BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Joint Trajectories of Body Mass Index and Waist Circumference in Early to Mid-life Adulthood and Incident Hypertension

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-059556
Article Type:	Original research
Date Submitted by the Author:	24-Nov-2021
Complete List of Authors:	Qu, Yanlin; Shandong University Cheeloo College of Medicine, Department of Biostatistics, School of Public Health; Shandong University Cheeloo College of Medicine, Institute for Medical Dataology Li, Chunxia; Shandong University, Department of Biostatistics; Shandong University Lv, Jiali; Shandong University, Department of Biostatistics; Shandong University Fan, Bingbing ; Shandong University Liu, Ying; Shandong University Cheeloo College of Medicine, Department of Biostatistics, School of Public Health; Shandong University Cheeloo College of Medicine, Institute for Medical Dataology Su, Chang; Chinese Center for Disease Control and Prevention National Institute for Nutrition and Health Zhao, Xiangjuan; Shandong University Cheeloo College of Medicine,
Keywords:	Hypertension < CARDIOLOGY, EPIDEMIOLOGY, PUBLIC HEALTH

SCHOLARONE™
Manuscripts

Joint Trajectories of Body Mass Index and Waist Circumference in Early to Mid-life Adulthood and Incident Hypertension

Yanlin Qu [1,2], Chunxia Li [1,2], Jiali Lv [1,2], Bingbing Fan [1,2], Ying Liu [1,2], Chang Su [3], Xiangjuan Zhao [4 #]

[1] Department of Biostatistics, School of Public Health, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

[2] Institute for Medical Dataology, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

[3] National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, Beijing 102206, China

[4] Maternal and Child Health Care of Shandong Province, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

Running Title: Joint trajectories of BMI and WC and hypertension

 # Correspondence & Reprints:

Xiangjuan Zhao, MD.

Maternal and Child Health Care of Shandong Province, Cheeloo College of Medicine, Shandong University, Jinan 250014, China.

Email: xzhao6@hotmail.com

The authors do not have any conflict of interest.

Text word count: 3421 (excluding abstract and references)

Abstract word count: 285

Number of references: 31

Number of tables: 3

Number of figures: 3

ABSTRACT

Objective This longitudinal study aims to identify distinct trajectories of body mass index (BMI) and waist circumference (WC) during 20~60 years old, and explore their joint effect on incident hypertension.

Design A longitudinal cohort study.

Setting China Health and Nutrition Survey 1993–2011.

Participants The longitudinal cohort included 6571 participants (3063 males and 3508 females) who had BMI and WC repeatedly measured 3~7 times before incident hypertension or loss to follow-up during 1993~2011.

Outcomes Hypertension was defined as SBP/DBP >140/90 mm Hg or diagnosis by medical records or taking anti-hypertensive medication.

Results Two distinct trajectories were characterized for both BMI and WC: low-increasing and high-increasing. Jointly, subjects were divided into four groups: normal (n = 4963), WC-increasing (n = 620), BMI-increasing (n = 309), and BMI&WC-increasing (n = 679). Compared with the normal group, the adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for hypertension were 1.43 (1.19~1.74), 1.51 (1.19~1.92), and 1.76 (1.45, 2.14) for WC-increasing, BMI-increasing and BMI&WC-increasing group, respectively. The associations between model-estimated levels and hypertension increased with age, with adjusted odds ratios (ORs) and 95% CIs ranging from 0.92 (0.86~0.98) to 1.57 (1.47~1.67) for BMI, and 0.98 (0.92~1.05) to 1.44 (1.35~1.53) for WC. Conversely, the ORs (95% CIs) of level-adjusted linear slopes decreased with age, ranging from 1.47 (1.38~1.57) to 0.97 (0.92~1.03) for BMI, and 1.36 (1.28~1.45) to 0.99 (0.93~1.06) for WC.

Conclusions Our study demonstrates the joint trajectories of BMI and WC have significant effect on future hypertension risk, and the changing slopes of BMI and WC during young adulthood are independent risk factors. As modifiable factors, both BMI and WC should be

paid more attention to prevent hypertension, and young adulthood may be a crucial period for intervention.

Key words: Body mass index; Waist circumference; Hypertension; Trajectory; Longitudinal studies

Strengths and limitations of this study

- The community-based longitudinal study, with large sample size and repeated measurements, was used to explore the distinct trajectories of BMI and WC in early to mid-life adulthood.
- Distinct trajectories of BMI and WC were identified by the latent class growth mixed model, and their joint effect on incident hypertension was explored.
- The trajectory parameters, model-estimated levels and linear slopes, were examined to identify the critical period for early prevention of hypertension.
- Unmeasurable covariates may cause potential confounding bias.

ABBREVIATIONS:

BMI = body mass index

WC = waist circumference

SBP = Systolic Blood Pressure

DBP = Diastolic Blood Pressure

CHNS = The China Health and Nutrition Survey

LCGMM = latent class growth mixed model

SD = standard deviation

HR = hazard ratio

OR = odds ratio

CI = confidence interval

INTRODUCTION

As a major risk factor for cardiovascular disease, hypertension is a severe problem in public health[1]. The prevalence of hypertension has increased rapidly among decades[2], caused heavy burden to the health system in China[3,4]. Obesity is regarded as an important risk factor for incident hypertension[5,6], and it could be evaluated by many indicators, such as body mass index (BMI) and waist circumference (WC)[7,8]. The relationship between single obesity indicator and incident hypertension has been well-established in observation studies[5-9]. However, the joint effect of those indicators on hypertension is largely unknown in a life course perspective.

Generally, obesity is divided into systemic obesity and abdominal obesity[8,9]. Systemic obesity is mainly defined by BMI, while the abdominal obesity is often defined by WC[8]. The levels of BMI and WC reflect different aspects of obesity[5-12], and their joint trajectories present the heterogeneous longitudinal changing patterns of body shape. Previous researches have showed that BMI and WC were associated with incident hypertension in both cross-sectional[5-12] and longitudinal studies[13-15]. However, these studies mainly focused on the BMI and WC separately[10-15], and the joint effect of BMI and WC trajectories on incident hypertension is still unclarified. We hypothesized that individuals in different joint trajectory group of BMI and WC may present different risk of hypertension, and a critical period may exist in early to mid-life adulthood for early prevention of hypertension.

Using data from the China Health and Nutrition Survey, this study aims to identify BMI and WC trajectories during early to mid-life adulthood (20~60 years), explore the joint effect of BMI and WC trajectories on incident hypertension, and determine the potential critical period for the development of hypertension.

Subjects AND METHODS

Study cohort

The China Health and Nutrition Survey (CHNS) is an ongoing longitudinal cohort implemented by national and local governments[16,17]. It is aimed at understanding how the social and economic transformation of Chinese society affects the health and nutritional status of Chinese population. A multi-stage, random cluster process was used to collect data from Beijing, Chongqing, Guangxi, Guizhou, Heilongjiang, Henan, Hubei, Hunan, Jiangsu, Liaoning, Shaanxi, Shandong, Shanghai, Yunnan, and Zhejiang. Nine cross-sectional surveys have been completed during 1989~2011, covering 4400 households with 33348 individuals.

In this current study, we excluded individuals younger than 20 years old or older than 60 years old (n = 12147), with BMI lower than15 kg/m^2 or higher than 40 kg/m^2 (n = 799), with WC greater than120 cm (n = 1632), and with less than three follow-up visits before loss to follow-up or incident hypertension (n = 12199). Finally, 6571 normotensive adult subjects, with 3-7 times visits, were included in this study. The mean follow-up time was 11.8 years (sd = 4.2 years). BMI and WC measurements after the onset of hypertension (outcome) were excluded in our analyses. **Supplement Table S1** shows excluded respondents (n = 26777) were generally younger male, with lower baseline BMI, lower proportion of smokers and alcohol consumers, higher systolic blood pressure (SBP) and diastolic blood pressure (DBP) than those included.

Study protocols were approved by the Institutional Review Committees of the University of North Carolina at Chapel Hill, NC, USA, and the China National Institute of Nutrition and Food Safety at the Chinese Center for Disease Control and Prevention, Beijing, China. Each study participants agreed the written informed consent.

Examinations

At each follow-up, standing height was measured without shoes to the nearest 0.2 cm using a portable SECA stadiometer (SECA, Hamburg, Germany). Weight in light clothing without shoes was measured to the nearest 0.1 kilograms on a dedicated scale that was routinely calibrated. BMI was calculated as weight in kilograms divided by height in meters squared. Smoking was defined as ever smoking cigarettes (including ex-smoker and current smoker). Alcohol drinking was defined as alcohol consumption (including beer, liquor or wine) ⩾25g (for male) or ⩾15g (for female) per week.

WC was measured in centimeters at the midway between the lowest rib margin and the top of the iliac crest using a SECA tape measure during 1993~2011. Blood pressure was measured at least three times using a standard mercury sphygmomanometer after the participants rested at least five minutes in a seated position during 1991~2011. SBP was measured at the first appearance of a pulse sound (Korotkoff phase 1) and DBP at the disappearance of the pulse sound (Korotkoff phase 5). We used the mean of the last two measurements for analyses.

Outcome

Hypertension was defined as SBP/DBP ⩾140/90 mm Hg or taking antihypertensive medication or diagnosis by medical records. Data for SBP, DBP, incidence of diagnosis hypertension and taking antihypertensive medication were first collected in 1991, and subsequently in 1993, 1997, 2000, 2004, 2006, 2009 and 2011 survey.

Statistical methods

The latent class growth mixed model (LCGMM) was used to identify different trajectory patterns of BMI and WC[18]. The latent class trajectories of BMI and WC were specified as functions of age (centered to 42 years, the mean age of the cohort). Multiple LCGMMs with different trajectory shapes including linear and nonlinear parameters were tested using the strategy we previously described[19]. We chose the best-fitting model for BMI and WC trajectory according to the BIC criterion while ensuring that each group has an acceptable proportion of the population and posterior probability. In the joint analyses, comprehensively considering the trajectories of BMI and WC, subjects were assigned into different joint groups.

Cox proportional hazard models were used to explore the association between the joint group membership and incident hypertension. We established four models: model 1 with no covariates, model 2 with adjustment for baseline age, sex, and baseline BMI, model 3 with further adjustment for baseline SBP, and model 4 with further adjustment for smoking and alcohol drinking. Baseline WC was not adjusted due to its collinearity with baseline BMI (r = 0.68).

The model-estimated levels and linear slopes of BMI and WC were calculated at each age point in one-year interval according to the model parameters and their first derivatives, respectively[19]. Logistic regression analyses were used to examine the associations of model-estimated levels and linear slopes of BMI and WC at each age point with incident hypertension. Before logistic regression analyses, the model-estimated linear slope values of BMI and WC at each age point were adjusted for their corresponding levels to avoid collinearity of levels and linear slopes in the same model[19,20]. Standardized odds ratios (ORs) of levels and level-adjusted slopes of BMI and WC for incident hypertension were estimated, adjusted for gender, baseline SBP, smoking and alcohol drinking.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

Table 1 presents baseline characteristics of study variables by incident hypertension groups during follow-up. Incident hypertension subjects (n = 1415) were more likely to be older males, with higher BMI, WC, SBP and DBP, higher proportions of smokers and alcohol drinkers than normotensives.

Supplement Table S2 and **S3** summarize LCGMM results of the BMI and WC trajectory model fitting process. We fitted models from one class to three classes of linear, quadratic and cubic curves. According to statistical criteria above, a model of quadratic parameters with two classes was chosen for both BMI and WC as the best fit. **Supplement Table S4** and **S5** present parameter estimates for the best fitting 2-class quadratic latent class growth mixed model of BMI and WC, respectively.

Figure 1 shows the longitudinal trajectories of BMI (**Figure 1A**) and WC (**Figure 1B**) during 20~60 years old for 6571 participants. Both BMI and WC had two distinct trajectories, labeled as low-increasing (n (%) = 5583 (84.96%) for BMI and 5272 (80.53%) for WC) and high-increasing (n (%) = 988 (15.04%) for BMI, and 1299 (19.47%) for WC). Compared with the subjects in low-increasing group, those in the high-increasing group had similar predicted levels at age 20 years but higher linear slopes from 20 years to 60 years.

Supplement Table S6 shows hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between the BMI trajectory group membership and incident hypertension. Compared with the BMI low-increasing group, HR (95% CI) for the BMI high-increasing group was 1.49 (1.26, 1.75), adjusted for baseline age, sex, baseline BMI, baseline WC, baseline SBP, smoking and alcohol drinking. **Supplement Table S7** presents HRs and 95% CIs for the relationship between the WC trajectory classes and incident hypertension. Compared with the WC low-increasing group, HR (95% CI) for the WC high-increasing group was 1.43 (1.22, 1.68), adjusted for the same covariates above.

Jointly, subjects were divided into four joint groups according to their BMI and WC trajectories, named as normal (n = 4963), WC-increasing (n = 620), BMI-increasing (n = 309), and BMI&WC-increasing (n = 679). Individuals in the normal, WC-increasing, BMI-increasing and BMI&WC-increasing group had low-increasing WC and BMI, low-increasing BMI and high-increasing WC, high-increasing BMI and low-increasing WC, and high-increasing BMI and WC, respectively. **Table 2** summarizes the baseline characteristics of study variables by joint classes. Compared with the normal group, individuals in the BMI&WC-increasing group were more likely to be younger males with higher baseline BMI, WC, SBP and DBP, and higher proportions of smoking and alcohol drinking.

Table 3 presents HRs and 95% CIs for the association between joint group membership and incident hypertension. Compared with the normal group, the HRs (95% CIs) for WC-increasing, BMI-increasing, and BMI&WC-increasing group were 1.55 (1.31, 1.83), 1.69 (1.36, 2.10), and 1.98 (1.71, 2.28) in unadjusted model, respectively. After adjustment for baseline age, sex, baseline BMI, SBP, smoking and drinking status, these joint groups were still significantly associated with incident hypertension, whose HRs (95% CIs) were 1.43 (1.19, 1.74), 1.51 (1.19, 1.92), and 1.76 (1.45, 2.14), respectively.

Supplement Table S8 and **S9** show model-estimated levels and linear slopes of BMI and WC in means (SD) by incident hypertension at follow-up. **Figure 2** shows the change of model-estimated levels and linear slopes of BMI and WC during age 20 to 60 years in hypertension and normotension group. In **Figure 2A**, the levels increased and linear slopes decreased with age during 20~60 in both hypertension and normotension group. However, the hypertension group had higher levels and steeper rate of change than the normotension group. Similar results were found in WC (**Figure 2B**). Noticeably, the difference in change rate of WC linear slopes was large between the hypertension group and normotension group.

Figure 3 presents ORs and 95% CIs of model-estimated levels and level-adjusted linear slopes of BMI and WC for incident hypertension, adjusted for gender, baseline SBP, smoking, and alcohol drinking. The association between model-estimated levels and hypertension increased during 20~60 years old, with adjusted ORs and 95% CIs ranging from 0.92 (0.86~0.98) to 1.57 (1.47~1.67) for BMI, and 0.98 (0.92~1.05) to 1.44 (1.35~1.53) for WC. This association became significant at age 25 or above for BMI, and at age 23 or above for WC. Conversely, the standardized ORs (95% CIs) of level-adjusted linear slopes decreased with age, ranging from 1.47 (1.38~1.57) to 0.97 (0.92~1.03) for BMI, and 1.36 (1.28~1.45) to 0.99 (0.93~1.06) for WC. The associations of level-adjusted linear slopes with incident hypertension were no longer significant at age 55, indicating the importance of BMI and WC slopes in young adulthood.

DISCUSSION

In this longitudinal study, we identified two distinct trajectories for both BMI and WC during 20~60 years old in Chinese population, and found a joint effect of BMI and WC trajectories on incident hypertension. The model-estimated levels and level adjusted slopes at each age point in a 1-year interval were further calculated for both BMI and WC, and their associations with hypertension were estimated. Though previous studies have proved BMI or WC trajectories were associated with hypertension separately, the joint effect of BMI and WC trajectories was unclarified. Our observations support that BMI and WC trajectories have synergistic effect on future hypertension risk, and the changing slopes of BMI and WC during young adulthood are independent risk factors. Therefore, we suggest controlling both BMI and WC in young adulthood to prevent hypertension.

In the current study, we identified two trajectories for BMI. The low-increasing group, with baseline BMI around 20 kg/m^2, increased slowly during the 20~60 years period, while the high-increasing group with lower baseline BMI increased rapidly. Some studies, using data from China, British, and Finland, explored BMI trajectories for childhood and early adulthood, showed that BMI may have 2-6 trajectories[13,14,19-24]. Though the numbers of trajectories were different among these studies, they all discovered a low-increasing or low-stable group and a high-increasing group[13,14,19-24], which was in line with our results. Two distinct trajectories of WC were also identified in this study. The low-increasing group, with baseline WC around 70 cm, persisted 70~80 cm during early to mid-life adulthood, while the high-increasing group with same baseline WC, increased gradually from 70 cm to 95 cm. To our knowledge, the literatures on WC trajectories are still limited. Jeon et al.[15] showed 5 trajectories for WC in 40 years or above person using data from Korea. Cheng et al.[25] presented that WC may have 4 trajectories among Chinese population during 18~50 years old. However, these previous researches[15,25] did not consider the subject-specific random effect, which was a strength in our study.

Generally, obesity is divided into systemic obesity and abdominal obesity. Only studying the relationship between BMI or WC and hypertension is insufficient[13-15,19,20]. The joint effect of BMI and WC on hypertension should be explored. In this study, we divided participants into four sub-groups according to their BMI and WC trajectories. Compared with the normal group, BMI&WC-increasing group had a higher risk of incident hypertension after adjustment for some covariates, indicating that the joint effect of BMI and WC trajectories was significant associated with hypertension. Previous researches showed BMI or WC trajectories were associated with hypertension[13-15,19,25]. However, these studies mainly focused on the BMI and WC trajectories separately[13-15,19,20,25], ignoring the complementary effect between BMI and WC on incident hypertension. Hu et al.[8] found a joint effect of BMI and WC on hypertension in a cross-sectional study, nevertheless, the longitudinal changing patterns of both BMI and WC were not considered in that study. To our knowledge, the joint effect of BMI and WC trajectories was largely unknown. Our study supports a synergistic effect between BMI and WC trajectories on incident hypertension, highlighted that we should take more attention to control both BMI and WC in early adulthood.

In this longitudinal study, the model-estimated levels increased with age and the model-estimated slopes decreased with age for both BMI and WC, which was in line with our previous studies[19,20]. The standardized ORs were calculated for both model-estimated levels and level-adjusted slopes, after adjusting for gender, baseline SBP, smoking and alcohol drinking. Our results showed that for both BMI and WC, level-adjusted slopes had higher ORs than model-estimated levels before 30 years old. It may indicate slopes of BMI and WC are more important than their levels in early adulthood and 20~30 may be a critical period for early prevention of hypertension, which is similar with previous studies[19,20]. Interestingly, our longitudinal study found that the linear slopes of BMI had higher ORs than those of WC during 20~25 years old. Similarly, in 43~60 years old, the levels of BMI had higher ORs than those of WC. These results may indicate that BMI plays a more important role than WC in incident hypertension during both early and mid-life adulthood in Chinese population.

According to the life-course epidemiology theory[26-28], exposure at a specific period in the life span has a long-lasting effect on the anatomical structure and physiological function that may eventually result in disease. Individuals with high-increasing of BMI and WC may have some changes in physiological aspect during early adulthood, including aorta root thickening, premature vascular aging and endothelial dysfunction[29-31]. These changes may have long-lasting and cumulative effects on the way to incident hypertension. Previous research has reported meaningful high prevalence of premature vascular aging in younger than 40 years people[30]. Endothelial dysfunction may also play an important role in developing hypertension[31] and it may impact early aorta root thickening[29]. Aorta root size may play a causative role in the pathogenesis of systolic hypertension[29].

There are some important strengths in our study. The current study is a community-based longitudinal study with large sample size and repeated measurements. It allows us to use LCGMM to explore trajectory of BMI and WC. The LCGMM can identify distinct trajectory for subgroup participants and permits us to analyze the relationship between model-estimated levels and level-adjusted slopes and hypertension to reveal the critical period in life-course. Moreover, the joint effect of BMI and WC trajectories on incident hypertension was explored, which was rarely reported in previous researches. On the other hand, some limitations should be acknowledged. Firstly, the covariates we used may be insufficient. Some unavailable covariates may impact the prevalence of incident hypertension. Secondly, CHNS was a survey concentrated on Chinese population, suggesting our study may not be generalizable to other ethnic population. Finally, there are many indicators of obesity, besides BMI and WC. Further studies should consider more indicators such as body fat rate and fat-free body to explore the relationship between those indicators and incident hypertension.

In conclusion, the current study identified two distinct trajectories of BMI and WC from early to mid-life adulthood, and found complementary trajectory patterns between BMI and WC (620 [9.4%] and 309 [4.7%] participants for WC-increasing only trajectory and BMI-increasing only trajectory). From a life-course perspective, our study demonstrates the joint trajectories of BMI and WC have significant effect on future hypertension risk, and the changing slopes of BMI and WC during young adulthood are independent risk factors. These results emphasize that both BMI and WC should be paid more attention to prevent hypertension, and young adulthood may be a crucial period for intervention. More targeted strategies in the prevention of hypertension should be emphasized among early adulthood. Public health intervention for controlling modifiable risk factors during young adulthood has the potential to reduce the future prevalence and burden of hypertension among Chinese.

Acknowledgements

This research uses data from China Health and Nutrition Survey (CHNS). We thank the National Institute of Nutrition and Food Safety, China Center for Disease Control and Prevention, Carolina Population Center, the University of North Carolina at Chapel Hill, the NIH (R01-HD30880, DK056350, and R01-HD38700) and the Fogarty International Center, NIH for financial support for the CHNS data collection and analysis files from 1989 to 2006 and both parties plus the China-Japan Friendship Hospital, Ministry of Health for support for CHNS 2009 and future surveys.

Author contributions YQ, CL, JL, BF, YL, CS and XZ generated the hypothesis and contributed to analytic strategy and wrote the manuscript. CS and XZ supervised the field activities and data collection and edited the manuscript.

Funding

This study was supported by grants 81973147 from National Natural Science Foundation of China and the Cheeloo Young Scholars Program of Shandong University.

Conflict of interest The authors declare that they have no conflict of interest.

Patient consent for publication Not required.

Ethics approval The protocol was approved by the Ethics Committee of the National Institute for Nutrition and Health, China CDC (NO. 201524). Informed consent was obtained from all subjects before the investigation.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository from China Health and Nutrition Survey (https://www.cpc.unc.edu/projects/china/data/).

References

1. Li Y, Yang L, Wang L, et al. Burden of hypertension in China: A nationally representative survey of 174,621 adults. Int J Cardiol. 2017;227:516-523.

2. Gu D, Reynolds K, Wu X, et al. The International Collaborative Study of Cardiovascular Disease in ASIA. Prevalence, awareness, treatment, and control of hypertension in china. Hypertension. 2002;40(6):920-7.

3. Ye R, Liu K, Zhang Z, et al. Health-related quality of life of hypertension in China: a systematic review and meta-analysis. J Cardiovasc Med (Hagerstown). 2018;19(8):430-438.

4. Feng YJ, Wang HC, Li YC, et al. Hypertension Screening and Follow-up Management by Primary Health Care System among Chinese Population Aged 35 Years and Above. Biomed Environ Sci. 2015;28(5):330-40.

5. Shihab HM, Meoni LA, Chu AY, et al. Body mass index and risk of incident hypertension over the life course: the Johns Hopkins Precursors Study. Circulation. 2012;126(25):2983-9.

6. Robinson RF, Batisky DL, Hayes JR, et al. Body mass index in primary and secondary pediatric hypertension. Pediatr Nephrol. 2004;19(12):1379-84.

7. Dong B, Wang Z, Yang Y, et al. Intensified association between waist circumference and hypertension in abdominally overweight children. Obes Res Clin Pract. 2016;10(1):24-32.

8. Hu L, Huang X, You C, et al. Prevalence and Risk Factors of Prehypertension and

Hypertension in Southern China. PLoS One. 2017;12(1):e0170238.

9. Feng RN, Zhao C, Wang C, et al. BMI is strongly associated with hypertension, and waist circumference is strongly associated with type 2 diabetes and dyslipidemia, in northern Chinese adults. J Epidemiol. 2012;22(4):317-23.

10. Javed F, Aziz EF, Sabharwal MS, et al. Association of BMI and cardiovascular risk stratification in the elderly African-American females. Obesity (Silver Spring). 2011;19(6):1182-6.

11. Levine DA, Calhoun DA, Prineas RJ, et al. Moderate waist circumference and hypertension prevalence: the REGARDS Study. Am J Hypertens. 2011;24(4):482-8.

12. Soltani S, Shirani F, Chitsazi MJ, et al. The effect of dietary approaches to stop hypertension (DASH) diet on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials. Obes Rev. 2016;17(5):442-54.

13. Buscot MJ, Thomson RJ, Juonala M, et al. Distinct child-to-adult body mass index trajectories are associated with different levels of adult cardiometabolic risk. Eur Heart J. 2018;39(24):2263-2270.

14. Ahanchi NS, Ramezankhani A, Munthali RJ, et al. Body mass index trajectories from adolescent to young adult for incident high blood pressure and high plasma glucose. PLoS One. 2019;14(5):e0213828.

15. Jeon J, Jung KJ, Jee SH. Waist circumference trajectories and risk of type 2 diabetes mellitus in Korean population: the Korean genome and epidemiology study (KoGES).

BMC Public Health. 2019;19(1):741.

16. Popkin BM, Du S, Zhai F, et al. The China Health and Nutrition Survey--monitoring and understanding socio-economic and health change in China, 1989-2011. Int J Epidemiol. 2010;39(6):1435-40.

17. Zhang B, Zhai FY, Du SF, et al. The China Health and Nutrition Survey, 1989-2011. Obes Rev. 2014;15 Suppl 1(0 1):2-7.

18. Proust-Lima C, Philipps V, Liquet B. Estimation of extended mixed models using latent classes and latent processes: the R package lcmm. J Stat Softw. 2015;78:1 – 56.

19. Fan B, Yang Y, Dayimu A, et al. Body Mass Index Trajectories During Young Adulthood and Incident Hypertension: A Longitudinal Cohort in Chinese Population. J Am Heart Assoc. 2019;8(8):e011937.

20. Lv J, Fan B, Wei M, et al. Trajectories of early to mid-life adulthood BMI and incident diabetes: the China Health and Nutrition Survey. BMJ Open Diabetes Res Care. 2020;8(1):e000972.

21. Kelly Y, Patalay P, Montgomery S, et al. BMI Development and Early Adolescent Psychosocial Well-Being: UK Millennium Cohort Study. Pediatrics. 2016;138(6):e20160967.

22. Nano J, Dhana K, Asllanaj E, et al. Trajectories of BMI Before Diagnosis of Type 2 Diabetes: The Rotterdam Study. Obesity (Silver Spring). 2020;28(6):1149-1156.

23. Viner RM, Costa S, Johnson W. Patterns of BMI development between 10 and 42 years of age and their determinants in the 1970 British Cohort Study. J Epidemiol Community Health. 2019;73(1):79-85.

24. Wang X, Dong B, Huang S, et al. Body Mass Index Trajectory and Incident Hypertension: Results From a Longitudinal Cohort of Chinese Children and Adolescents, 2006-2016. Am J Public Health. 2020;110(11):1689-1695.

25. Cheng C, Li Y, Ma W, et al. Trajectories of waist circumference during young adulthood and incident hypertension: the China Health and Nutrition Survey. J Hum Hypertens. 2021 Jun 18.

26. Ben-Shlomo Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. Int J Epidemiol. 2002;31:285 – 293.

27. Lynch J, Smith GD. A life course approach to chronic disease epidemiology. Annu Rev Public Health. 2005;26:1-35.

28. Mishra GD, Anderson D, Schoenaker DA, et al. InterLACE: A New International Collaboration for a Life Course Approach to Women's Reproductive Health and Chronic Disease Events. Maturitas. 2013;74(3):235-40.

29. Farasat SM, Morrell CH, Scuteri A, et al. Pulse pressure is inversely related to aortic root diameter implications for the pathogenesis of systolic hypertension. Hypertension. 2008;51(2):196-202.

30. Cunha PG, Cotter J, Oliveira P, et al. Pulse wave velocity distribution in a cohort study: from arterial stiffness to early vascular aging. J Hypertens.

2015;33(7):1438-45.

31. Scuteri A, Tesauro M, Rizza S, et al. Endothelial function and arterial stiffness in normotensive normoglycemic first-degree relatives of diabetic patients are independent of the metabolic syndrome. Nutr Metab Cardiovasc Dis. 2008;18(5):349-56.

Figure legends

Figure 1. (A) Predicted trajectories of BMI during 20-60 years old. The trajectories were shown in solid lines, and the 95% confidence intervals (CIs) were shown in shadow. The proportions in each trajectory were shown below solid lines. BMI = body mass index (see detailed information on the curve parameters in Supplemental Table S4) (B) Predicted trajectories of WC during 20-60 years old. The trajectories were shown in solid lines, and the 95% CIs were shown in shadow. The proportions in each trajectory were shown below solid lines. WC = waist circumference (see detailed information on the curve parameters in Supplemental Table S5)

Figure 2. (A) The mean of model-estimated levels and level-adjusted linear slopes of BMI during 20-60 years old by incident hypertension. (B) The mean of model-estimated levels and level-adjusted linear slopes of WC during 20-60 years old by incident hypertension. BMI, body mass index; WC, waist circumference.

Figure 3. Standardized Odds ratios (ORs) and 95% confidence intervals (CIs) of model-estimated levels and level-adjusted linear slopes of BMI and WC during 20-60 years old by age for incident hypertension, adjusted for gender, baseline SBP, smoking, and alcohol drinking.

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure.

Table 1. Baseline Characteristics by Incident Hypertension at Follow-Up

Variable	Total	Normotensives	Incident Hypertension	*P* Value
N	6571	5156	1415	
Age, ys	35.4 (8.6)	34.8 (8.8)	37.8 (7.4)	<0.001
Males, n (%)	3063 (46.6)	2329 (45.2)	734 (51.9)	<0.001
BMI, kg/m^2	22.0 (2.7)	21.8 (2.6)	22.9 (2.9)	<0.001
WC, cm	75.8 (8.4)	75.2 (8.2)	78.0 (8.8)	<0.001
SBP, mm Hg	111.3 (11.4)	110.3 (11.3)	114.8 (10.9)	<0.001
DBP, mm Hg	73.5 (8.5)	72.8 (8.5)	76.1 (8.1)	<0.001
Smoker, n (%)	2123 (32.5)	1578 (30.8)	545 (38.8)	<0.001
Drinker, n (%)	2312 (35.5)	1712 (33.6)	600 (42.7)	<0.001
Follow-up, ys	11.8 (4.2)	12.0 (4.3)	11.3 (3.9)	<0.001

Study variables are presented as mean (SD) or n (%). BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; WC, waist circumference.

Table 2. Characteristics at baseline and incident hypertension at follow-up by joint trajectory groups

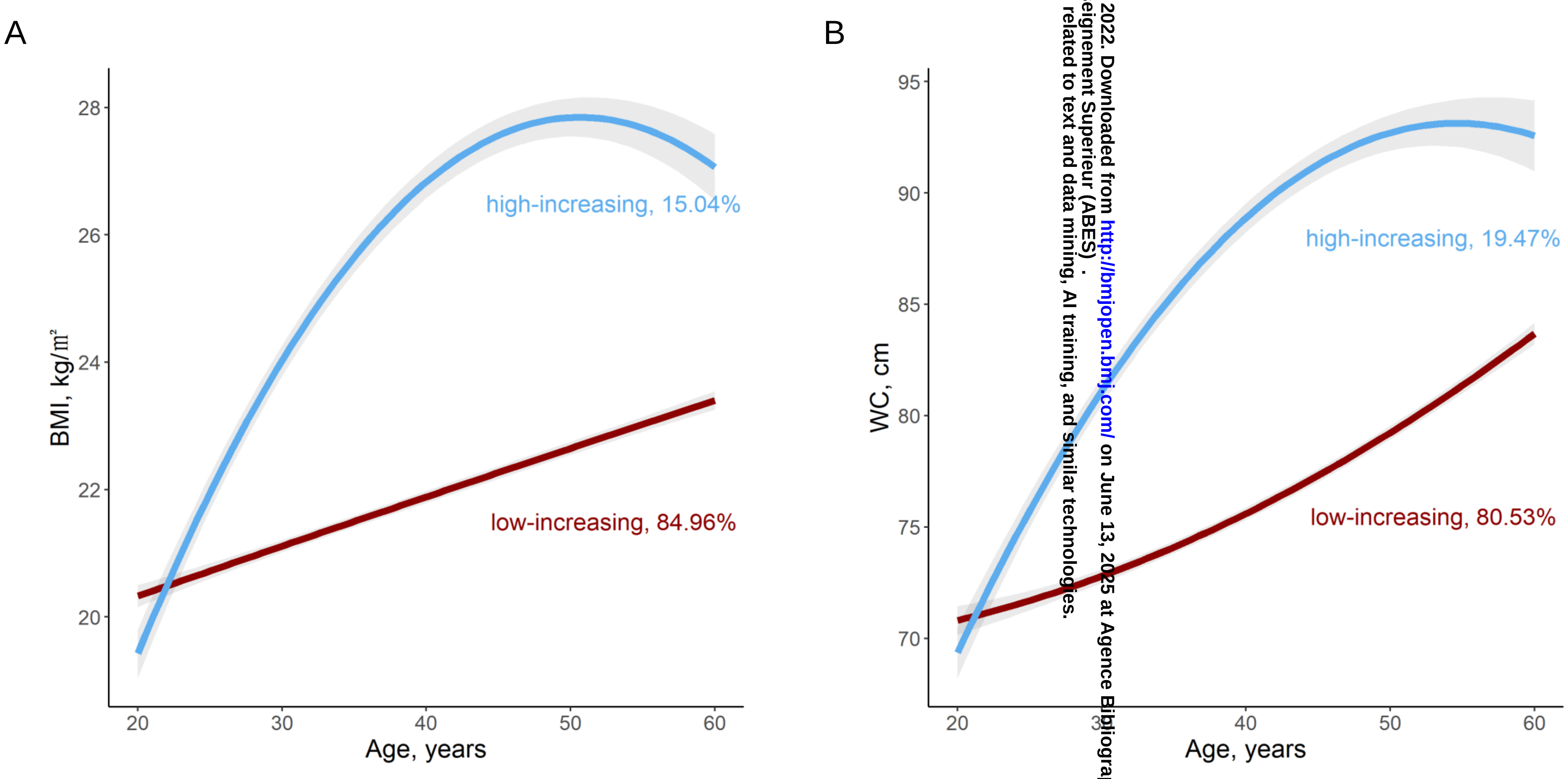
Variable	Normal	WC-increasing	BMI-increasing	BMI&WC-increasing	*P* Value
N	4963	620	309	679	
Age, years	36.3 (8.6)	32.8 (8.2)	34.3 (8.3)	31.8 (7.7)	<0.001
Males, n (%)	2019 (40.7)	557 (89.8)	33 (10.7)	454 (66.9)	<0.001
BMI, kg/m^2	21.3 (2.2)	22.8 (2.3)	24.5 (3.1)	25.0 (3.4)	<0.001
WC, cm	73.8 (7.0)	81.3 (8.7)	78.9 (8.2)	84.1 (9.9)	<0.001
SBP, mm Hg	110.3 (11.4)	115.6 (10.1)	111.3 (12.0)	114.4 (10.7)	<0.001
DBP, mm Hg	72.9 (8.6)	76.0 (7.5)	73.6 (8.6)	75.4 (8.3)	<0.001
Smoker, n (%)	1435 (29.1)	364 (59.4)	30 (9.8)	294 (43.5)	<0.001
Drinker, n (%)	1563 (31.8)	370 (60.3)	58 (18.9)	321 (48.0)	<0.001
Hypertension, n (%)	935 (18.8)	159 (25.6)	89 (28.8)	232 (34.2)	<0.001

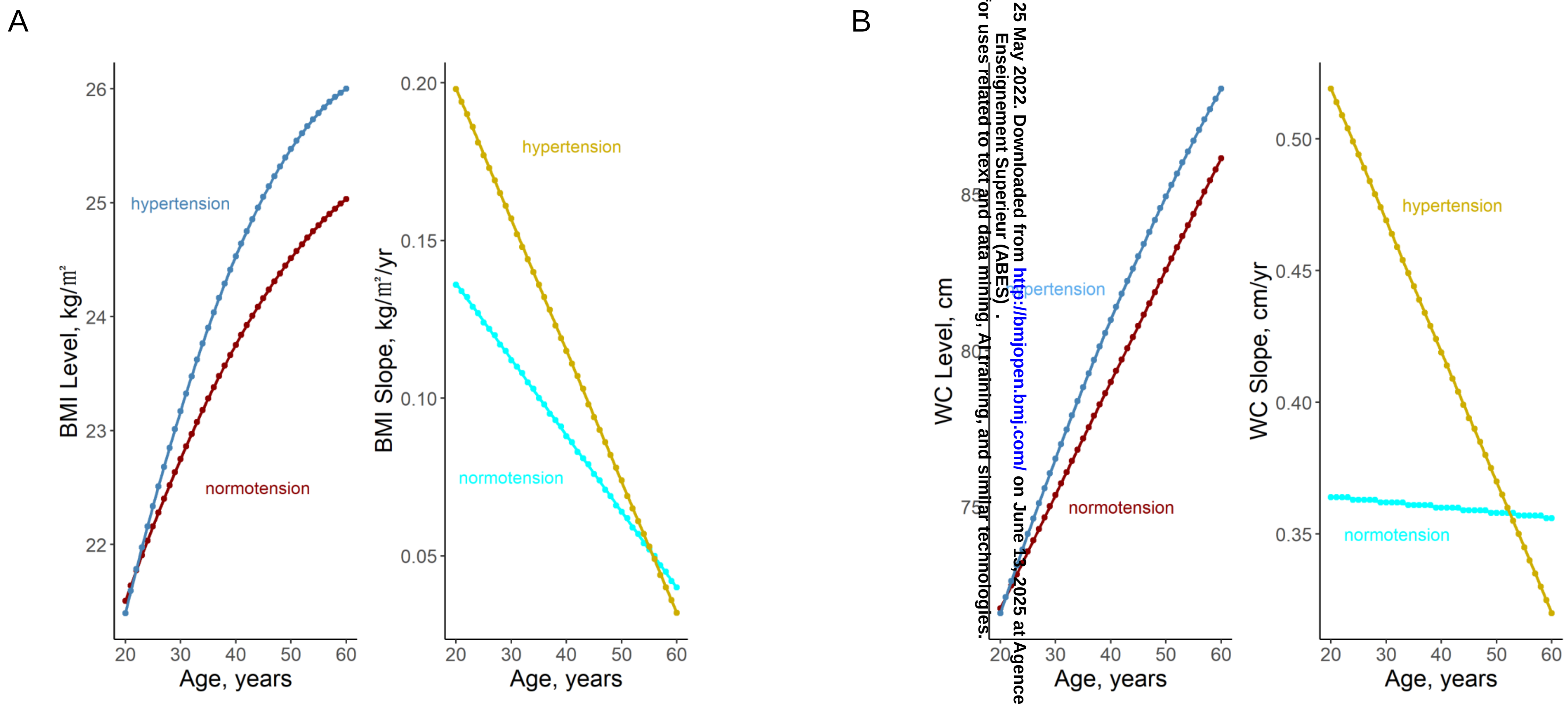
Study variables are presented as mean (SD) or n (%). BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; WC, waist circumference.

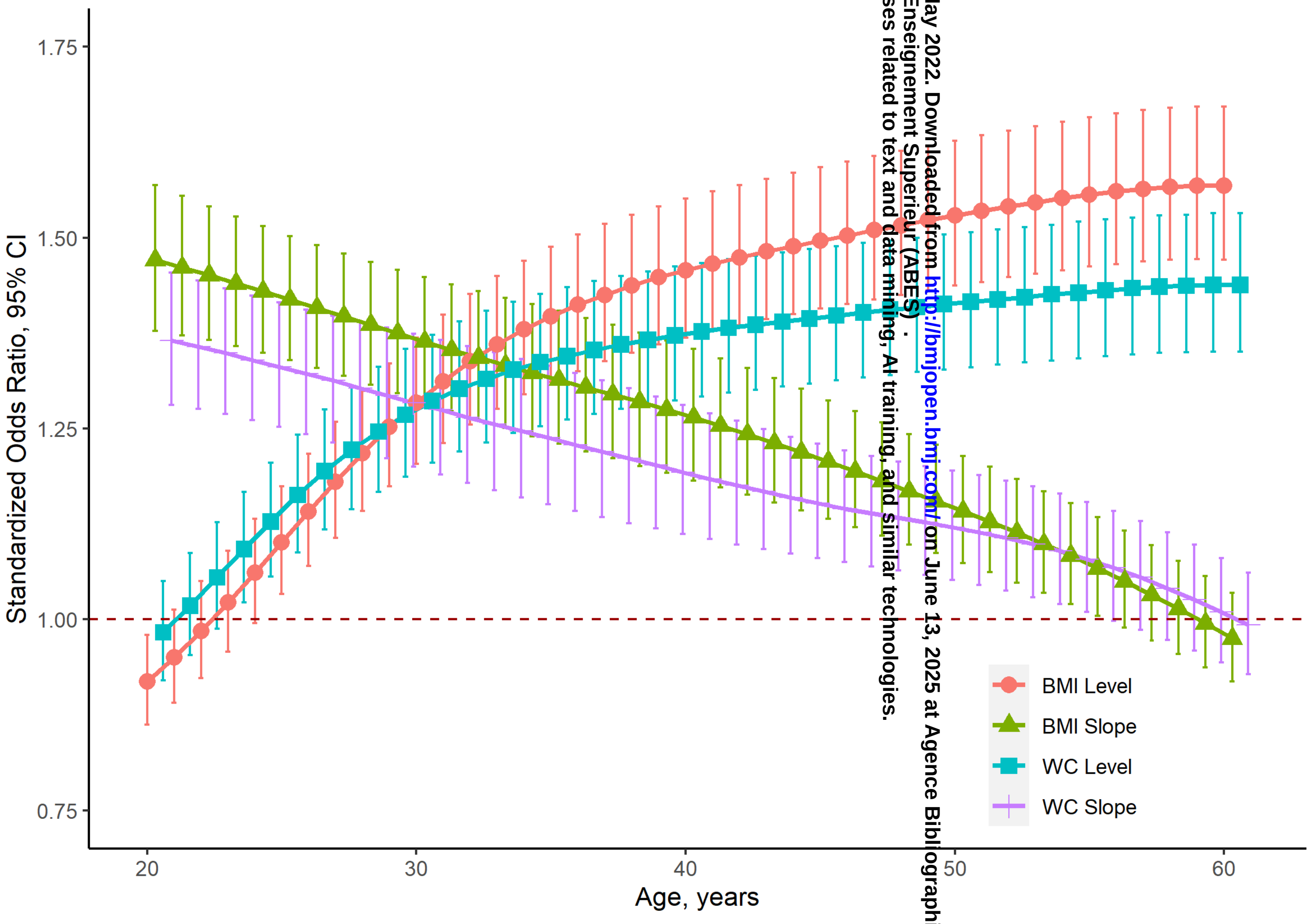
Table 3. Hazard Ratios and 95% CIs of Joint Trajectory Groups for Incident Hypertension

	Model 1	Model 2	Model 3	Model 4
Joint trajectory groups				
Normal	Reference	Reference	Reference	Reference
WC-increasing	1.55 (1.31, 1.83)	1.51 (1.25, 1.82)	1.41 (1.17, 1.71)	1.43 (1.19, 1.74)
BM-increasing	1.69 (1.36, 2.10)	1.47 (1.16, 1.87)	1.48 (1.17, 1.89)	1.51 (1.19, 1.92)
BMI&WC-increasing	1.98 (1.71, 2.28)	1.74 (1.44, 2.10)	1.73 (1.42, 2.10)	1.76 (1.45, 2.14)
Covariates				
Baseline Age		1.07 (1.06, 1.08)	1.07 (1.06, 1.08)	1.07 (1.06, 1.08)
Female		0.77 (0.69, 0.87)	0.89 (0.79, 1.00)	1.01 (0.85, 1.18)
Baseline BMI		1.10 (1.08, 1.13)	1.07 (1.05, 1.10)	1.07 (1.05, 1.10)
Baseline SBP			1.03 (1.02, 1.04)	1.03 (1.02, 1.04)
Smoker				1.12 (0.96, 1.30)
Drinker				1.10 (0.96, 1.26)

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure.


A
28
26
24
22
20
BMI, kg/㎡
high-increasing, 15.04%
low-increasing, 84.96%
20
30
40
50
60
Age, years
B
95
90
85
80
75
70
WC, cm
high-increasing, 19.47%
low-increasing, 80.53%
20
30
40
50
60
Age, years


A
BMI Level, kg/㎡
hypertension
normotension
Age, years
BMI Slope, kg/㎡/yr
hypertension
normotension
Age, years
B
WC Level, cm
hypertension
normotension
Age, years
WC Slope, cm/yr
hypertension
normotension
Age, years


Standardized Odds Ratio, 95% CI
1.75
1.50
1.25
1.00
0.75
20
30
40
50
60
Age, years
BMI Level
BMI Slope
WC Level
WC Slope

Supplemental Materials

Joint Trajectories of Body Mass Index and Waist Circumference in Early to Mid-life Adulthood and Incident Hypertension

Yanlin Qu [1,2], Chunxia Li [1,2], Jiali Lv [1,2], Bingbing Fan [1,2], Ying Liu [1,2], Chang Su [3], Xiangjuan Zhao [4 #]

[1] Department of Biostatistics, School of Public Health, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

[2] Institute for Medical Dataology, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

[3] National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, Beijing 102206, China

[4] Maternal and Child Health Care of Shandong Province, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

 # Correspondence & Reprints:

Xiangjuan Zhao, MD.

Maternal and Child Health Care of Shandong Province, Cheeloo College of Medicine, Shandong University, Jinan 250014, China.

Email: xzhao6@hotmail.com

Table S1. Baseline characteristics of participants included and excluded.

Variable	Excluded	Included	*P*-Value
N	26777	6571	
Age, y	30.8 (23.0)	35.4 (8.6)	<0.001
Male, n (%)	12931 (48.3)	3063 (46.6)	0.017
BMI, kg/m^2	20.9 (4.8)	22.0 (2.7)	<0.001
WC, cm	75.9 (15.6)	75.8 (8.4)	0.365
SBP, mm Hg	116.8 (20.9)	111.3 (11.4)	<0.001
DBP, mm Hg	75.1 (12.6)	73.5 (8.5)	<0.001
Smoker, n (%)	4475 (27.2)	2123 (32.5)	<0.001
Drinker, n (%)	5162 (29.4)	2312 (35.5)	<0.001

BMI indicates body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; WC, waist circumference.

Table S2. Latent Class Growth Mixture Models (LCGMM) results of model fitting process for BMI.

No. Latent class	Polynomial degree	Log-Lik	BIC	% Participants per class	Mean posterior probabilities	% Posterior probabilities > 70%
1	Linear	-59740	119525	100	na	na
	Quadratic	-59623	119308	100	na	na
	Cubic	-59604	119289	100	na	na
2	Linear	-59299	118678	9.98/90.02	0.79/0.95	66.92/95.38
	Quadratic	**-59122**	**118351**	**84.96/15.04**	**0.93/0.81**	**93.19/72.37**
	Cubic	-59120	118373	15.17/84.83	0.82/0.93	73.22/93.00
3	Linear	-59190	118495	24.97/72.12/2.91	0.74/0.87/0.79	56.98/84.30/67.02
	Quadratic	-58989	118128	73.40/23.09/3.51	0.88/0.73/0.78	85.32/57.61/64.07
	Cubic	-58985	118155	4.34/78.45/17.21	0.74/0.90/0.73	58.25/88.13/54.38

BMI indicate body mass index; NO. Latent class: latent class number of the model; Log-Lik: the maximum Log-Likelihood; BIC: the Bayesian information Criterion; % Participants per class: proportion of participants per class; The best fitting model is highlighted in bold characters. (na: not applicable)

Table S3. Latent Class Growth Mixture Models (LCGMM) results of model fitting process for WC

No. Latent class	Polynomial degree	Log-Lik	BIC	% Participants per class	Mean posterior probabilities	% Posterior probabilities > 70%
1	Linear	-98380	196839	100	na	na
	Quadratic	-98387	196836	100	na	na
	Cubic	-98397	196839	100	na	na
2	Linear	-98042	196163	83.32/16.68	0.92/0.78	91.98/65.42
	Quadratic	**-97946**	**195998**	**80.53/19.47**	**0.92/0.80**	**91.35/68.67**
	Cubic	-97940	196012	80.18/19.82	0.92/0.80	91.41/69.79
3	Linear	-98008	195918	50.95/36.74/12.81	0.95/0.89/0.7[illegible]	96.19/86.74/63.06
	Quadratic	-97875	195900	54.95/9.34/35.71	0.80/0.77/0.70	70.99/64.12/50.57
	Cubic	-97866	195112	50.46/36.74/12.80	0.71/0.87/0.6[illegible]	52.88/84.85/42.74

WC indicate waist circumference; NO. Latent class: latent class number of the model; Log-Lik: the maximum Log-Likelihood; BIC: the Bayesian information Criterion; % Participants per class: proportion of participants per class. The best fitting model is highlighted in bold characters. (na: not applicable)

Table S4. Parameters estimates for the best fitting 2-class quadratic Latent Class Growth Mixture Model for BMI.

		Intercept (se)*	Linear (se)	Quadratic (se)
Fixed effect				
	Group 1	23.519 (0.0487)	0.077 (0.0024)	-5×10^{-5} (0.0002)
	Group 2	27.177 (0.1337)	0.155 (0.0076)	-0.009 (0.0005)
Random effects: variance-covariance matrix				
$\sigma^2_{int} = 3.88$				
$\sigma^2_{linear\ slope} = 0.0105$				
$\sigma^2_{quadratic\ slope} < 0.001$				
$\sigma^2_{error} = 1.24$				

se = standard error; BMI = body mass index.

*: Intercept interpreted as the expected level of BMI in kg/m^2 at 42 years of age (centering to the mean age of the sample)

Table S5. Parameters estimates for the best fitting 2-class quadratic Latent Class Growth Mixture Model for WC.

		Intercept (se)*	Linear (se)	Quadratic (se)
Fixed effect				
	Group 1	76.890 (0.1459)	0.338 (0.0084)	0.004 (0.0006)
	Group 2	89.963 (0.3340)	0.501 (0.0226)	-0.020 (0.0015)
Random effects: variance-covariance matrix				
$\sigma^2_{int} = 24.31$				
$\sigma^2_{linear\ slope} = 0.0984$				
$\sigma^2_{quadratic\ slope} < 0.001$				
$\sigma^2_{error} = 5.38$				

se = standard error; WC = waist circumference.

*: Intercept interpreted as the expected level of WC in cm at 42 years of age (centering to the mean age of the sample)

Table S6. Hazard Ratios and 95% of BMI Trajectory Groups for Incident Hypertension

	Model 1	Model 2	Model 3	Model 4
Trajectory groups				
Low-increasing group	Reference	Reference	Reference	Reference
High-increasing group	1.79 (1.58, 2.03)	1.44 (1.22, 1.69)	1.47 (1.25, 1.73)	1.49 (1.26, 1.75)
Covariates				
Age, y		1.07 (1.06, 1.08)	1.06 (1.05, 1.07)	1.06 (1.05, 1.07)
Female		0.74 (0.67, 0.83)	0.86 (0.77, 0.96)	0.97 (0.83, 1.14)
Baseline BMI		1.09 (1.06, 1.12)	1.07 (1.04, 1.10)	1.07 (1.04, 1.10)
Baseline WC		1.01 (1.00,1.02)	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)
Baseline SBP			1.03 (1.02, 1.04)	1.03 (1.02, 1.04)
Smoker				1.11 (0.96, 1.30)
Drinker				1.11 (0.97, 1.27)

BMI, body mass index; SBP, systolic blood pressure; WC, waist circumference.

Table S7. Hazard Ratios and 95% of WC Trajectory Groups for Incident Hypertension

	Model 1	Model 2	Model 3	Model 4
Trajectory groups				
Low-increasing group	Reference	Reference	Reference	Reference
High-increasing group	1.71 (1.53, 1.93)	1.45 (1.24, 1.69)	1.42 (1.21, 1.66)	1.43 (1.22, 1.68)
Covariates				
Age, y		1.07 (1.06, 1.08)	1.06 (1.05, 1.07)	1.06 (1.05, 1.07)
Female		0.80 (0.72, 0.90)	0.92 (0.82, 1.03)	1.04 (0.89, 1.23)
Baseline BMI		1.10 (1.07, 1.13)	1.08 (1.05, 1.11)	1.08 (1.05, 1.11)
Baseline WC		1.01 (1.00, 1.02)	1.00 (0.99, 1.01)	1.01 (1.00, 1.02)
Baseline SBP			1.03 (1.02, 1.04)	1.03 (1.02, 1.04)
Smoker				1.12 (0.96, 1.30)
Drinker				1.10 (0.96, 1.26)

BMI, body mass index; SBP, systolic blood pressure; WC, waist circumference.

Table S8. Model-estimated levels and linear slopes of BMI in means (SD) by incident hypertension at follow-up

	BMI Level (kg/m^2)			BMI Slope (kg/m^2/year)		
Age, (years)	NTN	HTN	*P*-Value	NTN	HTN	*P*-Value
20	21.50 (2.03)	21.40 (1.95)	0.068	0.14 (0.17)	0.20 (0.21)	<0.001
21	21.64 (1.96)	21.59 (1.87)	0.407	0.13 (0.17)	0.19 (0.20)	<0.001
22	21.77 (1.90)	21.78 (1.82)	0.828	0.13 (0.16)	0.19 (0.19)	<0.001
23	21.90 (1.85)	21.97 (1.78)	0.199	0.13 (0.16)	0.19 (0.19)	<0.001
24	22.03 (1.82)	22.16 (1.76)	0.019	0.13 (0.15)	0.18 (0.18)	<0.001
25	22.16 (1.80)	22.34 (1.76)	<0.001	0.12 (0.15)	0.18 (0.17)	<0.001
26	22.28 (1.79)	22.51 (1.77)	<0.001	0.12 (0.14)	0.17 (0.17)	<0.001
27	22.40 (1.79)	22.68 (1.80)	<0.001	0.12 (0.14)	0.17 (0.16)	<0.001
28	22.52 (1.80)	22.85 (1.84)	<0.001	0.12 (0.13)	0.16 (0.15)	<0.001
29	22.64 (1.82)	23.01 (1.88)	<0.001	0.11 (0.13)	0.16 (0.15)	<0.001
30	22.75 (1.84)	23.17 (1.94)	<0.001	0.11 (0.12)	0.16 (0.14)	<0.001
31	22.86 (1.87)	23.32 (1.99)	<0.001	0.11 (0.12)	0.15 (0.13)	<0.001
32	22.97 (1.90)	23.48 (2.05)	<0.001	0.11 (0.11)	0.15 (0.13)	<0.001
33	23.07 (1.93)	23.62 (2.11)	<0.001	0.10 (0.11)	0.14 (0.12)	<0.001
34	23.18 (1.97)	23.76 (2.17)	<0.001	0.10 (0.10)	0.14 (0.11)	<0.001
35	23.28 (2.00)	23.90 (2.23)	<0.001	0.10 (0.10)	0.14 (0.11)	<0.001
36	23.38 (2.04)	24.04 (2.28)	<0.001	0.10 (0.09)	0.13 (0.10)	<0.001
37	23.48 (2.07)	24.16 (2.33)	<0.001	0.09 (0.09)	0.13 (0.10)	<0.001
38	23.57 (2.11)	24.29 (2.38)	<0.001	0.09 (0.09)	0.12 (0.09)	<0.001
39	23.66 (2.14)	24.41 (2.43)	<0.001	0.09 (0.08)	0.12 (0.09)	<0.001
40	23.75 (2.17)	24.53 (2.47)	<0.001	0.09 (0.08)	0.11 (0.08)	<0.001
41	23.84 (2.20)	24.64 (2.51)	<0.001	0.09 (0.07)	0.11 (0.08)	<0.001
42	23.92 (2.22)	24.75 (2.55)	<0.001	0.08 (0.07)	0.11 (0.07)	<0.001
43	24.01 (2.25)	24.85 (2.58)	<0.001	0.08 (0.07)	0.10 (0.07)	<0.001
44	24.08 (2.27)	24.96 (2.60)	<0.001	0.08 (0.07)	0.10 (0.07)	<0.001
45	24.16 (2.28)	25.05 (2.62)	<0.001	0.08 (0.07)	0.09 (0.07)	<0.001
46	24.24 (2.30)	25.14 (2.64)	<0.001	0.07 (0.07)	0.09 (0.07)	<0.001
47	24.31 (2.31)	25.23 (2.65)	<0.001	0.07 (0.07)	0.09 (0.07)	<0.001

48	24.38 (2.32)	25.32 (2.66)	<0.001	0.07 (0.07)	0.08 (0.07)	<0.001
49	24.45 (2.33)	25.40 (2.66)	<0.001	0.07 (0.07)	0.08 (0.07)	<0.001
50	24.51 (2.33)	25.47 (2.66)	<0.001	0.06 (0.07)	0.07 (0.07)	<0.001
51	24.58 (2.33)	25.54 (2.65)	<0.001	0.06 (0.07)	0.07 (0.07)	<0.001
52	24.64 (2.33)	25.61 (2.64)	<0.001	0.06 (0.07)	0.06 (0.08)	0.008
53	24.69 (2.33)	25.67 (2.62)	<0.001	0.06 (0.07)	0.06 (0.08)	0.075
54	24.75 (2.33)	25.73 (2.60)	<0.001	0.05 (0.08)	0.06 (0.09)	0.316
55	24.80 (2.32)	25.79 (2.58)	<0.001	0.05 (0.08)	0.05 (0.09)	0.766
56	24.85 (2.31)	25.84 (2.56)	<0.001	0.05 (0.08)	0.05 (0.10)	0.737
57	24.90 (2.30)	25.88 (2.53)	<0.001	0.05 (0.09)	0.04 (0.10)	0.367
58	24.95 (2.29)	25.93 (2.50)	<0.001	0.04 (0.09)	0.04 (0.11)	0.159
59	25.00 (2.28)	25.96 (2.48)	<0.001	0.04 (0.10)	0.04 (0.11)	0.063
60	25.03 (2.27)	26.00 (2.45)	<0.001	0.04 (0.10)	0.03 (0.12)	0.023

NTN = normotension; HTN = hypertension.

Table S9. Model-estimated levels and linear slopes of WC in means (SD) by incident hypertension at follow-up

	WC Level (cm)			WC Slope (cm/year)		
Age, (years)	NTN	HTN	*P*-Value	NTN	HTN	*P*-Value
20	71.75 (4.90)	71.60 (4.52)	0.271	0.36 (0.50)	0.52 (0.57)	<0.001
21	72.12 (4.80)	72.12 (4.45)	0.997	0.36 (0.48)	0.51 (0.55)	<0.001
22	72.48 (4.75)	72.63 (4.44)	0.272	0.36 (0.46)	0.51 (0.53)	<0.001
23	72.84 (4.73)	73.13 (4.48)	0.032	0.36 (0.45)	0.50 (0.51)	<0.001
24	73.21 (4.76)	73.64 (4.58)	0.002	0.36 (0.43)	0.50 (0.49)	<0.001
25	73.57 (4.81)	74.13 (4.71)	<0.001	0.36 (0.42)	0.49 (0.47)	<0.001
26	73.93 (4.89)	74.63 (4.88)	<0.001	0.36 (0.40)	0.49 (0.45)	<0.001
27	74.30 (5.00)	75.11 (5.06)	<0.001	0.36 (0.38)	0.48 (0.43)	<0.001
28	74.66 (5.12)	75.59 (5.26)	<0.001	0.36 (0.37)	0.48 (0.41)	<0.001
29	75.02 (5.25)	76.07 (5.47)	<0.001	0.36 (0.35)	0.47 (0.39)	<0.001
30	75.38 (5.38)	76.54 (5.68)	<0.001	0.36 (0.34)	0.47 (0.37)	<0.001
31	75.75 (5.25)	77.01 (5.90)	<0.001	0.36 (0.32)	0.46 (0.35)	<0.001
32	76.11 (5.67)	77.47 (6.10)	<0.001	0.36 (0.31)	0.46 (0.33)	<0.001
33	76.47 (5.81)	77.93 (6.30)	<0.001	0.36 (0.29)	0.45 (0.31)	<0.001
34	76.83 (5.95)	78.38 (6.50)	<0.001	0.36 (0.28)	0.45 (0.30)	<0.001
35	77.19 (6.08)	78.83 (6.68)	<0.001	0.36 (0.26)	0.44 (0.28)	<0.001
36	77.55 (6.21)	79.27 (6.85)	<0.001	0.36 (0.25)	0.44 (0.26)	<0.001
37	77.91 (6.33)	79.71 (7.01)	<0.001	0.36 (0.24)	0.43 (0.25)	<0.001
38	78.27 (6.44)	80.14 (7.15)	<0.001	0.36 (0.23)	0.43 (0.23)	<0.001
39	78.63 (6.54)	80.56 (7.28)	<0.001	0.36 (0.22)	0.42 (0.22)	<0.001
40	78.99 (6.63)	80.99 (7.39)	<0.001	0.36 (0.21)	0.42 (0.20)	<0.001
41	79.35 (6.71)	81.40 (7.49)	<0.001	0.36 (0.20)	0.41 (0.19)	<0.001
42	79.71 (6.78)	81.82 (7.58)	<0.001	0.36 (0.19)	0.41 (0.18)	<0.001
43	80.07 (6.83)	82.22 (7.64)	<0.001	0.36 (0.19)	0.40 (0.17)	<0.001
44	80.43 (6.88)	82.62 (7.70)	<0.001	0.36 (0.18)	0.40 (0.17)	<0.001
45	80.79 (6.92)	83.02 (7.73)	<0.001	0.36 (0.18)	0.39 (0.17)	<0.001
46	81.15 (6.94)	83.41 (7.75)	<0.001	0.36 (0.18)	0.39 (0.17)	<0.001
47	81.51 (6.95)	83.80 (7.75)	<0.001	0.36 (0.18)	0.38 (0.17)	<0.001

48	81.87 (6.96)	84.18 (7.74)	<0.001	0.36 (0.19)	0.38 (0.17)	<0.001
49	82.23 (6.95)	84.56 (7.72)	<0.001	0.36 (0.19)	0.37 (0.18)	0.006
50	82.59 (6.93)	84.93 (7.67)	<0.001	0.36 (0.20)	0.37 (0.19)	0.074
51	82.94 (6.90)	85.30 (7.72)	<0.001	0.36 (0.21)	0.36 (0.20)	0.355
52	83.30 (6.86)	85.66 (7.55)	<0.001	0.36 (0.22)	0.36 (0.22)	0.883
53	83.66 (6.81)	86.02 (7.46)	<0.001	0.36 (0.23)	0.35 (0.23)	0.586
54	84.02 (6.76)	86.37 (7.37)	<0.001	0.36 (0.24)	0.35 (0.25)	0.248
55	84.37 (6.70)	86.72 (7.26)	<0.001	0.36 (0.25)	0.34 (0.26)	0.091
56	84.73 (6.63)	87.06 (7.14)	<0.001	0.36 (0.26)	0.34 (0.28)	0.030
57	85.09 (6.56)	87.40 (7.02)	<0.001	0.36 (0.28)	0.33 (0.30)	0.010
58	85.45 (6.48)	87.73 (6.89)	<0.001	0.36 (0.29)	0.33 (0.32)	0.003
59	85.80 (6.41)	88.06 (6.75)	<0.001	0.36 (0.31)	0.32 (0.33)	0.001
60	86.16 (6.34)	88.38 (6.61)	<0.001	0.36 (0.32)	0.32 (0.35)	<0.001

NTN = normotension; HTN = hypertension.

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-4	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and time frame within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	1-4
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	7		
Objectives	3	State specific objectives, including any prespecified hypotheses	7		
Methods					
Study Design	4	Present key elements of study design early in the paper	8		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8		

Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	8	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	9	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	9
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8, 9		8, 9

Bias	9	Describe any efforts to address potential sources of bias	9, 10		
Study size	10	Explain how the study size was arrived at	8		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	8-10		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	9, 10		
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	8, 18

				RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	8
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	8	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	8
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)	10		
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure	10, 11		

		category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11-13		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	10, 11		
Discussion					
Key results	18	Summarise key results with reference to study objectives	13		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15, 16	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	15, 16
Interpretation	20	Give a cautious overall interpretation of results considering objectives,	13-16		

		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results	16		
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17		
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	18

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

BMJ Open

Joint Trajectories of Body Mass Index and Waist Circumference in Early to Mid-life Adulthood and Incident Hypertension: the China Health and Nutrition Survey

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-059556.R1
Article Type:	Original research
Date Submitted by the Author:	28-Feb-2022
Complete List of Authors:	Qu, Yanlin; Shandong University Cheeloo College of Medicine, Department of Biostatistics, School of Public Health; Shandong University Cheeloo College of Medicine, Institute for Medical Dataology Li, Chunxia; Shandong University, Department of Biostatistics; Shandong University Lv, Jiali; Shandong University, Department of Biostatistics; Shandong University Fan, Bingbing ; Shandong University Liu, Ying; Shandong University Cheeloo College of Medicine, Department of Biostatistics, School of Public Health; Shandong University Cheeloo College of Medicine, Institute for Medical Dataology Su, Chang; Chinese Center for Disease Control and Prevention National Institute for Nutrition and Health Zhao, Xiangjuan; Shandong Province Maternal and Child Health Care Hospital
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health, Cardiovascular medicine
Keywords:	Hypertension < CARDIOLOGY, EPIDEMIOLOGY, PUBLIC HEALTH

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Joint Trajectories of Body Mass Index and Waist Circumference in Early to Mid-life Adulthood and Incident Hypertension: the China Health and Nutrition Survey

Yanlin Qu [1,2], Chunxia Li [1,2], Jiali Lv [1,2], Bingbing Fan [1,2], Ying Liu [1,2], Chang Su [3], Xiangjuan Zhao [4 #]

[1] Department of Biostatistics, School of Public Health, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

[2] Institute for Medical Dataology, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

[3] National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, Beijing 102206, China

[4] Maternal and Child Health Care Hospital of Shandong Province, Jinan 250012, China

Running Title: Joint trajectories of BMI and WC and hypertension

 # Correspondence & Reprints:

Xiangjuan Zhao, MD.

Maternal and Child Health Care Hospital of Shandong Province, Jinan 250014, China.

Email: xzhao6@hotmail.com

The authors do not have any conflict of interest.

Text word count: 3438 (excluding abstract and references)

Abstract word count: 296

Number of references: 31

Number of tables: 3

Number of figures: 3

ABSTRACT

Objective This longitudinal study aims to identify distinct trajectories of body mass index (BMI) and waist circumference (WC) during 20~60 years old, and explore their joint effect on incident hypertension.

Design A longitudinal cohort study.

Setting China Health and Nutrition Survey 1993–2011.

Participants The longitudinal cohort included 6571 participants (3063 males) who had BMI and WC repeatedly measured 3~7 times before incident hypertension or loss to follow-up.

Outcomes Hypertension was defined as SBP/DBP >140/90 mmHg or diagnosis by medical records or taking anti-hypertensive medication.

Results Two distinct trajectories were characterized for both BMI and WC: low-increasing and high-increasing. Jointly, subjects were divided into four groups: normal (n=4963), WC-increasing (n=620), BMI-increasing (n=309), and BMI&WC-increasing (n=679). Compared with the normal group, the adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for hypertension were 1.43 (1.19~1.74), 1.51 (1.19~1.92), and 1.76 (1.45, 2.14) for WC-increasing, BMI-increasing and BMI&WC-increasing group, respectively. The model-estimated levels and slopes of BMI and WC were calculated at each age point in one-year interval according to the model parameters and their first derivatives, respectively. The associations between model-estimated levels and hypertension increased with age, with adjusted odds ratios (ORs) and 95% CIs ranging from 0.92 (0.86~0.98) to 1.57 (1.47~1.67) for BMI, and 0.98 (0.92~1.05) to 1.44 (1.35~1.53) for WC. Conversely, the ORs (95% CIs) of level-adjusted linear slopes decreased with age, ranging from 1.47 (1.38~1.57) to 0.97 (0.92~1.03) for BMI, and 1.36 (1.28~1.45) to 0.99 (0.93~1.06) for WC.

Conclusions Our study demonstrates the joint trajectories of BMI and WC have significant effect on future hypertension risk, and the changing slopes of BMI and WC during young

adulthood are independent risk factors. Both BMI and WC should be paid more attention to prevent hypertension, and young adulthood may be a crucial period for intervention.

Key words: Body mass index; Waist circumference; Hypertension; Trajectory; Longitudinal studies

Strengths and limitations of this study

- The community-based longitudinal study, with large sample size and repeated measurements, was used to explore the distinct trajectories of BMI and WC in early to mid-life adulthood.
- Distinct trajectories of BMI and WC were identified by the latent class growth mixed model, and their joint effect on incident hypertension was explored.
- The trajectory parameters, model-estimated levels and linear slopes, were examined to identify the critical period for early prevention of hypertension.
- Unmeasurable covariates may cause potential confounding bias.

ABBREVIATIONS:

BMI = body mass index

WC = waist circumference

SBP = Systolic Blood Pressure

DBP = Diastolic Blood Pressure

CHNS = The China Health and Nutrition Survey

LCGMM = latent class growth mixed model

SD = standard deviation

HR = hazard ratio

OR = odds ratio

CI = confidence interval

INTRODUCTION

As a major risk factor for cardiovascular disease, hypertension is a severe problem in public health[1]. The prevalence of hypertension has increased rapidly over decades[2], causing heavy burden to the health system in China[3,4]. Obesity is regarded as an important risk factor for incident hypertension[5,6], and it could be evaluated by many indicators, such as body mass index (BMI) and waist circumference (WC)[7,8]. The relationship between single obesity indicators and incident hypertension has been well-established in observation studies[5-9]. However, the joint effect of those indicators on hypertension is largely unknown in a life course perspective.

Generally, obesity is divided into systemic obesity and abdominal obesity[8,9]. Systemic obesity is mainly defined by BMI, while the abdominal obesity is often defined by WC[8]. The levels of BMI and WC reflect different aspects of obesity[5-12], and their joint trajectories present the heterogeneous longitudinal changing patterns of body shape. Previous research has showed that BMI and WC were associated with hypertension in both cross-sectional[5-12] and longitudinal studies[13-15]. However, these studies mainly focused on the BMI and WC separately[10-15], and the joint effect of BMI and WC trajectories on incident hypertension is still unclarified. We hypothesized that individuals in different joint trajectory group of BMI and WC may present different risk of hypertension, and a critical period may exist in early to mid-life adulthood for early prevention of hypertension.

Using data from the China Health and Nutrition Survey, this study aims to identify BMI and WC trajectories during early to mid-life adulthood (20~60 years), explore the joint effect of BMI and WC trajectories on incident hypertension, and determine the potential critical period for the development of hypertension.

Subjects AND METHODS

Study cohort

The China Health and Nutrition Survey (CHNS) is an ongoing longitudinal cohort implemented by national and local governments[16,17]. It is aimed at understanding how the social and economic transformation of Chinese society affects the health and nutritional status of Chinese population. A multi-stage, random cluster process was used to collect data from Beijing, Chongqing, Guangxi, Guizhou, Heilongjiang, Henan, Hubei, Hunan, Jiangsu, Liaoning, Shaanxi, Shandong, Shanghai, Yunnan, and Zhejiang. Nine cross-sectional surveys have been completed during 1989~2011, covering 4400 households with 33348 individuals.

In this current study, we excluded individuals younger than 20 years old or older than 60 years old (n = 12147), with BMI lower than15 kg/m^2 or higher than 40 kg/m^2 (n = 799), with WC greater than120 cm (n = 1632), and with less than three follow-up visits before loss to follow-up or incident hypertension (n = 12199). Finally, 6571 normotensive adult subjects, with 3-7 times visits, were included in this study. The mean follow-up time was 11.8 years (sd = 4.2 years). BMI and WC measurements after the onset of hypertension (outcome) were excluded in our analyses. **Supplement Table S1** shows excluded respondents (n = 26777) were generally younger male, with lower baseline BMI, lower proportion of smokers and alcohol consumers, higher systolic blood pressure (SBP) and diastolic blood pressure (DBP) than those included.

The protocol was approved by the Ethics Committee of the National Institute for Nutrition and Health, China CDC (NO. 201524). Informed consent was obtained from all subjects before the investigation.

Examinations

At each follow-up, standing height was measured without shoes to the nearest 0.2 cm using a portable SECA stadiometer (SECA, Hamburg, Germany). Weight in light clothing without shoes was measured to the nearest 0.1 kilograms on a dedicated scale that was routinely calibrated. BMI was calculated as weight in kilograms divided by height in meters squared. Smoking was defined as ever smoking cigarettes (including ex-smoker and current smoker). Alcohol drinking was defined as alcohol consumption (including beer, liquor or wine) ⩾25g (for male) or ⩾15g (for female) per week.

WC was measured in centimeters at the midway between the lowest rib margin and the top of the iliac crest using a SECA tape measure during 1993~2011. Blood pressure was measured at least three times using a standard mercury sphygmomanometer after the participants rested at least five minutes in a seated position during 1991~2011. SBP was measured at the first appearance of a pulse sound (Korotkoff phase 1) and DBP at the disappearance of the pulse sound (Korotkoff phase 5). We used the mean of the last two measurements for analyses.

Outcome

Hypertension was defined as SBP/DBP ⩾140/90 mmHg or taking antihypertensive medication or diagnosis by medical records. Data for SBP, DBP, incidence of diagnosis hypertension and taking antihypertensive medication were first collected in 1991, and subsequently in 1993, 1997, 2000, 2004, 2006, 2009 and 2011 survey.

Statistical methods

The latent class growth mixed model (LCGMM) was used to identify different trajectory patterns of BMI and WC[18]. The latent class trajectories of BMI and WC were specified as functions of age (centered to 42 years, the mean age of the cohort). Multiple LCGMMs with different trajectory shapes including linear and nonlinear parameters were tested using the strategy we previously described[19]. We chose the best-fitting model for BMI and WC trajectory according to the BIC criterion while ensuring that each group has an acceptable proportion of the population and posterior probability. In the joint analyses, comprehensively considering the trajectories of BMI and WC, subjects were assigned into different joint groups.

Cox proportional hazard models were used to explore the association between the joint group membership and incident hypertension. We established four models: model 1 with no covariates, model 2 with adjustment for baseline age, gender, and baseline BMI, model 3 with further adjustment for baseline SBP, and model 4 with further adjustment for smoking and alcohol drinking. Baseline WC was not adjusted due to its collinearity with baseline BMI (r = 0.68).

The model-estimated levels and linear slopes of BMI and WC were calculated at each age point in one-year interval according to the model parameters and their first derivatives, respectively[19]. Logistic regression analyses were used to examine the associations of model-estimated levels and linear slopes of BMI and WC at each age point with incident hypertension. Before logistic regression analyses, the model-estimated linear slope values of BMI and WC at each age point were adjusted for their corresponding levels to avoid collinearity of levels and linear slopes in the same model[19,20]. Standardized odds ratios (ORs) of levels and level-adjusted slopes of BMI and WC for incident hypertension were estimated, adjusted for gender, baseline SBP, smoking and alcohol drinking.

Variables were described using mean (sd), median [interquartile range] and n (%), as appropriate. All analyses were preformed using R version 4.0.4. Hypothesis tests were 2-sided, and P < .05 was considered statistically significant.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

Table 1 presents baseline characteristics of study variables by incident hypertension groups during follow-up. Incident hypertension subjects (n = 1415) were more likely to be older males, with higher BMI, WC, SBP and DBP, higher proportions of smokers and alcohol drinkers than normotensives.

Supplement Table S2 and **S3** summarize LCGMM results of the BMI and WC trajectory model fitting process. We fitted models from one class to three classes of linear, quadratic and cubic curves. According to statistical criteria above, a model of quadratic parameters with two classes was chosen for both BMI and WC as the best fit. **Supplement Table S4** and **S5** present parameter estimates for the best fitting 2-class quadratic latent class growth mixed model of BMI and WC, respectively.

Figure 1 shows the longitudinal trajectories of BMI (**Figure 1A**) and WC (**Figure 1B**) during 20~60 years old for 6571 participants. Both BMI and WC had two distinct trajectories, labeled as low-increasing (n (%) = 5583 (84.96%) for BMI and 5272 (80.53%) for WC) and high-increasing (n (%) = 988 (15.04%) for BMI, and 1299 (19.47%) for WC). Compared with the subjects in low-increasing group, those in the high-increasing group had similar predicted levels at age 20 years but higher linear slopes from 20 years to 60 years.

Supplement Table S6 shows hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between the BMI trajectory group membership and incident hypertension. Compared with the BMI low-increasing group, HR (95% CI) for the BMI high-increasing group was 1.49 (1.26, 1.75), adjusted for baseline age, gender, baseline BMI, baseline WC, baseline SBP, smoking and alcohol drinking. **Supplement Table S7** presents HRs and 95% CIs for the relationship between the WC trajectory classes and incident hypertension. Compared with the WC low-increasing group, HR (95% CI) for the WC high-increasing group was 1.43 (1.22, 1.68), adjusted for the same covariates above.

Jointly, subjects were divided into four joint groups according to their BMI and WC trajectories, named as normal (n = 4963), WC-increasing (n = 620), BMI-increasing (n = 309), and BMI&WC-increasing (n = 679). Individuals in the normal, WC-increasing, BMI-increasing and BMI&WC-increasing group had low-increasing WC and BMI, low-increasing BMI and high-increasing WC, high-increasing BMI and low-increasing WC, and high-increasing BMI and WC, respectively. **Table 2** summarizes the baseline characteristics of study variables by joint classes. Compared with the normal group, individuals in the BMI&WC-increasing group were more likely to be younger males with higher baseline BMI, WC, SBP and DBP, and higher proportions of smoking and alcohol drinking.

Table 3 presents HRs and 95% CIs for the association between joint group membership and incident hypertension. Compared with the normal group, the HRs (95% CIs) for WC-increasing, BMI-increasing, and BMI&WC-increasing group were 1.55 (1.31, 1.83), 1.69 (1.36, 2.10), and 1.98 (1.71, 2.28) in unadjusted model, respectively. After adjustment for baseline age, gender, baseline BMI, SBP, smoking and drinking status, these joint groups were still significantly associated with incident hypertension, whose HRs (95% CIs) were 1.43 (1.19, 1.74), 1.51 (1.19, 1.92), and 1.76 (1.45, 2.14), respectively.

Supplement Table S8 and **S9** show model-estimated levels and linear slopes of BMI and WC in means (SD) by incident hypertension at follow-up. **Figure 2** shows the change of model-estimated levels and linear slopes of BMI and WC during age 20 to 60 years in hypertension and normotension group. In **Figure 2A**, the levels increased and linear slopes decreased with age during 20~60 in both hypertension and normotension group. However, the hypertension group had higher levels and steeper rate of change than the normotension group. Similar results were found in WC (**Figure 2B**). Noticeably, the difference in change rate of WC linear slopes was large between the hypertension group and normotension group.

Figure 3 presents ORs and 95% CIs of model-estimated levels and level-adjusted linear slopes of BMI and WC for incident hypertension, adjusted for gender, baseline SBP, smoking, and alcohol drinking. The association between model-estimated levels and hypertension increased during 20~60 years old, with adjusted ORs and 95% CIs ranging from 0.92 (0.86~0.98) to 1.57 (1.47~1.67) for BMI, and 0.98 (0.92~1.05) to 1.44 (1.35~1.53) for WC. This association became significant at age 25 or above for BMI, and at age 23 or above for WC. Conversely, the standardized ORs (95% CIs) of level-adjusted linear slopes decreased with age, ranging from 1.47 (1.38~1.57) to 0.97 (0.92~1.03) for BMI, and 1.36 (1.28~1.45) to 0.99 (0.93~1.06) for WC. The associations of level-adjusted linear slopes with incident hypertension were no longer significant at age 55, indicating the importance of BMI and WC slopes in young adulthood.

DISCUSSION

In this longitudinal study, we identified two distinct trajectories for both BMI and WC during 20~60 years old in Chinese population, and found a joint effect of BMI and WC trajectories on incident hypertension. The model-estimated levels and level adjusted slopes at each age point in a 1-year interval were further calculated for both BMI and WC, and their associations with hypertension were estimated. Though previous studies have demonstrated BMI or WC trajectories were associated with hypertension separately, the joint effect of BMI and WC trajectories was unclarified. Our observations support that BMI and WC trajectories have synergistic effect on future hypertension risk, and the changing slopes of BMI and WC during young adulthood are independent risk factors. Therefore, we suggest controlling both BMI and WC in young adulthood to prevent hypertension.

In the current study, we identified two trajectories for BMI. The low-increasing group, with baseline BMI around 20 kg/m^2, increased slowly during the 20~60 years period, while the high-increasing group with lower baseline BMI increased rapidly. Some studies, using data from China, UK, and Finland, explored BMI trajectories for childhood and early adulthood, showed that BMI may have 2-6 trajectories[13,14,19-24]. Though the numbers of trajectories were different among these studies, they all discovered a low-increasing or low-stable group and a high-increasing group[13,14,19-24], which was in line with our results. Two distinct trajectories of WC were also identified in this study. The low-increasing group, with baseline WC around 70 cm, persisted 70~80 cm during early to mid-life adulthood, while the high-increasing group with same baseline WC, increased gradually from 70 cm to 95 cm. To our knowledge, the literatures on WC trajectories are still limited. Jeon et al.[15] showed 5 trajectories for WC in individuals aged 40 year or older using data from Korea. Cheng et al.[25] presented that WC may have 4 trajectories among Chinese population during 18~50 years old. However, these previous researches[15,25] did not consider the subject-specific random effect, which was a strength in our study.

Generally, obesity is divided into systemic obesity and abdominal obesity. Only studying the relationship between BMI or WC and hypertension is insufficient[13-15,19,20]. The joint effect of BMI and WC on hypertension should be explored. In this study, we divided participants into four sub-groups according to their BMI and WC trajectories. Compared with the normal group, BMI&WC-increasing group had a higher risk of incident hypertension after adjustment for some covariates, indicating that the joint effect of BMI and WC trajectories was significant associated with hypertension. Previous researches showed BMI or WC trajectories were associated with hypertension[13-15,19,25]. However, these studies mainly focused on the BMI and WC trajectories separately[13-15,19,20,25], ignoring the complementary effect between BMI and WC on incident hypertension. Hu et al.[8] found a joint effect of BMI and WC on hypertension in a cross-sectional study, nevertheless, the longitudinal changing patterns of both BMI and WC were not considered in that study. To our knowledge, the joint effect of BMI and WC trajectories was largely unknown. Our study supports a synergistic effect between BMI and WC trajectories on incident hypertension, highlighted that we should take more attention to control both BMI and WC in early adulthood.

In this longitudinal study, the model-estimated levels increased with age and the model-estimated slopes decreased with age for both BMI and WC, which was in line with our previous studies[19,20]. The standardized ORs were calculated for both model-estimated levels and level-adjusted slopes, after adjusting for gender, baseline SBP, smoking and alcohol drinking. Our results showed that for both BMI and WC, level-adjusted slopes had higher ORs than model-estimated levels before 30 years old. It may indicate slopes of BMI and WC are more important than their levels in early adulthood and 20~30 may be a critical period for early prevention of hypertension, which is similar with previous studies[19,20]. Interestingly, our longitudinal study found that the linear slopes of BMI had higher ORs than those of WC during 20~25 years old. Similarly, in 43~60 years old, the levels of BMI had higher ORs than those of WC. These results may indicate that BMI plays a more important role than WC in incident hypertension during both early and mid-life adulthood in Chinese population.

According to the life-course epidemiology theory[26-28], exposure at a specific period in the life span has a long-lasting effect on the anatomical structure and physiological function that may eventually result in disease. Individuals with high-increasing of BMI and WC may have some changes in physiological aspect during early adulthood, including aorta root thickening, premature vascular aging and endothelial dysfunction[29-31]. These changes may have long-lasting and cumulative effects on the way to incident hypertension. Previous research has reported meaningful high prevalence of premature vascular aging in younger than 40 years people[30]. Endothelial dysfunction may also play an important role in developing hypertension[31] and it may impact early aorta root thickening[29]. Aorta root size may play a causative role in the pathogenesis of systolic hypertension[29].

There are some important strengths in our study. The current study is a community-based longitudinal study with large sample size and repeated measurements. It allows us to use LCGMM to explore trajectory of BMI and WC. The LCGMM can identify distinct trajectory for subgroup participants and permits us to analyze the relationship between model-estimated levels and level-adjusted slopes and hypertension to reveal the critical period in life-course. Moreover, the joint effect of BMI and WC trajectories on incident hypertension was explored, which was rarely reported in previous researches. On the other hand, some limitations should be acknowledged. Firstly, the covariates we used may be insufficient. Some unavailable covariates, like physically fitness, may impact the prevalence of incident hypertension. Secondly, CHNS was a survey concentrated on Chinese population, suggesting our study may not be generalizable to other ethnic population. Finally, there are many indicators of obesity, besides BMI and WC. Further studies should consider more indicators such as body fat percentage and fat-free body to explore the relationship between those indicators and incident hypertension.

In conclusion, the current study identified two distinct trajectories of BMI and WC from early to mid-life adulthood, and found complementary trajectory patterns between BMI and WC (620 [9.4%] and 309 [4.7%] participants for WC-increasing only trajectory and BMI-increasing only trajectory). From a life-course perspective, our study demonstrates the joint trajectories of BMI and WC have significant effect on future hypertension risk, and the changing slopes of BMI and WC during young adulthood are independent risk factors. These results emphasize that both BMI and WC should be paid more attention to prevent hypertension, and young adulthood may be a crucial period for intervention. More targeted strategies in the prevention of hypertension should be emphasized among early adulthood.

Public health intervention for controlling modifiable risk factors during young adulthood has the potential to reduce the future prevalence and burden of hypertension among Chinese.

Acknowledgements

This research uses data from China Health and Nutrition Survey (CHNS). We thank the National Institute of Nutrition and Food Safety, China Center for Disease Control and Prevention, Carolina Population Center, the University of North Carolina at Chapel Hill, the NIH (R01-HD30880, DK056350, and R01-HD38700) and the Fogarty International Center, NIH for financial support for the CHNS data collection and analysis files from 1989 to 2006 and both parties plus the China-Japan Friendship Hospital, Ministry of Health for support for CHNS 2009 and future surveys.

Author contributions YQ, CL, JL, BF, YL, CS and XZ generated the hypothesis and contributed to analytic strategy and wrote the manuscript. CS and XZ supervised the field activities and data collection and edited the manuscript.

Funding

This study was supported by grants 81973147 from National Natural Science Foundation of China and the Cheeloo Young Scholars Program of Shandong University.

Conflict of interest The authors declare that they have no conflict of interest.

Patient consent for publication Not required.

Ethics approval The protocol was approved by the Ethics Committee of the National Institute for Nutrition and Health, China CDC (NO. 201524). Informed consent was obtained from all subjects before the investigation.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository from China Health and Nutrition Survey (https://www.cpc.unc.edu/projects/china/data/).

References

1. Li Y, Yang L, Wang L, et al. Burden of hypertension in China: A nationally representative survey of 174,621 adults. Int J Cardiol. 2017;227:516-523.
2. Gu D, Reynolds K, Wu X, et al. The International Collaborative Study of Cardiovascular Disease in ASIA. Prevalence, awareness, treatment, and control of hypertension in china. Hypertension. 2002;40(6):920-7.
3. Ye R, Liu K, Zhang Z, et al. Health-related quality of life of hypertension in China: a systematic review and meta-analysis. J Cardiovasc Med (Hagerstown). 2018;19(8):430-438.
4. Feng YJ, Wang HC, Li YC, et al. Hypertension Screening and Follow-up Management by Primary Health Care System among Chinese Population Aged 35 Years and Above. Biomed Environ Sci. 2015;28(5):330-40.
5. Shihab HM, Meoni LA, Chu AY, et al. Body mass index and risk of incident hypertension over the life course: the Johns Hopkins Precursors Study. Circulation. 2012;126(25):2983-9.
6. Robinson RF, Batisky DL, Hayes JR, et al. Body mass index in primary and secondary pediatric hypertension. Pediatr Nephrol. 2004;19(12):1379-84.
7. Dong B, Wang Z, Yang Y, et al. Intensified association between waist circumference and hypertension in abdominally overweight children. Obes Res Clin Pract. 2016;10(1):24-32.
8. Hu L, Huang X, You C, et al. Prevalence and Risk Factors of Prehypertension and

Hypertension in Southern China. PLoS One. 2017;12(1):e0170238.

9. Feng RN, Zhao C, Wang C, et al. BMI is strongly associated with hypertension, and waist circumference is strongly associated with type 2 diabetes and dyslipidemia, in northern Chinese adults. J Epidemiol. 2012;22(4):317-23.

10. Javed F, Aziz EF, Sabharwal MS, et al. Association of BMI and cardiovascular risk stratification in the elderly African-American females. Obesity (Silver Spring). 2011;19(6):1182-6.

11. Levine DA, Calhoun DA, Prineas RJ, et al. Moderate waist circumference and hypertension prevalence: the REGARDS Study. Am J Hypertens. 2011;24(4):482-8.

12. Soltani S, Shirani F, Chitsazi MJ, et al. The effect of dietary approaches to stop hypertension (DASH) diet on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials. Obes Rev. 2016;17(5):442-54.

13. Buscot MJ, Thomson RJ, Juonala M, et al. Distinct child-to-adult body mass index trajectories are associated with different levels of adult cardiometabolic risk. Eur Heart J. 2018;39(24):2263-2270.

14. Ahanchi NS, Ramezankhani A, Munthali RJ, et al. Body mass index trajectories from adolescent to young adult for incident high blood pressure and high plasma glucose. PLoS One. 2019;14(5):e0213828.

15. Jeon J, Jung KJ, Jee SH. Waist circumference trajectories and risk of type 2 diabetes mellitus in Korean population: the Korean genome and epidemiology study (KoGES).

BMC Public Health. 2019;19(1):741.

[dataset] 16. Popkin BM, Du S, Zhai F, et al. Cohort Profile: The China Health and Nutrition Survey--monitoring and understanding socio-economic and health change in China, 1989-2011. Int J Epidemiol. 2010 Dec;39(6):1435-40. doi: 10.1093/ije/dyp322.

[dataset] 17. Zhang B, Zhai FY, Du SF, et al. The China Health and Nutrition Survey, 1989-2011. Obes Rev. 2014 Jan;15 Suppl 1(0 1):2-7. doi: 10.1111/obr.12119.

18. Proust-Lima C, Philipps V, Liquet B. Estimation of extended mixed models using latent classes and latent processes: the R package lcmm. J Stat Softw. 2015;78:1 – 56.

19. Fan B, Yang Y, Dayimu A, et al. Body Mass Index Trajectories During Young Adulthood and Incident Hypertension: A Longitudinal Cohort in Chinese Population. J Am Heart Assoc. 2019;8(8):e011937.

20. Lv J, Fan B, Wei M, et al. Trajectories of early to mid-life adulthood BMI and incident diabetes: the China Health and Nutrition Survey. BMJ Open Diabetes Res Care. 2020;8(1):e000972.

21. Kelly Y, Patalay P, Montgomery S, et al. BMI Development and Early Adolescent Psychosocial Well-Being: UK Millennium Cohort Study. Pediatrics. 2016;138(6):e20160967.

22. Nano J, Dhana K, Asllanaj E, et al. Trajectories of BMI Before Diagnosis of Type 2 Diabetes: The Rotterdam Study. Obesity (Silver Spring). 2020;28(6):1149-1156.

23. Viner RM, Costa S, Johnson W. Patterns of BMI development between 10 and 42 years of age and their determinants in the 1970 British Cohort Study. J Epidemiol Community Health. 2019;73(1):79-85.

24. Wang X, Dong B, Huang S, et al. Body Mass Index Trajectory and Incident Hypertension: Results From a Longitudinal Cohort of Chinese Children and Adolescents, 2006-2016. Am J Public Health. 2020;110(11):1689-1695.

25. Cheng C, Li Y, Ma W, et al. Trajectories of waist circumference during young adulthood and incident hypertension: the China Health and Nutrition Survey. J Hum Hypertens. 2021 Jun 18.

26. Ben-Shlomo Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. Int J Epidemiol. 2002;31:285 – 293.

27. Lynch J, Smith GD. A life course approach to chronic disease epidemiology. Annu Rev Public Health. 2005;26:1-35.

28. Mishra GD, Anderson D, Schoenaker DA, et al. InterLACE: A New International Collaboration for a Life Course Approach to Women's Reproductive Health and Chronic Disease Events. Maturitas. 2013;74(3):235-40.

29. Farasat SM, Morrell CH, Scuteri A, et al. Pulse pressure is inversely related to aortic root diameter implications for the pathogenesis of systolic hypertension. Hypertension. 2008;51(2):196-202.

30. Cunha PG, Cotter J, Oliveira P, et al. Pulse wave velocity distribution in a cohort study: from arterial stiffness to early vascular aging. J Hypertens.

2015;33(7):1438-45.

31. Scuteri A, Tesauro M, Rizza S, et al. Endothelial function and arterial stiffness in normotensive normoglycemic first-degree relatives of diabetic patients are independent of the metabolic syndrome. Nutr Metab Cardiovasc Dis. 2008;18(5):349-56.

Figure legends

Figure 1. (A) Predicted trajectories of BMI during 20-60 years old. The trajectories were shown in solid lines, and the 95% confidence intervals (CIs) were shown in shadow. The proportions in each trajectory were shown below solid lines. BMI = body mass index (see detailed information on the curve parameters in Supplemental Table S4) (B) Predicted trajectories of WC during 20-60 years old. The trajectories were shown in solid lines, and the 95% CIs were shown in shadow. The proportions in each trajectory were shown below solid lines. WC = waist circumference (see detailed information on the curve parameters in Supplemental Table S5)

Figure 2. (A) The mean of model-estimated levels and level-adjusted linear slopes of BMI during 20-60 years old by incident hypertension. (B) The mean of model-estimated levels and level-adjusted linear slopes of WC during 20-60 years old by incident hypertension. BMI, body mass index; WC, waist circumference.

Figure 3. Standardized Odds ratios (ORs) and 95% confidence intervals (CIs) of model-estimated levels and level-adjusted linear slopes of BMI and WC during 20-60 years old by age for incident hypertension, adjusted for gender, baseline SBP, smoking, and alcohol drinking.

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure.

Table 1. Baseline Characteristics by Incident Hypertension at Follow-Up

Variable	Total	Normotensives	Incident Hypertension	*P* Value
N	6571	5156	1415	
Age, ys	35.4 (8.6)	34.8 (8.8)	37.8 (7.4)	<0.001
Males, n (%)	3063 (46.6)	2329 (45.2)	734 (51.9)	<0.001
BMI, kg/m^2	22.0 (2.7)	21.8 (2.6)	22.9 (2.9)	<0.001
WC, cm	75.8 (8.4)	75.2 (8.2)	78.0 (8.8)	<0.001
SBP, mmHg	110.0 [103.0, 120.0]	110.0 [101.0, 120.0]	116.0 [108.0, 120.0]	<0.001
DBP, mmHg	74.0 [70.0, 80.0]	72.5 [68.0, 80.0]	77.5 [70.0, 80.0]	<0.001
Smoker, n (%)	2123 (32.5)	1578 (30.8)	545 (38.8)	<0.001
Drinker, n (%)	2312 (35.5)	1712 (33.6)	600 (42.7)	<0.001
Follow-up, ys	11.8 (4.2)	12.0 (4.3)	11.3 (3.9)	<0.001

Study variables are presented as mean (SD), median [interquartile range] or n (%), appropriately. BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; WC, waist circumference.

Table 2. Characteristics at baseline and incident hypertension at follow-up by joint trajectory groups

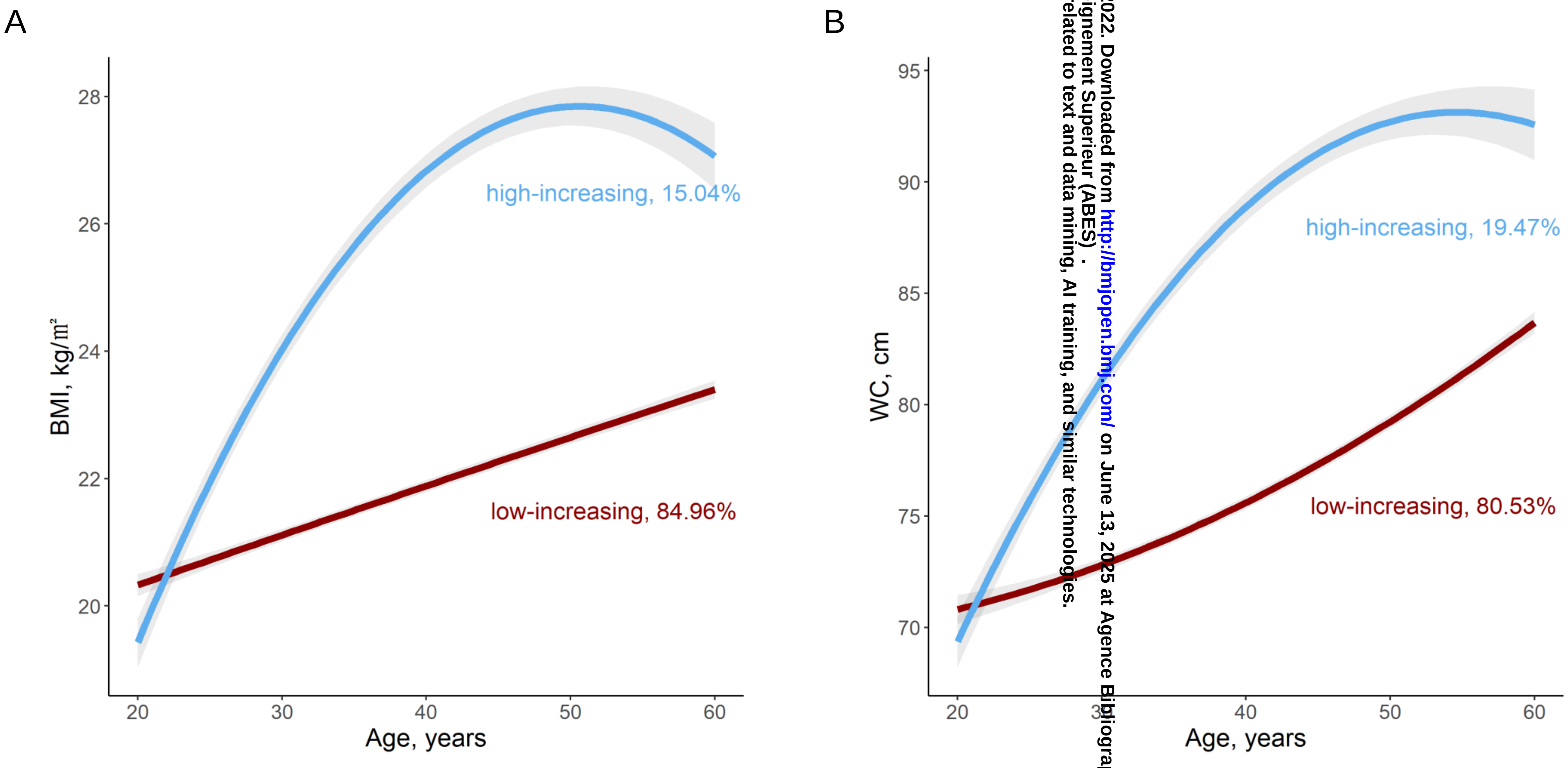
Variable	Normal	WC-increasing	BMI-increasing	BMI&WC-increasing	*P* Value
N	4963	620	309	679	
Age, years	36.3 (8.6)	32.8 (8.2)	34.3 (8.3)	31.8 (7.7)	<0.001
Males, n (%)	2019 (40.7)	557 (89.8)	33 (10.7)	454 (66.9)	<0.001
BMI, kg/m^2	21.3 (2.2)	22.8 (2.3)	24.5 (3.1)	25.0 (3.4)	<0.001
WC, cm	73.8 (7.0)	81.3 (8.7)	78.9 (8.2)	84.1 (9.9)	<0.001
SBP, mmHg	110.0 [101.0, 120.0]	117.5 [110.0, 120.0]	110.0 [105.0, 120.0]	116.0 [108.0, 120.0]	<0.001
DBP, mmHg	72.5 [68.0, 80.0]	77.0 [70.0, 80.0]	73.0 [68.8, 80.0]	77.0 [70.0, 80.0]	<0.001
Smoker, n (%)	1435 (29.1)	364 (59.4)	30 (9.8)	294 (43.5)	<0.001
Drinker, n (%)	1563 (31.8)	370 (60.3)	58 (18.9)	321 (48.0)	<0.001
Hypertension, n (%)	935 (18.8)	159 (25.6)	89 (28.8)	232 (34.2)	<0.001

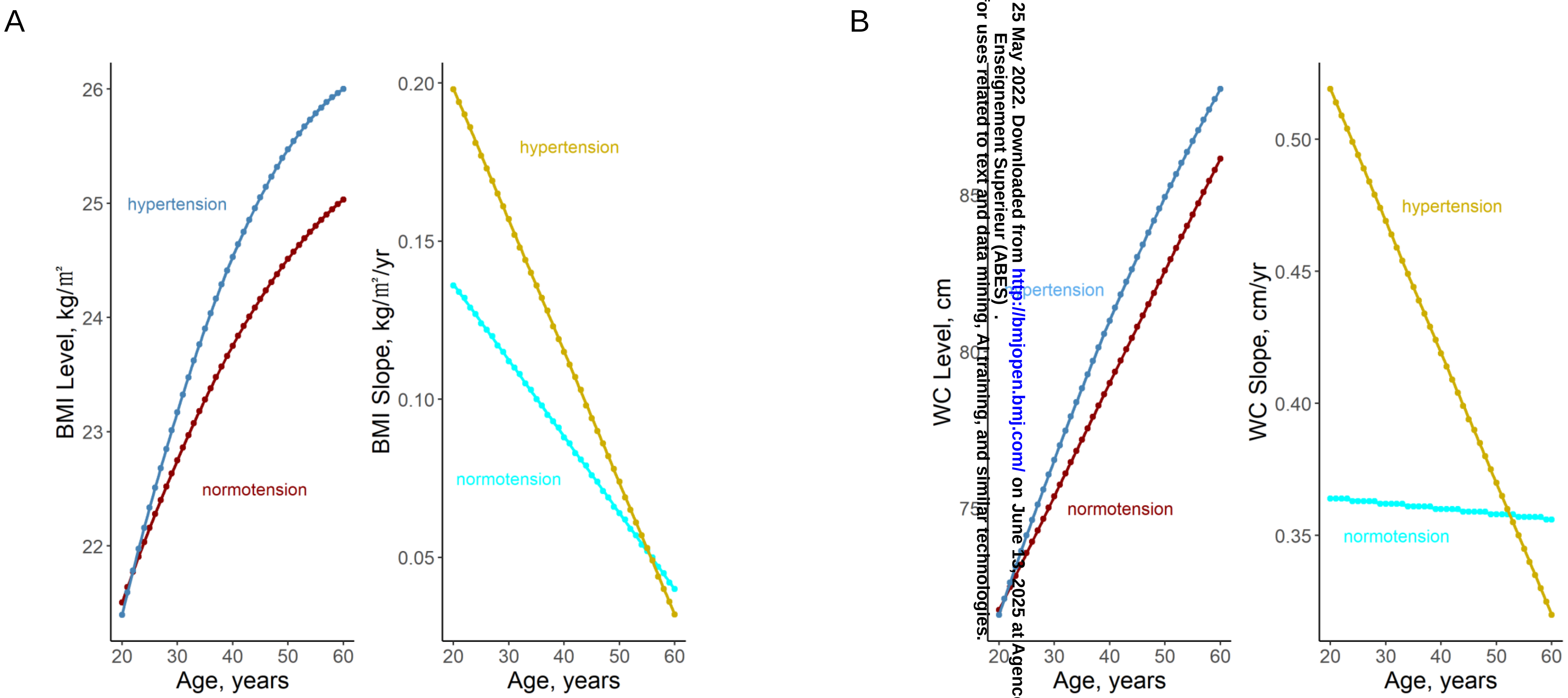
Study variables are presented as mean (SD), median [interquartile range] or n (%), appropriately. BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; WC, waist circumference.

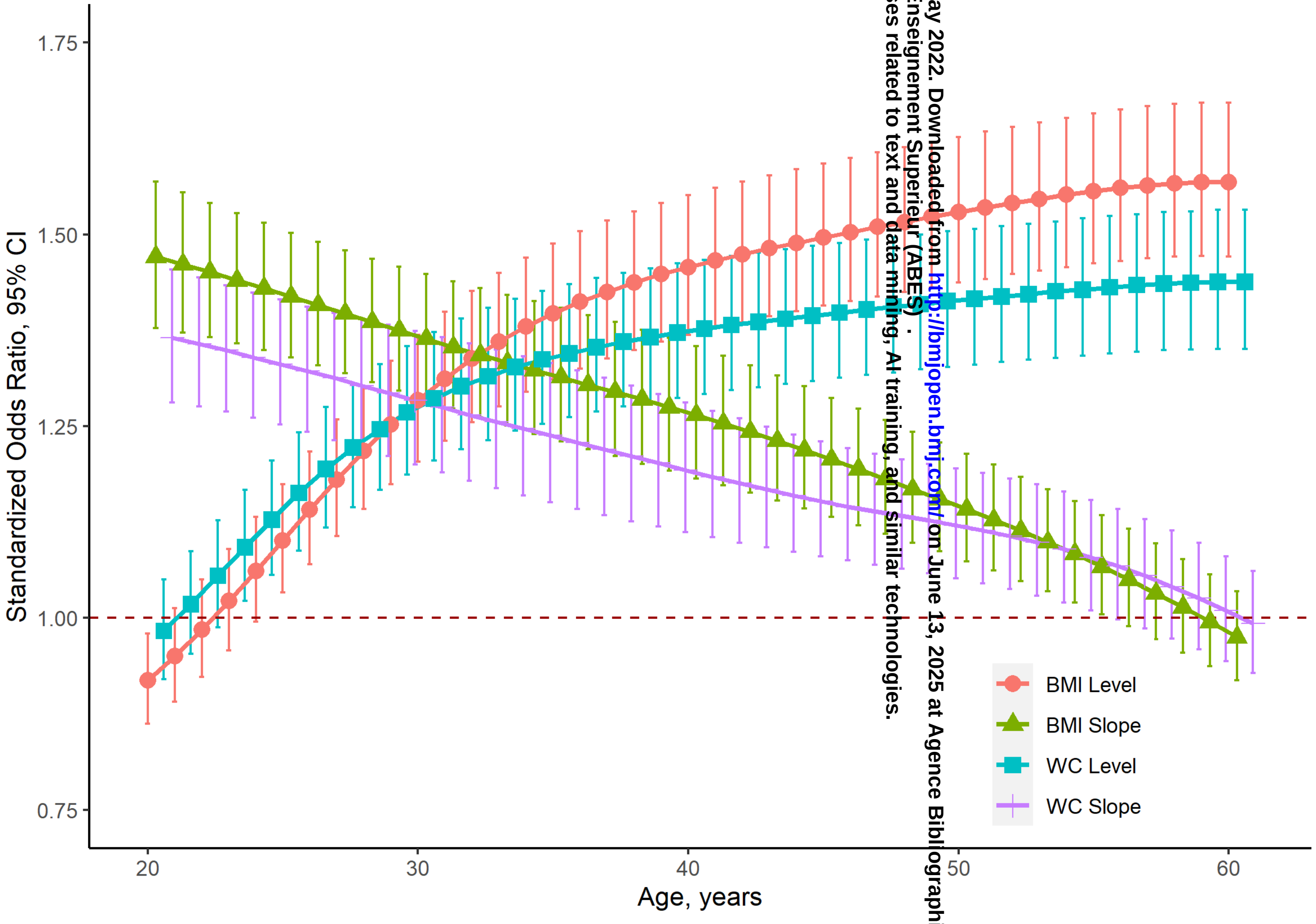
Table 3. Hazard Ratios and 95% CIs of Joint Trajectory Groups for Incident Hypertension

	Model 1	Model 2	Model 3	Model 4
Joint trajectory groups				
Normal	Reference	Reference	Reference	Reference
WC-increasing	1.55 (1.31, 1.83)	1.51 (1.25, 1.82)	1.41 (1.17, 1.71)	1.43 (1.19, 1.74)
BM-increasing	1.69 (1.36, 2.10)	1.47 (1.16, 1.87)	1.48 (1.17, 1.89)	1.51 (1.19, 1.92)
BMI&WC-increasing	1.98 (1.71, 2.28)	1.74 (1.44, 2.10)	1.73 (1.42, 2.10)	1.76 (1.45, 2.14)
Covariates				
Baseline Age		1.07 (1.06, 1.08)	1.07 (1.06, 1.08)	1.07 (1.06, 1.08)
Female		0.77 (0.69, 0.87)	0.89 (0.79, 1.00)	1.01 (0.85, 1.18)
Baseline BMI		1.10 (1.08, 1.13)	1.07 (1.05, 1.10)	1.07 (1.05, 1.10)
Baseline SBP			1.03 (1.02, 1.04)	1.03 (1.02, 1.04)
Smoker				1.12 (0.96, 1.30)
Drinker				1.10 (0.96, 1.26)

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure.


A
high-increasing, 15.04%
low-increasing, 84.96%
BMI, kg/m²
Age, years
20
22
24
26
28
30
40
50
60
B
high-increasing, 19.47%
low-increasing, 80.53%
WC, cm
Age, years
70
75
80
85
90
95
20
30
40
50
60


A
BMI Level, kg/㎡
hypertension
normotension
Age, years
BMI Slope, kg/㎡/yr
hypertension
normotension
Age, years
B
WC Level, cm
hypertension
normotension
Age, years
WC Slope, cm/yr
hypertension
normotension
Age, years


Standardized Odds Ratio, 95% CI
1.75
1.50
1.25
1.00
0.75
20
30
40
50
60
Age, years
BMI Level
BMI Slope
WC Level
WC Slope

Supplemental Materials

Joint Trajectories of Body Mass Index and Waist Circumference in Early to Mid-life Adulthood and Incident Hypertension: the China Health and Nutrition Survey

Yanlin Qu [1,2], Chunxia Li [1,2], Jiali Lv [1,2], Bingbing Fan [1,2], Ying Liu [1,2], Chang Su [3], Xiangjuan Zhao [4 #]

[1] Department of Biostatistics, School of Public Health, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

[2] Institute for Medical Dataology, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

[3] National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, Beijing 102206, China

[4] Maternal and Child Health Care Hospital of Shandong Province, Jinan 250012, China

 # Correspondence & Reprints:

Xiangjuan Zhao, MD.

Maternal and Child Health Care Hospital of Shandong Province, Jinan 250014, China.

Email: xzhao6@hotmail.com

Trajectory Analysis

Repeated trajectory analyses were performed to identify the latent classes by changing the number of groups from 2 to 3, with the same starting values calculated from the 1-group model. The shapes and optimal number of groups were determined by the following criteria: 1) Bayesian information criterion (BIC) decreased at least 20; 2) high mean posterior class membership probabilities (> 0.65); 3) high mean posterior probabilities (> 0.7). Estimation of latent class models was performed with lcmm (version 1.7.8) package in R (version 4.0.4). To avoid convergence towards local maxima, LCGMM models with 2 or 3 classes were performed for several times with different sets of random starting value based on 1-class model. Finally, according to criteria above, a model of quadratic parameters with two classes was chosen for both BMI and WC as the best fit. The final model of BMI was described as:

$$BMI_{ij}\,|_{c_{i=g}} = (\upsilon_{0g} + u_{0ig}) + (\upsilon_{1g} + u_{1ig})age + (\upsilon_{2g} + u_{2ig})age^2 + \varepsilon_{ij}$$

where υ =(υ_{0g}, υ_{1g}, υ_{2g}) is a vector of fixed effect parameters in the group "g", u =(u_{0ig}, u_{1ig}, u_{2ig}) is a vector of random effect parameters of the individual "i" in the group "g", ε_{ij} is an unknown error term (the model of WC is similar with BMI).

Table S1. Baseline characteristics of participants included and excluded.

Variable	Excluded	Included	*P*-Value
N	26777	6571	
Age, y	30.8 (23.0)	35.4 (8.6)	<0.001
Male, n (%)	12931 (48.3)	3063 (46.6)	0.017
BMI, kg/m^2	20.9 (4.8)	22.0 (2.7)	<0.001
WC, cm	75.9 (15.6)	75.8 (8.4)	0.365
SBP, mm Hg	116.0 [102.0, 129.0]	110.0 [103.0, 120.0]	<0.001
DBP, mm Hg	75.0 [68.0, 81.0]	74.0 [70.0, 80.0]	<0.001
Smoker, n (%)	4475 (27.2)	2123 (32.5)	<0.001
Drinker, n (%)	5162 (29.4)	2312 (35.5)	<0.001

BMI indicates body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; WC, waist circumference.

Table S2. Latent Class Growth Mixture Models (LCGMM) results of model fitting process for BMI.

No. Latent class	Polynomial degree	Log-Lik	BIC	% Participants per class	Mean posterior probabilities	% Posterior probabilities > 70%
1	Linear	-59740	119525	100	na	na
	Quadratic	-59623	119308	100	na	na
	Cubic	-59604	119289	100	na	na
2	Linear	-59299	118678	9.98/90.02	0.79/0.95	66.92/95.38
	Quadratic	**-59122**	**118351**	**84.96/15.04**	**0.93/0.81**	**93.19/72.37**
	Cubic	-59120	118373	15.17/84.83	0.82/0.93	73.22/93.00
3	Linear	-59190	118495	24.97/72.12/2.91	0.74/0.87/0.79	56.98/84.30/67.02
	Quadratic	-58989	118128	73.40/23.09/3.51	0.88/0.73/0.78	85.32/57.61/64.07
	Cubic	-58985	118155	4.34/78.45/17.21	0.74/0.90/0.78	58.25/88.13/54.38

BMI indicate body mass index; NO. Latent class: latent class number of the model; Log-Lik: the maximum Log-Likelihood; BIC: the Bayesian information Criterion; % Participants per class: proportion of participants per class; The best fitting model is highlighted in bold characters. (na: not applicable)

Table S3. Latent Class Growth Mixture Models (LCGMM) results of model fitting process for WC

No. Latent class	Polynomial degree	Log-Lik	BIC	% Participants per class	Mean posterior probabilities	% Posterior probabilities > 70%
1	Linear	-98380	196839	100	na	na
	Quadratic	-98387	196836	100	na	na
	Cubic	-98397	196839	100	na	na
2	Linear	-98042	196163	83.32/16.68	0.92/0.78	91.98/65.42
	Quadratic	**-97946**	**195998**	**80.53/19.47**	**0.92/0.80**	**91.35/68.67**
	Cubic	-97940	196012	80.18/19.82	0.92/0.80	91.41/69.79
3	Linear	-98008	195918	50.95/36.74/12.81	0.95/0.89/0.7[illegible]	96.19/86.74/63.06
	Quadratic	-97875	195900	54.95/9.34/35.71	0.80/0.77/0.70	70.99/64.12/50.57
	Cubic	-97866	195112	50.46/36.74/12.80	0.71/0.87/0.68	52.88/84.85/42.74

WC indicate waist circumference; NO. Latent class: latent class number of the model; Log-Lik: the maximum Log-Likelihood; BIC: the Bayesian information Criterion; % Participants per class: proportion of participants per class. The best fitting model is highlighted in bold characters. (na: not applicable)

Table S4. Parameters estimates for the best fitting 2-class quadratic Latent Class Growth Mixture Model for BMI.

		Intercept (se)*	Linear (se)	Quadratic (se)
Fixed effect				
	Group 1	23.519 (0.0487)	0.077 (0.0024)	-5×10^{-5} (0.0002)
	Group 2	27.177 (0.1337)	0.155 (0.0076)	-0.009 (0.0005)
Random effects: variance-covariance matrix				
σ^2_{int} = 3.88				
$\sigma^2_{linear\ slope}$ = 0.0105				
$\sigma^2_{quadratic\ slope}$ < 0.001				
σ^2_{error} = 1.24				

se = standard error; BMI = body mass index.

*: Intercept interpreted as the expected level of BMI in kg/m^2 at 42 years of age (centering to the mean age of the sample)

Table S5. Parameters estimates for the best fitting 2-class quadratic Latent Class Growth Mixture Model for WC.

		Intercept (se)*	Linear (se)	Quadratic (se)
Fixed effect				
	Group 1	76.890 (0.1459)	0.338 (0.0084)	0.004 (0.0006)
	Group 2	89.963 (0.3340)	0.501 (0.0226)	-0.020 (0.0015)
Random effects: variance-covariance matrix				
$\sigma^2_{int} = 24.31$				
$\sigma^2_{linear\ slope} = 0.0984$				
$\sigma^2_{quadratic\ slope} < 0.001$				
$\sigma^2_{error} = 5.38$				

se = standard error; WC = waist circumference.

*: Intercept interpreted as the expected level of WC in cm at 42 years of age (centering to the mean age of the sample)

Table S6. Hazard Ratios and 95% of BMI Trajectory Groups for Incident Hypertension

	Model 1	Model 2	Model 3	Model 4
Trajectory groups				
Low-increasing group	Reference	Reference	Reference	Reference
High-increasing group	1.79 (1.58, 2.03)	1.44 (1.22, 1.69)	1.47 (1.25, 1.73)	1.49 (1.26, 1.75)
Covariates				
Age, y		1.07 (1.06, 1.08)	1.06 (1.05, 1.07)	1.06 (1.05, 1.07)
Female		0.74 (0.67, 0.83)	0.86 (0.77, 0.96)	0.97 (0.83, 1.14)
Baseline BMI		1.09 (1.06, 1.12)	1.07 (1.04, 1.10)	1.07 (1.04, 1.10)
Baseline WC		1.01 (1.00,1.02)	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)
Baseline SBP			1.03 (1.02, 1.04)	1.03 (1.02, 1.04)
Smoker				1.11 (0.96, 1.30)
Drinker				1.11 (0.97, 1.27)

BMI, body mass index; SBP, systolic blood pressure; WC, waist circumference.

Table S7. Hazard Ratios and 95% of WC Trajectory Groups for Incident Hypertension

	Model 1	Model 2	Model 3	Model 4
Trajectory groups				
Low-increasing group	Reference	Reference	Reference	Reference
High-increasing group	1.71 (1.53, 1.93)	1.45 (1.24, 1.69)	1.42 (1.21, 1.66)	1.43 (1.22, 1.68)
Covariates				
Age, y		1.07 (1.06, 1.08)	1.06 (1.05, 1.07)	1.06 (1.05, 1.07)
Female		0.80 (0.72, 0.90)	0.92 (0.82, 1.03)	1.04 (0.89, 1.23)
Baseline BMI		1.10 (1.07, 1.13)	1.08 (1.05, 1.11)	1.08 (1.05, 1.11)
Baseline WC		1.01 (1.00, 1.02)	1.00 (0.99, 1.01)	1.01 (1.00, 1.02)
Baseline SBP			1.03 (1.02, 1.04)	1.03 (1.02, 1.04)
Smoker				1.12 (0.96, 1.30)
Drinker				1.10 (0.96, 1.26)

BMI, body mass index; SBP, systolic blood pressure; WC, waist circumference.

Table S8. Model-estimated levels and linear slopes of BMI in means (SD) by incident hypertension at follow-up

	BMI Level (kg/m^2)			BMI Slope (kg/m^2/year)		
Age, (years)	NTN	HTN	*P*-Value	NTN	HTN	*P*-Value
20	21.50 (2.03)	21.40 (1.95)	0.068	0.14 (0.17)	0.20 (0.21)	<0.001
21	21.64 (1.96)	21.59 (1.87)	0.407	0.13 (0.17)	0.19 (0.20)	<0.001
22	21.77 (1.90)	21.78 (1.82)	0.828	0.13 (0.16)	0.19 (0.19)	<0.001
23	21.90 (1.85)	21.97 (1.78)	0.199	0.13 (0.16)	0.19 (0.19)	<0.001
24	22.03 (1.82)	22.16 (1.76)	0.019	0.13 (0.15)	0.18 (0.18)	<0.001
25	22.16 (1.80)	22.34 (1.76)	<0.001	0.12 (0.15)	0.18 (0.17)	<0.001
26	22.28 (1.79)	22.51 (1.77)	<0.001	0.12 (0.14)	0.17 (0.17)	<0.001
27	22.40 (1.79)	22.68 (1.80)	<0.001	0.12 (0.14)	0.17 (0.16)	<0.001
28	22.52 (1.80)	22.85 (1.84)	<0.001	0.12 (0.13)	0.16 (0.15)	<0.001
29	22.64 (1.82)	23.01 (1.88)	<0.001	0.11 (0.13)	0.16 (0.15)	<0.001
30	22.75 (1.84)	23.17 (1.94)	<0.001	0.11 (0.12)	0.16 (0.14)	<0.001
31	22.86 (1.87)	23.32 (1.99)	<0.001	0.11 (0.12)	0.15 (0.13)	<0.001
32	22.97 (1.90)	23.48 (2.05)	<0.001	0.11 (0.11)	0.15 (0.13)	<0.001
33	23.07 (1.93)	23.62 (2.11)	<0.001	0.10 (0.11)	0.14 (0.12)	<0.001
34	23.18 (1.97)	23.76 (2.17)	<0.001	0.10 (0.10)	0.14 (0.11)	<0.001
35	23.28 (2.00)	23.90 (2.23)	<0.001	0.10 (0.10)	0.14 (0.11)	<0.001
36	23.38 (2.04)	24.04 (2.28)	<0.001	0.10 (0.09)	0.13 (0.10)	<0.001
37	23.48 (2.07)	24.16 (2.33)	<0.001	0.09 (0.09)	0.13 (0.10)	<0.001
38	23.57 (2.11)	24.29 (2.38)	<0.001	0.09 (0.09)	0.12 (0.09)	<0.001
39	23.66 (2.14)	24.41 (2.43)	<0.001	0.09 (0.08)	0.12 (0.09)	<0.001
40	23.75 (2.17)	24.53 (2.47)	<0.001	0.09 (0.08)	0.11 (0.08)	<0.001
41	23.84 (2.20)	24.64 (2.51)	<0.001	0.09 (0.07)	0.11 (0.08)	<0.001
42	23.92 (2.22)	24.75 (2.55)	<0.001	0.08 (0.07)	0.11 (0.07)	<0.001
43	24.01 (2.25)	24.85 (2.58)	<0.001	0.08 (0.07)	0.10 (0.07)	<0.001
44	24.08 (2.27)	24.96 (2.60)	<0.001	0.08 (0.07)	0.10 (0.07)	<0.001
45	24.16 (2.28)	25.05 (2.62)	<0.001	0.08 (0.07)	0.09 (0.07)	<0.001
46	24.24 (2.30)	25.14 (2.64)	<0.001	0.07 (0.07)	0.09 (0.07)	<0.001
47	24.31 (2.31)	25.23 (2.65)	<0.001	0.07 (0.07)	0.09 (0.07)	<0.001

48	24.38 (2.32)	25.32 (2.66)	<0.001	0.07 (0.07)	0.08 (0.07)	<0.001
49	24.45 (2.33)	25.40 (2.66)	<0.001	0.07 (0.07)	0.08 (0.07)	<0.001
50	24.51 (2.33)	25.47 (2.66)	<0.001	0.06 (0.07)	0.07 (0.07)	<0.001
51	24.58 (2.33)	25.54 (2.65)	<0.001	0.06 (0.07)	0.07 (0.07)	<0.001
52	24.64 (2.33)	25.61 (2.64)	<0.001	0.06 (0.07)	0.06 (0.08)	0.008
53	24.69 (2.33)	25.67 (2.62)	<0.001	0.06 (0.07)	0.06 (0.08)	0.075
54	24.75 (2.33)	25.73 (2.60)	<0.001	0.05 (0.08)	0.06 (0.09)	0.316
55	24.80 (2.32)	25.79 (2.58)	<0.001	0.05 (0.08)	0.05 (0.09)	0.766
56	24.85 (2.31)	25.84 (2.56)	<0.001	0.05 (0.08)	0.05 (0.10)	0.737
57	24.90 (2.30)	25.88 (2.53)	<0.001	0.05 (0.09)	0.04 (0.10)	0.367
58	24.95 (2.29)	25.93 (2.50)	<0.001	0.04 (0.09)	0.04 (0.11)	0.159
59	25.00 (2.28)	25.96 (2.48)	<0.001	0.04 (0.10)	0.04 (0.11)	0.063
60	25.03 (2.27)	26.00 (2.45)	<0.001	0.04 (0.10)	0.03 (0.12)	0.023

NTN = normotension; HTN = hypertension.

Table S9. Model-estimated levels and linear slopes of WC in means (SD) by incident hypertension at follow-up

	WC Level (cm)			WC Slope (cm/year)		
Age, (years)	NTN	HTN	*P*-Value	NTN	HTN	*P*-Value
20	71.75 (4.90)	71.60 (4.52)	0.271	0.36 (0.50)	0.52 (0.57)	<0.001
21	72.12 (4.80)	72.12 (4.45)	0.997	0.36 (0.48)	0.51 (0.55)	<0.001
22	72.48 (4.75)	72.63 (4.44)	0.272	0.36 (0.46)	0.51 (0.53)	<0.001
23	72.84 (4.73)	73.13 (4.48)	0.032	0.36 (0.45)	0.50 (0.51)	<0.001
24	73.21 (4.76)	73.64 (4.58)	0.002	0.36 (0.43)	0.50 (0.49)	<0.001
25	73.57 (4.81)	74.13 (4.71)	<0.001	0.36 (0.42)	0.49 (0.47)	<0.001
26	73.93 (4.89)	74.63 (4.88)	<0.001	0.36 (0.40)	0.49 (0.45)	<0.001
27	74.30 (5.00)	75.11 (5.06)	<0.001	0.36 (0.38)	0.48 (0.43)	<0.001
28	74.66 (5.12)	75.59 (5.26)	<0.001	0.36 (0.37)	0.48 (0.41)	<0.001
29	75.02 (5.25)	76.07 (5.47)	<0.001	0.36 (0.35)	0.47 (0.39)	<0.001
30	75.38 (5.38)	76.54 (5.68)	<0.001	0.36 (0.34)	0.47 (0.37)	<0.001
31	75.75 (5.25)	77.01 (5.90)	<0.001	0.36 (0.32)	0.46 (0.35)	<0.001
32	76.11 (5.67)	77.47 (6.10)	<0.001	0.36 (0.31)	0.46 (0.33)	<0.001
33	76.47 (5.81)	77.93 (6.30)	<0.001	0.36 (0.29)	0.45 (0.31)	<0.001
34	76.83 (5.95)	78.38 (6.50)	<0.001	0.36 (0.28)	0.45 (0.30)	<0.001
35	77.19 (6.08)	78.83 (6.68)	<0.001	0.36 (0.26)	0.44 (0.28)	<0.001
36	77.55 (6.21)	79.27 (6.85)	<0.001	0.36 (0.25)	0.44 (0.26)	<0.001
37	77.91 (6.33)	79.71 (7.01)	<0.001	0.36 (0.24)	0.43 (0.25)	<0.001
38	78.27 (6.44)	80.14 (7.15)	<0.001	0.36 (0.23)	0.43 (0.23)	<0.001
39	78.63 (6.54)	80.56 (7.28)	<0.001	0.36 (0.22)	0.42 (0.22)	<0.001
40	78.99 (6.63)	80.99 (7.39)	<0.001	0.36 (0.21)	0.42 (0.20)	<0.001
41	79.35 (6.71)	81.40 (7.49)	<0.001	0.36 (0.20)	0.41 (0.19)	<0.001
42	79.71 (6.78)	81.82 (7.58)	<0.001	0.36 (0.19)	0.41 (0.18)	<0.001
43	80.07 (6.83)	82.22 (7.64)	<0.001	0.36 (0.19)	0.40 (0.17)	<0.001
44	80.43 (6.88)	82.62 (7.70)	<0.001	0.36 (0.18)	0.40 (0.17)	<0.001
45	80.79 (6.92)	83.02 (7.73)	<0.001	0.36 (0.18)	0.39 (0.17)	<0.001
46	81.15 (6.94)	83.41 (7.75)	<0.001	0.36 (0.18)	0.39 (0.17)	<0.001
47	81.51 (6.95)	83.80 (7.75)	<0.001	0.36 (0.18)	0.38 (0.17)	<0.001

48	81.87 (6.96)	84.18 (7.74)	<0.001	0.36 (0.19)	0.38 (0.17)	<0.001
49	82.23 (6.95)	84.56 (7.72)	<0.001	0.36 (0.19)	0.37 (0.18)	0.006
50	82.59 (6.93)	84.93 (7.67)	<0.001	0.36 (0.20)	0.37 (0.19)	0.074
51	82.94 (6.90)	85.30 (7.72)	<0.001	0.36 (0.21)	0.36 (0.20)	0.355
52	83.30 (6.86)	85.66 (7.55)	<0.001	0.36 (0.22)	0.36 (0.22)	0.883
53	83.66 (6.81)	86.02 (7.46)	<0.001	0.36 (0.23)	0.35 (0.23)	0.586
54	84.02 (6.76)	86.37 (7.37)	<0.001	0.36 (0.24)	0.35 (0.25)	0.248
55	84.37 (6.70)	86.72 (7.26)	<0.001	0.36 (0.25)	0.34 (0.26)	0.091
56	84.73 (6.63)	87.06 (7.14)	<0.001	0.36 (0.26)	0.34 (0.28)	0.030
57	85.09 (6.56)	87.40 (7.02)	<0.001	0.36 (0.28)	0.33 (0.30)	0.010
58	85.45 (6.48)	87.73 (6.89)	<0.001	0.36 (0.29)	0.33 (0.32)	0.003
59	85.80 (6.41)	88.06 (6.75)	<0.001	0.36 (0.31)	0.32 (0.33)	0.001
60	86.16 (6.34)	88.38 (6.61)	<0.001	0.36 (0.32)	0.32 (0.35)	<0.001

NTN = normotension; HTN = hypertension.

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-4	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	1-4
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	7		
Objectives	3	State specific objectives, including any prespecified hypotheses	7		
Methods					
Study Design	4	Present key elements of study design early in the paper	8		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8		

Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	8	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	9	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	9
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8, 9		8, 9

Bias	9	Describe any efforts to address potential sources of bias	9, 10		
Study size	10	Explain how the study size was arrived at	8		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	8-10		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	9, 10		
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	8, 18

				RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	8
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	8	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	8
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)	10		
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure	10, 11		

		category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11-13		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	10, 11		
Discussion					
Key results	18	Summarise key results with reference to study objectives	13		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15, 16	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	15, 16
Interpretation	20	Give a cautious overall interpretation of results considering objectives,	13-16		

		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results	16		
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17		
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	18

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

BMJ Open

Joint Trajectories of Body Mass Index and Waist Circumference in Early to Mid-life Adulthood and Incident Hypertension: the China Health and Nutrition Survey

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-059556.R2
Article Type:	Original research
Date Submitted by the Author:	07-Apr-2022
Complete List of Authors:	Qu, Yanlin; Shandong University Cheeloo College of Medicine, Department of Biostatistics, School of Public Health; Shandong University Cheeloo College of Medicine, Institute for Medical Dataology Li, Chunxia; Shandong University, Department of Biostatistics; Shandong University Lv, Jiali; Shandong University, Department of Biostatistics; Shandong University Fan, Bingbing ; Shandong University Liu, Ying; Shandong University Cheeloo College of Medicine, Department of Biostatistics, School of Public Health; Shandong University Cheeloo College of Medicine, Institute for Medical Dataology Su, Chang; Chinese Center for Disease Control and Prevention National Institute for Nutrition and Health Zhao, Xiangjuan; Shandong Province Maternal and Child Health Care Hospital
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health, Cardiovascular medicine
Keywords:	Hypertension < CARDIOLOGY, EPIDEMIOLOGY, PUBLIC HEALTH

SCHOLARONE™
Manuscripts

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Joint Trajectories of Body Mass Index and Waist Circumference in Early to Mid-life Adulthood and Incident Hypertension: the China Health and Nutrition Survey

Yanlin Qu [1,2], Chunxia Li [1,2], Jiali Lv [1,2], Bingbing Fan [1,2], Ying Liu [1,2], Chang Su [3], Xiangjuan Zhao [4 #]

[1] Department of Biostatistics, School of Public Health, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

[2] Institute for Medical Dataology, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

[3] National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, Beijing 102206, China

[4] Maternal and Child Health Care Hospital of Shandong Province, Jinan 250012, China

Running Title: Joint trajectories of BMI and WC and hypertension

 # Correspondence & Reprints:

Xiangjuan Zhao, MD.

Maternal and Child Health Care Hospital of Shandong Province, Jinan 250014, China.

Email: xzhao6@hotmail.com

The authors do not have any conflict of interest.

Text word count: 3418 (excluding abstract and references)

Abstract word count: 296

Number of references: 32

Number of tables: 3

Number of figures: 3

ABSTRACT

Objective This longitudinal study aims to identify distinct trajectories of body mass index (BMI) and waist circumference (WC) during 20~60 years old, and explore their joint effect on incident hypertension.

Design A longitudinal cohort study.

Setting China Health and Nutrition Survey 1993–2011.

Participants The longitudinal cohort included 6571 participants (3063 males) who had BMI and WC repeatedly measured 3~7 times before incident hypertension or loss to follow-up.

Outcomes Hypertension was defined as SBP/DBP >140/90 mmHg or diagnosis by medical records or taking anti-hypertensive medication.

Results Two distinct trajectories were characterized for both BMI and WC: low-increasing and high-increasing. Jointly, subjects were divided into four groups: normal (n=4963), WC-increasing (n=620), BMI-increasing (n=309), and BMI&WC-increasing (n=679). Compared with the normal group, the adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for hypertension were 1.43 (1.19~1.74), 1.51 (1.19~1.92), and 1.76 (1.45, 2.14) for WC-increasing, BMI-increasing and BMI&WC-increasing group, respectively. The model-estimated levels and slopes of BMI and WC were calculated at each age point in one-year interval according to the model parameters and their first derivatives, respectively. The associations between model-estimated levels and hypertension increased with age, with adjusted odds ratios (ORs) and 95% CIs ranging from 0.92 (0.86~0.98) to 1.57 (1.47~1.67) for BMI, and 0.98 (0.92~1.05) to 1.44 (1.35~1.53) for WC. Conversely, the ORs (95% CIs) of level-adjusted linear slopes decreased with age, ranging from 1.47 (1.38~1.57) to 0.97 (0.92~1.03) for BMI, and 1.36 (1.28~1.45) to 0.99 (0.93~1.06) for WC.

Conclusions Our study demonstrates the joint trajectories of BMI and WC have significant effect on future hypertension risk, and the changing slopes of BMI and WC during young

adulthood are independent risk factors. Both BMI and WC should be paid more attention to prevent hypertension, and young adulthood may be a crucial period for intervention.

Key words: Body mass index; Waist circumference; Hypertension; Trajectory; Longitudinal studies

Strengths and limitations of this study

- The community-based longitudinal study, with large sample size and repeated measurements, was used to explore the distinct trajectories of BMI and WC in early to mid-life adulthood.
- Distinct trajectories of BMI and WC were identified by the latent class growth mixed model, and their joint effect on incident hypertension was explored.
- The trajectory parameters, model-estimated levels and linear slopes, were examined to identify the critical period for early prevention of hypertension.
- Unmeasurable covariates may cause potential confounding bias.

ABBREVIATIONS:

BMI = body mass index

WC = waist circumference

SBP = Systolic Blood Pressure

DBP = Diastolic Blood Pressure

CHNS = The China Health and Nutrition Survey

LCGMM = latent class growth mixed model

SD = standard deviation

HR = hazard ratio

OR = odds ratio

CI = confidence interval

INTRODUCTION

As a major risk factor for cardiovascular disease, hypertension is a severe problem in public health[1]. The prevalence of hypertension has increased rapidly over decades[2], causing heavy burden to the health system in China[3,4]. Obesity is regarded as an important risk factor for incident hypertension[5,6], and it could be evaluated by many indicators, such as body mass index (BMI) and waist circumference (WC)[7,8]. The relationship between single obesity indicators and incident hypertension has been well-established in observation studies[5-9]. However, the joint effect of those indicators on hypertension is largely unknown in a life course perspective.

Generally, obesity is divided into systemic obesity and abdominal obesity[8,9]. Systemic obesity is mainly defined by BMI, while the abdominal obesity is often defined by WC[8]. The levels of BMI and WC reflect different aspects of obesity[5-12], and their joint trajectories present the heterogeneous longitudinal changing patterns of body shape. Previous research has showed that BMI and WC were associated with hypertension in both cross-sectional[5-12] and longitudinal studies[13-15]. However, these studies mainly focused on the BMI and WC separately[10-15], and the joint effect of BMI and WC trajectories on incident hypertension is still unclarified. We hypothesized that individuals in different joint trajectory group of BMI and WC may present different risk of hypertension, and a critical period may exist in early to mid-life adulthood for early prevention of hypertension.

Using data from the China Health and Nutrition Survey, this study aims to identify BMI and WC trajectories during early to mid-life adulthood (20~60 years), explore the joint effect of BMI and WC trajectories on incident hypertension, and determine the potential critical period for the development of hypertension.

Subjects AND METHODS

Study cohort

As an ongoing longitudinal cohort, the China Health and Nutrition Survey (CHNS) is implemented by national and local governments[16,17]. It is aimed at understanding how the economic and social transformation of Chinese society affects the health and nutritional status of Chinese population. Data from Beijing, Shanghai, Guizhou, Henan, Chongqing, Heilongjiang, Liaoning, Jiangsu, Zhejiang, Hubei, Hunan, Shaanxi, Shandong, Guangxi, and Yunnan were collected by a multi-stage, random cluster process. During 1989~2011, a total of nine cross-sectional surveys have been completed, covering 4400 households with 33348 individuals.

In this current study, we excluded individuals younger than 20 years old or older than 60 years old (n = 12147), with BMI lower than15 kg/m^2 or higher than 40 kg/m^2 (n = 799), with WC greater than120 cm (n = 1632), and with less than three follow-up visits before loss to follow-up or incident hypertension (n = 12199). Finally, 6571 normotensive adult subjects, with 3-7 times visits, were included in this study. The mean follow-up time was 11.8 years (sd = 4.2 years). BMI and WC measurements after the onset of hypertension (outcome) were excluded in our analyses. **Supplement Table S1** shows excluded respondents (n = 26777) were generally younger male, with lower baseline BMI, higher baseline systolic blood pressure (SBP) and diastolic blood pressure (DBP), lower proportion of smokers and alcohol consumers than those included.

The protocol was approved by the Ethics Committee of the National Institute for Nutrition and Health, China CDC (NO. 201524). Informed consent was obtained from all subjects before the investigation.

Examinations

Standing height without shoes was measured to the nearest 0.2 centimeters using a portable SECA stadiometer (SECA, Hamburg, Germany) at each follow up[18]. Weight was measured to the nearest 0.1 kilograms in light clothing without shoes on a dedicated scale that was routinely calibrated[18]. We calculated BMI as weight in kilograms divided by height in meters squared. Smoker was defined as ever smoking cigarettes (including ex-smoker and current smoker). Alcohol drinker was defined as alcohol consumption (including beer, liquor or wine) ⩾25g (for male) or ⩾15g (for female) per week.

WC was defined as the midway between the lowest costal margin and the superior margin of the iliac crest, and was measured in centimeters using a SECA tapeline during 1993~2011[18]. After resting five minutes in a seated position, SBP and DBP were measured three times on the right upper arm using a standard mercury sphygmomanometer during 1991~2011[18]. The mean of the last two measurements were used for analyses.

Outcome

Hypertension was defined as SBP/DBP ⩾140/90 mmHg and/or diagnosis by medical records and/or taking antihypertensive medication. Data for SBP, DBP, taking antihypertensive medication and incidence of diagnosis hypertension were first collected in 1991, and subsequently in 1993, 1997, 2000, 2004, 2006, 2009 and 2011 survey.

Statistical methods

The latent class growth mixed model (LCGMM) was used to identify different trajectory patterns of BMI and WC[19]. The latent class trajectories of BMI and WC were specified as functions of age (centered to 42 years, the mean age of the cohort). Multiple LCGMMs with different trajectory shapes including linear and nonlinear parameters were tested using the strategy we previously described[19]. We chose the best-fitting model for BMI and WC trajectory according to the BIC criterion while ensuring that each group has an acceptable proportion of the population and posterior probability. In the joint analyses, comprehensively considering the trajectories of BMI and WC, subjects were assigned into different joint groups.

The relationship between the joint group membership and incident hypertension were explored using Cox proportional hazard models. We established four models: model 1 with no covariates, model 2 with adjustment for baseline age, gender, and baseline BMI, model 3 with further adjustment for baseline SBP, and model 4 with further adjustment for smoking and alcohol drinking. Baseline WC was not adjusted due to its collinearity with baseline BMI (r = 0.68).

According to the model parameters and their first derivatives, the model-estimated levels and linear slopes of BMI and WC were calculated at each age point in one-year interval, respectively[20]. Logistic regression models were used to examine the associations of model-estimated levels and linear slopes of BMI and WC at each age point with incident hypertension. Before logistic regression analyses, the model-estimated linear slope values of BMI and WC at each age point were adjusted for their corresponding levels to avoid collinearity of levels and linear slopes in the same model[20,21]. Standardized odds ratios (ORs) of levels and level-adjusted slopes of BMI and WC for incident hypertension were estimated, adjusted for gender, baseline SBP, smoking and alcohol drinking.

Variables were described using mean (sd), median [interquartile range] and n (%), as appropriate. All analyses were performed using R version 4.0.4. Hypothesis tests were 2-sided, and P < .05 was considered statistically significant.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

Table 1 presents baseline characteristics of study variables by incident hypertension groups during follow-up. Incident hypertension subjects (n = 1415) were more likely to be older males, with higher BMI, WC, SBP and DBP, higher proportions of smokers and alcohol drinkers than normotensives.

Supplement Table S2 and **S3** summarize LCGMM results of the BMI and WC trajectory model fitting process. We fitted models from one class to three classes of linear, quadratic and cubic curves. According to statistical criteria above, a model of quadratic parameters with two classes was chosen for both BMI and WC as the best fit. **Supplement Table S4** and **S5** present parameter estimates for the best fitting 2-class quadratic latent class growth mixed model of BMI and WC, respectively.

Figure 1 shows the longitudinal trajectories of BMI (**Figure 1A**) and WC (**Figure 1B**) during 20~60 years old for 6571 participants. Both BMI and WC had two distinct trajectories, labeled as low-increasing (n (%) = 5583 (84.96%) for BMI and 5272 (80.53%) for WC) and high-increasing (n (%) = 988 (15.04%) for BMI, and 1299 (19.47%) for WC). Compared with the subjects in low-increasing group, those in the high-increasing group had similar predicted levels at age 20 years but higher linear slopes from 20 years to 60 years.

Supplement Table S6 shows hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between the BMI trajectory group membership and incident hypertension. Compared with the BMI low-increasing group, HR (95% CI) for the BMI high-increasing group was 1.49 (1.26, 1.75), adjusted for baseline age, gender, baseline BMI, baseline WC, baseline SBP, smoking and alcohol drinking. **Supplement Table S7** presents HRs and 95% CIs for the relationship between the WC trajectory classes and incident hypertension. Compared with the WC low-increasing group, HR (95% CI) for the WC high-increasing group was 1.43 (1.22, 1.68), adjusted for the same covariates above.

Jointly, subjects were divided into four joint groups according to their BMI and WC trajectories, named as normal (n = 4963), WC-increasing (n = 620), BMI-increasing (n = 309), and BMI&WC-increasing (n = 679). Individuals in the normal, WC-increasing, BMI-increasing and BMI&WC-increasing group had low-increasing WC and BMI, low-increasing BMI and high-increasing WC, high-increasing BMI and low-increasing WC, and high-increasing BMI and WC, respectively. **Table 2** summarizes the baseline characteristics of study variables by joint classes. Compared with the normal group, individuals in the BMI&WC-increasing group were more likely to be younger males with higher baseline BMI, WC, SBP and DBP, and higher proportions of smoking and alcohol drinking.

Table 3 presents HRs and 95% CIs for the association between joint group membership and incident hypertension. Compared with the normal group, the HRs (95% CIs) for WC-increasing, BMI-increasing, and BMI&WC-increasing group were 1.55 (1.31, 1.83), 1.69 (1.36, 2.10), and 1.98 (1.71, 2.28) in unadjusted model, respectively. After adjustment for baseline age, gender, baseline BMI, SBP, smoking and drinking status, these joint groups were still significantly associated with incident hypertension, whose HRs (95% CIs) were 1.43 (1.19, 1.74), 1.51 (1.19, 1.92), and 1.76 (1.45, 2.14), respectively.

Supplement Table S8 and **S9** show model-estimated levels and linear slopes of BMI and WC in means (SD) by incident hypertension at follow-up. **Figure 2** shows the change of model-estimated levels and linear slopes of BMI and WC during age 20 to 60 years in hypertension and normotension group. In **Figure 2A**, the levels increased and linear slopes decreased with age during 20~60 in both hypertension and normotension group. However, the hypertension group had higher levels and steeper rate of change than the normotension group. Similar results were found in WC (**Figure 2B**). Noticeably, the difference in change rate of WC linear slopes was large between the hypertension group and normotension group.

Figure 3 presents ORs and 95% CIs of model-estimated levels and level-adjusted linear slopes of BMI and WC for incident hypertension, adjusted for gender, baseline SBP, smoking, and alcohol drinking. The association between model-estimated levels and hypertension increased during 20~60 years old, with adjusted ORs and 95% CIs ranging from 0.92 (0.86~0.98) to 1.57 (1.47~1.67) for BMI, and 0.98 (0.92~1.05) to 1.44 (1.35~1.53) for WC. This association became significant at age 25 or above for BMI, and at age 23 or above for WC. Conversely, the standardized ORs (95% CIs) of level-adjusted linear slopes decreased with age, ranging from 1.47 (1.38~1.57) to 0.97 (0.92~1.03) for BMI, and 1.36 (1.28~1.45) to 0.99 (0.93~1.06) for WC. The associations of level-adjusted linear slopes with incident hypertension were no longer significant at age 55, indicating the importance of BMI and WC slopes in young adulthood.

DISCUSSION

In this longitudinal study, we identified two distinct trajectories for both BMI and WC during 20~60 years old in Chinese population, and found a joint effect of BMI and WC trajectories on incident hypertension. The model-estimated levels and level adjusted slopes at each age point in a 1-year interval were further calculated for both BMI and WC, and their associations with hypertension were estimated. Though previous studies have demonstrated BMI or WC trajectories were associated with hypertension separately, the joint effect of BMI and WC trajectories was unclarified. Our observations support that BMI and WC trajectories have synergistic effect on future hypertension risk, and the changing slopes of BMI and WC during young adulthood are independent risk factors. Therefore, we suggest controlling both BMI and WC in young adulthood to prevent hypertension.

In the current study, we identified two trajectories for BMI. The low-increasing group, with baseline BMI around 20 kg/m^2, increased slowly during the 20~60 years period, while the high-increasing group with lower baseline BMI increased rapidly. Some studies, using data from China, UK, and Finland, explored BMI trajectories for childhood and early adulthood, showed that BMI may have 2-6 trajectories[13,14,20-25]. Though the numbers of trajectories were different among these studies, they all discovered a low-increasing or low-stable group and a high-increasing group[13,14,20-25], which was in line with our results. Two distinct trajectories of WC were also identified in this study. The low-increasing group, with baseline WC around 70 cm, persisted 70~80 cm during early to mid-life adulthood, while the high-increasing group with same baseline WC, increased gradually from 70 cm to 95 cm. To our knowledge, the literatures on WC trajectories are still limited. Jeon et al.[15] showed 5 trajectories for WC in individuals aged 40 years or older using data from Korea. Cheng et al.[26] presented that WC may have 4 trajectories among Chinese population during 18~50 years old. However, these previous researches[15,26] did not consider the subject-specific random effect, which was a strength in our study.

Generally, obesity is divided into systemic obesity and abdominal obesity. Only studying the relationship between BMI or WC and hypertension is insufficient[13-15,20,21]. The joint effect of BMI and WC on hypertension should be explored. In this study, we divided participants into four sub-groups according to their BMI and WC trajectories. Compared with the normal group, BMI&WC-increasing group had a higher risk of incident hypertension after adjustment for some covariates, indicating that the joint effect of BMI and WC trajectories was significant associated with hypertension. Previous researches showed BMI or WC trajectories were associated with hypertension[13-15,20,26]. However, these studies mainly focused on the BMI and WC trajectories separately[13-15,20,21,26], ignoring the complementary effect between BMI and WC on incident hypertension. Hu et al.[8] found a joint effect of BMI and WC on hypertension in a cross-sectional study, nevertheless, the longitudinal changing patterns of both BMI and WC were not considered in that study. To our knowledge, the joint effect of

BMI and WC trajectories was largely unknown. Our study supports a synergistic effect between BMI and WC trajectories on incident hypertension, highlighted that we should take more attention to control both BMI and WC in early adulthood.

In this longitudinal study, the model-estimated levels increased with age and the model-estimated slopes decreased with age for both BMI and WC, which was in line with our previous studies[20,21]. The standardized ORs were calculated for both model-estimated levels and level-adjusted slopes, after adjusting for gender, baseline SBP, smoking and alcohol drinking. Our results showed that for both BMI and WC, level-adjusted slopes had higher ORs than model-estimated levels before 30 years old. It may indicate slopes of BMI and WC are more important than their levels in early adulthood and 20~30 may be a critical period for early prevention of hypertension, which is similar with previous studies[20,21]. Interestingly, our longitudinal study found that the linear slopes of BMI had higher ORs than those of WC during 20~25 years old. Similarly, in 43~60 years old, the levels of BMI had higher ORs than those of WC. These results may indicate that BMI plays a more important role than WC in incident hypertension during both early and mid-life adulthood in Chinese population.

According to the life-course epidemiology theory[27-29], exposure at a particular period in the life span has a long-term effect on the physiological function and anatomical structure and may eventually lead to some diseases. In the current study, individuals with high-increasing trajectory patterns of BMI and WC may have some changes in physiological aspect during early adulthood, including aorta root thickening, premature vascular aging and endothelial dysfunction[30-32]. These changes may have accumulated effects on the way to incident hypertension. Previous research has reported meaningful high prevalence of premature vascular aging in younger than 40 years people[31]. Endothelial dysfunction may also play an important role in developing hypertension[32] and it may impact early aorta root thickening[30]. Furthermore, aorta root size may play a causative role in the pathogenesis of systolic hypertension[30].

There are some important strengths in our study. The current study is a community-based longitudinal study with large sample size and repeated measurements. It allows us to use LCGMM to explore trajectory of BMI and WC. The LCGMM can identify distinct trajectory for subgroup participants and permits us to analyze the relationship between model-estimated levels and level-adjusted slopes and hypertension to reveal the critical period in life-course. Moreover, the joint effect of BMI and WC trajectories on incident hypertension was explored, which was rarely reported in previous researches. On the other hand, some limitations should be acknowledged. Firstly, the covariates we used may be insufficient. Some unavailable covariates, like physically fitness, may impact the prevalence of incident hypertension. Secondly, CHNS was a survey concentrated on Chinese population, suggesting our study may not be generalizable to other ethnic population. Finally, there are many indicators of obesity, besides BMI and WC. Further studies should consider more indicators such as body fat percentage and fat free mass to explore the relationship between those indicators and incident hypertension.

In conclusion, the current study identified two distinct trajectories of BMI and WC from early to mid-life adulthood, and found complementary trajectory patterns between BMI and WC (620 [9.4%] and 309 [4.7%] participants for WC-increasing only trajectory and BMI-increasing only trajectory). From a life-course perspective, our study demonstrates the joint trajectories of BMI and WC have significant effect on future hypertension risk, and the changing slopes of BMI and WC during young adulthood are independent risk factors. These results emphasize that both BMI and WC should be paid more attention to prevent hypertension, and young adulthood may be a crucial period for intervention. More targeted strategies in the prevention of hypertension should be emphasized among early adulthood. Public health intervention for controlling modifiable risk factors during young adulthood may reduce the future prevalence and burden of hypertension among Chinese.

Acknowledgements

The current study uses data from CHNS. We thank the National Institute of Nutrition and Food Safety, China Center for Disease Control and Prevention, Carolina Population Center, the University of North Carolina at Chapel Hill, the NIH (R01-HD30880, DK056350, and R01-HD38700) and the Fogarty International Center, NIH for financial support for the CHNS data collection and analysis files from 1989 to 2006 and both parties plus the China-Japan Friendship Hospital, Ministry of Health for support for CHNS 2009 and future surveys.

Author contributions YQ, CL, JL, BF, YL, CS and XZ generated the hypothesis and contributed to analytic strategy and wrote the manuscript. CS and XZ supervised the field activities and data collection and edited the manuscript.

Funding

This study was supported by grants 81973147 from National Natural Science Foundation of China and the Cheeloo Young Scholars Program of Shandong University.

Conflict of interest The authors declare that they have no conflict of interest.

Patient consent for publication Not required.

Ethics approval The protocol was approved by the Ethics Committee of the National Institute for Nutrition and Health, China CDC (NO. 201524). Informed consent was obtained from all subjects before the investigation.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository from China Health and Nutrition Survey (https://www.cpc.unc.edu/projects/china/data/).

References

1. Li Y, Yang L, Wang L, et al. Burden of hypertension in China: A nationally representative survey of 174,621 adults. Int J Cardiol. 2017;227:516-523.

2. Gu D, Reynolds K, Wu X, et al. The International Collaborative Study of Cardiovascular Disease in ASIA. Prevalence, awareness, treatment, and control of hypertension in china. Hypertension. 2002;40(6):920-7.

3. Ye R, Liu K, Zhang Z, et al. Health-related quality of life of hypertension in China: a systematic review and meta-analysis. J Cardiovasc Med (Hagerstown). 2018;19(8):430-438.

4. Feng YJ, Wang HC, Li YC, et al. Hypertension Screening and Follow-up Management by Primary Health Care System among Chinese Population Aged 35 Years and Above. Biomed Environ Sci. 2015;28(5):330-40.

5. Shihab HM, Meoni LA, Chu AY, et al. Body mass index and risk of incident hypertension over the life course: the Johns Hopkins Precursors Study. Circulation. 2012;126(25):2983-9.

6. Robinson RF, Batisky DL, Hayes JR, et al. Body mass index in primary and secondary pediatric hypertension. Pediatr Nephrol. 2004;19(12):1379-84.

7. Dong B, Wang Z, Yang Y, et al. Intensified association between waist circumference and hypertension in abdominally overweight children. Obes Res Clin Pract. 2016;10(1):24-32.

8. Hu L, Huang X, You C, et al. Prevalence and Risk Factors of Prehypertension and

Hypertension in Southern China. PLoS One. 2017;12(1):e0170238.

9. Feng RN, Zhao C, Wang C, et al. BMI is strongly associated with hypertension, and waist circumference is strongly associated with type 2 diabetes and dyslipidemia, in northern Chinese adults. J Epidemiol. 2012;22(4):317-23.

10. Javed F, Aziz EF, Sabharwal MS, et al. Association of BMI and cardiovascular risk stratification in the elderly African-American females. Obesity (Silver Spring). 2011;19(6):1182-6.

11. Levine DA, Calhoun DA, Prineas RJ, et al. Moderate waist circumference and hypertension prevalence: the REGARDS Study. Am J Hypertens. 2011;24(4):482-8.

12. Soltani S, Shirani F, Chitsazi MJ, et al. The effect of dietary approaches to stop hypertension (DASH) diet on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials. Obes Rev. 2016;17(5):442-54.

13. Buscot MJ, Thomson RJ, Juonala M, et al. Distinct child-to-adult body mass index trajectories are associated with different levels of adult cardiometabolic risk. Eur Heart J. 2018;39(24):2263-2270.

14. Ahanchi NS, Ramezankhani A, Munthali RJ, et al. Body mass index trajectories from adolescent to young adult for incident high blood pressure and high plasma glucose. PLoS One. 2019;14(5):e0213828.

15. Jeon J, Jung KJ, Jee SH. Waist circumference trajectories and risk of type 2 diabetes mellitus in Korean population: the Korean genome and epidemiology study (KoGES).

BMC Public Health. 2019;19(1):741.

[dataset] 16. Popkin BM, Du S, Zhai F, et al. Cohort Profile: The China Health and Nutrition Survey--monitoring and understanding socio-economic and health change in China, 1989-2011. Int J Epidemiol. 2010 Dec;39(6):1435-40. doi: 10.1093/ije/dyp322.

[dataset] 17. Zhang B, Zhai FY, Du SF, et al. The China Health and Nutrition Survey, 1989-2011. Obes Rev. 2014 Jan;15 Suppl 1(0 1):2-7. doi: 10.1111/obr.12119.

18. Huang L, Wang H, Wang Z, Zhang J, Zhang B, Ding G. Regional Disparities in the Association between Cereal Consumption and Metabolic Syndrome: Results from the China Health and Nutrition Survey. Nutrients. 2019 Apr 1;11(4):764.

19. Proust-Lima C, Philipps V, Liquet B. Estimation of extended mixed models using latent classes and latent processes: the R package lcmm. J Stat Softw. 2015;78:1 – 56.

20. Fan B, Yang Y, Dayimu A, et al. Body Mass Index Trajectories During Young Adulthood and Incident Hypertension: A Longitudinal Cohort in Chinese Population. J Am Heart Assoc. 2019;8(8):e011937.

21. Lv J, Fan B, Wei M, et al. Trajectories of early to mid-life adulthood BMI and incident diabetes: the China Health and Nutrition Survey. BMJ Open Diabetes Res Care. 2020;8(1):e000972.

22. Kelly Y, Patalay P, Montgomery S, et al. BMI Development and Early Adolescent Psychosocial Well-Being: UK Millennium Cohort Study. Pediatrics. 2016;138(6):e20160967.

23. Nano J, Dhana K, Asllanaj E, et al. Trajectories of BMI Before Diagnosis of Type 2 Diabetes: The Rotterdam Study. Obesity (Silver Spring). 2020;28(6):1149-1156.

24. Viner RM, Costa S, Johnson W. Patterns of BMI development between 10 and 42 years of age and their determinants in the 1970 British Cohort Study. J Epidemiol Community Health. 2019;73(1):79-85.

25. Wang X, Dong B, Huang S, et al. Body Mass Index Trajectory and Incident Hypertension: Results From a Longitudinal Cohort of Chinese Children and Adolescents, 2006-2016. Am J Public Health. 2020;110(11):1689-1695.

26. Cheng C, Li Y, Ma W, et al. Trajectories of waist circumference during young adulthood and incident hypertension: the China Health and Nutrition Survey. J Hum Hypertens. 2021 Jun 18.

27. Ben-Shlomo Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. Int J Epidemiol. 2002;31:285 – 293.

28. Lynch J, Smith GD. A life course approach to chronic disease epidemiology. Annu Rev Public Health. 2005;26:1-35.

29. Mishra GD, Anderson D, Schoenaker DA, et al. InterLACE: A New International Collaboration for a Life Course Approach to Women's Reproductive Health and Chronic Disease Events. Maturitas. 2013;74(3):235-40.

30. Farasat SM, Morrell CH, Scuteri A, et al. Pulse pressure is inversely related to aortic root diameter implications for the pathogenesis of systolic hypertension.

Hypertension. 2008;51(2):196-202.

31. Cunha PG, Cotter J, Oliveira P, et al. Pulse wave velocity distribution in a cohort study: from arterial stiffness to early vascular aging. J Hypertens. 2015;33(7):1438-45.

32. Scuteri A, Tesauro M, Rizza S, et al. Endothelial function and arterial stiffness in normotensive normoglycemic first-degree relatives of diabetic patients are independent of the metabolic syndrome. Nutr Metab Cardiovasc Dis. 2008;18(5):349-56.

Figure legends

Figure 1. (A) Predicted trajectories of BMI during 20-60 years old. The trajectories were shown in solid lines, and the 95% confidence intervals (CIs) were shown in shadow. The proportions in each trajectory were shown below solid lines. BMI = body mass index (see detailed information on the curve parameters in Supplemental Table S4) (B) Predicted trajectories of WC during 20-60 years old. The trajectories were shown in solid lines, and the 95% CIs were shown in shadow. The proportions in each trajectory were shown below solid lines. WC = waist circumference (see detailed information on the curve parameters in Supplemental Table S5)

Figure 2. (A) The mean of model-estimated levels and level-adjusted linear slopes of BMI during 20-60 years old by incident hypertension. (B) The mean of model-estimated levels and level-adjusted linear slopes of WC during 20-60 years old by incident hypertension. BMI, body mass index; WC, waist circumference.

Figure 3. Standardized Odds ratios (ORs) and 95% confidence intervals (CIs) of model-estimated levels and level-adjusted linear slopes of BMI and WC during 20-60 years old by age for incident hypertension, adjusted for gender, baseline SBP, smoking, and alcohol drinking.

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure.

Table 1. Baseline Characteristics by Incident Hypertension at Follow-Up

Variable	Total	Normotensives	Incident Hypertension	*P* Value
N	6571	5156	1415	
Age, ys	35.4 (8.6)	34.8 (8.8)	37.8 (7.4)	<0.001
Males, n (%)	3063 (46.6)	2329 (45.2)	734 (51.9)	<0.001
BMI, kg/m^2	22.0 (2.7)	21.8 (2.6)	22.9 (2.9)	<0.001
WC, cm	75.8 (8.4)	75.2 (8.2)	78.0 (8.8)	<0.001
SBP, mmHg	110.0 [103.0, 120.0]	110.0 [101.0, 120.0]	116.0 [108.0, 120.0]	<0.001
DBP, mmHg	74.0 [70.0, 80.0]	72.5 [68.0, 80.0]	77.5 [70.0, 80.0]	<0.001
Smoker, n (%)	2123 (32.5)	1578 (30.8)	545 (38.8)	<0.001
Drinker, n (%)	2312 (35.5)	1712 (33.6)	600 (42.7)	<0.001
Follow-up, ys	11.8 (4.2)	12.0 (4.3)	11.3 (3.9)	<0.001

Study variables are presented as mean (SD), median [interquartile range] or n (%), appropriately. BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; WC, waist circumference.

Table 2. Characteristics at baseline and incident hypertension at follow-up by joint trajectory groups

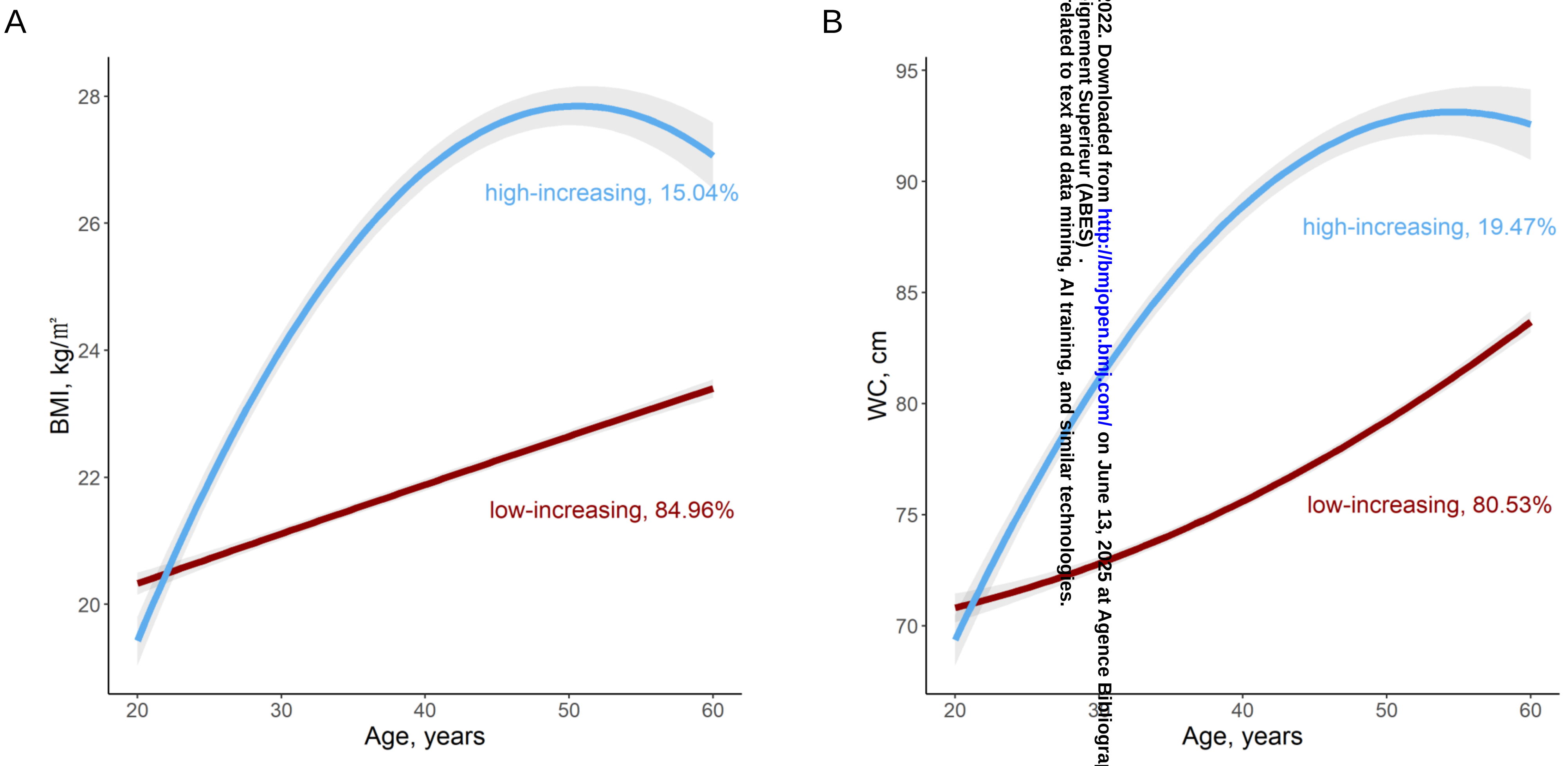
Variable	Normal	WC-increasing	BMI-increasing	BMI&WC-increasing	*P* Value
N	4963	620	309	679	
Age, years	36.3 (8.6)	32.8 (8.2)	34.3 (8.3)	31.8 (7.7)	<0.001
Males, n (%)	2019 (40.7)	557 (89.8)	33 (10.7)	454 (66.9)	<0.001
BMI, kg/m^2	21.3 (2.2)	22.8 (2.3)	24.5 (3.1)	25.0 (3.4)	<0.001
WC, cm	73.8 (7.0)	81.3 (8.7)	78.9 (8.2)	84.1 (9.9)	<0.001
SBP, mmHg	110.0 [101.0, 120.0]	117.5 [110.0, 120.0]	110.0 [105.0, 120.0]	116.0 [108.0, 120.0]	<0.001
DBP, mmHg	72.5 [68.0, 80.0]	77.0 [70.0, 80.0]	73.0 [68.8, 80.0]	77.0 [70.0, 80.0]	<0.001
Smoker, n (%)	1435 (29.1)	364 (59.4)	30 (9.8)	294 (43.5)	<0.001
Drinker, n (%)	1563 (31.8)	370 (60.3)	58 (18.9)	321 (48.0)	<0.001
Hypertension, n (%)	935 (18.8)	159 (25.6)	89 (28.8)	232 (34.2)	<0.001

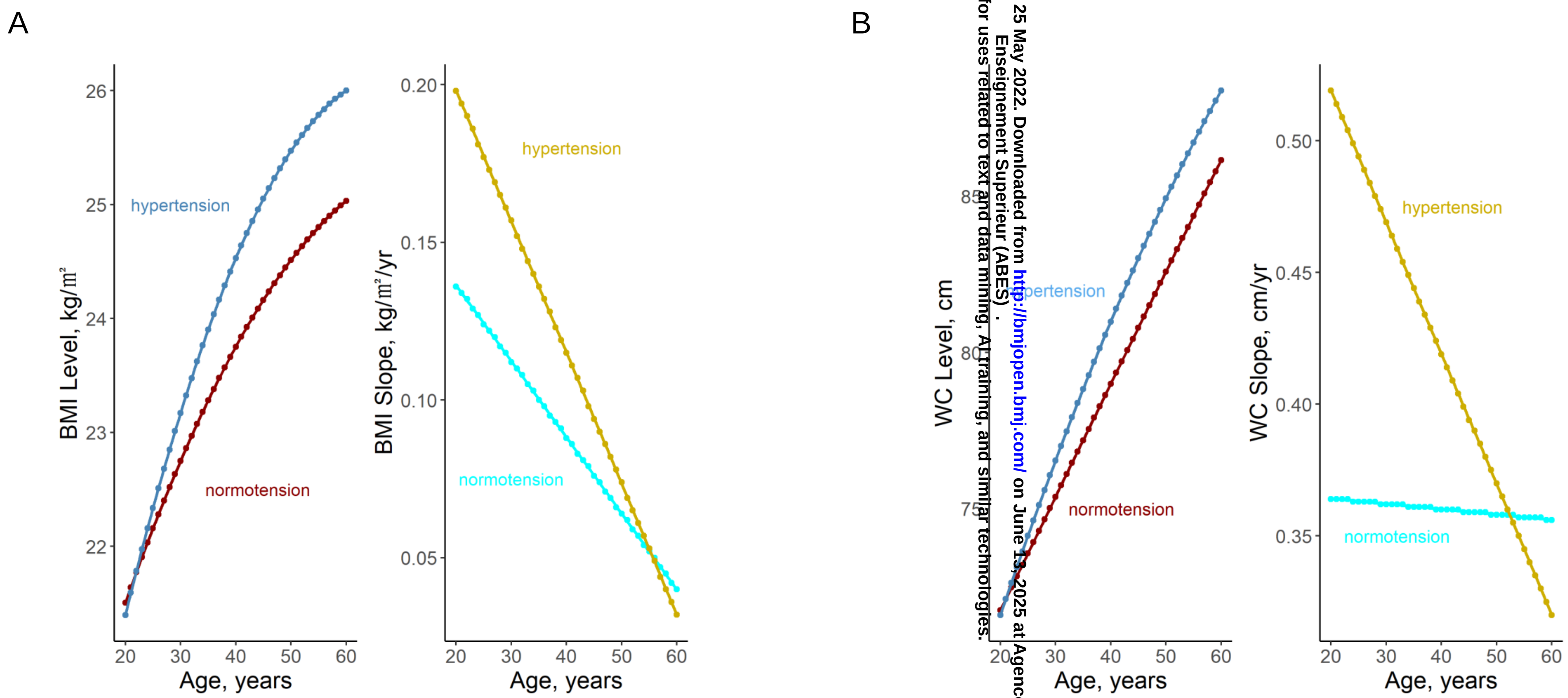
Study variables are presented as mean (SD), median [interquartile range] or n (%), appropriately. BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; WC, waist circumference.

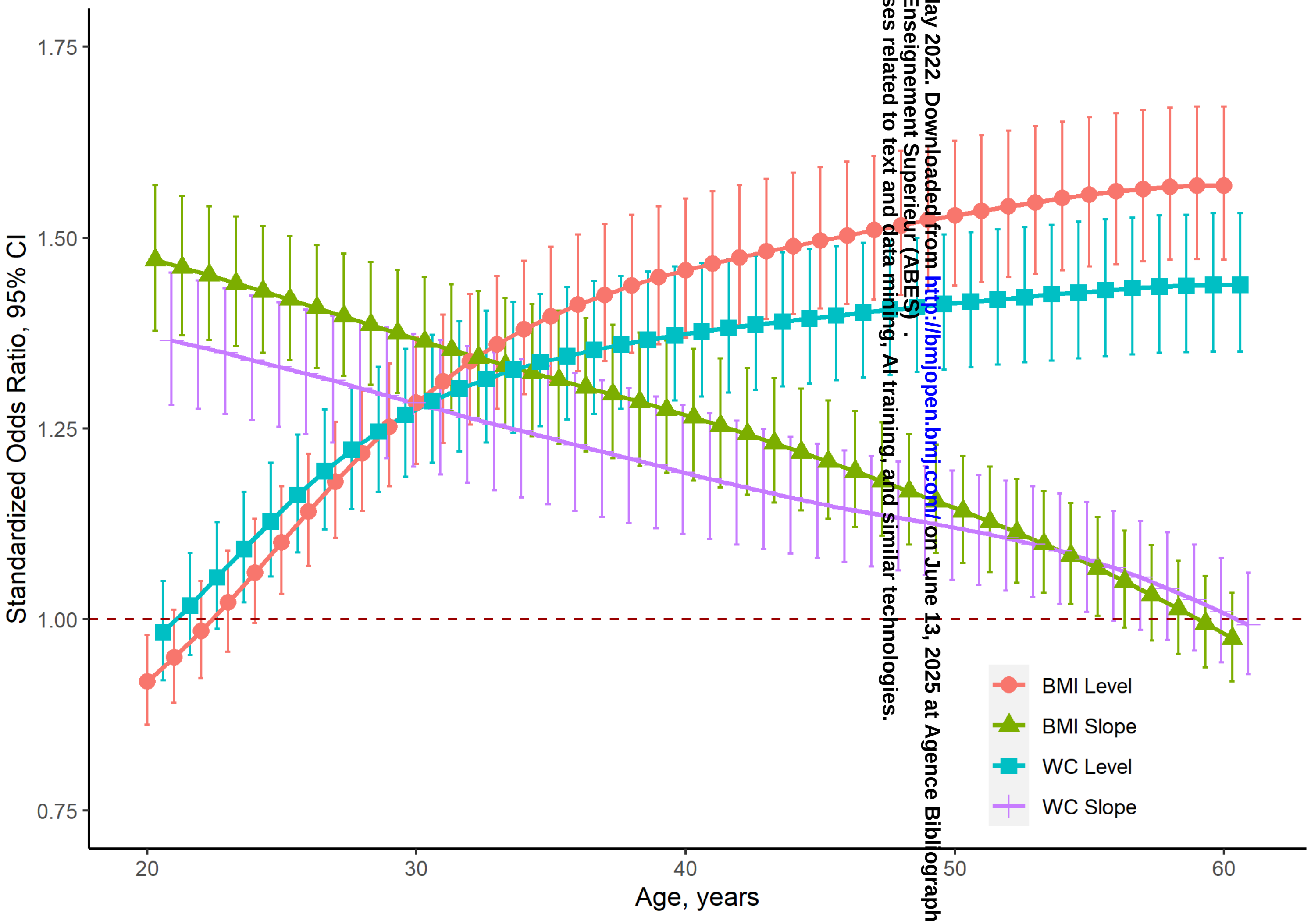
Table 3. Hazard Ratios and 95% CIs of Joint Trajectory Groups for Incident Hypertension

	Model 1	Model 2	Model 3	Model 4
Joint trajectory groups				
Normal	Reference	Reference	Reference	Reference
WC-increasing	1.55 (1.31, 1.83)	1.51 (1.25, 1.82)	1.41 (1.17, 1.71)	1.43 (1.19, 1.74)
BM-increasing	1.69 (1.36, 2.10)	1.47 (1.16, 1.87)	1.48 (1.17, 1.89)	1.51 (1.19, 1.92)
BMI&WC-increasing	1.98 (1.71, 2.28)	1.74 (1.44, 2.10)	1.73 (1.42, 2.10)	1.76 (1.45, 2.14)
Covariates				
Baseline Age		1.07 (1.06, 1.08)	1.07 (1.06, 1.08)	1.07 (1.06, 1.08)
Female		0.77 (0.69, 0.87)	0.89 (0.79, 1.00)	1.01 (0.85, 1.18)
Baseline BMI		1.10 (1.08, 1.13)	1.07 (1.05, 1.10)	1.07 (1.05, 1.10)
Baseline SBP			1.03 (1.02, 1.04)	1.03 (1.02, 1.04)
Smoker				1.12 (0.96, 1.30)
Drinker				1.10 (0.96, 1.26)

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure.


A
28
26
24
22
20
BMI, kg/㎡
20
30
40
50
60
Age, years
high-increasing, 15.04%
low-increasing, 84.96%
B
95
90
85
80
75
70
WC, cm
20
30
40
50
60
Age, years
high-increasing, 19.47%
low-increasing, 80.53%


A
BMI Level, kg/㎡
26
25
24
23
22
hypertension
normotension
20
30
40
50
60
Age, years
BMI Slope, kg/㎡/yr
0.20
0.15
0.10
0.05
hypertension
normotension
B
WC Level, cm
85
80
75
normotension
WC Slope, cm/yr
0.50
0.45
0.40
0.35
hypertension
normotension


Standardized Odds Ratio, 95% CI
1.75
1.50
1.25
1.00
0.75
20
30
40
50
60
Age, years
BMI Level
BMI Slope
WC Level
WC Slope

Supplemental Materials

Joint Trajectories of Body Mass Index and Waist Circumference in Early to Mid-life Adulthood and Incident Hypertension: the China Health and Nutrition Survey

Yanlin Qu [1,2], Chunxia Li [1,2], Jiali Lv [1,2], Bingbing Fan [1,2], Ying Liu [1,2], Chang Su [3], Xiangjuan Zhao [4 #]

[1] Department of Biostatistics, School of Public Health, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

[2] Institute for Medical Dataology, Cheeloo College of Medicine, Shandong University, Jinan 250012, China

[3] National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, Beijing 102206, China

[4] Maternal and Child Health Care Hospital of Shandong Province, Jinan 250012, China

 # Correspondence & Reprints:

Xiangjuan Zhao, MD.

Maternal and Child Health Care Hospital of Shandong Province, Jinan 250014, China.

Email: xzhao6@hotmail.com

Trajectory Analysis

Repeated trajectory analyses were performed to identify the latent classes by changing the number of groups from 2 to 3, with the same starting values calculated from the 1-group model. The shapes and optimal number of groups were determined by the following criteria: 1) Bayesian information criterion (BIC) decreased at least 20; 2) high mean posterior class membership probabilities (> 0.65); 3) high mean posterior probabilities (> 0.7). Estimation of latent class models was performed with lcmm (version 1.7.8) package in R (version 4.0.4). To avoid convergence towards local maxima, LCGMM models with 2 or 3 classes were performed for several times with different sets of random starting value based on 1-class model. Finally, according to criteria above, a model of quadratic parameters with two classes was chosen for both BMI and WC as the best fit. The final model of BMI was described as:

$$BMI_{ij} |_{c_{i=g}} = (\upsilon_{0g} + u_{0ig}) + (\upsilon_{1g} + u_{1ig})age + (\upsilon_{2g} + u_{2ig})age^2 + \varepsilon_{ij}$$

where υ =(υ_{0g}, υ_{1g}, υ_{2g}) is a vector of fixed effect parameters in the group "g", u =(u_{0ig}, u_{1ig}, u_{2ig}) is a vector of random effect parameters of the individual "i" in the group "g", ε_{ij} is an unknown error term (the model of WC is similar with BMI).

Table S1. Baseline characteristics of participants included and excluded.

Variable	Excluded	Included	*P*-Value
N	26777	6571	
Age, y	30.8 (23.0)	35.4 (8.6)	<0.001
Male, n (%)	12931 (48.3)	3063 (46.6)	0.017
BMI, kg/m^2	20.9 (4.8)	22.0 (2.7)	<0.001
WC, cm	75.9 (15.6)	75.8 (8.4)	0.365
SBP, mm Hg	116.0 [102.0, 129.0]	110.0 [103.0, 120.0]	<0.001
DBP, mm Hg	75.0 [68.0, 81.0]	74.0 [70.0, 80.0]	<0.001
Smoker, n (%)	4475 (27.2)	2123 (32.5)	<0.001
Drinker, n (%)	5162 (29.4)	2312 (35.5)	<0.001

BMI indicates body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; WC, waist circumference.

Table S2. Latent Class Growth Mixture Models (LCGMM) results of model fitting process for BMI.

No. Latent class	Polynomial degree	Log-Lik	BIC	% Participants per class	Mean posterior probabilities	% Posterior probabilities > 70%
1	Linear	-59740	119525	100	na	na
	Quadratic	-59623	119308	100	na	na
	Cubic	-59604	119289	100	na	na
2	Linear	-59299	118678	9.98/90.02	0.79/0.95	66.92/95.38
	Quadratic	**-59122**	**118351**	**84.96/15.04**	**0.93/0.81**	**93.19/72.37**
	Cubic	-59120	118373	15.17/84.83	0.82/0.93	73.22/93.00
3	Linear	-59190	118495	24.97/72.12/2.91	0.74/0.87/0.7[illegible]	56.98/84.30/67.02
	Quadratic	-58989	118128	73.40/23.09/3.51	0.88/0.73/0.7[illegible]	85.32/57.61/64.07
	Cubic	-58985	118155	4.34/78.45/17.21	0.74/0.90/0.7[illegible]	58.25/88.13/54.38

BMI indicate body mass index; NO. Latent class: latent class number of the model; Log-Lik: the maximum Log-Likelihood; BIC: the Bayesian information Criterion; % Participants per class: proportion of participants per class; The best fitting model is highlighted in bold characters. (na: not applicable)

Table S3. Latent Class Growth Mixture Models (LCGMM) results of model fitting process for WC.

No. Latent class	Polynomial degree	Log-Lik	BIC	% Participants per class	Mean posterior probabilities	% Posterior probabilities > 70%
1	Linear	-98380	196839	100	na	na
	Quadratic	-98387	196836	100	na	na
	Cubic	-98397	196839	100	na	na
2	Linear	-98042	196163	83.32/16.68	0.92/0.78	91.98/65.42
	Quadratic	**-97946**	**195998**	**80.53/19.47**	**0.92/0.80**	**91.35/68.67**
	Cubic	-97940	196012	80.18/19.82	0.92/0.80	91.41/69.79
3	Linear	-98008	195918	50.95/36.74/12.81	0.95/0.89/0.7[illegible]	96.19/86.74/63.06
	Quadratic	-97875	195900	54.95/9.34/35.71	0.80/0.77/0.70	70.99/64.12/50.57
	Cubic	-97866	195112	50.46/36.74/12.80	0.71/0.87/0.68	52.88/84.85/42.74

WC indicate waist circumference; NO. Latent class: latent class number of the model; Log-Lik: the maximum Log-Likelihood; BIC: the Bayesian information Criterion; % Participants per class: proportion of participants per class. The best fitting model is highlighted in bold characters. (na: not applicable)

Table S4. Parameters estimates for the best fitting 2-class quadratic Latent Class Growth Mixture Model for BMI.

		Intercept (se)*	Linear (se)	Quadratic (se)
Fixed effect				
	Group 1	23.519 (0.0487)	0.077 (0.0024)	-5×10^{-5} (0.0002)
	Group 2	27.177 (0.1337)	0.155 (0.0076)	-0.009 (0.0005)
Random effects: variance-covariance matrix				
$\sigma^2_{int} = 3.88$				
$\sigma^2_{linear\ slope} = 0.0105$				
$\sigma^2_{quadratic\ slope} < 0.001$				
$\sigma^2_{error} = 1.24$				

se = standard error; BMI = body mass index.

*: Intercept interpreted as the expected level of BMI in kg/m^2 at 42 years of age (centering to the mean age of the sample)

Table S5. Parameters estimates for the best fitting 2-class quadratic Latent Class Growth Mixture Model for WC.

		Intercept (se)*	Linear (se)	Quadratic (se)
Fixed effect				
	Group 1	76.890 (0.1459)	0.338 (0.0084)	0.004 (0.0006)
	Group 2	89.963 (0.3340)	0.501 (0.0226)	-0.020 (0.0015)
Random effects: variance-covariance matrix				
$\sigma^2_{int} = 24.31$				
$\sigma^2_{linear\ slope} = 0.0984$				
$\sigma^2_{quadratic\ slope} < 0.001$				
$\sigma^2_{error} = 5.38$				

se = standard error; WC = waist circumference.

*: Intercept interpreted as the expected level of WC in cm at 42 years of age (centering to the mean age of the sample)

Table S6. Hazard Ratios and 95% of BMI Trajectory Groups for Incident Hypertension

	Model 1	Model 2	Model 3	Model 4
Trajectory groups				
Low-increasing group	Reference	Reference	Reference	Reference
High-increasing group	1.79 (1.58, 2.03)	1.44 (1.22, 1.69)	1.47 (1.25, 1.73)	1.49 (1.26, 1.75)
Covariates				
Age, y		1.07 (1.06, 1.08)	1.06 (1.05, 1.07)	1.06 (1.05, 1.07)
Female		0.74 (0.67, 0.83)	0.86 (0.77, 0.96)	0.97 (0.83, 1.14)
Baseline BMI		1.09 (1.06, 1.12)	1.07 (1.04, 1.10)	1.07 (1.04, 1.10)
Baseline WC		1.01 (1.00,1.02)	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)
Baseline SBP			1.03 (1.02, 1.04)	1.03 (1.02, 1.04)
Smoker				1.11 (0.96, 1.30)
Drinker				1.11 (0.97, 1.27)

BMI, body mass index; SBP, systolic blood pressure; WC, waist circumference.

Table S7. Hazard Ratios and 95% of WC Trajectory Groups for Incident Hypertension

	Model 1	Model 2	Model 3	Model 4
Trajectory groups				
Low-increasing group	Reference	Reference	Reference	Reference
High-increasing group	1.71 (1.53, 1.93)	1.45 (1.24, 1.69)	1.42 (1.21, 1.66)	1.43 (1.22, 1.68)
Covariates				
Age, y		1.07 (1.06, 1.08)	1.06 (1.05, 1.07)	1.06 (1.05, 1.07)
Female		0.80 (0.72, 0.90)	0.92 (0.82, 1.03)	1.04 (0.89, 1.23)
Baseline BMI		1.10 (1.07, 1.13)	1.08 (1.05, 1.11)	1.08 (1.05, 1.11)
Baseline WC		1.01 (1.00, 1.02)	1.00 (0.99, 1.01)	1.01 (1.00, 1.02)
Baseline SBP			1.03 (1.02, 1.04)	1.03 (1.02, 1.04)
Smoker				1.12 (0.96, 1.30)
Drinker				1.10 (0.96, 1.26)

BMI, body mass index; SBP, systolic blood pressure; WC, waist circumference.

Table S8. Model-estimated levels and linear slopes of BMI in means (SD) by incident hypertension at follow-up

	BMI Level (kg/m^2)			BMI Slope (kg/m^2/year)		
Age, (years)	NTN	HTN	*P*-Value	NTN	HTN	*P*-Value
20	21.50 (2.03)	21.40 (1.95)	0.068	0.14 (0.17)	0.20 (0.21)	<0.001
21	21.64 (1.96)	21.59 (1.87)	0.407	0.13 (0.17)	0.19 (0.20)	<0.001
22	21.77 (1.90)	21.78 (1.82)	0.828	0.13 (0.16)	0.19 (0.19)	<0.001
23	21.90 (1.85)	21.97 (1.78)	0.199	0.13 (0.16)	0.19 (0.19)	<0.001
24	22.03 (1.82)	22.16 (1.76)	0.019	0.13 (0.15)	0.18 (0.18)	<0.001
25	22.16 (1.80)	22.34 (1.76)	<0.001	0.12 (0.15)	0.18 (0.17)	<0.001
26	22.28 (1.79)	22.51 (1.77)	<0.001	0.12 (0.14)	0.17 (0.17)	<0.001
27	22.40 (1.79)	22.68 (1.80)	<0.001	0.12 (0.14)	0.17 (0.16)	<0.001
28	22.52 (1.80)	22.85 (1.84)	<0.001	0.12 (0.13)	0.16 (0.15)	<0.001
29	22.64 (1.82)	23.01 (1.88)	<0.001	0.11 (0.13)	0.16 (0.15)	<0.001
30	22.75 (1.84)	23.17 (1.94)	<0.001	0.11 (0.12)	0.16 (0.14)	<0.001
31	22.86 (1.87)	23.32 (1.99)	<0.001	0.11 (0.12)	0.15 (0.13)	<0.001
32	22.97 (1.90)	23.48 (2.05)	<0.001	0.11 (0.11)	0.15 (0.13)	<0.001
33	23.07 (1.93)	23.62 (2.11)	<0.001	0.10 (0.11)	0.14 (0.12)	<0.001
34	23.18 (1.97)	23.76 (2.17)	<0.001	0.10 (0.10)	0.14 (0.11)	<0.001
35	23.28 (2.00)	23.90 (2.23)	<0.001	0.10 (0.10)	0.14 (0.11)	<0.001
36	23.38 (2.04)	24.04 (2.28)	<0.001	0.10 (0.09)	0.13 (0.10)	<0.001
37	23.48 (2.07)	24.16 (2.33)	<0.001	0.09 (0.09)	0.13 (0.10)	<0.001
38	23.57 (2.11)	24.29 (2.38)	<0.001	0.09 (0.09)	0.12 (0.09)	<0.001
39	23.66 (2.14)	24.41 (2.43)	<0.001	0.09 (0.08)	0.12 (0.09)	<0.001
40	23.75 (2.17)	24.53 (2.47)	<0.001	0.09 (0.08)	0.11 (0.08)	<0.001
41	23.84 (2.20)	24.64 (2.51)	<0.001	0.09 (0.07)	0.11 (0.08)	<0.001
42	23.92 (2.22)	24.75 (2.55)	<0.001	0.08 (0.07)	0.11 (0.07)	<0.001
43	24.01 (2.25)	24.85 (2.58)	<0.001	0.08 (0.07)	0.10 (0.07)	<0.001
44	24.08 (2.27)	24.96 (2.60)	<0.001	0.08 (0.07)	0.10 (0.07)	<0.001
45	24.16 (2.28)	25.05 (2.62)	<0.001	0.08 (0.07)	0.09 (0.07)	<0.001
46	24.24 (2.30)	25.14 (2.64)	<0.001	0.07 (0.07)	0.09 (0.07)	<0.001
47	24.31 (2.31)	25.23 (2.65)	<0.001	0.07 (0.07)	0.09 (0.07)	<0.001

48	24.38 (2.32)	25.32 (2.66)	<0.001	0.07 (0.07)	0.08 (0.07)	<0.001
49	24.45 (2.33)	25.40 (2.66)	<0.001	0.07 (0.07)	0.08 (0.07)	<0.001
50	24.51 (2.33)	25.47 (2.66)	<0.001	0.06 (0.07)	0.07 (0.07)	<0.001
51	24.58 (2.33)	25.54 (2.65)	<0.001	0.06 (0.07)	0.07 (0.07)	<0.001
52	24.64 (2.33)	25.61 (2.64)	<0.001	0.06 (0.07)	0.06 (0.08)	0.008
53	24.69 (2.33)	25.67 (2.62)	<0.001	0.06 (0.07)	0.06 (0.08)	0.075
54	24.75 (2.33)	25.73 (2.60)	<0.001	0.05 (0.08)	0.06 (0.09)	0.316
55	24.80 (2.32)	25.79 (2.58)	<0.001	0.05 (0.08)	0.05 (0.09)	0.766
56	24.85 (2.31)	25.84 (2.56)	<0.001	0.05 (0.08)	0.05 (0.10)	0.737
57	24.90 (2.30)	25.88 (2.53)	<0.001	0.05 (0.09)	0.04 (0.10)	0.367
58	24.95 (2.29)	25.93 (2.50)	<0.001	0.04 (0.09)	0.04 (0.11)	0.159
59	25.00 (2.28)	25.96 (2.48)	<0.001	0.04 (0.10)	0.04 (0.11)	0.063
60	25.03 (2.27)	26.00 (2.45)	<0.001	0.04 (0.10)	0.03 (0.12)	0.023

NTN = normotension; HTN = hypertension.

Table S9. Model-estimated levels and linear slopes of WC in means (SD) by incident hypertension at follow-up

	WC Level (cm)			WC Slope (cm/year)		
Age, (years)	NTN	HTN	*P*-Value	NTN	HTN	*P*-Value
20	71.75 (4.90)	71.60 (4.52)	0.271	0.36 (0.50)	0.52 (0.57)	<0.001
21	72.12 (4.80)	72.12 (4.45)	0.997	0.36 (0.48)	0.51 (0.55)	<0.001
22	72.48 (4.75)	72.63 (4.44)	0.272	0.36 (0.46)	0.51 (0.53)	<0.001
23	72.84 (4.73)	73.13 (4.48)	0.032	0.36 (0.45)	0.50 (0.51)	<0.001
24	73.21 (4.76)	73.64 (4.58)	0.002	0.36 (0.43)	0.50 (0.49)	<0.001
25	73.57 (4.81)	74.13 (4.71)	<0.001	0.36 (0.42)	0.49 (0.47)	<0.001
26	73.93 (4.89)	74.63 (4.88)	<0.001	0.36 (0.40)	0.49 (0.45)	<0.001
27	74.30 (5.00)	75.11 (5.06)	<0.001	0.36 (0.38)	0.48 (0.43)	<0.001
28	74.66 (5.12)	75.59 (5.26)	<0.001	0.36 (0.37)	0.48 (0.41)	<0.001
29	75.02 (5.25)	76.07 (5.47)	<0.001	0.36 (0.35)	0.47 (0.39)	<0.001
30	75.38 (5.38)	76.54 (5.68)	<0.001	0.36 (0.34)	0.47 (0.37)	<0.001
31	75.75 (5.25)	77.01 (5.90)	<0.001	0.36 (0.32)	0.46 (0.35)	<0.001
32	76.11 (5.67)	77.47 (6.10)	<0.001	0.36 (0.31)	0.46 (0.33)	<0.001
33	76.47 (5.81)	77.93 (6.30)	<0.001	0.36 (0.29)	0.45 (0.31)	<0.001
34	76.83 (5.95)	78.38 (6.50)	<0.001	0.36 (0.28)	0.45 (0.30)	<0.001
35	77.19 (6.08)	78.83 (6.68)	<0.001	0.36 (0.26)	0.44 (0.28)	<0.001
36	77.55 (6.21)	79.27 (6.85)	<0.001	0.36 (0.25)	0.44 (0.26)	<0.001
37	77.91 (6.33)	79.71 (7.01)	<0.001	0.36 (0.24)	0.43 (0.25)	<0.001
38	78.27 (6.44)	80.14 (7.15)	<0.001	0.36 (0.23)	0.43 (0.23)	<0.001
39	78.63 (6.54)	80.56 (7.28)	<0.001	0.36 (0.22)	0.42 (0.22)	<0.001
40	78.99 (6.63)	80.99 (7.39)	<0.001	0.36 (0.21)	0.42 (0.20)	<0.001
41	79.35 (6.71)	81.40 (7.49)	<0.001	0.36 (0.20)	0.41 (0.19)	<0.001
42	79.71 (6.78)	81.82 (7.58)	<0.001	0.36 (0.19)	0.41 (0.18)	<0.001
43	80.07 (6.83)	82.22 (7.64)	<0.001	0.36 (0.19)	0.40 (0.17)	<0.001
44	80.43 (6.88)	82.62 (7.70)	<0.001	0.36 (0.18)	0.40 (0.17)	<0.001
45	80.79 (6.92)	83.02 (7.73)	<0.001	0.36 (0.18)	0.39 (0.17)	<0.001
46	81.15 (6.94)	83.41 (7.75)	<0.001	0.36 (0.18)	0.39 (0.17)	<0.001
47	81.51 (6.95)	83.80 (7.75)	<0.001	0.36 (0.18)	0.38 (0.17)	<0.001

48	81.87 (6.96)	84.18 (7.74)	<0.001	0.36 (0.19)	0.38 (0.17)	<0.001
49	82.23 (6.95)	84.56 (7.72)	<0.001	0.36 (0.19)	0.37 (0.18)	0.006
50	82.59 (6.93)	84.93 (7.67)	<0.001	0.36 (0.20)	0.37 (0.19)	0.074
51	82.94 (6.90)	85.30 (7.72)	<0.001	0.36 (0.21)	0.36 (0.20)	0.355
52	83.30 (6.86)	85.66 (7.55)	<0.001	0.36 (0.22)	0.36 (0.22)	0.883
53	83.66 (6.81)	86.02 (7.46)	<0.001	0.36 (0.23)	0.35 (0.23)	0.586
54	84.02 (6.76)	86.37 (7.37)	<0.001	0.36 (0.24)	0.35 (0.25)	0.248
55	84.37 (6.70)	86.72 (7.26)	<0.001	0.36 (0.25)	0.34 (0.26)	0.091
56	84.73 (6.63)	87.06 (7.14)	<0.001	0.36 (0.26)	0.34 (0.28)	0.030
57	85.09 (6.56)	87.40 (7.02)	<0.001	0.36 (0.28)	0.33 (0.30)	0.010
58	85.45 (6.48)	87.73 (6.89)	<0.001	0.36 (0.29)	0.33 (0.32)	0.003
59	85.80 (6.41)	88.06 (6.75)	<0.001	0.36 (0.31)	0.32 (0.33)	0.001
60	86.16 (6.34)	88.38 (6.61)	<0.001	0.36 (0.32)	0.32 (0.35)	<0.001

NTN = normotension; HTN = hypertension.

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-4	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	1-4
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	7		
Objectives	3	State specific objectives, including any prespecified hypotheses	7		
Methods					
Study Design	4	Present key elements of study design early in the paper	8		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8		

Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	8	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	9	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	9
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8, 9		8, 9

Bias	9	Describe any efforts to address potential sources of bias	9, 10		
Study size	10	Explain how the study size was arrived at	8		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	8-10		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	9, 10		
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	8, 18

				RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	8
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	8	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	8
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)	10		
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure	10, 11		

		category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11-13		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	10, 11		
Discussion					
Key results	18	Summarise key results with reference to study objectives	13		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15, 16	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	15, 16
Interpretation	20	Give a cautious overall interpretation of results considering objectives,	13-16		

		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results	16		
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17		
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	18

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.