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

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

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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 ($1.19 \sim 1.74$), 1.51 ($1.19 \sim 1.92$), 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 ($0.86 \sim 0.98$) to 1.57 ($1.47 \sim 1.67$) for BMI, and 0.98 ($0.92 \sim 1.05$) to 1.44 ($1.35 \sim 1.53$) for WC. Conversely, the ORs (95% CIs) of level-adjusted linear slopes decreased with age, ranging from 1.47 ($1.38 \sim 1.57$) to 0.97($0.92 \sim 1.03$) for BMI, and 1.36 ($1.28 \sim 1.45$) to 0.99 ($0.93 \sim 1.06$) 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

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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

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INTRODUCTION

As a major risk factor for cardiovascular disease, hypertension is a severe problem in public health¹. The prevalence of hypertension has increased rapidly among decades², 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 studies⁵⁻⁹. 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 WC⁸. The levels of BMI and WC reflect different aspects of obesity⁵⁻¹², 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-sectional⁵⁻¹² and longitudinal studies¹³⁻¹⁵. However, these studies mainly focused on the BMI and WC separately¹⁰⁻¹⁵, 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 than 15 kg/m² or higher than 40 kg/m² (n = 799), with WC greater than 120 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

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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) $\geq 25g$ (for male) or $\geq 15g$ (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 \geq 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 WC¹⁸. 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 described¹⁹. We chose the best-fitting model for BMI and WC

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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, respectively¹⁹. 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.

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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),

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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. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

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

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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/m², increased slowly during the 20~60 years period, while the high-increasing group with lower baseline BMI increased rapidly. Some studies, using

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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

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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 theory²⁶⁻²⁸, 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 dysfunction²⁹⁻³¹. 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 people³⁰. Endothelial dysfunction may also play an important role in developing hypertension³¹ and it may impact early aorta root thickening²⁹. Aorta root size may play a causative role in the pathogenesis of systolic hypertension²⁹.

There are some important strengths in our study. The current study is a

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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. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

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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.

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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 (<u>https://www.cpc.unc.edu/projects/china/data/</u>).

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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.

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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.

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	Total	Normotensives	Incident Hypertension	
	TULAI	Normolensives		
Ν	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

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

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 hypertens	ion at follow-up by joint trajectory
groups	

`	Variable	Normal	WC-increasing	BMI-increasing	BMI&WC-increasing	P Value
,	Ν	4963	620	309	679	
- } L	Age, years	36.3 (8.6)	32.8 (8.2)	34.3 (8.3)	31.8 (7.7)	<0.001
r 5	Males, n (%)	2019 (40.7)	557 (89.8)	33 (10.7)	454 (66.9)	<0.001
, , ,	BMI, kg/m²	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
5	DBP, mm Hg	72.9 (8.6)	76.0 (7.5)	73.6 (8.6)	75.4 (8.3)	<0.001
5	Smoker, n (%)	1435 (29.1)	364 (59.4)	30 (9.8)	294 (43.5)	<0.001
7 3	Drinker, n (%)	1563 (31.8)	370 (60.3)	58 (18.9)	321 (48.0)	<0.001
))	Hypertension,	935 (18.8)	159 (25.6)	89 (28.8)	232 (34.2)	<0.001
<u>)</u>	n (%)					

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

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

	Model 1	Model 2	Model 3	Model 4
Joint trajectory grou	ıps			
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, 1.7
BM-increasing	1.69 (1.36, 2.10)	1.47 (1.16, 1.87)	1.48 (1.17, 1.89)	1.51 (1.19, 1.9
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, 2.1
Covariates				
Baseline Age		1.07 (1.06, 1.08)	1.07 (1.06, 1.08)	1.07 (1.06, 1.0
Female		0.77 (0.69, 0.87)	0.89 (0.79, 1.00)	1.01 (0.85, 1.1
Baseline BMI		1.10 (1.08, 1.13)	1.07 (1.05, 1.10)	1.07 (1.05, 1.1
Baseline SBP			1.03 (1.02, 1.04)	1.03 (1.02, 1.0
Smoker				1.12 (0.96, 1.3
Drinker				1.10 (0.96, 1.2







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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 Su³, 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 ³National 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

Variable	Excluded	Included	<i>P</i> -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/m²	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

Table S1. Baseline characteristics of participants included and excluded.

BMI indicates body mass index; DBP, diastolic blood pressure; SBP, systolic blood

pressure; WC, waist circumference.

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rable S2. Latent Class Growth Mixture Models (LCGMM) results of model fitting process for الملقى المقلقي المقلقي المتحدية المتحدية المتحدية المتحدية المتحدية المتحدية المحدية المح										
No. Latent class	Polynomial degree	Log-Lik	BIC	% Participants per class	Mean posterior	% Posterior				
					probabiliti	probabilities > 70%				
1	Linear	-59740	119525	100	na reigna	na				
	Quadratic	-59623	119308	100	na to nov	na				
	Cubic	-59604	119289	100	na text	na				
2	Linear	-59299	118678	9.98/90.02	0.79/0.95 and erie	66.92/95.38				
	Quadratic	-59122	118351	84.96/15.04	$0.93/0.81 \stackrel{dat}{ta} \stackrel{from}{P}$	93.19/72.37				
	Cubic	-59120	118373	15.17/84.83		73.22/93.00				
3	Linear	-59190	118495	24.97/72.12/2.91	0.74/0.87	56.98/84.30/67.02				
	Quadratic	-58989	118128	73.40/23.09/3.51	0.88/0.73/2.7	85.32/57.61/64.07				
	Cubic	-58985	118155	4.34/78.45/17.21	0.74/0.90	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)
				BMJ Open	bmjopen-20 I by copyrig	
Table S3. Latent (Class Growth Mixture	Models (LCGMM)	results of model fitting pro	cess for Would in	
No. Latent class	Polynomial degree	Log-Lik	BIC	% Participants per class	Mean post	% Posterior
					probabiliti	probabilities > 70 ^o
1	Linear	-98380	196839	100	na eign	na
	Quadratic	-98387	196836	100		na
	Cubic	-98397	196839	100	na text	na
2	Linear	-98042	196163	83.32/16.68	0.92/0.78 and berged	91.98/65.42
	Quadratic	-97946	195998	80.53/19.47	0.92/0.80 data from	91.35/68.67
	Cubic	-97940	196012	80.18/19.82	0.92/0.80 m K	91.41/69.79
3	Linear	-98008	195918	50.95/36.74/12.81	0.95/0.89	96.19/86.74/63.06
	Quadratic	-97875	195900	54.95/9.34/35.71	0.80/0.77	70.99/64.12/50.57
	Cubic	-97866	195112	50.46/36.74/12.80	0.71/0.87	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 highlighted in bold characters. (na: not applicable)

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

		Intercept (se)"	Linear (se)	Quadratic (se)
Fixed effect				
	Group 1	23.519 (0.0487)	0.077 (0.0024)	-5x10 ⁻⁵ (0.0002)
	Group 2	27.177 (0.1337)	0.155 (0.0076)	-0.009 (0.0005)
Random effect	cts: varianc	e-covariance mat	rix.	
σ^{2}_{int} = 3.88				
$\sigma^{2}_{\text{linear slope}} = 0.$	0105			
σ^2 quadratic slope <	0.001			
σ^{2}_{error} = 1.24				
se = standard e	error; BMI =	body mass index.		
*: Intercept inte	rpreted as th	ne expected level or	f BMI in kg/m² at 4	42 years of age (cente
to the mean ag	e of the sam	nple)		

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

Intercept (ac) Enter (ac) Outdrane (ac) 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 P ² intear stope = 0.0984 P ² quadratic stope < 0.001 P ² quadratic stope < 0.001 P ² quadratic stope < 0.001 P ² quadratic stope < 0.001 P ² quadratic stope < 0.001 P ² mor = 5.38 P P = standard error; WC = waist circumference. Intercept interpreted as the expected level of WC in cm at 42 years of age (center e mean age of the sample)	intercept (sc) Entrain(sc) education (sc) ixed 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) iandom effects: variance-covariance matrix ² mt = 24.31 ² mt = 24.31 ² mear slope < 0.001 ² error = 5.38 = standard error; WC = waist circumference. Intercept interpreted as the expected level of WC in cm at 42 years of age (center a mean age of the sample)			Intercent (se)*	Linear (se)	Quadratic (se)
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 Prime 24.31 Prime 3000 Prime 2000 Prim 2000 Prim 2000 P	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) andom effects: variance-covariance matrix ² _{imt} = 24.31 ² _{imear slope} = 0.0984 ² _{quadratic slope} < 0.001 ² _{error} = 5.38 = standard error; WC = waist circumference. Intercept interpreted as the expected level of WC in cm at 42 years of age (center a mean age of the sample)	Fixed offect				
Group 2 89.963 (0.3340) 0.501 (0.0226) -0.020 (0.0015) Random effects: variance-covariance matrix P ² _{int} = 24.31 P ² _{intear stope} = 0.0984 P ² _{error} = 5.38 P ² = standard error, WC = waist circumference. Intercept interpreted as the expected level of WC in cm at 42 years of age (center e mean age of the sample)	Group 2 89.963 (0.3340) 0.501 (0.0226) -0.020 (0.0015) andom effects: variance-covariance matrix ² _{Int} = 24.31 ² _{Intear slope} = 0.0984 ² _{quadratic slope} < 0.001 ² _{error} = 5.38 = standard error; WC = waist circumference. Intercept interpreted as the expected level of WC in cm at 42 years of age (center e mean age of the sample)	i ikeu ellect	Group 1	76 800 (0 1450)	0 338 (0 0094)	0.004 (0.0006)
Cloup 2 25.363 (0.3340) 0.301 (0.0226) -0.020 (0.0013) Random effects: variance-covariance matrix P ² Int = 24.31 P ² Intear slope = 0.0984 P ² quadratic slope < 0.001	andom effects: variance-covariance matrix ² _{int} = 24.31 ² _{intear slope} = 0.0984 ² _{quadratic slope} < 0.001 ² _{error} = 5.38 = standard error; WC = waist circumference. Intercept interpreted as the expected level of WC in cm at 42 years of age (center a mean age of the sample)		Group 2	70.090 (0.1439) 80.062 (0.2240)	0.556 (0.0064)	0.004 (0.0000)
P ² _{pht} = 24.31 P ² _{intear stope} = 0.0984 P ² _{quadratic stope} < 0.001 P ² _{error} = 5.38 P = standard error; WC = waist circumference. Intercept interpreted as the expected level of WC in cm at 42 years of age (center e mean age of the sample)	² _{int} = 24.31 ² _{intear slope} = 0.0984 ² _{quadratic stope} < 0.001 ² _{error} = 5.38 = standard error; WC = waist circumference. Intercept interpreted as the expected level of WC in cm at 42 years of age (center a mean age of the sample)	Bandom offe		09.903(0.3340)	0.501 (0.0220)	-0.020 (0.0013)
Print = 24.31 Plinear slope = 0.0984 P ² quadratic slope < 0.001 P ² error = 5.38 P = standard error; WC = waist circumference. Intercept interpreted as the expected level of WC in cm at 42 years of age (center e mean age of the sample)	The - 24-31 ² linear slope = 0.0984 ² quadratic slope < 0.001 ² error = 5.38 = standard error; WC = waist circumference. Intercept interpreted as the expected level of WC in cm at 42 years of age (center a mean age of the sample)	$\frac{1}{\sigma^2} = 24.21$				
P ² quadratic slope < 0.001 P ² error = 5.38 P = standard error; WC = waist circumference. Intercept interpreted as the expected level of WC in cm at 42 years of age (center e mean age of the sample)	<pre>#mear stope < 0.001 2error = 5.38 = standard error; WC = waist circumference. Intercept interpreted as the expected level of WC in cm at 42 years of age (center e mean age of the sample)</pre>	$\sigma^{2} = -0$	0084			
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		J J - 1		51
	Model 1	Model 2	Model 3	Model 4
Trajectory groups				
Low-increasing group	Reference	Reference	Reference	Reference
High-increasing group	1.79 (1.58,	1.44 (1.22,	1.47 (1.25,	1.49 (1.26,
	2.03)	1.69)	1.73)	1.75)
Covariates				
Age, y		1.07 (1.06,	1.06 (1.05,	1.06 (1.05,
		1.08)	1.07)	1.07)
Female		0.74 (0.67,	0.86 (0.77,	0.97 (0.83,
		0.83)	0.96)	1.14)
Baseline BMI		1.09 (1.06,	1.07 (1.04,	1.07 (1.04,
		1.12)	1.10)	1.10)
Baseline WC		1.01	1.01 (1.00,	1.01 (1.00,
		(1.00,1.02)	1.02)	1.02)
Baseline SBP			1.03 (1.02,	1.03 (1.02,
			1.04)	1.04)
Smoker				1.11 (0.96,
				1.30)
Drinker				1.11 (0.97,
				1.27)
BMI, body mass index; SI	3P, systolic bloo	d pressure; WC,	waist circumfere	ence.

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

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30 31	В
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Table S7. Hazard Ratios and 95% of WC	Trajectory Groups for Incident Hypertension
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	Model 1	Model 2	Model 3	Model 4
Trajectory groups				
Low-increasing	Reference	Reference	Reference	Reference
group				
High-increasing	1.71 (1.53,	1.45 (1.24,	1.42 (1.21,	1.43 (1.22,
group	1.93)	1.69)	1.66)	1.68)
Covariates				
Age, y		1.07 (1.06,	1.06 (1.05,	1.06 (1.05,
		1.08)	1.07)	1.07)
Female		0.80 (0.72,	0.92 (0.82,	1.04 (0.89,
		0.90)	1.03)	1.23)
Baseline BMI		1.10 (1.07,	1.08 (1.05,	1.08 (1.05,
		1.13)	1.11)	1.11)
Baseline WC		1.01 (1.00,	1.00 (0.99,	1.01 (1.00,
		1.02)	1.01)	1.02)
Baseline SBP			1.03 (1.02,	1.03 (1.02,
			1.04)	1.04)
Smoker				1.12 (0.96,
				1.30)
Drinker				1.10 (0.96,
				1.26)

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

1 2 3

4

	BMI Level (k	g/m²)		BMI Slope	(kg/m²/year)	
Age, (years)	NTN	HTN	P-Value	NTN	HTN	<i>P</i> -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)	<0.0
49	24.45 (2.33)	25.40 (2.66)	<0.001	0.07 (0.07)	0.08 (0.07)	<0.0
50	24.51 (2.33)	25.47 (2.66)	<0.001	0.06 (0.07)	0.07 (0.07)	<0.0
51	24.58 (2.33)	25.54 (2.65)	<0.001	0.06 (0.07)	0.07 (0.07)	<0.0
52	24.64 (2.33)	25.61 (2.64)	<0.001	0.06 (0.07)	0.06 (0.08)	0.00
53	24.69 (2.33)	25.67 (2.62)	<0.001	0.06 (0.07)	0.06 (0.08)	0.07
54	24.75 (2.33)	25.73 (2.60)	<0.001	0.05 (0.08)	0.06 (0.09)	0.31
55	24.80 (2.32)	25.79 (2.58)	<0.001	0.05 (0.08)	0.05 (0.09)	0.76
56	24.85 (2.31)	25.84 (2.56)	<0.001	0.05 (0.08)	0.05 (0.10)	0.73
57	24.90 (2.30)	25.88 (2.53)	<0.001	0.05 (0.09)	0.04 (0.10)	0.36
58	24.95 (2.29)	25.93 (2.50)	<0.001	0.04 (0.09)	0.04 (0.11)	0.15
59	25.00 (2.28)	25.96 (2.48)	<0.001	0.04 (0.10)	0.04 (0.11)	0.06
60	25.03 (2.27)	26.00 (2.45)	<0.001	0.04 (0.10)	0.03 (0.12)	0.02

NTN = normotension; HTN = hypertension.

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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	<i>P</i> -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	

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48	81.87 (6.96)	84.18 (7.74)	<0.001	0.36 (0.19)	0.38 (0.17)	<0.0
49	82.23 (6.95)	84.56 (7.72)	<0.001	0.36 (0.19)	0.37 (0.18)	0.00
50	82.59 (6.93)	84.93 (7.67)	<0.001	0.36 (0.20)	0.37 (0.19)	0.07
51	82.94 (6.90)	85.30 (7.72)	<0.001	0.36 (0.21)	0.36 (0.20)	0.35
52	83.30 (6.86)	85.66 (7.55)	<0.001	0.36 (0.22)	0.36 (0.22)	0.88
53	83.66 (6.81)	86.02 (7.46)	<0.001	0.36 (0.23)	0.35 (0.23)	0.58
54	84.02 (6.76)	86.37 (7.37)	<0.001	0.36 (0.24)	0.35 (0.25)	0.24
55	84.37 (6.70)	86.72 (7.26)	<0.001	0.36 (0.25)	0.34 (0.26)	0.09
56	84.73 (6.63)	87.06 (7.14)	<0.001	0.36 (0.26)	0.34 (0.28)	0.03
57	85.09 (6.56)	87.40 (7.02)	<0.001	0.36 (0.28)	0.33 (0.30)	0.01
58	85.45 (6.48)	87.73 (6.89)	<0.001	0.36 (0.29)	0.33 (0.32)	0.00
59	85.80 (6.41)	88.06 (6.75)	<0.001	0.36 (0.31)	0.32 (0.33)	0.00
60	86.16 (6.34)	88.38 (6.61)	<0.001	0.36 (0.32)	0.32 (0.35)	<0.0

NTN = normotension; HTN = hypertension.

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	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items including fo	Location in manuscript where items are reported
Title and abstra	ct				
	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 State used should be specified in the state or abstract. When possible, the mame of the databases used should B included. RECORD 1.2: If applications the geographic region and time the within which the study the state 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		1		d si D	
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	7	on June 1	
Objectives	3	State specific objectives, including any prespecified hypotheses	7	3, 2025 at hnologies.	
Methods		-		Ag	
Study Design	4	Present key elements of study design early in the paper	8	эпсе В	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8	ibliographiqu	

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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 details. If this is not possible, an explanation house of provided. RECORD 6.2: Any validation of select the population should be referenced. If validation of sconducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study of a flow diagram or other graphical display to demonstrate the data finkage process, including the number of individuals with linked that 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, conformeders, and effect modifiers should be provided. If these cannot be reported and 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	Agence Bibliographiq	8,9

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Bias	9	Describe any efforts to address potential sources of bias	9, 10	jøpen-2	
Study size	10	Explain how the study size was arrived at	8	021-05 yht, inc	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	8-10	9556 on 25 May 2 Ense luding for uses	
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) <i>Cohort study</i> - If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> - If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses 	9, 10	2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at eignement Superieur (ABES) . related to text and data mining, Al training, and similar technologies	
Data access and cleaning methods				RECORD 12.1: Authors showld 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 hogild provide information on the data	
Linkage	· · ·		RECORD 12.3: State whether the study included person-legel, institutional-level, or other data linkage across two or more dataleases. The methods of linkage and methods of	8
			linkage quality evaluation and fould be provided.	
Results Participants	13 (a) Report the numbers of individuals at each stage of the study (<i>e.g.</i> , numbers potentially eligible, examined for eligibility confirmed eligible, included in the study, completing follow-up and analysed) (b) Give reasons for non-	8	RECORD 13.1: Describe selection of the persons is selection) including filtering based is that a quality, data availability selection) the selection of includes in the selection of includes in the text is the selection of the study flow grag am.	8
Descriptive data	participation at each stage.(c) Consider use of a flowdiagram14(a) Give characteristics of studyparticipants (e.g., demographic,clinical, social) and informationon exposures and potentialconfounders(b) Indicate the number ofparticipants with missing datafor each variable of interest(c) Cohort study - summarisefollow-up time (e.g., average an	10 d	open.bmj.com/ on June 13, 2025 at Agen I training, and similar technologies.	
Outcome data	total amount)15Cohort study - Report numbers of outcome events or summary measures over time Case-control study - Report numbers in each exposure	10, 11	se Bibliographique c	

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		category, or summary measures of exposure <i>Cross-sectional study</i> - Report numbers of outcome events or summary measures		open-2021-0595t copyright, inclu	
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	56 on 25 May 2022. Downloaded from http://bm Enseignement Superieur (ABES) . ding for uses related to text and data mining, <i>μ</i>	
Other analyses	17	Report other analyses done— e.g., analyses of subgroups and interactions, and sensitivity analyses	10, 11	njopen.bmj.co Al training, ar	
Discussion				nd m	
Key results	18	Summarise key results with reference to study objectives	13	similar Ju	
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 date that were not created or collected to an swee 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	13-16	l aphi	

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			limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		jopen-2021-05 copyright, inc	
	Generalisability	21	Discuss the generalisability (external validity) of the study results	16	9556 on 2 Sluding fo	
	Other Information	n		1	<u> </u>	
) 1 2 3 4	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	17	ay 2022. Down inseignement s ses related to te	
5 – 5 – 7 – 8	Accessibility of protocol, raw data, and				RECORD 22.1: Authors and any supplemental information on the supplemental information supplementation	18 Inccess Inch as
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<pre>* C 3 C 5 ii 6 7 * 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3</pre>	Reference: Bench Committee. The R n press. Checklist is protec	imol EI, Eporting	Smeeth L, Guttmann A, Harron K, g of studies Conducted using Observ er Creative Commons Attribution (Moher D, Petersen I, Sø vational Routinely-collec <u>CC BY</u>) license.	prensen HT, von Elm E, Langan Sl cted health Data (RECOR ing, and similar technologies. Bibliographique C	M, the RECORD Working ment. <i>PLoS Medicine</i> 2015;
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Joint Trajectories of Body Mass Index and Waist Circumference in Early to Mid-life Adulthood and Incident Hypertension: the China Health and Nutrition Survey

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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

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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 (Cls) 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% Cls 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% Cls) 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 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

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 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
- ked I. LCGMM = latent class growth mixed model
- SD = standard deviation
 - HR = hazard ratio
 - OR = odds ratio
 - CI = confidence interval

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INTRODUCTION

As a major risk factor for cardiovascular disease, hypertension is a severe problem in public health¹. The prevalence of hypertension has increased rapidly over decades², 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 studies⁵⁻⁹. 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 WC⁸. The levels of BMI and WC reflect different aspects of obesity⁵⁻¹², 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-sectional⁵⁻¹² and longitudinal studies¹³⁻¹⁵. However, these studies mainly focused on the BMI and WC separately¹⁰⁻¹⁵, 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/m² or higher than 40 kg/m² (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.

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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

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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) $\geq 25g$ (for male) or $\geq 15g$ (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 \geq 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 WC¹⁸. 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 described¹⁹. We chose the best-fitting model for BMI and WC

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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, respectively¹⁹. 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.

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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.

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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 (Cls) for the association between the BMI trajectory group membership and incident hypertension. Compared with the BMI low-increasing group, HR (95% Cl) 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% Cls for the relationship between the WC trajectory classes and incident hypertension. Compared with the WC low-increasing group, HR (95% Cl) for the WC high-increasing

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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. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

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

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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. SIR

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.

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In the current study, we identified two trajectories for BMI. The low-increasing group, with baseline BMI around 20 kg/m², 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

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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 in incident hypertension during both early and mid-life adulthood in Chinese population.

According to the life-course epidemiology theory²⁶⁻²⁸, 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 dysfunction²⁹⁻³¹. 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 people³⁰. Endothelial dysfunction may also play an important role in developing

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hypertension³¹ and it may impact early aorta root thickening²⁹. Aorta root size may play a causative role in the pathogenesis of systolic hypertension²⁹.

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.

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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.

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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.

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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.

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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 (<u>https://www.cpc.unc.edu/projects/china/data/</u>).

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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.

Variable	Total	Normotensives	Incident	P Value
			Hypertension	
Ν	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/m²	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,	110.0 [101.0, 120.0]	116.0 [108.0, 120.0]	<0.001
	120.0]			
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

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

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.

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N 4963 620 309 Age, years 36.3 (8.6) 32.8 (8.2) 34.3 (8.3) 77.7) <0	Variable	Normal	WC-increasing	BMI-increasing	B M	&WC-increasing	P Value
Age, years 36.3 (8.6) 32.8 (8.2) 34.3 (8.3) 36.3 (8.6) 32.8 (8.2) 34.3 (8.3) Males, n (%) 2019 (40.7) 557 (89.8) 33 (10.7) 459 (66.9) <0 BMI, kg/m ² 21.3 (2.2) 22.8 (2.3) 24.5 (3.1) 459 (6.9) <0 VC, cm 73.8 (7.0) 81.3 (8.7) 78.9 (8.2) 450 (3.4) <0 SBP, mmHg 110.0 [101.0, 120.0] 117.5 [110.0, 120.0] 110.0 [105.0, 120.0] 100 [108.0, 120.0] <0 OBP, 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	N	4963	620	309	÷ وي:	5 May	
Males, n (%) 2019 (40.7) 557 (89.8) 33 (10.7) 557 (66.9) <0	Age, years	36.3 (8.6)	32.8 (8.2)	34.3 (8.3)	seigne s réligite	₿ <mark>3</mark> (7.7)	<0.002
BMI, kg/m ² 21.3 (2.2) 22.8 (2.3) 24.5 (3.1) 250 (3.4) <0 NC, cm 73.8 (7.0) 81.3 (8.7) 78.9 (8.2) 24.5 (3.1) <0 SBP, mmHg 110.0 [101.0, 120.0] 117.5 [110.0, 120.0] 110.0 [105.0, 120.0] 110.0 [108.0, 120.0] <0 DBP, mmHg 72.5 [68.0, 80.0] 77.0 [70.0, 80.0] 73.0 [68.8, 80.0] 70.0 [70.0, 80.0] <0	Males, n (%)	2019 (40.7)	557 (89.8)	33 (10.7)		9 66.9)	<0.002
NC, cm 73.8 (7.0) 81.3 (8.7) 78.9 (8.2) and	BMI, kg/m²	21.3 (2.2)	22.8 (2.3)	24.5 (3.1)	ext an	02 02(3.4)	<0.001
SBP, mmHg 110.0 [101.0, 120.0] 117.5 [110.0, 120.0] 110.0 [105.0, 120.0] 120.0] <0 DBP, mmHg 72.5 [68.0, 80.0] 77.0 [70.0, 80.0] 73.0 [68.8, 80.0] 72.0 [70.0, 80.0] <0	WC, cm	73.8 (7.0)	81.3 (8.7)	78.9 (8.2)	ieur (15(9.9)	<0.001
DBP, mmHg 72.5 [68.0, 80.0] 77.0 [70.0, 80.0] 73.0 [68.8, 80.0] 72.5 [68.0, 80.0] <77.0 [70.0, 80.0] <0	SBP, mmHg	110.0 [101.0, 120.0]	117.5 [110.0, 120.0]	110.0 [105.0, 120.0]	a naini	a [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]	ng7 Al	و [70.0, 80.0]	<0.001
Smoker, n (%) 1435 (29.1) 364 (59.4) 30 (9.8) 20 (9.8) <0	Smoker, n (%)	1435 (29.1)	364 (59.4)	30 (9.8)		43.5)	<0.001
Drinker, n (%) 1563 (31.8) 370 (60.3) 58 (18.9) $\frac{3}{2}$ 21 $\frac{3}{4}$ 48.0) <0	Drinker, n (%)	1563 (31.8)	370 (60.3)	58 (18.9)	ng Sar	48.0)	<0.001
Hypertension, n (%) 935 (18.8) 159 (25.6) 89 (28.8) 23/34.2) <0	Hypertension, n (%)	935 (18.8)	159 (25.6)	89 (28.8)	2 2 3 2 3 2	234.2)	<0.00

	Model 1	Model 2	Model 3	Model 4
Joint trajectory grou	ups			
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, ⁻
BM-increasing	1.69 (1.36, 2.10)	1.47 (1.16, 1.87)	1.48 (1.17, 1.89)	1.51 (1.19, ⁻
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
Covariates				
Baseline Age		1.07 (1.06, 1.08)	1.07 (1.06, 1.08)	1.07 (1.06,
Female		0.77 (0.69, 0.87)	0.89 (0.79, 1.00)	1.01 (0.85, ²
Baseline BMI		1.10 (1.08, 1.13)	1.07 (1.05, 1.10)	1.07 (1.05, ⁻
Baseline SBP			1.03 (1.02, 1.04)	1.03 (1.02,
Smoker				1.12 (0.96,
Drinker				1.10 (0.96, ²



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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 Su³, 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

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

where $v = (v_{0g}, v_{1g}, v_{2g})$ 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_{ii} is an unknown error term (the model of WC is similar with BMI).

Variable	Excluded	Included	<i>P</i> -Value
Ν	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

Table S1. Baseline characteristics of participants included and excluded.

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

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fable S2 . Latent (Class Growth Mixture	Models (LCGMM)	results of model fitting pro	cess for BMa. 555	
No. Latent class	Polynomial degree	Log-Lik	BIC	% Participants per class	Mean posteriar	% Posterior
					probabiliti	probabilities > 70%
1	Linear	-59740	119525	100	na reign 2022	na
	Quadratic	-59623	119308	100	na to Dov	na
	Cubic	-59604	119289	100	na tesu	na
2	Linear	-59299	118678	9.98/90.02	0.79/0.95 and erie de	66.92/95.38
	Quadratic	-59122	118351	84.96/15.04	$0.93/0.81 \stackrel{dat}{ta} \stackrel{from}{A}$	93.19/72.37
	Cubic	-59120	118373	15.17/84.83		73.22/93.00
3	Linear	-59190	118495	24.97/72.12/2.91	0.74/0.87	56.98/84.30/67.02
	Quadratic	-58989	118128	73.40/23.09/3.51	0.88/0.73	85.32/57.61/64.07
	Cubic	-58985	118155	4.34/78.45/17.21	0.74/0.90	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)

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Table S3. Latent (Class Growth Mixture	Models (LCGMM)	results of model fitting pro	ght, ingluding	
No. Latent class	Polynomial degree	Log-Lik	BIC	% Participants per class	Mean posteriar	% Posterior
					probabiliti	probabilities > 709
1	Linear	-98380	196839	100		na
	Quadratic	-98387	196836	100		na
	Cubic	-98397	196839	100	na text	na
2	Linear	-98042	196163	83.32/16.68	0.92/0.78 and e	91.98/65.42
	Quadratic	-97946	195998	80.53/19.47	0.92/0.80 tata from	91.35/68.67
	Cubic	-97940	196012	80.18/19.82	0.92/0.80 mig	91.41/69.79
3	Linear	-98008	195918	50.95/36.74/12.81	0.95/0.89%	96.19/86.74/63.06
	Quadratic	-97875	195900	54.95/9.34/35.71	0.80/0.77	70.99/64.12/50.57
	Cubic	-97866	195112	50.46/36.74/12.80	0.71/0.87	52.88/84.85/42.74

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

		Intercept (se)*	Linear (se)	Quadratic (se)
Fixed effect				
	Group 1	23.519 (0.0487)	0.077 (0.0024)	-5x10 ⁻⁵ (0.0002)
	Group 2	27.177 (0.1337)	0.155 (0.0076)	-0.009 (0.0005)
Random effe	cts: varianc	e-covariance mati	rix	
σ^{2}_{int} = 3.88				
$\sigma^{2}_{\text{linear slope}} = 0$.0105			
σ^2 quadratic slope <	0.001			
σ^{2}_{error} = 1.24				
se = standard e	error; BMI =	body mass index.		
: Intercept inte	rpreted as tl	he expected level of	f BMI in kg/m² at 4	42 years of age (cente
o the mean ag	e of the sam	nple)		

Table S5. Parameters estimates for the best fitting 2-class quadratic Latent Class GrowthMixture 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 effec	ts: varianc	e-covariance mat	rix	
$\sigma^{2}_{int} = 24.31$				
$\sigma^{2}_{\text{linear slope}} = 0.$	0984			
σ^2 quadratic slope <	0.001			
$\sigma^{2}_{error} = 5.38$				
e = standard e	rror; WC = v	waist circumferenc	e.	
: Intercept inter	rpreted as th	ne expected level o	of WC in cm at 42	years of age (centeri
ne mean age o	f the sample	e)		

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		J J - 1		51
	Model 1	Model 2	Model 3	Model 4
Trajectory groups				
Low-increasing group	Reference	Reference	Reference	Reference
High-increasing group	1.79 (1.58,	1.44 (1.22,	1.47 (1.25,	1.49 (1.26,
	2.03)	1.69)	1.73)	1.75)
Covariates				
Age, y		1.07 (1.06,	1.06 (1.05,	1.06 (1.05,
		1.08)	1.07)	1.07)
Female		0.74 (0.67,	0.86 (0.77,	0.97 (0.83,
		0.83)	0.96)	1.14)
Baseline BMI		1.09 (1.06,	1.07 (1.04,	1.07 (1.04,
		1.12)	1.10)	1.10)
Baseline WC		1.01	1.01 (1.00,	1.01 (1.00,
		(1.00,1.02)	1.02)	1.02)
Baseline SBP			1.03 (1.02,	1.03 (1.02,
			1.04)	1.04)
Smoker				1.11 (0.96,
				1.30)
Drinker				1.11 (0.97,
				1.27)
BMI, body mass index; SI	BP, systolic bloo	d pressure; WC,	waist circumfere	ence.

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

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20 27 28 29	В
30 31 32	В
33 34 35 36	S
37 38 39 40	D
41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59	

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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	Reference	Reference	Reference	Reference
group				
High-increasing	1.71 (1.53,	1.45 (1.24,	1.42 (1.21,	1.43 (1.22,
group	1.93)	1.69)	1.66)	1.68)
Covariates				
Age, y		1.07 (1.06,	1.06 (1.05,	1.06 (1.05,
		1.08)	1.07)	1.07)
Female		0.80 (0.72,	0.92 (0.82,	1.04 (0.89,
		0.90)	1.03)	1.23)
Baseline BMI		1.10 (1.07,	1.08 (1.05,	1.08 (1.05,
		1.13)	1.11)	1.11)
Baseline WC		1.01 (1.00,	1.00 (0.99,	1.01 (1.00,
		1.02)	1.01)	1.02)
Baseline SBP			1.03 (1.02,	1.03 (1.02,
			1.04)	1.04)
Smoker				1.12 (0.96,
				1.30)
Drinker				1.10 (0.96,
				1.26)
BMI, body mass	index; SBP, systo	lic blood pressure;	WC, waist circum	ference.

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

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	BMI Level (kg/m ²)			BMI Slope (kg/m²/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)	<0.00
49	24.45 (2.33)	25.40 (2.66)	<0.001	0.07 (0.07)	0.08 (0.07)	<0.00
50	24.51 (2.33)	25.47 (2.66)	<0.001	0.06 (0.07)	0.07 (0.07)	<0.00
51	24.58 (2.33)	25.54 (2.65)	<0.001	0.06 (0.07)	0.07 (0.07)	<0.0
52	24.64 (2.33)	25.61 (2.64)	<0.001	0.06 (0.07)	0.06 (0.08)	0.00
53	24.69 (2.33)	25.67 (2.62)	<0.001	0.06 (0.07)	0.06 (0.08)	0.07
54	24.75 (2.33)	25.73 (2.60)	<0.001	0.05 (0.08)	0.06 (0.09)	0.31
55	24.80 (2.32)	25.79 (2.58)	<0.001	0.05 (0.08)	0.05 (0.09)	0.76
56	24.85 (2.31)	25.84 (2.56)	<0.001	0.05 (0.08)	0.05 (0.10)	0.73
57	24.90 (2.30)	25.88 (2.53)	<0.001	0.05 (0.09)	0.04 (0.10)	0.36
58	24.95 (2.29)	25.93 (2.50)	<0.001	0.04 (0.09)	0.04 (0.11)	0.15
59	25.00 (2.28)	25.96 (2.48)	<0.001	0.04 (0.10)	0.04 (0.11)	0.06
60	25.03 (2.27)	26.00 (2.45)	<0.001	0.04 (0.10)	0.03 (0.12)	0.02

NTN = normotension; HTN = hypertension.

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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)	<0.0
49	82.23 (6.95)	84.56 (7.72)	<0.001	0.36 (0.19)	0.37 (0.18)	0.00
50	82.59 (6.93)	84.93 (7.67)	<0.001	0.36 (0.20)	0.37 (0.19)	0.07
51	82.94 (6.90)	85.30 (7.72)	<0.001	0.36 (0.21)	0.36 (0.20)	0.35
52	83.30 (6.86)	85.66 (7.55)	<0.001	0.36 (0.22)	0.36 (0.22)	0.88
53	83.66 (6.81)	86.02 (7.46)	<0.001	0.36 (0.23)	0.35 (0.23)	0.58
54	84.02 (6.76)	86.37 (7.37)	<0.001	0.36 (0.24)	0.35 (0.25)	0.24
55	84.37 (6.70)	86.72 (7.26)	<0.001	0.36 (0.25)	0.34 (0.26)	0.09
56	84.73 (6.63)	87.06 (7.14)	<0.001	0.36 (0.26)	0.34 (0.28)	0.03
57	85.09 (6.56)	87.40 (7.02)	<0.001	0.36 (0.28)	0.33 (0.30)	0.01
58	85.45 (6.48)	87.73 (6.89)	<0.001	0.36 (0.29)	0.33 (0.32)	0.00
59	85.80 (6.41)	88.06 (6.75)	<0.001	0.36 (0.31)	0.32 (0.33)	0.00
60	86.16 (6.34)	88.38 (6.61)	<0.001	0.36 (0.32)	0.32 (0.35)	<0.0

NTN = normotension; HTN = hypertension.

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BMJ Open 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 including for 2	Location in manuscript where items are reported
Title and abstra	ct				
	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 State used should be specified in the dite or abstract. When possible, dife name of the databases used should be included. RECORD 1.2: If applications within which the study the be included should be reported in the time 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	imilar tecl	
Objectives	3	State specific objectives, including any prespecified hypotheses	7	3, 2025 at hnologies.	
Methods		1	1	Age	1
Study Design	4	Present key elements of study design early in the paper	8	nce B	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8	ibliographiqu	

47 of 50			BMJ Open	36/bm	
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 of this is not possible, an explanation should be provided.	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, conformeders, and effect modifiers should be provided. If these cannot be reported and 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	Agence Bibliographiq	8,9

			BMJ Open	6/bm ed by	Page 4
Bias	9	Describe any efforts to address potential sources of bias	9, 10	jopen-2	
Study size	10	Explain how the study size was arrived at	8	021-05; yht, inc	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	8-10	9556 on 25 May 2 Ense Juding for uses	
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) <i>Cohort study</i> - If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> - If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses 	9, 10	2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at eignement Superieur (ABES) . related to text and data mining, Al training, and similar technologies	
Data access and cleaning methods				RECORD 12.1: Authors showed 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 showid provide information on the data	
			cleaning methods used ig the study.	
Linkage			RECORD 12.3: State whether the study included person-level, g institutional-level, or other data linkage	8
			across two or more dataleases. The methods of linkage and methods of linkage quality evaluation are bould be	
			provided.	
Results			ateo	
Participants	 (a) Report the numbers of individuals at each stage of the study (<i>e.g.</i>, 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 Retail the selection of the persons Red ded in the study (<i>i.e.</i> , study population detection) including filtering based at quality, data availability data the selection of included resons 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 (<i>e.g.</i>, 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) <i>Cohort study</i> - summarise follow-up time (<i>e.g.</i>, average ar total amount) 	nd 10	icom/ on June 13, 2025 at Agence E and similar technologies.	
Outcome data	15Cohort study - Report numbers of outcome events or summary measures over time Case-control study - Report numbers in each exposure	10, 11	3ibliographique d	

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		category, or summary measures of exposure <i>Cross-sectional study</i> - Report numbers of outcome events or summary measures		open-2021-05955 copyright, inclu	
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	56 on 25 May 2022. Downloaded from http://bm Enseignement Superieur (ABES) . ding for uses related to text and data mining, <i>A</i>	
Other analyses	17	Report other analyses done— e.g., analyses of subgroups and interactions, and sensitivity analyses	10, 11	njopen.bmj.co Al training, ar	
Discussion				d j	
Key results	18	Summarise key results with reference to study objectives	13	imilar Ju	
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 date that were not created or collected to a sweet 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	13-16	raphiq	

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

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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

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Running Title: Joint trajectories of BMI and WC and hypertension

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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 (Cls) 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% Cls 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% Cls) 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

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 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
- di LCGMM = latent class growth mixed model
- SD = standard deviation
 - HR = hazard ratio
 - OR = odds ratio
 - CI = confidence interval

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INTRODUCTION

As a major risk factor for cardiovascular disease, hypertension is a severe problem in public health¹. The prevalence of hypertension has increased rapidly over decades², 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 studies⁵⁻⁹. 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 WC⁸. The levels of BMI and WC reflect different aspects of obesity⁵⁻¹², 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-sectional⁵⁻¹² and longitudinal studies¹³⁻¹⁵. However, these studies mainly focused on the BMI and WC separately¹⁰⁻¹⁵, 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/m² or higher than 40 kg/m² (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.

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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

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Standing height without shoes was measured to the nearest 0.2 centimeters using a portable SECA stadiometer (SECA, Hamburg, Germany) at each follow up¹⁸. Weight was measured to the nearest 0.1 kilograms in light clothing without shoes on a dedicated scale that was routinely calibrated¹⁸. 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) \geq 25g (for male) or \geq 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 1993~2011¹⁸. 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 1991~2011¹⁸. The mean of the last two measurements were used for analyses.

Outcome

Hypertension was defined as SBP/DBP \geq 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 WC¹⁹. 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 described¹⁹. 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

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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, respectively²⁰. 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. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

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

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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 (Cls) 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% Cls 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. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

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.

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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/m², increased slowly during the 20~60 years period, while

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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 Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

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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 theory²⁷⁻²⁹, 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 dysfunction³⁰⁻³². 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 people³¹. Endothelial dysfunction may also play an important role in developing hypertension³² and it may impact early aorta root thickening³⁰. Furthermore, aorta root size may play a causative role in the pathogenesis of

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systolic hypertension³⁰.

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.

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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

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reduce the future prevalence and burden of hypertension among Chinese.

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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.

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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 (<u>https://www.cpc.unc.edu/projects/china/data/</u>).

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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.

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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.

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Variable	Total	Normotensives	Incident	P Value
			Hypertension	
Ν	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/m²	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,	110.0 [101.0, 120.0]	116.0 [108.0, 120.0]	<0.001
	120.0]			
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

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

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.

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3 4

6

N 4963 620 309 Age, years 36.3 (8.6) 32.8 (8.2) 34.3 (8.3) Males, n (%) 2019 (40.7) 557 (89.8) 33 (10.7) BMI, kg/m ² 21.3 (2.2) 22.8 (2.3) 24.5 (3.1) WC, cm 73.8 (7.0) 81.3 (8.7) 78.9 (8.2) 844 (9.9) SBP, mmHg 110.0 [101.0, 120.0] 117.5 [110.0, 120.0] 110.0 [105.0, 120.0] 110.0 [108.0, 120.0] 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]	<0.00 <0.00
Age, years36.3 (8.6)32.8 (8.2)34.3 (8.3)34.3 (8.3)Males, n (%)2019 (40.7)557 (89.8)33 (10.7)557 (89.8)BMI, kg/m²21.3 (2.2)22.8 (2.3)24.5 (3.1)WC, cm73.8 (7.0)81.3 (8.7)78.9 (8.2)SBP, mmHg110.0 [101.0, 120.0]117.5 [110.0, 120.0]110.0 [105.0, 120.0]DBP, mmHg72.5 [68.0, 80.0]77.0 [70.0, 80.0]73.0 [68.8, 80.0]77.0 [70.0, 80.0]	<0.00 <0.00
Males, n (%) 2019 (40.7) 557 (89.8) 33 (10.7) 557 (66.9) BMI, kg/m² 21.3 (2.2) 22.8 (2.3) 24.5 (3.1) 556 (3.4) WC, cm 73.8 (7.0) 81.3 (8.7) 78.9 (8.2) 557 (108.0, 120.0) SBP, mmHg 110.0 [101.0, 120.0] 117.5 [110.0, 120.0] 110.0 [105.0, 120.0] 110.0 [108.0, 120.0] 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]	<0.00
BMI, kg/m² 21.3 (2.2) 22.8 (2.3) 24.5 (3.1) 250 (3.4) WC, cm 73.8 (7.0) 81.3 (8.7) 78.9 (8.2) 84 (100 (100 (100 (100 (100 (100 (100 (10	
WC, cm 73.8 (7.0) 81.3 (8.7) 78.9 (8.2) 84.1 (9.9) SBP, mmHg 110.0 [101.0, 120.0] 117.5 [110.0, 120.0] 110.0 [105.0, 120.0] 110.0 [108.0, 120.0] 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]	<0.00
SBP, mmHg 110.0 [101.0, 120.0] 117.5 [110.0, 120.0] 110.0 [105.0, 120.0]	<0.00
DBP. mmHg 72.5 [68.0. 80.0] 77.0 [70.0. 80.0] 73.0 [68.8. 80.0]	<0.00
	<0.00
Smoker, n (%) 1435 (29.1) 364 (59.4) 30 (9.8) 20 (9.8)	<0.00
Drinker, n (%) 1563 (31.8) 370 (60.3) 58 (18.9) $321\frac{3}{4}$ 48.0)	<0.00
Hypertension, n (%) 935 (18.8) 159 (25.6) 89 (28.8) 2332 34.2)	<0.00

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

	Model 1	Model 2	Model 3	Model 4
Joint trajectory grou	lps			
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, 1.7
BM-increasing	1.69 (1.36, 2.10)	1.47 (1.16, 1.87)	1.48 (1.17, 1.89)	1.51 (1.19, 1.9
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, 2.1
Covariates				
Baseline Age		1.07 (1.06, 1.08)	1.07 (1.06, 1.08)	1.07 (1.06, 1.0
Female		0.77 (0.69, 0.87)	0.89 (0.79, 1.00)	1.01 (0.85, 1.1
Baseline BMI		1.10 (1.08, 1.13)	1.07 (1.05, 1.10)	1.07 (1.05, 1.1
Baseline SBP			1.03 (1.02, 1.04)	1.03 (1.02, 1.0
Smoker				1.12 (0.96, 1.3
Drinker				1 10 (0 06 1 3
BMI, body mass ir	ndex; WC, waist cir	cumference; SBP,	systolic blood pres	sure.
BMI, body mass ir	ndex; WC, waist cir	cumference; SBP,	systolic blood pres	sure.
BMI, body mass in	ndex; WC, waist cir	cumference; SBP,	systolic blood pres	sure.
BMI, body mass in	ndex; WC, waist cir	cumference; SBP,	systolic blood pres	sure.
BMI, body mass in	ndex; WC, waist cir	cumference; SBP,	systolic blood pres	sure.
BMI, body mass in	ndex; WC, waist cir	cumference; SBP,	systolic blood pres	sure.
BMI, body mass in	ndex; WC, waist cir	cumference; SBP,	systolic blood pres	sure.
BMI, body mass in	ndex; WC, waist cir	cumference; SBP,	systolic blood pres	sure.
BMI, body mass in	ndex; WC, waist cir	cumference; SBP,	systolic blood pres	sure.
BMI, body mass in	ndex; WC, waist cir	cumference; SBP,	systolic blood pres	sure.

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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

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

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where $v = (v_{0g}, v_{1g}, v_{2g})$ 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_{ii} is an unknown error term (the model of WC is similar with BMI).

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Variable	Excluded	Included	<i>P</i> -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

Table S1. Baseline characteristics of participants included and excluded.

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

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Fable S2. Latent C	Class Growth Mixture	Models (LCGMM)	results of model fitting pro	cess for BMudin	
No. Latent class	Polynomial degree	Log-Lik	BIC	% Participants per class	Mean posteria	% Posterior
					probabiliti	probabilities > 70%
1	Linear	-59740	119525	100	na reign	na
	Quadratic	-59623	119308	100		na
	Cubic	-59604	119289	100	na text	na
2	Linear	-59299	118678	9.98/90.02	0.79/0.95 and see	66.92/95.38
	Quadratic	-59122	118351	84.96/15.04	0.93/0.81 data (A from	93.19/72.37
	Cubic	-59120	118373	15.17/84.83		73.22/93.00
3	Linear	-59190	118495	24.97/72.12/2.91	0.74/0.87	56.98/84.30/67.02
	Quadratic	-58989	118128	73.40/23.09/3.51	0.88/0.73/2.7	85.32/57.61/64.07
	Cubic	-58985	118155	4.34/78.45/17.21	0.74/0.90	58.25/88.13/54.38

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

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Fable S3. Latent (Class Growth Mixture	Models (LCGMM)	results of model fitting pro	cess for Wouding	
No. Latent class	Polynomial degree	Log-Lik	BIC	% Participants per class	Mean pos t eri <mark>g</mark> r	% Posterior
					probabilitiଞ୍ଜିଙ୍କୁ ଛୁ	probabilities > 70%
1	Linear	-98380	196839	100	na eign	na
	Quadratic	-98387	196836	100	na tempo	na
	Cubic	-98397	196839	100		na
2	Linear	-98042	196163	83.32/16.68	0.92/0.78 and ed	91.98/65.42
	Quadratic	-97946	195998	80.53/19.47	0.92/0.80 tat from	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	96.19/86.74/63.06
	Quadratic	-97875	195900	54.95/9.34/35.71	0.80/0.77	70.99/64.12/50.57
	Cubic	-97866	195112	50.46/36.74/12.80	0.71/0.87	52.88/84.85/42.74

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

Intercept (se)*Fixed effectGroup 123.519 (0.0487)Group 227.177 (0.1337)Random effects: variance-covariance matri $\sigma^2_{int} = 3.88$ $\sigma^2_{iinear slope} = 0.0105$ $\sigma^2_{quadratic slope} < 0.001$ $\sigma^2_{error} = 1.24$ e = standard error; BMI = body mass index.: Intercept interpreted as the expected level of the mean age of the sample)		
Fixed effect Group 1 23.519 (0.0487) Group 2 27.177 (0.1337) Random effects: variance-covariance matri $\sigma^{2}_{int} = 3.88$ $\sigma^{2}_{iinear slope} = 0.0105$ $\sigma^{2}_{quadratic slope} < 0.001$ $\sigma^{2}_{error} = 1.24$ se = standard error; BMI = body mass index. : Intercept interpreted as the expected level of the mean age of the sample)	Linear (se)	Quadratic (se)
Group 1 23.519 (0.0487) Group 2 27.177 (0.1337) Random effects: variance-covariance matri $\sigma^{2}_{int} = 3.88$ $\sigma^{2}_{linear slope} = 0.0105$ $\sigma^{2}_{quadratic slope} < 0.001$ $\sigma^{2}_{error} = 1.24$ e = standard error; BMI = body mass index. Intercept interpreted as the expected level of the mean age of the sample)		
Group 2 27.177 (0.1337) Random effects: variance-covariance matri $\sigma^2_{int} = 3.88$ $\sigma^2_{linear slope} = 0.0105$ $\sigma^2_{quadratic slope} < 0.001$ $\sigma^2_{error} = 1.24$ e = standard error; BMI = body mass index. : Intercept interpreted as the expected level of the mean age of the sample)	0.077 (0.0024)	-5x10 ⁻⁵ (0.0002)
Random effects: variance-covariance matri $\sigma^{2}_{int} = 3.88$ $\sigma^{2}_{iinear slope} = 0.0105$ $\sigma^{2}_{quadratic slope} < 0.001$ $\sigma^{2}_{error} = 1.24$ e = standard error; BMI = body mass index. : Intercept interpreted as the expected level of the mean age of the sample)	0.155 (0.0076)	-0.009 (0.0005)
$\sigma^{2}_{int} = 3.88$ $\sigma^{2}_{linear slope} = 0.0105$ $\sigma^{2}_{quadratic slope} < 0.001$ $\sigma^{2}_{error} = 1.24$ e = standard error; BMI = body mass index. : Intercept interpreted as the expected level of the mean age of the sample)	x	
σ ² linear slope = 0.0105 σ ² quadratic slope < 0.001 σ ² error = 1.24 e = standard error; BMI = body mass index. Intercept interpreted as the expected level of o the mean age of the sample)		
$\sigma^2_{quadratic slope} < 0.001$ $\sigma^2_{error} = 1.24$ e = standard error; BMI = body mass index. : Intercept interpreted as the expected level of the mean age of the sample)		
σ ² error = 1.24 e = standard error; BMI = body mass index. the nean age of the sample)		
e = standard error; BMI = body mass index. : Intercept interpreted as the expected level of o the mean age of the sample)		
: Intercept interpreted as the expected level of the mean age of the sample)		
o the mean age of the sample)	BMI in kg/m² at 4	12 years of age (cen

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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 effe	cts: varianc	e-covariance mat	rix	
$\sigma^{2}_{int} = 24.31$				
$\sigma^{2}_{\text{linear slope}} = 0$.0984			
σ^2 quadratic slope <	< 0.001			
$\sigma^{2}_{error} = 5.38$				
se = standard o	error; WC = v	waist circumferenc	e.	
: Intercept inte	erpreted as th	he expected level o	of WC in cm at 42	years of age (centering) و
he mean age o	of the sample	e)		

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Trajectory groups Low-increasing group Re High-increasing group 1. 2. Covariates Age, y Female Baseline BMI	eference 79 (1.58, 03)	Reference 1.44 (1.22, 1.69) 1.07 (1.06, 1.08) 0.74 (0.67,	Reference 1.47 (1.25, 1.73) 1.06 (1.05, 1.07)	Reference 1.49 (1.26 1.75) 1.06 (1.05 1.07)
Low-increasing group Re High-increasing group 1. 2. Covariates Age, y Female Baseline BMI	eference 79 (1.58, 03)	Reference 1.44 (1.22, 1.69) 1.07 (1.06, 1.08) 0.74 (0.67,	Reference 1.47 (1.25, 1.73) 1.06 (1.05, 1.07)	Reference 1.49 (1.26 1.75) 1.06 (1.05 1.07)
High-increasing group 1. 2. Covariates Age, y Female Baseline BMI	79 (1.58, 03)	1.44 (1.22, 1.69) 1.07 (1.06, 1.08) 0.74 (0.67,	1.47 (1.25, 1.73) 1.06 (1.05, 1.07)	1.49 (1.26 1.75) 1.06 (1.05 1.07)
2. Covariates Age, y Female Baseline BMI	03)	1.69) 1.07 (1.06, 1.08) 0.74 (0.67,	1.73) 1.06 (1.05, 1.07)	1.75) 1.06 (1.05 1.07)
Covariates Age, y Female Baseline BMI		1.07 (1.06, 1.08) 0.74 (0.67,	1.06 (1.05, 1.07)	1.06 (1.05 1.07)
Age, y Female Baseline BMI		1.07 (1.06, 1.08) 0.74 (0.67,	1.06 (1.05, 1.07)	1.06 (1.05 1.07)
Female Baseline BMI		1.08) 0.74 (0.67,	1.07)	1.07)
Female Baseline BMI		0.74 (0.67,		•
Baseline BMI			0.86 (0.77,	0.97 (0.83
Baseline BMI		0.83)	0.96)	1.14)
		1.09 (1.06,	1.07 (1.04,	1.07 (1.04
		1.12)	1.10)	1.10)
Baseline WC		1.01	1.01 (1.00,	1.01 (1.00
		(1.00,1.02)	1.02)	1.02)
Baseline SBP			1.03 (1.02,	1.03 (1.02
			1.04)	1.04)
Smoker				1.11 (0.96
				1.30)
Drinker				1.11 (0.97
				1.27)
MI, body mass index; SBP, s	systolic bloc	od pressure; WC	waist circumfere	1.27) ence.

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

		Model 3	wodel 4
Reference	Reference	Reference	Reference
1.71 (1.53,	1.45 (1.24,	1.42 (1.21,	1.43 (1.22,
1.93)	1.69)	1.66)	1.68)
	1.07 (1.06,	1.06 (1.05,	1.06 (1.05,
	1.08)	1.07)	1.07)
	0.80 (0.72,	0.92 (0.82,	1.04 (0.89
	0.90)	1.03)	1.23)
	1.10 (1.07,	1.08 (1.05,	1.08 (1.05
	1.13)	1.11)	1.11)
	1.01 (1.00,	1.00 (0.99,	1.01 (1.00,
	1.02)	1.01)	1.02)
		1.03 (1.02,	1.03 (1.02
		1.04)	1.04)
			1.12 (0.96
			1.30)
			1.10 (0.96
			1.26)
index: SBP. svsto	lic blood pressure:	WC, waist circum	ference
, , ,	,	_,	
	Reference 1.71 (1.53, 1.93)	Reference Reference 1.71 (1.53, 1.45 (1.24, 1.93) 1.69) 1.93) 1.07 (1.06, 1.08) 0.80 (0.72, 0.90) 0.80 (0.72, 0.90) 1.10 (1.07, 1.13) 1.01 (1.00, 1.02)	Reference Reference Reference 1.71 (1.53, 1.45 (1.24, 1.42 (1.21, 1.93) 1.69) 1.66) 1.07 (1.06, 1.06 (1.05, 1.08) 1.07) 0.80 (0.72, 0.92 (0.82, 0.90) 1.03) 1.10 (1.07, 1.08 (1.05, 1.13) 1.11) 1.01 (1.00, 1.00 (0.99, 1.02) 1.01) 1.03 (1.02, 1.04)
4

5 6 **Table S8**. Model-estimated levels and linear slopes of BMI in means (SD) by incidenthypertension at follow-up

	BMI Level (k	g/m²)		BMI Slope	(kg/m²/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

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	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
5		ormatanajan. L	JTN - hyporto	naian			

NTN = normotension; HTN = hypertension.

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5 6 **Table S9**. Model-estimated levels and linear slopes of WC in means (SD) by incidenthypertension at follow-up

	WC Level (c	m)		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

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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
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NTN = normotension; HTN = hypertension.

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	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items including for 2	Location in manuscript where items an reported
Title and abstra	ct	1	1		T
	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 the used should be specified in the type of the or abstract. When possible, and the or the databases used should be included. RECORD 1.2: If applications the geographic region and time frame within which the study the frame within which the study the frame should be reported in the true 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				d s	
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	7	on June 1 imilar tecl	
Objectives	3	State specific objectives, including any prespecified hypotheses	7	3, 2025 at mologies	
Methods				P g	
Study Design	4	Present key elements of study design early in the paper	8	ence B	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8	libliographic	

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 	8	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in details If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms are detailed to select the population should be referenced. If validation available delsewhere, detailed method and results should be provided. RECORD 6.3: If the study over the study of a flow diagram or other graphical display	8
Variables	7	 and number of exposed and unexposed <i>Case-control study</i> - For matched studies, give matching criteria and the number of controls per case Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic 	9	to demonstrate the data finkage process, including the number of individuals with linked data at each stage.	9
Data sources/ measurement	8	criteria, if applicable.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	these cannot be reported Gan S explanation should be provided.	8,9

Blas	9	Describe any efforts to address	9, 10	c op	
		potential sources of bias		yrig	
Study size	10	Explain how the study size was arrived at	8)21-05	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	8-10	9556 on 25 May 2 Ense cluding for uses	
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) <i>Cohort study</i> - If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> - If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses 	9, 10	2022. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 a eignement Superieur (ABES) . related to text and data mining, Al training, and similar technologies	
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

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				RECORD 12.2: Authorseshorid	
				provide information on the data	
				cleaning methods used in the study.	
Linkage				RECORD 12.3: State whether the	8
				study included person-legel,g	
				institutional-level, or other data linka	ge
				across two or more datals as the	
				methods of linkage and methods of	
				linkage quality evaluation and be	
				provided.	
Results					
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		confirmed eligible, included in		quality, data availability	
		the study, completing follow-up,		The selection of include	1
		and analysed)		be described in the text and br	
		(b) Give reasons for non-		means of the study flow giag am.	
		participation at each stage.		L tr	
		(c) Consider use of a flow		ain en	
		diagram	N N	ing m	
Descriptive data	14	(a) Give characteristics of study	10	an co	
		participants (e.g., demographic,		d si n	
		clinical, social) and information			
		on exposures and potential		ar t	
		confounders		ect	
		(b) Indicate the number of		ino	
		participants with missing data		logi	
		for each variable of interest		es at	
		(c) <i>Cohort study</i> - summarise		Ag	
		follow-up time (<i>e.g.</i> , average and		enc	
		total amount)		Ö	
Outcome data	15	<i>Cohort study</i> - Report numbers	10, 11		
		of outcome events or summary		ogr	
		measures over time		apt apt	
		Case-control study - Report		viq	
		numbers in each exposure		ō 0	

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		category, or summary measures of exposure <i>Cross-sectional study</i> - Report numbers of outcome events or summary measures		open-2021-05955 copyright, inclu	
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	56 on 25 May 2022. Downloaded from http://bm Enseignement Superieur (ABES) . ding for uses related to text and data mining, <i>i</i>	
Other analyses	17	Report other analyses done— e.g., analyses of subgroups and interactions, and sensitivity analyses	10, 11	njopen.bmj.c Al training, a	
Discussion				nd "	
Key results	18	Summarise key results with reference to study objectives	13	imilar	
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 any 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	raphique	

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		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		jøpen-2021-05 , copyright, inc		
Generalisability	21	Discuss the generalisability (external validity) of the study results	16	9556 on 2 cluding fo		
Other Information	on			<u>, , , , , , , , , , , , , , , , , , , </u>		
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	ay 2022. Downlines related to te		
Accessibility of protocol, raw data, and programming			Pr	RECORD 22.1: Authors	ld o access a such as or	18
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