

Decreasing Blood Pressure Trajectories Are Associated with Reduced Stroke Risk: A Group-Based Trajectory Analysis

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Abstract

Objective: This study aims to identify the independent and multiple trajectories of systolic blood pressure (SBP) and diastolic blood pressure (DBP), and to explore their associations with the risk of incident stroke.

Methods: This study included 10,420 participants who underwent at least three measurements of blood pressure. Group-based trajectory modeling and group-based multi-trajectory modeling were used to identify the trajectory patterns of blood pressure. Logistic regression models were used to assess the association between the trajectories and the risk of stroke.

Results: During a median 11.07-year follow-up, 788 incident stroke cases were observed. We identified three SBP and DBP trajectory groups respectively, and five multi-trajectory groups. Among the SBP trajectories, compared to the normotensive-stable group, the high normal-slight increase and hypertension-decrease groups had 133% and 179% higher stroke risks when compared to the normotensive-slight decrease group. In DBP trajectories, the high normal-slight decrease and hypertension-decrease groups had 50% and 96% higher risks, respectively. In multi-trajectories of SBP and DBP, compared with participants with normal stable SBP and normal decreased DBP levels, the other four groups had a significantly higher stroke risk; individuals with high initial blood pressure and a decreasing pattern had the highest stroke risk (3.04-fold increase), followed by those with increasing SBP and stable DBP patterns (1.96-fold increase). When further adjusting for baseline blood pressure levels, the stroke risk of the participants with a hypertension-decrease SBP pattern was lower than that in the high normal-slight increase trajectory group; the multi-trajectory group, whose SBP decreased from stage 1 hypertension to high normal while DBP decreased from high normal to normal, showed no significant difference in stroke risk compared to the low-level group.

Conclusion: Participants with persistently high SBP and DBP levels have a higher stroke risk, while a decreasing trend in blood pressure is independently associated with reduced stroke risk regardless of baseline levels. This study emphasizes the importance of controlling blood pressure, especially SBP, for stroke prevention; it offers epidemiological evidence for stroke prevention and control.

Keywords: blood pressure; stroke; group-based trajectory model; multi-trajectory; cohort study

INTRODUCTION

Stroke, defined by the World Health Organization as an acute neurological deficit caused by focal cerebrovascular injury, remains a disease with high incidence and recurrence, resulting in significant disability, mortality, and economic burden^[1, 2]. Data from the Global Burden of Disease Study 2021 show that there were 11.95 million incident strokes worldwide, 93.82 million people living with stroke, 7.29 million deaths, and 160 million disability-adjusted life years (DALYs); it ranked stroke third for mortality and fourth for DALYs lost^[2, 3]. In China, there were 4.09 million new stroke patients and 2.59 million deaths in 2021, with stroke now the leading cause of disability nationally^[3, 4]. These figures highlight an urgent need for comprehensive, life-course prevention and control strategies.

Hypertension, one of the most prevalent chronic diseases worldwide, remains the most significant modifiable risk factor for stroke^[2]. Blood pressure (BP) levels change with factors such as age and behavioral lifestyle patterns^[5]. Most previous studies^[6, 7] relied on single BP measurements, which may only reflect the current state of research subjects, ignoring long-term variations and potentially leading to misclassification. Trajectory analysis models based on repeated measurements are now widely used to evaluate long-term changes in various disease risk factors^[8]. Although several studies have explored the association between longitudinal BP trajectories and stroke, their findings remain inconsistent. Some studies have reported that a stable trajectory at high BP levels is associated with an increased risk of stroke^[9], while others have found that fluctuating^[10] or high-level decreasing trajectories^[11] are linked to a higher stroke risk. Additionally, previous studies based on Chinese subjects^[4, 9] were conducted in occupational or non-hypertensive populations, limiting generalizability to the general population. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) may follow distinct co-variation patterns, yet previous research has mostly focused on single BP parameter trajectories rather than multi-trajectory analysis. One US study using cluster analysis, based on the Cardiovascular Health Study, identified three joint SBP-DBP trajectory groups: compared to the first group (both SBP and DBP increasing from low initial level), the third group (both decreasing from high initial level) showed a higher cardiovascular disease risk (Hazard Ratio [HR]: 1.32)^[11]. While studies in Chinese populations have shown significant associations between multiple BP trajectories and overall cardiovascular disease risk, the specific relationship between joint SBP-DBP trajectories and stroke risk remains unclear. It is therefore necessary to conduct trajectory analysis, especially multi-trajectory analysis, on SBP and DBP in Chinese populations to identify BP change patterns and explore their associations with stroke risk.

This research aimed to identify distinct long-term trajectory patterns for SBP, DBP, and their multi-trajectories, and to evaluate the association between these BP trajectory patterns and the risk of stroke, while also exploring potential factors that might modify this association, thus providing evidence upon which to formulate stroke prevention strategies.

MATERIAL AND METHODS

Study population and study design

The study population was drawn from the Rural Chinese Cohort study, an ongoing study investigating noncommunicable disease and risk factors. The detailed study design and methodology have been previously described^[12]. In brief, this cohort was established between July 2007 and August 2008, using cluster random sampling to select 81 natural villages from two representative towns: Tiemen and Cijian in Xin'an County, Luoyang City. The baseline survey was conducted with 20,194 residents aged 18 and older. The first and second follow-up surveys were conducted in July 2013 and October 2014, and July 2018 and August 2020, respectively. A total of 10,420 participants were included in this study after

excluding participants with stroke at baseline or at the first follow-up survey (n=1,379), those with less than 3 BP measurements (n=7,891), and those of unknown stroke status (n=504). Approval for this study was granted by the Ethics Committees of Shenzhen University. All participants fully understood and voluntarily participated in the study, providing written informed consent.

Data collection and definition

In this study, a face-to-face questionnaire survey was administered by uniformly trained and certified interviewers to collect information on demographic and socioeconomic characteristics, behavioral risk factors, and medical histories. A tape was used to measure height, requiring the subject to be barefoot, upright, and looking straight ahead, with the heels, hips, and shoulder blades in a line. Height measurements were taken to the nearest 0.1 cm, with the average over two measurements recorded. A calibrated electronic scale was used to measure weight, with participants being asked to remove shoes, hats, and heavy clothing, and to wear only light clothing. Weight was measured to the nearest 0.5 kg, with two measurements taken and their average recorded. BP was measured on the right upper arm with participants in a seated position using a calibrated electronic sphygmomanometer (HEM-770AFuzzy, Omron, Kyoto, Japan). After resting for at least 5 minutes, BP was measured three times with at least 30 seconds interval between measurements, then the average of the three measurements recorded. Peripheral venous blood samples collected after overnight fasting (for at least 8 hours) were used to measure fasting plasma glucose (FPG), total cholesterol (TC), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) levels; it was assayed using an enzyme method with the Hitachi 7060 automatic biochemical analyzer (Hitachi 7060, Tokyo, Japan). Low-density lipoprotein cholesterol (LDL-C) levels were calculated using the Friedewald formula^[13].

Smoking was defined as having smoked more than 100 cigarettes in one's lifetime^[14]. Drinking was defined as having consuming alcoholic beverages (including beer, spirits, wine, rice wine, and yellow wine) more than 12 times in the past year^[15]. Ideal physical activity (PA) was defined according to recommended PA guidelines, engaging in ≥ 150 minutes of moderate-intensity PA per week, or ≥ 75 minutes of vigorous-intensity PA per week, or an equivalent combination of both^[16]. Family history of stroke was defined as having at least one parent or sibling with a history of stroke. Healthy diet was defined by subjects meeting two or more intake measures: fish ≥ 200 g/week, vegetables and fruits ≥ 500 g/day, soy products ≥ 125 g/day, red meat < 75 g/day, and tea ≥ 50 g/month^[17]. Body mass index (BMI) was calculated by dividing the square of height (m^2) by weight (kg). Obesity^[18] defined as BMI ≥ 28.0 kg/ m^2 . TC level ≥ 6.2 mmol/L and/or TG ≥ 2.3 mmol/L and/or LDL-C level ≥ 4.1 mmol/L, and/or HDL-C level < 1.0 mmol/L was diagnosed as dyslipidemia^[19]. Type 2 diabetes mellitus (T2DM) was defined as self-reported history of T2DM and/or FPG ≥ 7.0 mmol/L and/or current use of antihyperglycemic medications^[20]. Hypertension was diagnosed by SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg, and/or current use of antihypertension medications^[21].

Assessment of stroke

New-onset stroke was identified as first occurrence of stroke during the period from baseline to the 2018-2020 follow-up survey. Information on stroke was collected by interviewing study participants or their relatives, then further checking of medical records or death certificates for verification. Stroke was classified according to the International Classification of Diseases, 10th Edition (ICD-10). In this study, stroke refers to the first fatal or non-fatal stroke event (ICD-10 codes I60-I69) diagnosed during the follow-up period.

Data analysis

The trajectory patterns of SBP and DBP during the baseline examination and up to the final visits were

determined by the group-based trajectory model (GBTM) within the Proc Traj procedure of SAS software^[22, 23]. GBTM was used with the maximum likelihood estimation to identify subgroups of participants that are homogeneous with BP change. A group-based multi-trajectory model (GBMTM), which is an extension of GBTM, was used to model the joint trajectories of SBP and DBP^[24]. In this study, a censored normal model deemed appropriate was used for continuous variables. We launched a model that started with two groups and then added 3, 4, 5 and up to 6 groups. Cubic, quadratic, and linear terms were considered and evaluated based on their significance level, starting with the highest polynomial. Selecting the best-fitting model was determined by the minimum absolute value of the Bayesian information criterion (BIC) and the proportion of participants in any single trajectory group being no less than 5%. We then assessed the goodness of fit for the final model based on the following criteria: an average posterior probability (AvePP) of assignment for each trajectory group higher than 0.7; the odds of correct classification (OCC) equal to 5 or higher for all groups; and the reasonable similarity between the proportion of samples assigned to a particular group and the group probabilities estimated by the model. Continuous variables, found to be non-normally distributed after normality tests, were described using medians and interquartile ranges, while differences between trajectory groups were assessed using the Wilcoxon rank sum test. Categorical variables were described using frequency and percentage, with differences between groups compared using the χ^2 test. A logistic model was used to explore the association between the BP trajectories of study participants and the risk of stroke, and to calculate the odds ratio (OR) and 95% confidence interval (CI). Three models were constructed in this study: model 1 was adjusted for baseline sex and age; model 2 was adjusted for baseline smoking, drinking, education, income, marital status, ideal PA, healthy diet, and family history of stroke on the basis of model 1; and model 3 was further adjusted for baseline obesity, dyslipidemia, T2DM, and use of antihypertension agents, based on Model 2. Subgroup analyses, stratified by sex (male and female), age (<60 and ≥ 60), smoking (yes and no), drinking (yes and no), and ideal PA (yes and no), obesity (yes and no), dyslipidemia (yes and no), and T2DM (yes and no), were undertaken to explore the association between BP trajectory patterns and risk of stroke in various characterized populations. The multiple terms of the above stratification factors with BP trajectory patterns were included in Model 3 to assess the multiple interaction effect. We also conducted a series of sensitivity analyses to assess the robustness of the results by excluding those taking antihypertensive agents at baseline and during follow-up, those with other cardiovascular diseases, and those with chronic conditions (cancer and renal failure), then additionally adjusting for baseline BP levels.

In this study, a two-sided test was used with a significance level set at $\alpha = 0.05$. All statistical analyses were performed using SAS 9.4 (SAS Institute, Inc., Cary, NC).

RESULTS

Table 1 presents the baseline demographic characteristics of 10,420 participants in this study. The median age was 50 years (interquartile range: 42–58), and 3,633 (34.87%) were male. Compared with those without stroke, participants in the stroke group were older and had higher levels of BMI, SBP, DBP, FPG, TC, TG, and LDL-C. They were also more likely to have a monthly income below ¥1,000, a family history of stroke, obesity, T2DM, and to be using antihypertensive medications; conversely, fewer had attained a high school education or above, were married or cohabiting, or engaged in ideal levels of physical activity (all $P < 0.05$). No significant differences were observed in sex distribution, smoking status, drinking, healthy diet adherence, dyslipidemia, or HDL-C levels ($P > 0.05$).

As shown in Figure 1 and Figure 2, this study revealed that there are 3 distinct trajectories for SBP changes

over time, 3 trajectories for DBP, and 5 multi-trajectories for joint SBP and DBP. Fitting parameters for trajectory models are shown in Table S1. All subgroups showed robust classification quality, with AvePP > 0.70, the OCC > 5.00, and there was good agreement between P_j and Π_j (Table S2).

Regarding SBP, 48.45% of participants showed normotensive stable SBP, maintaining between 111.91 and 114.44 mmHg in 3 surveys (normotensive-slight decrease group); 41.58% of participants showed high normal and slowly increasing SBP, increasing from 130.83 to 134.31 mmHg (high normal-slight increase group); and 9.97% of participants showed hypertension and decreasing SBP, maintaining SBP around 160.00 mmHg during the first and second surveys, but decreasing to 153.02 mmHg in the third survey (hypertension-decrease group). Regarding DBP, 37.95% of participants showed normotensive and slowly decreasing DBP, decreasing from 69.92 to 66.97 mmHg in 3 waves (normotensive-slight decrease group); 48.76% of participants showed high normal and slowly decreasing DBP, decreasing from 80.56 to 77.80 mmHg in 3 waves (high normal-slight decrease group); and 13.29% of participants showed hypertension and decreasing DBP, maintaining DBP around 95.00 mmHg during the first and second waves, decreasing to 88.03 mmHg in the third wave (hypertension-decrease group).

In the multi-trajectory models, group 1 (26.42% of participants) and group 2 (41.59% of participants) showed normotensive stable DBP patterns. Group 1 maintained between 65.77 and 68.10 mmHg, while group 2 maintained between 75.11 and 76.83 mmHg; however, group 1 showed a normotensive stable SBP pattern with SBP staying between 107.96 to 109.53 mmHg, while group 2 showed a high normal increasing SBP, with SBP increasing from 120.74 to 125.19 mmHg. Group 3 (17.91% of participants) showed an increasing in SBP from high normal to stage 1 hypertension, with SBP increasing from 132.47 to 149.53 mmHg and maintaining stable high normal DBP, with DBP range from 85.43 to 88.21 mmHg. Group 4 (8.47% of participants) and group 5 (5.61% of participants) showed decreasing blood pressure patterns. In group 4, SBP decreased from stage 1 hypertension to high normal, with SBP decreasing from 151.24 to 133.87 mmHg, and DBP decreasing from high normal to normal, from 89.05 to 72.13 mmHg. In group 5, SBP decreased from stage 2 hypertension to stage 1 hypertension, with SBP decreasing from 164.10 to 153.69 mmHg, and DBP decreasing from stage 2 hypertension to normal high, from 100.06 to 87.49 mmHg.

During a median follow-up of 11.07 years, 788 incident stroke cases were observed. The association between groups and stroke risk are shown in Table 2. In multi-variable models, all groups show higher risk of stroke incidence compared with the reference group. In SBP trajectories, compared with participants in the normotensive-slight decrease group, the risk of incident stroke increased by 133% and 179% in high normal-slight increase and hypertension-decrease group; the risk of stroke remained significant in these two groups after additional adjustments for baseline SBP levels but the risk was lower in the hypertension-decrease group than the high normal-slight increase group. In DBP trajectories, compared with participants in the normotensive-slight decrease group, the risk of incident stroke increased by 50% and 96% in the high normal-slight decrease and hypertension-decrease groups, while the associations were not significant after adjustment for baseline DBP levels. In multi-trajectories, compared with participants in group1, the risk of incident stroke increased by 102%, 196%, 159% and 304% in groups 2, 3, 4 and 5, respectively. After adjusting for baseline blood pressure, the associations remained significant in all groups except group 4, while the risk of stroke was lower in group 5 than in group 3. The results of the SBP trajectory and multi-trajectories remained stable after excluding participants with other cardiovascular diseases, cancer, or renal failure, and those taking antihypertensive medications during the follow-up period (Table S3 and Table S4).

The subgroup analyses are shown in Table 3, Table S5, and Table S6. The effect directions in each

subgroup were consistent with the counterparts in general. In addition, we found that the association of multi-trajectory patterns of blood pressure, trajectory patterns of SBP, and trajectory pattern of DBP with stroke may be modified by age ($P_{\text{interaction}} < 0.05$), and the relationship between trajectory patterns of SBP may be modified by obesity ($P_{\text{interaction}} = 0.018$).

Discussion

In this large prospective study, we identified 3 trajectories for SBP, 3 trajectories for DBP, and 5 multi-trajectories for BP based on 10,240 eligible participants. In multi-variable adjusted models, when compared with group 1, all other groups had greater stroke risk. As for SBP, participants in the hypertension-decrease group had the highest risk of incident stroke (OR: 2.79, 95%CI: 2.17-3.60), compared with those in the normotensive-slight decrease group. As for DBP, there were similar results, with the hypertension-decrease group having the worst risk (OR: 1.96 and 95%CI: 1.55-2.48). As for the multi-trajectories model, taking participants in group 1 as reference, group 5 showed the highest risk of incident stroke (OR: 4.04, 95%CI: 2.91-5.62). In subgroup analyses we found that the association between all BP trajectories and stroke could be affected by age, while obesity could modify the association between SBP trajectory patterns and stroke.

Our study indicated that in the SBP trajectory groups, participants in the high normal-slight increase group, even with sustained high normal SBP (120-140 mmHg), had a 1.33-fold higher stroke risk compared to the normotensive-slight decrease group. This is consistent with findings from the US Atherosclerosis Risk in Communities Study^[25], suggesting that stricter BP control (maintaining measures below 120 mmHg) may be an effective primary stroke prevention strategy. Additionally, the hypertension-decrease group had the highest risk, with a 1.79-fold increase relative to the normotensive-slight decrease group. Although participants in the hypertension-decrease group were likely to have implemented intentional BP management leading to SBP reduction, the results remained robust after excluding those taking antihypertensive agents during the survey. When baseline SBP levels were adjusted, the hypertension-decrease group showed a lower stroke risk than the high normal-slight increase group. This indicates that the trend of decreasing SBP significantly affects stroke risk independently of baseline levels, demonstrating that SBP change trajectories are more accurate for assessing stroke risk than single-timepoint SBP measurements. Our findings show that a decreasing trend independent of baseline levels can significantly reduce stroke risk, a result which aligns with previous research^[26]. This highlights the importance of proactive BP control for individuals with normal-high BP or hypertension in stroke prevention. In addition, we identified 3 trajectory groups with decreased DBP, finding that individuals with abnormally high baseline DBP (>80 mmHg) had an elevated risk of stroke, consistent with findings from the Kailuan study^[26]. After adjusting for baseline DBP levels, however, their stroke risk showed no significant difference from the normotensive-slight decrease group, suggesting that the effect of the DBP trajectories on stroke may be driven by the initial DBP level. After excluding individuals taking antihypertensive medications, neither the high normal-slight decrease group nor the hypertension-decrease group was associated with stroke risk. This may be because patients taking antihypertensive drugs typically have higher BP or greater cardiovascular risk, thereby masking the potential harm of elevated DBP itself^[27, 28].

In the present study, we identified 5 distinct multi-trajectories for the joint of SBP and DBP, based on repeated BP measurements from 3 waves. Taking participants with optimal stable SBP and DBP (group 1) as reference, we found that other trajectories were strongly associated with the increased risk of stroke. Participants with stable normal high SBP and normal DBP (group 2), the risk of stroke was doubled, which confirmed that even within the normotensive range, higher BP increased the risk of CVD events^[29].

Participants with increasing BP (group 3) had almost 3 times the risk of stroke, which was inconsistent with Christopher's study^[11]. This may be due to the reference group in Christopher's study showed increasing SBP and DBP, as well as the limited number of groupings, which may not have been sufficient to distinguish between populations with different BP trajectories. Participants with lower baseline BP but increasing BP trajectories (group 3) had higher stroke risk, comparing to those with higher initial BP but decreasing patterns (group 4). More importantly, in sensitivity analyses, after further adjusted the baseline BP based on model 3, we found that the association for group 4 was attenuated (OR:1.49, 95%CI: 0.98-2.27), indicating that concurrent decreases in SBP and DBP independently reduce stroke risk. However, in Chen's study, the risk cardiovascular disease increased as the trajectory group increased^[30]. This difference can be explained by the fact that in Chen's study, both SBP and DBP of each group remained stable and did not show any great upward or downward trends. These findings therefore suggest that we should pay more attention on the long-term BP trajectories, and taking interventions aimed at maintaining or lowering BP over time for the further stroke prevention.

Our study clearly revealed a strong interaction effect of age. Specifically, the impact of adverse BP trajectories on stroke risk was more pronounced in individuals younger than 60 years. which could be explained by those older participants have more CVD risk factors, and these factors may mask the relationship between BP trajectories and stroke risk. Besides age, we found that obesity was also a possible modifier of the SBP trajectory with stroke ($P>0.05$). The association between SBP trajectory was more pronounced in non-obese individuals, which could be due to that obesity population always with higher SBP and obesity interacts with more CVD risk factors such as insulin resistance and dyslipidemia, which attenuate the association between SBP trajectory and stroke risk^[31, 32].

This study has several notable strengths. This study is based on a prospective cohort design, which provides a high level of epidemiological evidence. This design strengthens the inference of a temporal sequence between exposure and outcome and mitigates common biases, such as recall bias, found in retrospective studies. whereas most previous studies have relied on single-time-point BP measurements, thereby ignoring the dynamic nature of this physiological parameter. Our study utilized repeated measurement data from a prospective cohort and employed GBTM to delineate long-term BP change patterns more precisely, which helps identify risks that might be overlooked by conventional methods. Most importantly, our study not only examined the individual trajectories of SBP and DBP but applied GBMTM to assess the impact of their combined change patterns on stroke risk. It helps to identify high-risk populations more accurately for stroke, thereby providing a new scientific basis for the development of comprehensive and effective prevention and control strategies.

Nevertheless, this study has several limitations. First, the generalizability of our findings is limited. As all participants were from a rural area in Henan, caution is warranted when extrapolating the results to urban populations in China. Furthermore, despite our quality control measures, some loss to follow-up was unavoidable over the decade-long study period. Additionally, while we adjusted for numerous potential confounders in our analysis, the possibility of residual confounding cannot be entirely dismissed.

CONCLUSION

Participants with persistently high SBP and DBP levels have a higher stroke risk, while a decreasing trend in BP is independently associated with reduced stroke risk regardless of baseline levels. This study emphasizes the importance of controlling BP, especially SBP, for stroke prevention and offers epidemiological evidence for stroke prevention and control.

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Table 1. Baseline characteristics of participants.

Characteristics	Overall (n=10,420)	Stroke (n=788)	Non-stroke (n=9,632)	P value
Age, years	50.00 (42.00-58.00)	58.00 (52.00-63.00)	50.00 (41.00-58.00)	<0.001
Male, %	3633 (34.87)	289 (36.68)	3344 (34.72)	0.268
High school and above, %	972 (9.33)	42 (5.33)	930 (9.66)	<0.001
Average income < 1000 ¥/month, %	9723 (93.50)	750 (95.30)	8973 (93.35)	0.033
Married or cohabiting, %	9688 (93.01)	715 (90.74)	8973 (93.20)	0.009
Smoking, %	2624 (25.18)	201 (25.51)	2423 (25.16)	0.828
Drinking, %	1117 (10.72)	69 (8.76)	1048 (10.88)	0.064
Healthy diet, %	5260 (50.50)	378 (47.97)	4882 (50.71)	0.139
Ideal physical activity, %	8628 (82.80)	631 (80.08)	7997 (83.03)	0.035
Family history of stroke, %	1404 (13.47)	138 (17.51)	1359 (14.11)	<0.001
BMI, kg/m ²	24.22 (21.88-26.74)	24.89 (22.48-27.44)	24.17 (21.83-26.68)	<0.001
SBP, mmHg	121.33 (110.83-135.00)	132.83 (120.17-147.33)	120.67 (110.33-133.67)	<0.001
DBP, mmHg	77.33 (70.67-85.00)	82.00 (75.00-90.00)	77.00 (70.33-84.67)	<0.001
FPG, mmol/L	5.35 (5.00-5.78)	5.48 (5.10-6.04)	5.34 (4.99-5.76)	<0.001
TC, mmol/L	4.40 (3.84-5.03)	4.66 (4.12-5.28)	4.37 (3.82-5.01)	<0.001
TG, mmol/L	1.37 (0.96-1.99)	1.51 (1.09-2.19)	1.36 (0.96-1.97)	<0.001
HDL-C, mmol/L	1.14 (0.99-1.32)	1.13 (0.99-1.32)	1.14 (0.99-1.32)	0.816
LDL-C, mmol/L	2.50 (2.10-3.00)	2.70 (2.20-3.20)	2.50 (2.10-3.00)	<0.001
Obesity, %	1624 (15.59)	166 (21.07)	1458 (15.14)	<0.001
T2DM, %	724 (6.95)	104 (13.20)	620 (6.44)	<0.001
Dyslipidemia, %	4533 (43.55)	367 (46.63)	4166 (43.30)	0.070
Use of antihypertensive agents, %	1245 (11.95)	207 (26.27)	1038 (10.78)	<0.001

Data are presented as median (interquartile range) for continuous and frequency (percentage) for categorical variables.

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; T2DM, type 2 diabetes mellitus.

Table 2. Association between blood pressure trajectory patterns and stroke.

Trajectory group	Cases/ Participants	OR (95%CI)		
		Model 1	Model 2	Model 3
SBP trajectories				
Normotensive-Slight decrease	186/5049	1.00	1.00	1.00
High normal-Slight increase	445/4333	2.64 (2.20-3.16)	2.64 (2.20-3.16)	2.33 (1.94-2.80)
Hypertension-Decrease	157/1038	3.62 (2.87-4.58)	3.63 (2.87-4.60)	2.79 (2.17-3.60)
DBP trajectories				
Normotensive-Slight decrease	206/3954	1.00	1.00	1.00
High normal-Slight decrease	422/5081	1.68 (1.41-2.00)	1.69 (1.42-2.01)	1.50 (1.25-1.79)
Hypertension-Decrease	160/1385	2.52 (2.03-3.14)	2.54 (2.04-3.17)	1.96 (1.55-2.48)
Multi-trajectories				
Group 1	86/2753	1.00	1.00	1.00
Group 2	298/4334	2.16 (1.69-2.76)	2.16 (1.69-2.77)	2.02 (1.58-2.59)
Group 3	191/1866	3.39 (2.60-4.41)	3.42 (2.63-4.45)	2.96 (2.26-3.88)
Group 4	116/883	3.43 (2.54-4.62)	3.43 (2.54-4.62)	2.59 (1.90-3.55)
Group 5	97/584	5.28 (3.87-7.20)	5.33 (3.91-7.28)	4.04 (2.91-5.62)

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; OR, odds ratio; CI, confidence interval.

Model 1 adjusted for baseline sex and age;

Model 2 adjusted for baseline smoking, drinking, education, income, marital status, ideal physical activity, healthy diet, and family history of stroke in the basis of model 1;

Model 3 included variables in model 2 and further adjusted for baseline obesity, dyslipidemia, type 2 diabetes mellitus, and use of antihypertensive agents.

Table 3. Subgroup analyses for the association between multi-trajectory patterns of blood pressure and stroke.

	Group 1	Group 2	Group 3	Group 4	Group 5	P interaction
Sex						0.394
Male	1.00	1.56 (1.07-2.27)	2.69 (1.78-4.04)	1.48 (0.85-2.58)	3.58 (2.05-6.27)	
Female	1.00	2.42 (1.74-3.38)	3.19 (2.22-4.58)	3.39 (2.28-5.04)	4.51 (2.97-6.85)	
Age (years)						<0.001
< 60	1.00	1.91 (1.40-2.59)	2.91 (2.09-4.05)	3.56 (2.36-5.38)	4.40 (2.90-6.68)	
≥ 60	1.00	2.08 (1.36-3.18)	2.76 (1.72-4.43)	1.93 (1.19-3.13)	3.05 (1.78-5.24)	
Smoking						0.434
Yes	1.00	1.44 (0.94-2.22)	2.78 (1.74-4.43)	1.51 (0.78-2.96)	3.29 (1.66-6.51)	
No	1.00	2.33 (1.71-3.15)	3.04 (2.18-4.24)	3.03 (2.10-4.38)	4.40 (2.99-6.48)	
Drinking						0.861
Yes	1.00	1.19 (0.57-2.45)	1.83 (0.82-4.08)	1.42 (0.44-4.64)	3.14 (1.02-9.60)	

No	1.00	2.14 2.79)	(1.65- 3.12 4.16)	(2.34- 2.74 3.80)	(1.97- 4.22 (2.98-5.97)	0.539
Ideal PA						
Yes	1.00	1.87 2.45)	(1.43- 3.04 4.07)	(2.28- 2.53 3.58)	(1.79- 3.27 (2.24-4.77)	0.081
No	1.00	3.05 5.94)	(1.57- 2.60 5.49)	(1.24- 3.26 7.00)	(1.52- 7.96 (3.71-17.08)	
Obesity						0.275
Yes	1.00	1.60 3.34)	(0.76- 1.75 3.76)	(0.82- 1.78 4.01)	(0.79- 2.76 (1.22-6.24)	
No	1.00	2.05 2.67)	(1.57- 3.21 4.29)	(2.40- 2.74 3.87)	(1.94- 4.25 (2.93-6.17)	0.554
Dyslipidemia						
Yes	1.00	1.88 2.76)	(1.28- 2.94 4.43)	(1.95- 2.25 3.63)	(1.40- 4.04 (2.47-6.61)	0.554
No	1.00	2.10 2.90)	(1.51- 2.84 4.09)	(1.98- 2.82 4.28)	(1.86- 3.83 (2.45-6.00)	
T2DM						0.554
Yes	1.00	2.18 4.86)	(0.98- 2.49 6.12)	(1.01- 2.71 6.64)	(1.10- 5.37 (1.90-15.15)	
No	1.00	1.99 2.58)	(1.53- 2.98 3.96)	(2.24- 2.54 3.55)	(1.81- 3.81 (2.69-5.41)	

Abbreviations: PA, physical activity; T2DM, type 2 diabetes mellitus. Adjusted for baseline sex, age, smoking, drinking, education, income, marital status, ideal physical activity, healthy diet, family history of stroke, obesity, dyslipidemia, and type 2 diabetes mellitus (except for the stratification factors).

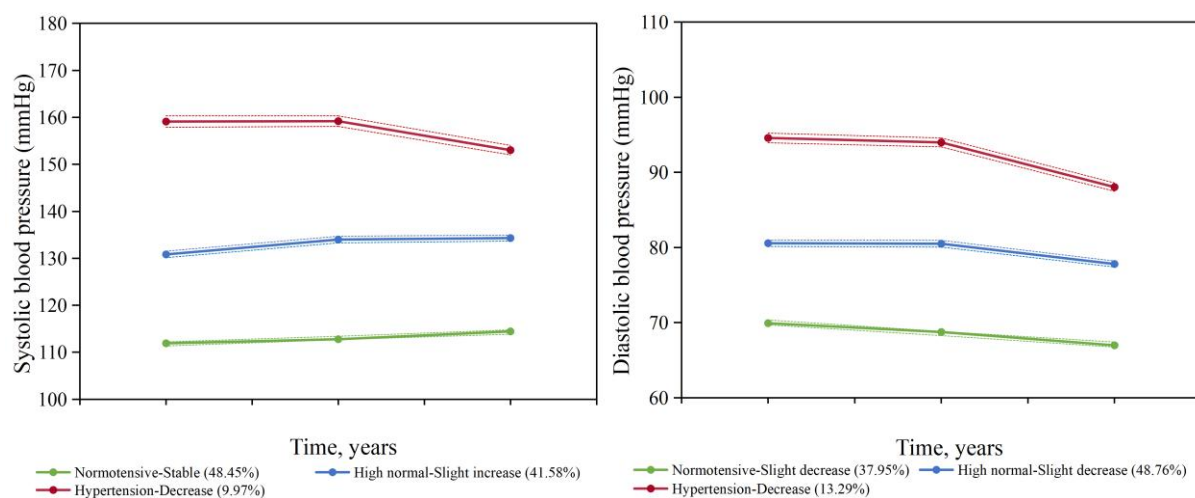


Figure 1. Single trajectory patterns of systolic blood pressure and diastolic blood pressure.

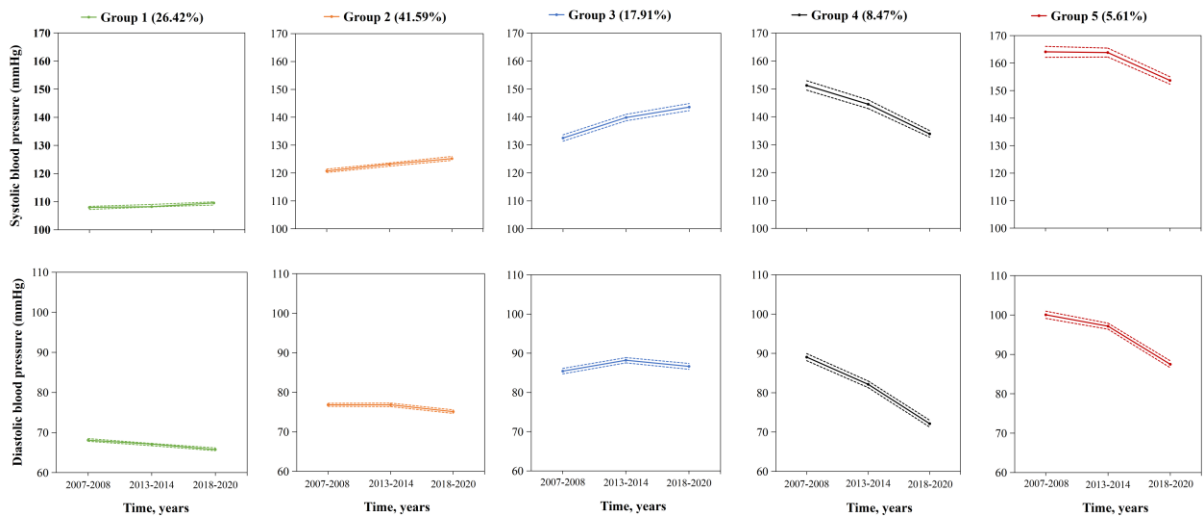


Figure 2. Multi-trajectories patterns of systolic blood pressure and diastolic blood pressure.

Table S1. Fit parameters for trajectory models.

Number of groups	Polynomi al order*	BIC	Percentage in each class	Average probability	posterior
SBP trajectories					
2	1, 2	132243. 7	69.41; 30.59	0.95; 0.90	
3	1, 2, 2	130956. 1	48.29; 41.28; 10.43	0.91; 0.86; 0.89	
4	1, 1, 2, 2	130607. 0	36.94; 41.23; 18.23; 3.60	0.87; 0.81; 0.83; 0.88	
5	1, 2, 2, 1, 2	130330. 0	38.95; 41.78; 6.94; 10.10; 2.23	0.89; 0.83; 0.77; 0.77; 0.86	
6	1, 1, 2, 2, 2, 1	130180. 4	28.09; 37.16; 23.18; 5.17; 5.30; 1.11	0.83; 0.75; 0.76; 0.77; 0.80; 0.87	
DBP trajectories					
2	2, 2	115509. 8	62.80; 37.20	0.93; 0.90	
3	1, 2, 2	114520. 4	38.34; 47.58; 14.08	0.88; 0.85; 0.87	
4	1, 2, 2, 2	114216. 9	22.69; 46.36; 26.79; 4.17	0.82; 0.81; 0.83; 0.85	
5	1, 2, 2, 1, 2	114060. 5	22.26; 45.95; 23.04; 4.85; 3.91	0.83; 0.81; 0.78; 0.70; 0.82	
6	1, 2, 2, 2, 1, 1	113961. 4	12.55; 40.75; 31.02; 9.12; 5.06; 1.50	0.79; 0.79; 0.76; 0.76; 0.69; 0.81	

Multi-trajectories of blood pressure

SBP		1, 2	-		
DBP	2	2, 2	245261.0	61.09; 38.91	0.96; 0.95
SBP		2, 2, 2	-		
DBP	3	1, 2, 2	242024.5	39.49; 44.99; 15.52	0.93; 0.91; 0.93
SBP		1, 1, 2, 2	-		
DBP	4	1, 2, 2, 2	240951.5	26.26; 41.20; 26.01; 6.52	0.90; 0.86; 0.88; 0.90
SBP		1, 1, 2, 2, 2	-		
DBP	5	1, 2, 2, 2, 2	240019.2	26.77; 40.57; 17.86; 9.21; 5.59	0.90; 0.87; 0.84; 0.82; 0.90
SBP		1, 1, 2, 2, 2, 2	-		
DBP	6	1, 2, 2, 2, 2, 2	239448.9	16.77; 36.00; 25.32; 9.29; 9.25; 3.38	0.87; 0.84; 0.81; 0.84; 0.82; 0.91

*Polynomial order: 3, cubic; 2, quadratic; 1, linear. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; BIC, Bayesian information criterion.

Table S2. Diagnostic criteria for judging the adequacy of the final models.

Trajectory group	AvePP (%)	OCC	Pj (%)	Π_j (%)
SBP trajectories				
1	0.91	10.50	48.45	48.29
2	0.86	8.69	41.58	41.28
3	0.89	71.86	9.97	10.43
DBP trajectories				
1	0.88	11.68	37.95	38.34
2	0.85	6.07	48.76	47.58
3	0.87	41.14	13.29	14.08
Multi-trajectories of blood pressure				
1	0.90	25.77	26.42	26.77
2	0.87	9.66	41.59	40.57
3	0.84	24.01	17.91	17.86
4	0.82	45.85	8.47	9.21
5	0.90	144.83	5.61	5.59

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; AvePP, average posterior probability; OCC, odds of correct classification; Pj, actual proportion of subjects assigned to each trajectory group using the maximum probability rule; π_j , the posterior probability of group membership estimated by the model.

Table S3. Sensitivity analyses for the association between single systolic and diastolic blood pressure trajectory patterns and stroke.

Trajectory group	Cases	Participants	OR (95%CI)
Sensitivity analysis 1			
SBP trajectories			
Normotensive-Slight decrease	171	4879	1.00
High normal-Slight increase	410	4071	2.41 (1.99-2.93)
Hypertension-Decrease	141	957	2.86 (2.19-3.72)
DBP trajectories			
Normotensive-Slight decrease	190	3796	1.00
High normal-Slight decrease	387	4811	1.51 (1.25-1.81)
Hypertension-Decrease	145	1300	1.96 (1.53-2.51)
Sensitivity analysis 2			
SBP trajectories			
Normotensive-Slight decrease	144	4646	1.00
High normal-Slight increase	124	2225	1.54 (1.19-1.98)
Hypertension-Decrease	13	129	2.42 (1.29-4.52)
DBP trajectories			
Normotensive-Slight decrease	130	3535	1.00
High normal-Slight decrease	136	3150	1.21 (0.94-1.56)
Hypertension-Decrease	15	315	1.39 (0.79-2.43)
Sensitivity analysis 3			
SBP trajectories			
Normotensive-Slight decrease	186	5049	1.00
High normal-Slight increase	445	4333	1.83 (1.48-2.27)
Hypertension-Decrease	157	1038	1.55 (1.07-2.24)
DBP trajectories			
Normotensive-Slight decrease	206	3954	1.00
High normal-Slight decrease	422	5081	1.11 (0.90-1.37)
Hypertension-Decrease	160	1385	1.00 (0.70-1.42)

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; OR, odds ratio; CI, confidence interval.

Sensitivity analysis 1: excluded the participants with other cardiovascular diseases, cancer, and renal failure at baseline and the first follow-up survey based on model 3;

Sensitivity analysis 2: excluded participants using antihypertension agents at baseline and during the follow-up surveys based on model 3;

Sensitivity analysis 3: based on model 3 with additional adjustment for baseline blood pressure.

Table S4. Sensitivity analyses for the association between multi-trajectory patterns of blood pressure and stroke.

Trajectory group	Cases	Participants	OR (95%CI)
Sensitivity analysis 1			
Group 1	79	2661	1.00
Group 2	278	4128	2.08 (1.61-2.69)
Group 3	176	1766	3.04 (2.30-4.03)
Group 4	102	813	2.55 (1.83-3.54)
Group 5	87	539	4.08 (2.89-5.76)
Sensitivity analysis 2			
Group 1	78	2658	1.00
Group 2	143	3297	1.38 (1.04-1.83)
Group 3	38	814	1.56 (1.05-2.34)
Group 4	16	190	2.00 (1.12-3.59)
Group 5	6	41	4.73 (1.87-11.93)
Sensitivity analysis 3			
Group 1	86	2753	1.00
Group 2	298	4334	1.73 (1.32-2.26)
Group 3	191	1866	2.24 (1.60-3.11)
Group 4	116	883	1.49 (0.98-2.27)
Group 5	97	584	2.01 (1.20-3.34)

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; OR, odds ratio; CI, confidence interval.

Sensitivity analysis 1: excluded the participants with other cardiovascular diseases, cancer, and renal failure at baseline and the first follow-up survey based on model 3;

Sensitivity analysis 2: excluded participants using antihypertension agents at baseline and during the follow-up surveys based on model 3;

Sensitivity analysis 3: based on model 3 with additional adjustment for baseline blood pressure.

Table S5. Subgroup analyses for the association between SBP trajectory patterns and stroke.

	Normotensive -Slight decrease	High normal-Slight increase	Hypertension- Decrease	P _{interaction}
Sex				0.579
Male	1.00	1.90 (1.43-2.52)	2.73 (1.76-4.23)	
Female	1.00	2.70 (2.11-3.46)	2.97 (2.16-4.08)	
Age (years)				<0.001
< 60	1.00	2.34 (1.87-2.93)	3.38 (2.43-4.70)	
≥ 60	1.00	1.94 (1.39-2.72)	1.95 (1.30-2.91)	
Smokin g				0.774
Yes	1.00	2.11 (1.52-2.94)	3.10 (1.81-5.30)	
No	1.00	2.42 (1.94-3.03)	2.76 (2.06-3.69)	
Drinkin g				0.695
Yes	1.00	1.95 (1.12-3.39)	2.89 (1.10-7.60)	
No	1.00	2.37 (1.95-2.88)	2.82 (2.17-3.67)	
Ideal PA				0.547
Yes	1.00	2.21 (1.81-2.70)	2.56 (1.93-3.41)	
No	1.00	3.27 (1.96-5.45)	4.30 (2.36-7.82)	
Obesity				0.018
Yes	1.00	1.50 (0.96-2.35)	1.78 (1.03-3.09)	
No	1.00	2.50 (2.04-3.06)	2.61 (1.98-3.43)	
Dyslipidemia				0.549
Yes	1.00	2.26 (1.72-2.98)	3.12 (2.17-4.50)	
No	1.00	2.35 (1.83-3.01)	2.43 (1.71-3.46)	

T2DM				0.162
Yes	1.00	2.02 (1.16-3.53)	2.43 (1.17-5.09)	
No	1.00	2.35 (1.93-2.86)	2.81 (2.14-3.68)	

Abbreviations: PA, physical activity; T2DM, type 2 diabetes mellitus. Adjusted for baseline sex, age, smoking, drinking, education, income, marital status, ideal physical activity, healthy diet, family history of stroke, obesity, dyslipidemia, and type 2 diabetes mellitus (except for the stratification factors).

Table S6. Subgroup analyses for the association between DBP trajectory patterns and stroke.

	Normotensive- Slight decrease	High normal- Slight decrease	Hypertension- Decrease	P interaction
Sex				0.330
Male	1.00	1.24 (0.94-1.65)	1.75 (1.19-2.60)	
Female	1.00	1.68 (1.33-2.12)	2.13 (1.58-2.87)	
Age (years)				0.012
< 60	1.00	1.69 (1.33-2.16)	2.16 (1.59-2.94)	
≥ 60	1.00	1.28 (0.98-1.68)	1.52 (1.02-2.25)	
Smoking				0.872
Yes	1.00	1.35 (0.96-1.89)	2.10 (1.32-3.33)	
No	1.00	1.54 (1.25-1.91)	1.92 (1.46-2.53)	
Drinking				0.466
Yes	1.00	0.94 (0.52-1.68)	1.23 (0.56-2.73)	
No	1.00	1.56 (1.30-1.89)	2.06 (1.61-2.64)	
Ideal PA				0.472
Yes	1.00	1.49 (1.22-1.81)	1.83 (1.40-2.39)	
No	1.00	1.56 (1.03-2.37)	2.48 (1.47-4.17)	
Obesity				0.135
Yes	1.00	0.85 (0.54-1.35)	1.20 (0.72-2.00)	
No	1.00	1.65 (1.36-2.00)	2.12 (1.62-2.78)	
Dyslipidemia				0.813
Yes	1.00	1.30 (1.00-1.70)	2.09 (1.49-2.93)	
No	1.00	1.65 (1.29-2.09)	1.73 (1.24-2.43)	
T2DM				0.966
Yes	1.00	1.48 (0.88-2.48)	1.64 (0.77-3.49)	
No	1.00	1.47 (1.22-1.78)	1.97 (1.53-2.53)	

Abbreviations: PA, physical activity; T2DM, type 2 diabetes mellitus. Adjusted for baseline sex, age, smoking, drinking, education, income, marital status, ideal physical activity, healthy diet, family history of stroke, obesity, dyslipidemia, and type 2 diabetes mellitus (except for the stratification factors).