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ORIGINAL RESEARCH

Inflection Points in Blood Pressure Trajectories Preceding Hypertension Onset in Different Age Groups

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BACKGROUND: Understanding the natural history of elevated blood pressure (BP) is important to determine the window for primary prevention of hypertension. The authors aimed to investigate the natural history of elevated BP and examine whether there were inflection points in BP trajectories preceding hypertension onset in Chinese adults.

METHODS AND RESULTS: A total of 8688 participants with an average of 5 BP measurements were included from the CHNS (China Health and Nutrition Survey). In each wave, triplicate measurements on the same arm were taken, and the mean systolic BP (SBP) and diastolic BP (DBP) were used in the analysis. Hypertension onset was defined as SBP ≥140 mm Hg or DBP ≥90 mm Hg or diagnosed by physician or currently under antihypertensive treatment. The median follow-up time was 13.0 years. Overall, BP elevation with age prior to the onset of hypertension showed a nonlinear trajectory. The increased rates in both SBP and DBP were obviously faster after the inflection point than before. According to hypertension onset at age 30 to 39, 40 to 49, 50 to 59, 60 to 69, and 70 to 79 years, at the inflection point, patients were ≈29, 38, 48, 57, and 67 years, SBP levels were 112.6, 114.8, 116.8, 117.4, and 118.0 mm Hg, and DBP levels were 73.4, 75.7, 76.9, 76.2, and 73.8 mm Hg, respectively.

CONCLUSIONS: There was a nonlinear trajectory of BP elevation preceding hypertension onset. The inflection points for SBP and DBP were in the range of 112 to 118 mm Hg and 73 to 77 mm Hg, respectively. Once BP levels exceeded the changing points, the level of SBP and DBP increased more rapidly.

Key Words: age of hypertension onset ■ blood pressure trajectory ■ inflection point ■ longitudinal study

Hypertension is the leading risk factor of premature death and disability-adjusted life-years worldwide.[1,2] By 2019, the number of patients with hypertension in the world had exceeded 1.2 billion.[3] Therefore, the natural history of elevated blood pressure (BP) should be further understood in order to determine the window period for primary prevention of hypertension.

The body maintains normal BP levels by regulating cardiac output and peripheral vascular resistance.[4] Aging of blood vessels, such as arterial stiffness, will weaken this regulation, leading to an inevitable increase in BP levels and the prevalence of hypertension with advancing age.[5,6] In a healthy state, the body's repair and metabolic damage are in balance. However, the ability of the body's repair has an upper limit, and when the continuous exposure of risk factors increases to a certain level, it will cause accelerated aging of blood vessels.[7–9] Therefore, there may be an inflection point in the trajectory of BP preceding hypertension onset, and the BP will rise relatively faster after the inflection point. Accordingly, a previous study[10] reported that systolic BP (SBP) levels are generally stable until they approach ≈120 to 125 mm Hg, after which SBP rises at a relatively rapid rate toward overt hypertension. However, this

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CLINICAL PERSPECTIVE

What Is New?

- There was a nonlinear trajectory of blood pressure (BP) elevation preceding hypertension onset.
- The inflection points for systolic BP and diastolic BP were in the range of 112 to 118 mm Hg and 73 to 77 mm Hg, respectively.
- Once BP levels exceeded the changing points, the level of systolic BP and diastolic BP increase more rapidly.

What Are the Clinical Implications?

- Maintaining systolic BP levels <115 mm Hg regardless of age, and diastolic BP levels <75 mm Hg before age 50, may possibly contribute to primary prevention of hypertension in the general population.

Nonstandard Abbreviations and Acronyms

CHNS	China Health and Nutrition Survey
DBP	diastolic blood pressure
SBP	systolic blood pressure

study only included 1252 European American adults, did not include participants who had hypertension onset before age 40 years, and investigated the possible inflection point of diastolic BP (DBP).

As such, in the present study, we aimed to investigate the natural history of elevated BP and examine whether there were inflection points in SBP and DBP trajectories preceding hypertension onset in Chinese adults with varying ages of hypertension onset.

METHODS

Our article adheres to the American Heart Association journals' implementation of the Transparency and Openness Promotion Guidelines. The institutional review boards of the University of North Carolina at Chapel Hill and the National Institute of Nutrition and Food Safety, and Chinese Center for Disease Control and Prevention, approved the study. Each CHNS (China Health and Nutrition Survey) participant provided their written informed consent. The data and study materials that support the findings of this study can be found on the CHNS official website (http://www.cpc.unc.edu/projects/china).

Population and Study Design

Our study population was from the CHNS. Details of the original design, sampling methods, and response rates of the CHNS have been described elsewhere.[11–15] Briefly, CHNS is an ongoing multipurpose longitudinal open cohort study initiated in 1989 and has been followed up every 2 to 4 years. By 2011, the provinces included in the CHNS constituted 47% of China's population.[13] The CHNS rounds have been completed in 1989, 1991, 1993, 1997, 2000, 2004, 2006, 2009, 2011, and 2015.

We conducted a longitudinal study based on the repeat measurement setting in the CHNS. The same standard procedure and calibrated mercury sphygmomanometers were used for measuring BP in each wave since 1991. From 1991 to 2015, there were 26 941 adults (86 642 person waves) with complete BP measurements. In order to evaluate the trajectories of BP preceding hypertension onset, the following inclusion and exclusion criteria were implemented one by one: including the survey waves for each participant at or before hypertension onset; excluding participants with fewer than 3 survey waves; excluding participants with hypertension onset before age 30 years or at or after age 80 years considering the limited sample size in these 2 age groups. Finally, 8688 participants (42 570 person waves) with an average of 5 BP measurements were included in this study (Figure 1).

BP Measurements

After the participants had rested for 5 minutes, seated BP was measured by trained research staff. Triplicate measurements on the same arm were taken in a quiet and bright room. The mean SBP and DBP of the 3 independent measures were used in the analysis.

Definition of Hypertension Onset

Hypertension onset was defined as an SBP ≥140 mm Hg or a DBP ≥90 mm Hg or diagnosed by a physician or currently under antihypertensive treatment. In a series of consecutive repeated surveys, we truncated data at the onset of hypertension once participants met criteria for hypertension. If participants were taking antihypertensive medicine at a given survey wave, then SBP was adjusted by adding 10 mm Hg and DBP was adjusted by adding 5 mm Hg.[10,16]

To test whether the component of physician diagnosis in the definition of hypertension onset had an influence on the results, we further defined hypertension onset as a BP ≥140/90 mm Hg or taking antihypertensive drugs in a given wave. Moreover, considering the influence of the reproducibility of hypertension diagnosis on the results, another definition of hypertension onset was also made according to previous study,[17] which was defined as BP ≥160/95 mm Hg or taking antihypertensive medicine at a given wave or BP ≥140/90 mm Hg at ≥2 consecutive waves.

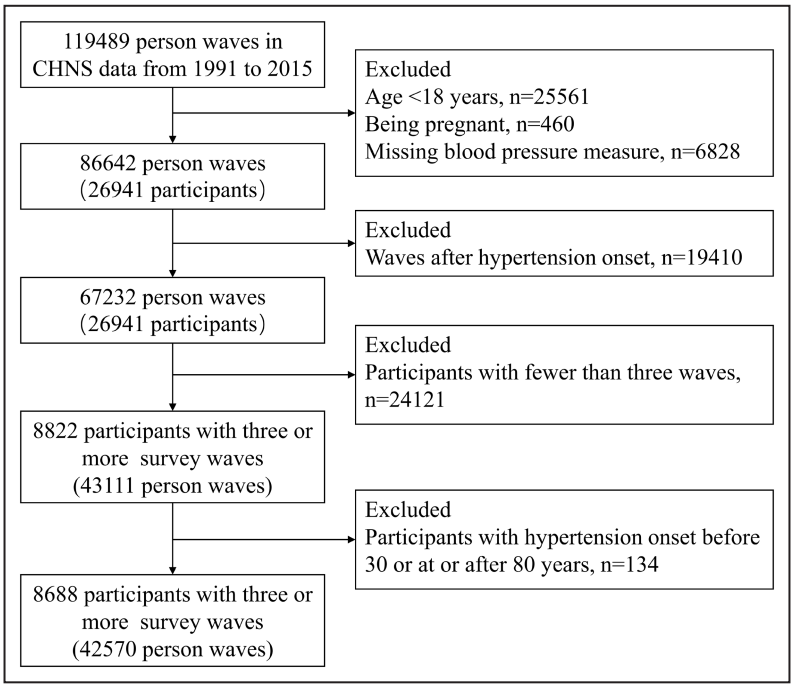

Figure 1. Flowchart of the study population.
CHNS indicates China Health and Nutrition Survey.

Covariates Measurements

Demographic and lifestyle information was obtained through questionnaires, including age, sex, smoking, alcohol drinking, occupation, education level, residence, regions, physical activity, and concomitant diseases at each survey wave. Height and weight were measured following a standard procedure with calibrated equipment. Body mass index was calculated as weight (kg) by height squared (m^2).

Statistical Analysis

The first survey wave was considered as baseline, and baseline characteristics were described by age groups of hypertension onset (30–39, 40–49, 50–59, 60–69, and 70–79 years, or no onset). Population characteristics are presented as mean±SD for continuous variables and proportions for categorical variables. Differences in population characteristics across these age groups of hypertension onset were compared using ANOVA or chi-square tests, accordingly.

Mixed linear regression models were used to evaluate the nonlinear BP trajectories with age in each age group of hypertension onset. Specifically, BP was considered as a response variable, the restricted cubic spline term with 4 knots of age was fitted as fixed effect, and a random intercept was used to account for the interindividual differences in each mixed linear model. The trajectory of BP showed an abrupt change in the rate of BP increase with increasing age, which suggested that there was an inflection point in the relationship between BP and age. Accordingly, segmented models, which extended from simple segmented linear regression to permit application within a mixed model framework, were applied to estimate the inflection point.[10] Those identified by age, including the inflection point, had the slope before and after the inflection point, and their respective CIs, obtained by segmented mixed linear model. The CIs for BP corresponding to the inflection points were calculated through 1000 bootstrap. In addition, the heterogeneity in the estimates across the age groups of hypertension onset was examined using the Cochran Q test. The main statistical analyses were performed by using R package *nlme* and *segmented*.

All statistical analyses were performed using R version 3.6.3 (R Foundation for Statistical Computing). A 2-sided *P* value of <0.05 was considered as statistically significant.

RESULTS

Characteristics of the Study Participants

A total of 8688 Chinese adults with an average of 5 BP measurements were included in this longitudinal study from 1991 to 2015 (Figure 1). The baseline mean age was 37.3 years (SD, 12.4 years), and the median follow-up time was 13.0 years (25th percentile to 75th percentile, 8.9–18.0 years).

As presented in Table 1, participants with later onset of hypertension were older; were more likely to

be women and urban residents; were less likely to be smokers, alcohol drinkers, and farmers; and had lower body mass index, SBP, and DBP levels.

BP Trajectories and the Inflection Point Characteristics

BP continued to increase with advancing age in those without hypertension onset and in each age categories of hypertension onset (Figure 2). In the group without new-onset hypertension, SBP and DBP increased at a lower rate with the advancing age than groups with new-onset hypertension (age at hypertension onset: 30–39, 40–49, 50–59, 60–69, and 70–79 years), and the relationship was approximately linear. However, a nonlinear trajectory was observed between increasing SBP or DBP and advancing age in each group with hypertension onset. The rate of increase in both SBP and DBP was obviously faster after the inflection point than before.

The change point characteristics in BP trajectories are shown in Table 2. For SBP trajectories, according to participants with hypertension onset at age 30 to 39, 40 to 49, 50 to 59, 60 to 69, and 70 to 79 years, the ages at the change point were 29.0 years (95% CI, 27.7–30.4), 38.9 years (95% CI, 38.3–39.5), 48.6 years (95% CI, 48.0–49.2), 57.4 years (95% CI, 56.7–58.2), and 67.8 years (95% CI, 66.9–68.8); and the SBP values at the inflection point were 112.6 mm Hg (95% CI, 111.2–114.1), 114.8 mm Hg (95% CI, 114.0–115.5), 116.8 mm Hg (95% CI, 116.2–117.5), 117.4 mm Hg (95% CI, 116.3–118.1), and 118.0 mm Hg (95% CI, 116.7–119.2), respectively. Overall, with the increase of age of hypertension onset, SBP at the inflection point (heterogeneity $P<0.001$) became higher, and SBP before (heterogeneity $P=0.043$) and after (heterogeneity $P<0.001$) the inflection point raised faster. The range of SBP at the inflection points in age groups of hypertension onset was from 112.6 mm Hg to 118.0 mm Hg.

For DBP trajectories, with the increase of age of hypertension onset, DBP level at the inflection point and slopes before the inflection points both increased first and then decreased. The highest levels of DBP at the inflection point (76.9 mm Hg; 95% CI, 76.4–77.4) and the slope before the inflection point (0.41 mm Hg per year; 95% CI, 0.34–0.47) were seen in the group of hypertension onset at 50 to 59 years. More importantly, unlike the gradual increase of the SBP slope after the inflection point, with

Table 1. Baseline Characteristics

Characteristics	Age of hypertension onset, y						*P* value
	30–39	40–49	50–59	60–69	70–79	No-onset	
No.	391	915	1033	699	338	5312	
Age, mean (SD), y	26.2 (4.2)	32.9 (5.6)	41.0 (6.2)	51.0 (6.7)	60.5 (6.4)	34.8 (12.3)	<0.001
Women, n (%)	144 (36.8)	449 (49.1)	534 (51.7)	385 (55.1)	194 (57.4)	2963 (55.8)	<0.001
BMI, mean (SD), kg/m^2	22.0 (2.6)	22.5 (2.9)	22.2 (2.8)	22.0 (2.8)	21.5 (3.1)	21.4 (2.6)	<0.001
SBP, mean (SD), mm Hg	112.2 (10.1)	112.4 (10.3)	112.6 (11.6)	113.9 (11.8)	112.7 (13.2)	109.1 (11.3)	<0.001
DBP, mean (SD), mm Hg	73.5 (7.7)	74.1 (7.7)	73.6 (8.3)	73.5 (8.2)	72.7 (8.3)	71.3 (8.3)	<0.001
Smoking, n (%)	139 (35.7)	354 (38.8)	389 (37.9)	272 (39.0)	123 (36.6)	1520 (28.7)	<0.001
Alcohol drinking, n (%)	159 (41.0)	356 (39.1)	433 (42.3)	286 (41.2)	119 (35.4)	1682 (31.9)	<0.001
Occupation, n (%)							<0.001
Farmer	89 (48.6)	112 (41.3)	90 (37.0)	56 (34.8)	21 (30.4)	824 (31.8)	
Worker	34 (18.6)	35 (12.9)	28 (11.5)	7 (4.3)	3 (4.3)	371 (14.3)	
Inoccupation	22 (12.0)	29 (10.7)	45 (18.5)	63 (39.1)	39 (56.5)	648 (25.0)	
Other	38 (20.8)	95 (35.1)	80 (32.9)	35 (21.7)	6 (8.7)	746 (28.8)	
Education, n (%)							<0.001
Illiteracy	32 (8.4)	156 (17.2)	336 (32.7)	361 (52.3)	235 (71.6)	915 (17.5)	
Primary school	85 (22.2)	208 (23.0)	261 (25.4)	170 (24.6)	57 (17.4)	1087 (20.8)	
Middle school	178 (46.5)	353 (39.0)	261 (25.4)	87 (12.6)	21 (6.4)	1930 (36.9)	
High school or above	88 (23.0)	188 (20.8)	170 (16.5)	72 (10.4)	15 (4.6)	1302 (24.9)	
Urban resident, n (%)	95 (24.3)	232 (25.4)	249 (24.1)	172 (24.6)	106 (31.4)	1655 (31.2)	<0.001
Region, n (%)							<0.001
Central	182 (46.5)	460 (50.3)	507 (49.1)	323 (46.2)	138 (40.8)	2194 (41.3)	
North	94 (24.0)	186 (20.3)	177 (17.1)	101 (14.4)	34 (10.1)	904 (17.0)	
South	115 (29.4)	269 (29.4)	349 (33.8)	275 (39.3)	166 (49.1)	2214 (41.7)	
Self-reported diabetes	0 (0.0)	1 (0.4)	2 (0.8)	5 (3.2)	1 (1.5)	10 (0.4)	<0.001

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

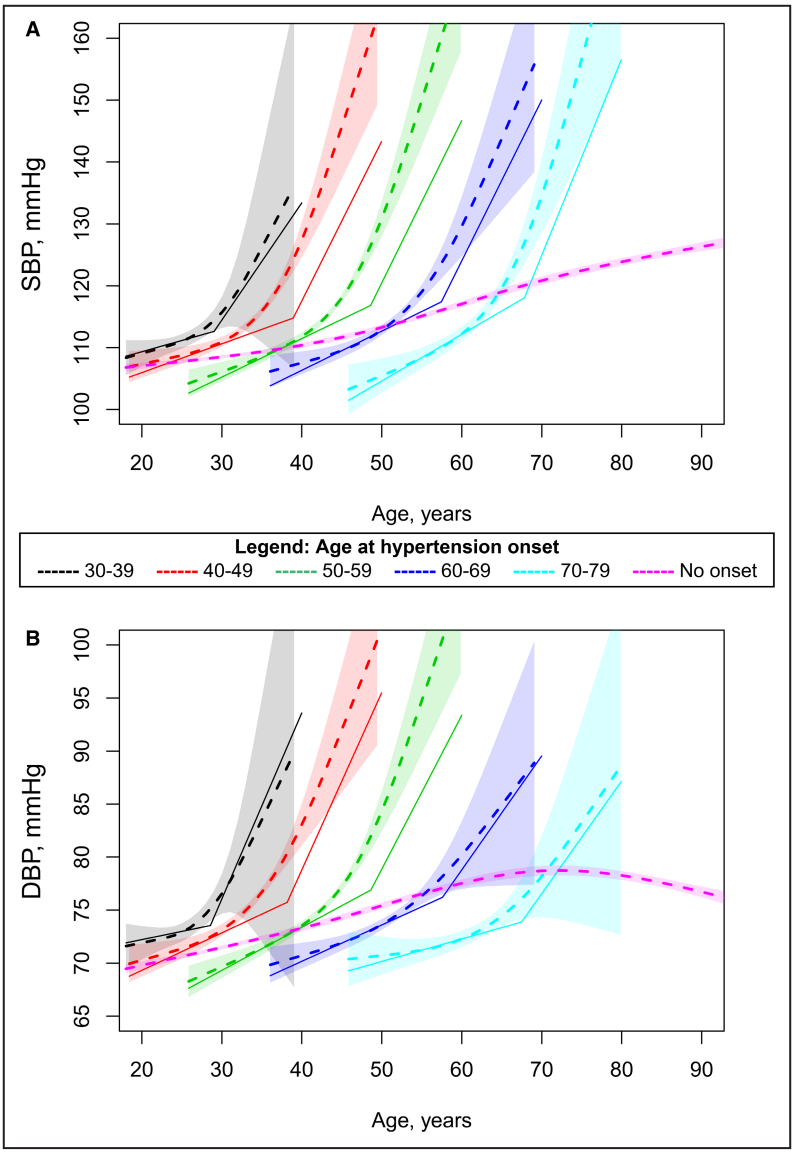

Figure 2. A, SBP and B, DBP trajectories preceding hypertension by onset age.*

*Mixed linear models with restricted cubic splines (dash line) were used to assess the BP-increased trajectories with age and their 95% CIs; mixed segmented linear models (solid line) were used to identify the inflection points in the BP-increased trajectories. BP indicates blood pressure; DBP, diastolic blood pressure; and SBP, systolic blood pressure.

the increase of age of hypertension onset, the DBP slope after the inflection point decreased gradually. The range of DBP at the inflection points in age groups of hypertension onset was from 73.4 mm Hg to 76.9 mm Hg.

Sensitivity Analysis

Similar results were found when we defined hypertension onset based on BP ≥140/90 mm Hg or taking antihypertensive medicine (Table S1). When the definition of hypertension onset was defined as BP ≥160/95 mm Hg or taking antihypertensive medicine at a given wave or BP ≥140/90 mm Hg at ≥2 consecutive waves, we found that the BP levels were slightly higher than our main findings. SBP levels at inflection points were in the range of 118 mm Hg to 124 mm Hg, and DBP levels were in the range of 76 mm Hg to 82 mm Hg (Table S2).

DISCUSSION

We found a nonlinear trajectory of BP elevation with age prior to the onset of hypertension. The observed inflection points for SBP and DBP were in the range of

Table 2. Change Point Characteristics by Age of Hypertension Onset Using Mixed Segmented Models

Change point characteristic, estimate (95% CI)*	Age of hypertension onset, y					P value†
	30–39	40–49	50–59	60–69	70–79	
SBP						
Age at change point, y	29.0 (27.7–30.4)	38.9 (38.3–39.5)	48.6 (48.0–49.2)	57.4 (56.7–58.2)	67.8 (66.9–68.8)	<0.001
SBP at change point, mm Hg	112.6 (111.2–114.1)	114.8 (114.0–115.5)	116.8 (116.2–117.5)	117.4 (116.3–118.1)	118.0 (116.7–119.2)	<0.001
Slope before change point, mm Hg per y	0.36 (0.03–0.70)	0.47 (0.34–0.59)	0.62 (0.53–0.72)	0.63 (0.51–0.76)	0.75 (0.58–0.93)	0.043
Slope after change point, mm Hg per y	1.90 (1.67–2.13)	2.58 (2.41–2.76)	2.62 (2.46–2.79)	2.60 (2.41–2.80)	3.18 (2.85–3.51)	<0.001
DBP						
Age at change point, y	28.6 (27.6–29.6)	38.2 (37.5–38.9)	48.6 (47.9–49.4)	57.6 (56.3–58.9)	67.5 (65.7–69.2)	<0.001
DBP at change point, mm Hg	73.4 (72.1–74.5)	75.7 (75.1–76.1)	76.9 (76.4–77.4)	76.2 (75.5–76.7)	73.8 (73.0–74.6)	<0.001
Slope before change point, mm Hg per y	0.15 (−0.11–0.42)	0.35 (0.26–0.44)	0.41 (0.34–0.47)	0.34 (0.26–0.42)	0.21 (0.09–0.33)	0.035
Slope after change point, mm Hg per y	1.76 (1.59–1.92)	1.67 (1.56–1.79)	1.45 (1.34–1.56)	1.08 (0.95–1.21)	1.06 (0.86–1.27)	<0.001

DBP indicates diastolic blood pressure; and SBP, systolic blood pressure.
*Change point estimates were derived using the mixed segmented model. Empirical confidence limits were derived from bootstrapping. Percentile limits are reported to accommodate for potentially nonnormal sampling distributions of parameter estimates.
†We used the Cochran Q test to assess heterogeneities among groups.

112 mm Hg to 118 mm Hg and 73 mm Hg to 77 mm Hg, respectively. For the rate of increase in both SBP and DBP, it was relatively faster after the inflection point than before.

Our study showed that the rate of increase in BP preceding hypertension onset was not constant. There was a transitional period in the increase of individual BP, beyond which the increase would accelerate. A similar rising pattern of SBP was found in the previous Framingham Heart Study.[10] In that study, the estimated SBP levels at the turning point were in a range of 120 mm Hg to 125 mm Hg, which is higher than our findings (112–118 mm Hg). The possible explanations may include that, first, the definition of hypertension onset was based on a single examination, which may misclassify normotension as hypertension and underestimate change points. Consistently, in our sensitivity analysis, SBP levels at inflection points were in the range of 118 mm Hg to 124 mm Hg (Table S2). Second, the BP level in Chinese is lower than Americans among nonhypertensive people.[18] In fact, the cutoff point of body mass index for the definition of obesity is higher for Americans than Chinese,[19,20] which means that the normal body size of Americans is higher than that of Chinese, and therefore Americans may need a relatively higher BP level to promote blood circulation.

Hypertension onset age is a highly heritable trait,[21] and previous studies have identified numerous genetic loci and gene variants that are associated with early-onset hypertension.[22–24] Furthermore, the associations between hypertension and cardiovascular disease and all-cause mortality have been shown to be stronger in those with early onset age.[25] As such, we hypothesize that a higher genetic susceptibility to early-onset hypertension may represent a lower ability to repair damage to vessels, with the upper limit of repair capacity being reached earlier as damage accumulates. In addition, the BP level at the inflection point may partly represent a critical threshold of extant vascular remodeling.[10] Vascular remodeling is the common pathological basis of hypertension and end-organ damage such as heart, brain, and kidney.[26] Hence, once the corresponding BP level reaches or exceeds this threshold, the risk of cardiovascular and cerebrovascular diseases will be significantly increased, even if the BP level is still within the normal range.

SBP is mainly affected by the elasticity of the large arterial vessels.[27] Arterial elasticity decreases with age, and pulse wave velocity increased at an accelerated rate with advancing age.[28] Therefore, the slower increase in SBP in young people, either before or after the inflection point, may be attributed to the better vascular elasticity and better adaptation to the pressure on the large arteries caused by the heart pumping.

DBP was related to peripheral vascular resistance, arterial elasticity, and atherosclerosis. Remodeling of

peripheral small vessels usually occurs earlier than large arteries and cardiac hypertrophy.[29] Peripheral vascular resistance and degree of arteriosclerosis increase with age, but arteriosclerosis symptoms begin to appear in middle and old age.[30] In addition, the accelerated progression of arteriosclerosis was observed in healthy people aged 40 to 50 years.[31] Thus, the DBP level at the inflection point and the slope before the inflection point first increased and then decreased with age, which may indicate that the influence of peripheral vascular resistance on DBP in younger people plays a leading role for the first stage increase trend, while in older people arterial stiffness plays a major role for the second stage decline trend. BP level beyond the changing point is a sign that the arteries are starting to harden more quickly, and the effect of arterial elasticity on DBP begins to dominate. Therefore, the slope after the inflection points appears to decrease with age. Because the change points in groups of age of hypertension onset over 60 years were lower than those in the no-onset group of the same age, we speculated that DBP levels should be maintained below 75 mm Hg until at least age 50 for primary prevention of the accelerated progression of vascular remodeling. In addition, when we included the data after the onset of hypertension (Figure S1), we found that DBP increased first and then decreased in any group with hypertension onset age over 40 years (Figure S2; Table S3), suggesting that the symptoms of arterial stiffness may begin to be overt near or after the onset of hypertension.

If further confirmed, our study showed that in the primary prevention of hypertension in the general population, SBP level should be maintained below 115 mm Hg regardless of age, and DBP level should be maintained below 75 mm Hg before age 50. Consistently, a previous meta-analysis of individual data for 1 million adults in prospective studies suggested that death from both ischemic heart disease and stroke increases progressively and linearly from BP levels as low as 115 mm Hg systolic and 75 mm Hg diastolic upward.[32] The World Health Organization also reports that suboptimal SBP level (>115 mm Hg) is responsible for 62% of cerebrovascular disease and 49% of ischemic heart disease.[33] However, of note, among those who did not develop hypertension, the overall proportion of data points with SBP ≥115 mm Hg was 42.7%. When the age was in the range of <30, 30 to 40, 40 to 50, 50 to 60, 60 to 70, and ≥70 years, the proportion was 31.8%, 36.1%, 43.5%, 51.5%, 58.5%, and 66.0%, respectively (Table S4). These results mean that if our recommendations are followed, a portion of people who will not develop hypertension may also need to pay more attention to their BP and take more action to help control their SBP <115 mm Hg. Therefore, the cost–benefit ratio should be further evaluated. Moreover, all of the findings should be further confirmed by interventional trials.

Although compared with the previous study,[10] the current study had the strengths of a larger sample size, inclusion of an early-onset hypertension population, and extended analysis of DBP trajectory, some limitations should also be noted. First, previous studies[10,34] mentioned that the mixed segmented model may not perform optimally in certain situations, such as data with extreme noise. Nonetheless, our results suggest that the model fits the data relatively well, and the results can be explained reasonably. Second, we did not explore the effect of modifiers on BP trajectories and inflection points, because of methodological complexity and sample size limitations. Third, this study included Chinese adults with age of hypertension onset in the range of 30 to 80 years, and caution is required when generalizing the findings to other age ranges and ethnicities. Fourth, in our study, participants with hypertension at baseline were excluded. Because participants who were older than 30 years at baseline were included, there may be selection bias when excluding those with hypertension at baseline, who would have been classified into a younger hypertensive-onset group. However, among the 26 941 participants (Figure 1), the mean age of the excluded participants with hypertension (n=5304) was 55.5 years, which was similar to the age of hypertension onset of the included participants (mean age, 54.0 years). Fifth, in the current study, diabetes was defined as having a self-reported physician diagnosis of diabetes, which may have underestimated the prevalence of diabetes.[35] Finally, because of the different mechanisms affecting DBP in younger and older adults, mean baseline age older than 50 years in the late-onset group does not provide a complete picture of the impact of DBP trajectory or inflection point on the development of hypertension. More studies are needed to validate our findings and further elucidate the trajectory of DBP.

CONCLUSIONS

Our study showed a nonlinear trajectory of BP elevation preceding hypertension onset. The inflection points for SBP and DBP were in the range of 112 to 118 mm Hg and 73 to 77 mm Hg, respectively. Once BP levels exceeded the changing points, the level of SBP and DBP will increase more rapidly.

ARTICLE INFORMATION

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Disclosures

No disclosures were reported.

Supplemental Material

Tables S1–S4
Figures S1–S2

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SUPPLEMENTAL MATERIAL

Table S1. Change point characteristics by age of hypertension onset using mixed segmented models when hypertension onset was defined as BP ≥140/90 mmHg or taking antihypertensive medicine

Change point characteristic, estimate (95% CI) *	Age of hypertension onset, years					*P* value †
	30-39	40-49	50-59	60-69	70-79	
SBP						
Age at change point, years	29.2 (27.9, 30.5)	38.9 (38.3, 39.5)	48.6 (48.1, 49.2)	57.6 (56.9, 58.3)	67.9 (67.0, 68.8)	<0.001
SBP at change point, mmHg	112.8 (111.6, 114.2)	114.8 (113.9, 115.4)	117.0 (116.4, 117.7)	117.6 (116.6, 118.3)	118.4 (117.0, 119.5)	<0.001
Slope before change point, mmHg/year	0.38 (0.05, 0.70)	0.46 (0.34, 0.59)	0.62 (0.52, 0.71)	0.64 (0.52, 0.77)	0.76 (0.59, 0.94)	0.032
Slope after change point, mmHg/year	1.94 (1.71, 2.18)	2.62 (2.44, 2.80)	2.70 (2.53, 2.87)	2.70 (2.50, 2.90)	3.26 (2.93, 3.59)	<0.001
DBP						
Age at change point, years	28.6 (27.6, 29.6)	38.2 (37.5, 38.9)	48.7 (47.9, 49.4)	57.9 (56.7, 59.2)	67.8 (66.2, 69.4)	<0.001
DBP at change point, mmHg	73.5 (72.1, 74.5)	75.8 (75.1, 76.2)	77.1 (76.7, 77.6)	76.5 (75.8, 76.9)	74.2 (73.4, 74.9)	<0.001
Slope before change point, mmHg/year	0.15 (-0.11, 0.42)	0.35 (0.26, 0.45)	0.41 (0.34, 0.47)	0.35 (0.28, 0.43)	0.22 (0.10, 0.33)	0.036
Slope after change point, mmHg/year	1.77 (1.61, 1.94)	1.70 (1.58, 1.81)	1.49 (1.37, 1.60)	1.13 (0.99, 1.26)	1.12 (0.91, 1.33)	<0.001

* Change point estimates were derived using the mixed segmented model. Empirical confidence limits were derived from bootstrapping. Percentile limits are reported to accommodate for potentially non-normal sampling distributions of parameter estimates.

† We used the Cochran Q test to assess heterogeneities among groups.

Abbreviations: BP = Blood pressure, CI = Confidence interval, DBP = Diastolic blood pressure, SBP = Systolic blood pressure

Table S2. Change point characteristics by age of hypertension onset using mixed segmented models when hypertension onset was defined as BP ≥160/95 mmHg or taking antihypertensive medicine or BP ≥140/90 mmHg at 2 or more consecutive waves

Change point characteristic, estimate (95% CI) *	Age of hypertension onset, years					*P* value †
	30-39	40-49	50-59	60-69	70-79	
SBP						
Age at change point, years	33.6 (32.4, 34.9)	39.5 (38.7, 40.3)	48.8 (48.1, 49.5)	57.3 (56.3, 58.3)	68.4 (67.3, 69.5)	<0.001
SBP at change point, mmHg	120.7 (119.1, 122.8)	118.3 (117.2, 119.3)	120.2 (119.4, 121.0)	121.3 (120.3, 122.2)	123.8 (122.4, 125.4)	<0.001
Slope before change point, mmHg/year	0.69 (0.41, 0.97)	0.68 (0.52, 0.84)	0.71 (0.59, 0.84)	0.76 (0.61, 0.91)	0.70 (0.49, 0.92)	0.964
Slope after change point, mmHg/year	3.38 (2.56, 4.20)	2.82 (2.57, 3.08)	2.82 (2.60, 3.04)	2.61 (2.38, 2.84)	3.22 (2.80, 3.64)	0.073
DBP						
Age at change point, years	33.5 (32.3, 34.7)	39.2 (38.3, 40.1)	48.9 (48.0, 49.7)	57.9 (56.1, 59.7)	67.5 (65.8, 69.2)	<0.001
DBP at change point, mmHg	81.6 (80.4, 83.3)	78.8 (78.0, 79.5)	79.2 (78.6, 79.7)	78.9 (78.2, 79.6)	76.3 (75.4, 77.3)	<0.001
Slope before change point, mmHg/year	0.63 (0.41, 0.84)	0.50 (0.38, 0.62)	0.41 (0.33, 0.50)	0.40 (0.30, 0.49)	0.18 (0.04, 0.32)	0.002
Slope after change point, mmHg/year	2.78 (2.18, 3.38)	1.86 (1.70, 2.03)	1.58 (1.43, 1.73)	1.04 (0.88, 1.19)	1.15 (0.93, 1.38)	<0.001

* Change point estimates were derived using the mixed segmented model. Empirical confidence limits were derived from bootstrapping. Percentile limits are reported to accommodate for potentially non-normal sampling distributions of parameter estimates.

† We used the Cochran Q test to assess heterogeneities among groups.

Abbreviations: BP = Blood pressure, CI = Confidence interval, DBP = Diastolic blood pressure, SBP = Systolic blood pressure

Table S3. DBP change point characteristics by age of hypertension onset using mixed segmented models when further including data after the onset of hypertension

Change point characteristic of DBP, estimate (95% CI) *	Age of hypertension onset, years					*P* value †
	30-39	40-49	50-59	60-69	70-79	
Age at change point, years	36.8 (35.5, 38.0)	47.9 (47.1, 48.6)	57.6 (57.0, 58.3)	67.7 (66.7, 68.6)	77.7 (75.7, 79.7)	<0.001
DBP at change point, mmHg	85.9 (85.2, 86.7)	89.0 (88.6, 89.5)	87.9 (87.5, 88.3)	86.7 (86.3, 87.2)	83.9 (83.0, 84.5)	<0.001
Slope before change point, mmHg/year	1.03 (0.92, 1.14)	0.94 (0.89, 0.98)	0.81 (0.77, 0.84)	0.69 (0.64, 0.73)	0.59 (0.52, 0.65)	<0.001
Slope after change point, mmHg/year	0.24 (0.18, 0.31)	0.00 (-0.06, 0.06)	-0.10 (-0.16, -0.04)	-0.10 (-0.19, -0.01)	-0.05 (-0.26, 0.16)	<0.001

* Change point estimates were derived using the mixed segmented model. Empirical confidence limits were derived from bootstrapping. Percentile limits are reported to accommodate for potentially non-normal sampling distributions of parameter estimates.

† We used the Cochran Q test to assess heterogeneities among groups.

Abbreviations: CI = Confidence interval, DBP = Diastolic blood pressure

Table S4. The proportion of data points with SBP ≥115 mmHg in non-hypertension onset group

Age, years	Total person-waves	SBP ≥115 mmHg
		n (%)
<30	4758	1513 (31.8)
30-40	7256	2616 (36.1)
40-50	7256	3158 (43.5)
50-60	4553	2346 (51.5)
60-70	2101	1229 (58.5)
≥70	860	568 (66.0)
Overall	26784	11430 (42.7)

Abbreviations: SBP = Systolic blood pressure

Figure S1. Flowchart of the study population by further including data after the onset of hypertension

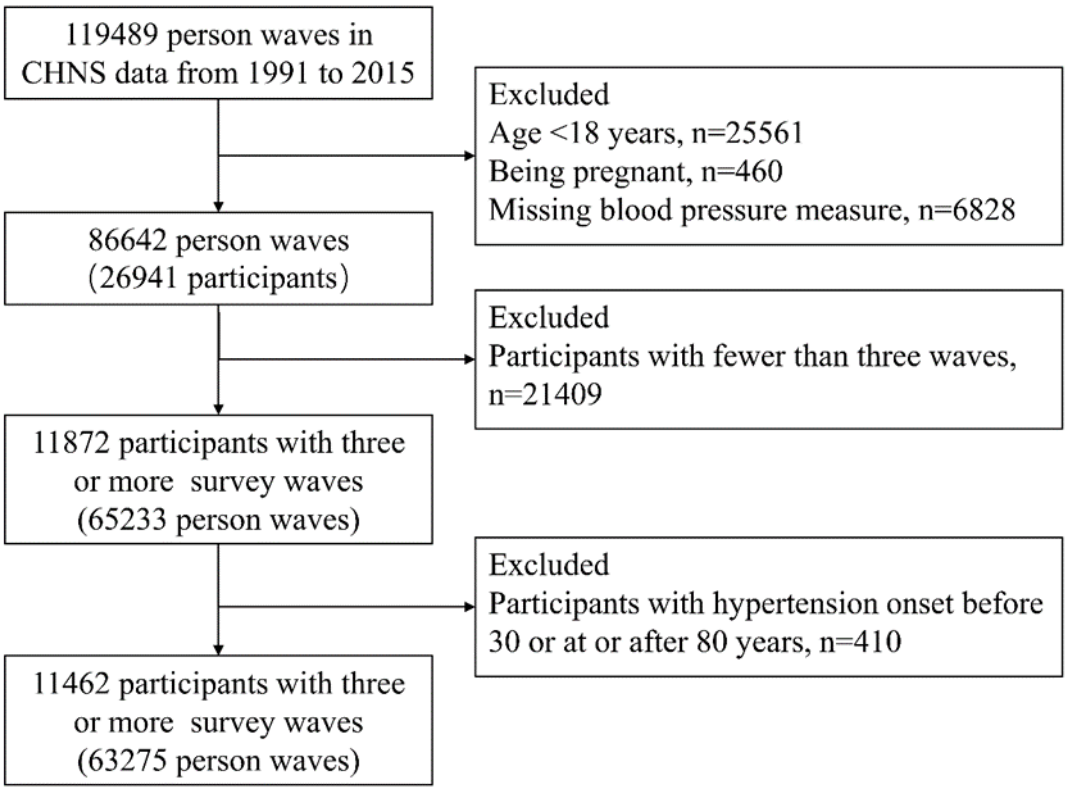
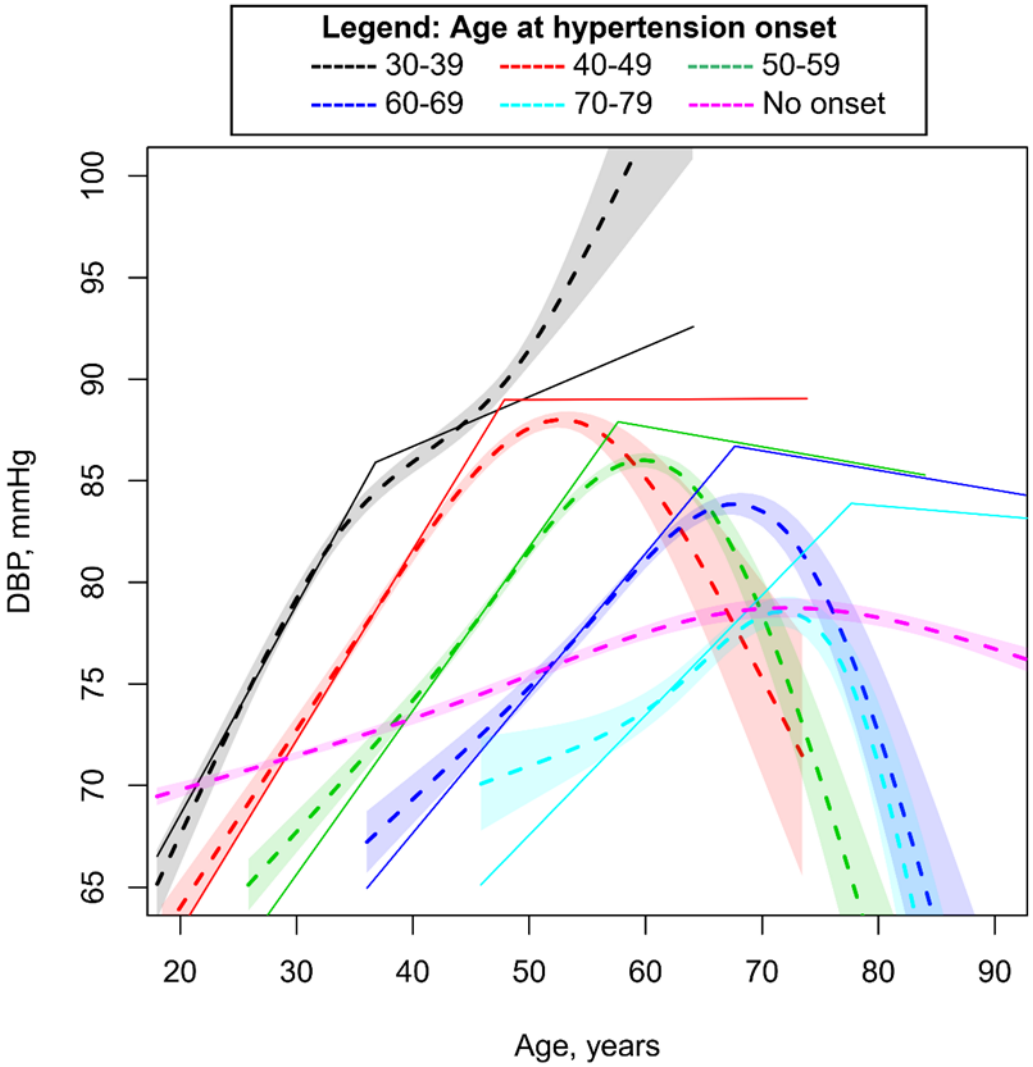


Figure S2. The DBP trajectory when further including data after the onset of hypertension*



*Mixed Linear models with restricted cubic splines (dash line) were used to assess the DBP increased trajectories with age and its' 95% confidence intervals; mixed segmented linear models (solid line) were used to identify the inflection points in the DBP increased trajectories.

Abbreviations: DBP = Diastolic blood pressure