles in insulin resistance, which occurs in insulin-responsive tissues, impairing systemic glucose and lipid homeostasis and body weight control and serving as an important mechanism for the development of metabolic syndrome [19]. The discovery of endocrine and immune properties of adipocytes has provided further mechanistic insights into the development of MetS. Previous studies found that adiponectin was a protective factor against the development of hypertension, diabetes, and acute coronary syndrome [20]. Moreover, activation of the renin-angiotensin system (RAS) serves as an important neurohumoral pathway contributing to the development of MetS. Obesity and insulin resistance are associated with increased production of Ang II, which can activate nicotinamide adenine dinucleotide phosphate oxidase, leading to the generation of reactive oxygen species [21]. These studies focusing on the etiology of MetS supported that at the molecular level, obesity is a dynamic evolution process of continuous fat accumulation. The BMI trajectory not only represents changes in body shape but, more importantly, changes in various nutrient metabolism pathways in the organism, which are closely related to the pathogenesis of MetS.

Our study has limitations. First, the retrospective study design prevented us from making causal conclusions. Second, the CHNS was not focused on child development, and most adult participants were excluded from our study. However, the young people we enrolled were still geographically representative. Third, since the diagnosis of MetS requires multiple combined indicators and the CHNS did not collect blood samples at baseline when adolescents were enrolled, we could not identify those with diagnosed MetS at baseline and exclude them.

Conclusion

In summary, our study identified three BMI trajectories between childhood or adolescence and the end of a 16-year follow-up. In addition to baseline BMI, the low-high and high-high trajectories of BMI are also

independent risk factors for MetS in early adulthood, especially in males. The control of BMI in childhood or adolescence would improve public health.

Declarations

Data Availability Statement

The clinical data used to support the findings of this study were supplied by the China Health and Nutrition Survey.The survey data are publicly available on the Internet for data users and researchers throughout the world https://www.cpc.unc.edu/projects/china.

Conflict of Interest

The authors declared no conflict of interest.

Author Contributions

Research idea and study design: MY; Data acquisition: MY, QL; Data analysis/interpretation: XMH; Statistical analysis: XMH; Supervision and mentorship: ZJC, YLZ. Each author contributed important intellectual content during manuscript drafting or revision.

Funding

Our research was supported by The National Key Research and Development Program of China (No. 2016YFC1301202).

Acknowledgments

We thank the investigators who worked hard for the CHNS, and the CHNS participants and their families for the data provided.

References

1. M. Gierach, J. Gierach, M. Ewertowska, A. Arndt, R. Junik Correlation between Body Mass Index and Waist Circumference in Patients with Metabolic Syndrome. ISRN endocrinology 2014: 514589, 2014; M. Ng, T. Fleming, Robinson Met al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet (London, England) 384: 766-781, 2014
2. A.F. Cicero, G. Derosa, Are there mild and serious metabolic syndromes? The need for a graded diagnosis. J. Cardiovasc. Med. **15**, 759–760 (2014)
3. V. Burke, Obesity in childhood and cardiovascular risk. Clin. Exp. Pharmacol. Physiol. **33**, 831–837 (2006)

4. J.B. Meigs, P.W. Wilson, C.Set Fox, al. Body mass index, metabolic syndrome, and risk of type 2 diabetes or cardiovascular disease. J. Clin. Endocrinol. Metab. **91**, 2906–2912 (2006)
5. F. Lifshitz Obesity in children. Journal of clinical research in pediatric endocrinology 1: 53-60, 2008; S. Owens, Galloway R Childhood obesity and the metabolic syndrome. Current atherosclerosis reports 16: 436, 2014
6. E. Fisher, R.Y. Brzezinski, M. Ehrenwald al. Increase of body mass index and waist circumference predicts development of metabolic syndrome criteria in apparently healthy individuals with 2 and 5 years follow-up. International journal of obesity (2005) 43: 800-807, 2019
7. S.S. Guo, W. Wu, W.C. Chumlea, Roche AF Predicting overweight and obesity in adulthood from body mass index values in childhood and adolescence. Am. J. Clin. Nutr. **76**, 653–658 (2002)
8. J. Koskinen, C.G. Magnussen, A. Sinaiko al. Childhood Age and Associations Between Childhood Metabolic Syndrome and Adult Risk for Metabolic Syndrome, Type 2 Diabetes Mellitus and Carotid Intima Media Thickness: The International Childhood Cardiovascular Cohort Consortium. Journal of the American Heart Association 6, 2017; E. Zimmermann, L.G. Bjerregaard, M. Gamborg, A.A. Vaag, T.I.A. Sørensen, Baker JL Childhood body mass index and development of type 2 diabetes throughout adult life-A large-scale danish cohort study. Obesity (Silver Spring, Md.) 25: 965-971, 2017; A.M. Pimenta, J.J. Beunza, A. Sanchez-Villegas, M. Bes-Rastrollo, Martinez-Gonzalez MA Childhood underweight, weight gain during childhood to adolescence/young adulthood and incidence of adult metabolic syndrome in the SUN (Seguimiento Universidad de Navarra) Project. Public health nutrition 14: 1237-1244, 2011
9. B. Liu, Y. Li, J. Guo, Y. Fan, L. Li, P.Body Li Mass Index and Its Change from Adolescence to Adulthood Are Closely Related to the Risk of Adult Metabolic Syndrome in China. International journal of endocrinology 2021: 8888862, 2021
10. B. Zhang, F.Y. Zhai, S.F. Du, B.M. Popkin, The China Health and N. Survey, 1989–2011. Obesity reviews: an official journal of the International Association for the Study of Obesity 15 Suppl 1: 2–7, 2014
11. K.G. Alberti, P. Zimmet, J. Shaw, The metabolic syndrome--a new worldwide definition. Lancet **366**, 1059–1062 (2005)
12. K.S. Berlin, G.R. Parra, Williams NA An introduction to latent variable mixture modeling (part 2): longitudinal latent class growth analysis and growth mixture models. J. Pediatr. Psychol. **39**, 188–203 (2014)
13. O. Kobo, R. Leiba, O. Avizohar, Karban A Normal body mass index (BMI) can rule out metabolic syndrome: An Israeli cohort study. Medicine **98**, e14712 (2019)
14. S.C. Stolzman, J. Skelton, A. Harkins, M. Hoeger Bement, Does Weight Status Impact Metabolic Health in Adolescents When Controlling for Physical Fitness? Pediatric physical therapy: the official publication of the Section on Pediatrics of the American. Physical Therapy Association **31**, 134–140 (2019)

15. J.A. Morrison, L.A. Friedman, P. Wang, C.J. Glueck Metabolic syndrome in childhood predicts adult metabolic syndrome and type 2 diabetes mellitus 25 to 30 years later. The Journal of pediatrics 152: 201-206, 2008; S.R. Srinivasan, L. Myers, Berenson GS Predictability of childhood adiposity and insulin for developing insulin resistance syndrome (syndrome X) in young adulthood: the Bogalusa Heart Study. Diabetes 51: 204-209, 2002
16. A. Engin, The Definition and Prevalence of Obesity and Metabolic Syndrome. Adv. Exp. Med. Biol. **960**, 1–17 (2017)
17. P.M. McKeigue, T. Pierpoint, J.E. Ferrie, M.G. Marmot, Relationship of glucose intolerance and hyperinsulinaemia to body fat pattern in south Asians and Europeans. Diabetologia **35**, 785–791 (1992)
18. H.E. Lebovitz, Insulin resistance: definition and consequences. Experimental and clinical endocrinology & diabetes: official journal. German Society of Endocrinology [and] German Diabetes Association **109**(Suppl 2), S135–S148 (2001)
19. A. Ben Maamer, H. Zaafouri, Noomene Ret al. Colouterine fistula complicating diverticulitis. La Tunisie medicale **91**, 617–618 (2013)
20. W.P. Charlton, D.A. Randolph Jr., S. Lemos, C.L. Shields Jr.. Clinical outcome of anterior cruciate ligament reconstruction with quadrupled hamstring tendon graft and bioabsorbable interference screw fixation. The American journal of sports medicine 31: 518-521, 2003; T. Pischon, C.J. Girman, G.S. Hotamisligil, N. Rifai, F.B. Hu, Rimm EB Plasma adiponectin levels and risk of myocardial infarction in men. Jama 291: 1730-1737, 2004
21. I. Vaněčková, L. Maletínská, M. Behuliak, V. Nagelová, J. Zicha, Kuneš J Obesity-related hypertension: possible pathophysiological mechanisms. J. Endocrinol. **223**, R63–R78 (2014)

Figures

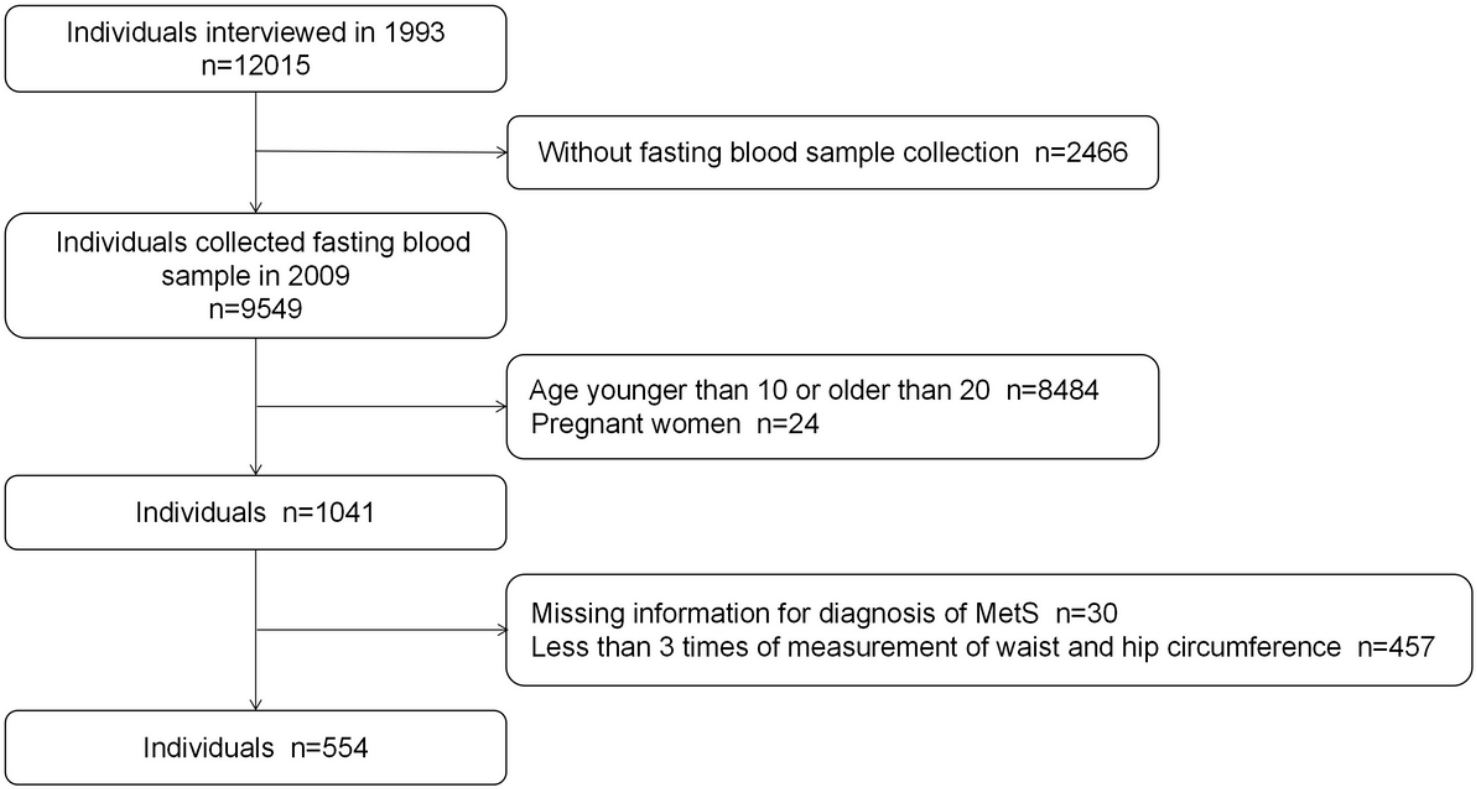

Figure 1

Flow chart.

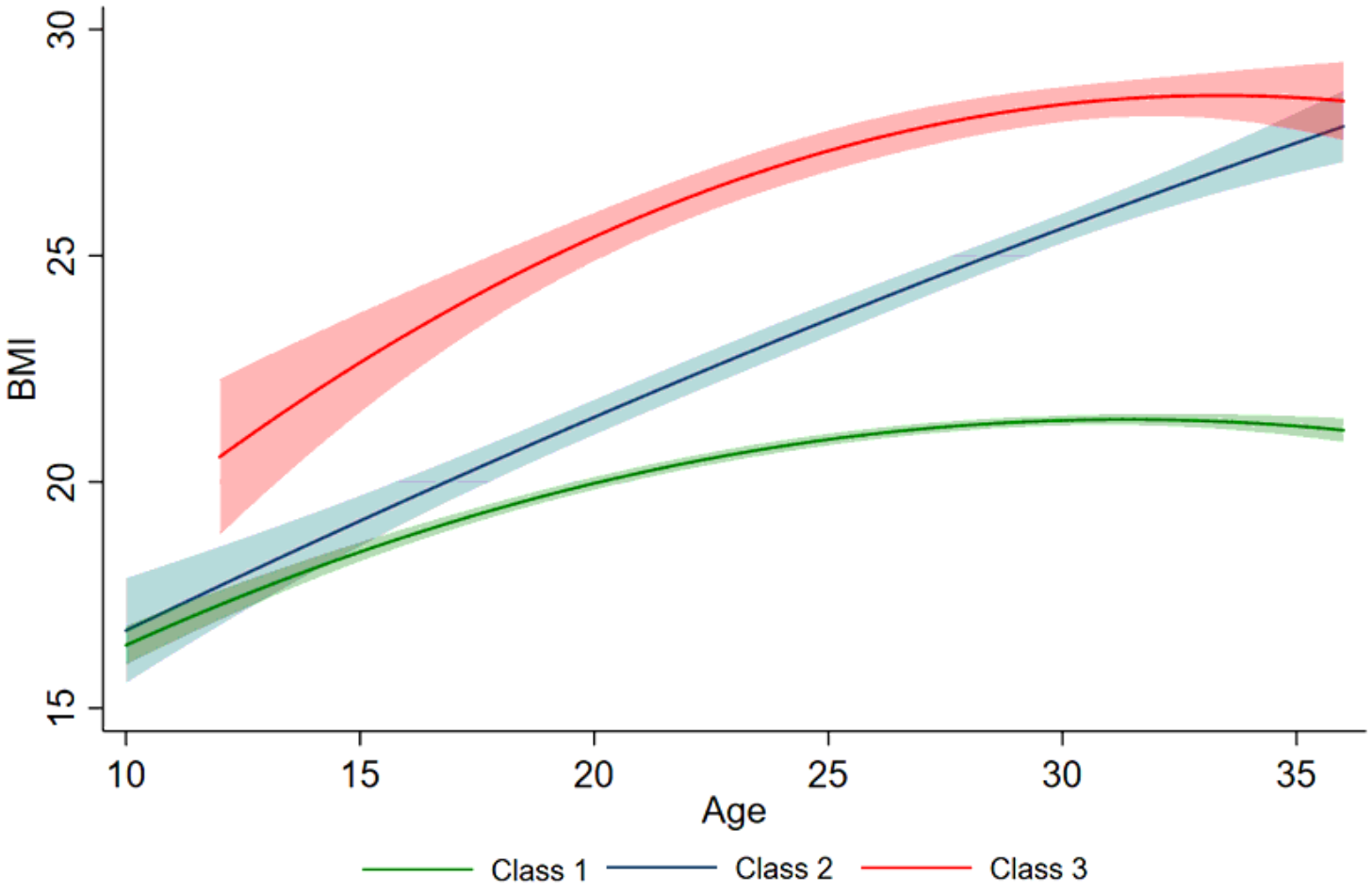

Figure 2

Predicted trajectory of BMI with age is presented by the solid line, and 95% of the CI is represented by shading.

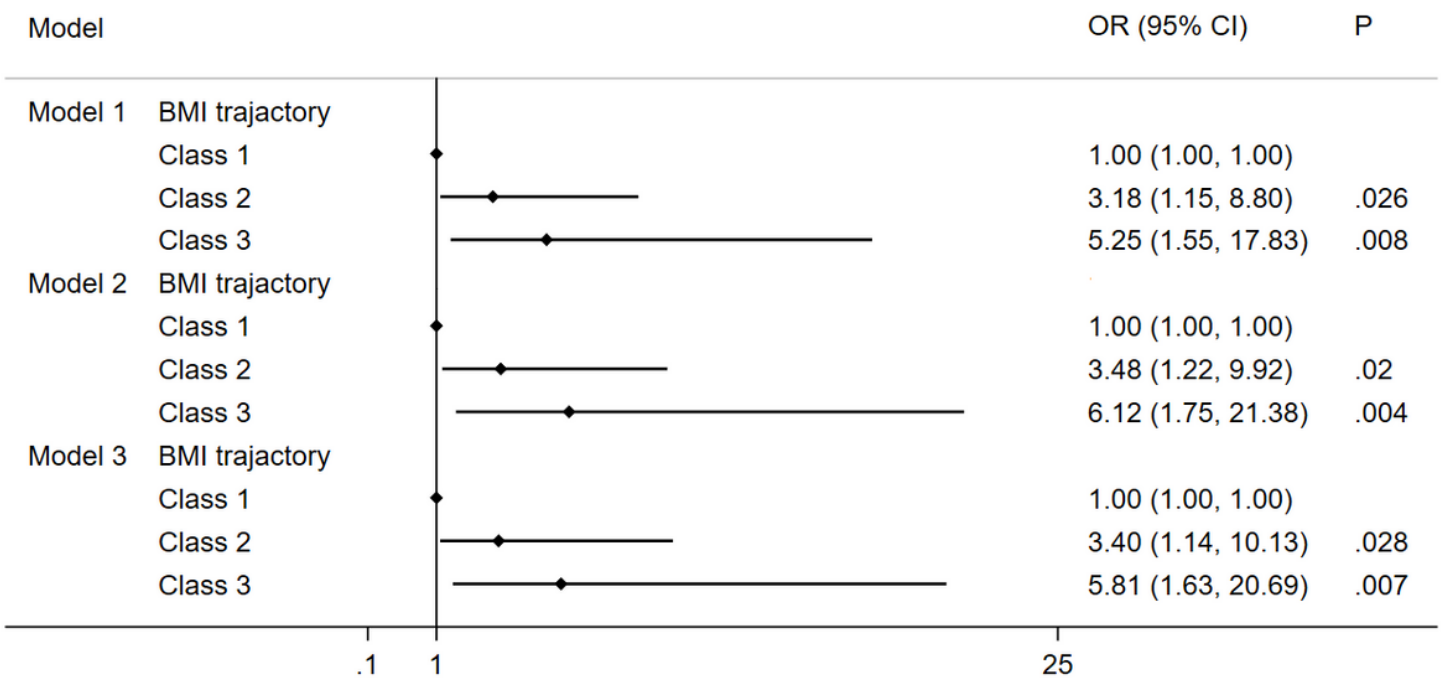

Figure 3

Association of MetS and BMI trajectory in the study subjects.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementalTableS1.docx
- YingBMIandMetSSupp.Fig.S1.tif
- YingBMIandMetSSupp.Fig.S2..tif