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Lifestyle Factors and Antihypertensive Treatment on the Risks of Ischemic and Hemorrhagic Stroke

Yurong Zhang, Jaakko Tuomilehto, Pekka Jousilahti, Yujie Wang, Riitta Antikainen, Gang Hu

Abstract—The joint relationship between healthy lifestyle and antihypertensive treatment with stroke risk is unclear. We prospectively investigated the individual and joint effects of healthy lifestyle factors and antihypertensive treatment on stroke risk among 36 686 Finnish participants aged 25 to 74 years and free of coronary heart disease and stroke at baseline. During a mean follow-up of 13.7 years, 1478 people developed stroke event (1167 ischemic and 311 hemorrhagic). The stroke risk was significantly decreased in people who adhered to ≥ 3 healthy lifestyle factors (never smoking, normal weight, moderate/high level of exercise, vegetable consumption ≥ 3 times per week, and light/moderate alcohol drinking) compared with those who adhered to < 3 healthy lifestyle factors. The stroke risk was significantly increased in unaware untreated, aware untreated, aware treated and controlled, and aware treated and uncontrolled hypertensive people than in normotensive people. The risks of stroke were decreased in people who adhered to ≥ 3 healthy lifestyle factors compared with those who adhered to < 3 healthy lifestyle factors within different hypertensive status. Compared with hypertensive people who did not use antihypertensive drugs and adhered to ≥ 3 healthy lifestyle factors, the multivariable-adjusted hazard ratios in hypertensive people who used antihypertensive drugs and adhered to < 3 healthy lifestyle factors were associated with 37% to 42% increased risks of total, ischemic, and hemorrhagic stroke in men and 121% to 131% increased risks of stroke in women. The present study demonstrates that a healthy lifestyle significantly decreases stroke risk in both men and women in different strata of hypertension status and antihypertensive drug treatments. (*Hypertension*. 2012;60:906-912.) • [Online Data Supplement](#)

Key Words: lifestyle factors ■ antihypertensive drug ■ stroke risk

Stroke is one of the leading causes of death and disability worldwide.^{1,2} Although stroke poses a major public health challenge, it can be prevented.³ Modification of risk factors is an effective way to reduce stroke risk, and most risk factors can be altered with lifestyle changes and medications.^{4,5} Recent prospective studies have demonstrated that a healthy lifestyle (including no smoking, physical activity, and maintaining a healthy diet and normal body mass index [BMI]) can significantly reduce stroke risk.^{6,7} Our previous study indicated that there is a graded inverse association between the number of healthy lifestyle indicators and the risks of total, ischemic, and hemorrhagic stroke.⁸ Hypertension as a potential intermediate factor on the causal pathway of lifestyle factor with stroke risk is generally considered to be the most important risk factor for stroke in the general population. Clinical trials have unequivocally demonstrated that blood pressure (BP) lowering in people with hypertension reduces stroke risk. However, little is known about the joint association between

healthy lifestyle and antihypertensive drug treatment on the risk of stroke. The aims of the present study were to assess in a randomly selected population sample the effect of healthy lifestyle factors on total, ischemic, and hemorrhagic stroke risks among the subgroups of the hypertension status defined by awareness, treatment, and BP control status at baseline and differences of stroke risk among hypertensive men and women between antihypertensive drug treatment and lifestyle traits at baseline.

Methods

Participants

Five independent cross-sectional population surveys were carried out in 6 geographic areas of Finland in 1982, 1987, 1992, 1997, and 2002.⁹ The sample was stratified by area, sex, and 10-year age group according to the World Health Organization Monitoring Trends and Determinants of Cardiovascular Disease protocol.¹⁰ The participation rate varied by year from 65% to 88%.⁹ The subjects included in the 5 surveys were 25 to 64 years of age, and the 1997 and 2002

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surveys also included people aged 65 to 74 years. People who participated in >1 survey were only included in the first survey cohort in this analysis. The total sample size of the 5 surveys was 38 737. After excluding people with a history of coronary heart disease (n=1090) or stroke (n=775) at baseline and those with incomplete data on any required variables (n=186), the present analysis is composed of 17 287 men and 19 399 women. The participants gave an informed consent (verbal in 1982–1992 and signed in 1997 and 2002). These surveys were conducted according to the ethical rules of the National Public Health Institute, and the investigations were performed in accordance with the Declaration of Helsinki.

Baseline Measurements

A self-administered questionnaire was sent to the participants to be completed at home. The questionnaire included questions on medical history, socioeconomic factors, physical activity, smoking habits, alcohol consumption, and diet. Education level, measured as the total number of school years, was divided into birth cohort–specific tertiles. Family history of stroke was defined as a history of those whose mothers or fathers were once diagnosed as having stroke. History of myocardial infarction, stroke, or diabetes mellitus at baseline was obtained from the questionnaire and collected by hospital discharge or National Social Insurance Institution drug register (diabetes mellitus only).¹¹

A detailed description of the questions on occupational and leisure-time physical activity has been presented elsewhere.^{11–14} Because we found that moderate and high occupational or leisure time physical activity independently and significantly reduced stroke risk, these activities were merged into 3 categories, low, moderate, and high.¹² Based on the response, participants were classified as never, ever, and current smokers. Alcohol consumption was categorized into 4 groups, 0, 1 to 34, 35 to 209, and ≥ 210 g/wk in men and 0, 1 to 34, 35 to 139, and ≥ 140 g/wk in women. The frequency of consumption of vegetables over the last week (<1, 1–2, 3–6, and ≥ 7 times per week) was inquired.¹⁵

At the study center, specially trained nurses measured height, weight, and BP using the standardized protocol as described in the World Health Organization Monitoring Trends and Determinants of Cardiovascular Disease project.¹⁰ Height and weight were measured without shoes and with light clothing. The measurements of height were rounded to the nearest centimeter and weight to the nearest 100 g. BMI was calculated as weight in kilograms divided by the square of height in meters. BP was measured from the right arm of the participant after 5 minutes of sitting using a mercury sphygmomanometer in each survey. After BP measurement, venous blood specimen was taken. Serum total cholesterol was determined by an enzymatic method (CHOD-PAP, Boehringer Mannheim, Mannheim, Germany). All of the samples were analyzed in the same central laboratory at the National Public Health Institute.¹⁶

Definition of Healthy Lifestyle and Hypertension

In our previous publications, healthy lifestyle factors were defined as never smoking, maintaining normal BMI (BMI <25 kg/m²), moderate/high level of physical activity, vegetable consumption ≥ 3 times per week, and light/moderate alcohol drinking (1–209 g/wk in men and 1–139 g/wk in women), and a graded inverse association between the number of healthy lifestyle factors and the risk of stroke was found.⁸ In the present analyses, a healthy lifestyle was defined as having ≥ 3 healthy lifestyle factors.

Hypertension was defined as systolic BP ≥ 160 mm Hg and/or diastolic BP ≥ 95 mm Hg or using antihypertensive drugs. The reason for choosing these BP levels rather than the currently recommended 140/90 mm Hg for the definition of hypertension is that, during most of the follow up, they were the official treatment thresholds of the national guidelines in Finland.¹⁷ Information on awareness of hypertension and using antihypertensive drugs was obtained with a self-administered questionnaire. Awareness of hypertension was defined as a participant having reported a previous diagnosis of hypertension or current use of antihypertensive drug treatment. People on antihypertensive drug treatment, whose measured BP

level was <160/95 mm Hg, were considered to be adequately treated (controlled). The study population was classified into 5 groups according to their BP status at baseline, normotensive participants, hypertensive people unaware of their hypertensive status and untreated, hypertensive people aware of their hypertensive status but untreated, hypertensive patients treated with antihypertensive drugs and controlled, and hypertensive patients treated with antihypertensive drugs but not controlled.

Prospective Follow-Up

The survey cohorts were followed until the end of 2007 through computerized register linkage by a unique personal identification number. Mortality data were obtained from Statistics Finland, and data on nonfatal events were from the National Hospital Discharge Register. The International Classification of Diseases (ICD) was used to identify hemorrhagic stroke (ICD-8 and -9, 430–431 and ICD-10, I60–I62), ischemic stroke (ICD-8 and -9, 432–438 and ICD-10, I63–I66), and any stroke (ICD-8 and -9, 430–438 and ICD-10, I60–I66) events, but the ICD-9 code 432 was classified as a hemorrhagic stroke. The stroke events occurred before the baseline survey were identified from the Hospital Discharge Register retrospectively and excluded from the analyses. The validity of the diagnosis of acute stroke in Finland is good for hospital discharge register (agreement in 90% for all strokes, 82% for hemorrhage, and 90% for ischemic stroke) and death register (agreement in 97% for all strokes, 95% for hemorrhage, and 92% for ischemic stroke).¹⁸ End points during the follow-up were incident stroke events, defined as either the first nonfatal stroke event or stroke death without a preceding nonfatal event.

Statistical Analyses

Differences in risk factors at different levels of healthy lifestyle factors and different hypertensive status were tested using ANOVA or logistic regression after adjustment for age and study year, and a *P* value for trend across all 10 of the categories was given. The Cox proportional hazards model was used to evaluate the associations between healthy lifestyle factors and hypertension subgroups with stroke risk. All of the analyses were carried out first adjusting for age and study year (model 1) and then for education and family history of stroke (model 2). To avoid a potential bias because of severe or subclinical diseases at baseline, additional analyses were carried out excluding participants who were subsequently diagnosed with stroke (n=107) or died (n=181) during the first 2 years of follow-up after baseline survey. Statistical significance was considered to be *P*<0.05. All of the statistical analyses were performed with PASW for Windows, version 18.0 (SPSS Inc, Chicago, IL).

Results

General characteristics of the study population at baseline are presented in Table 1. During a mean follow-up of 13.7 years, we identified 1478 stroke events (1167 ischemic and 311 hemorrhagic) in the study cohort. After adjustment for age, study year, education, and family history of stroke (multivariable model 2), the risks of stroke were significantly lower in the groups with ≥ 3 healthy lifestyle factors compared with the groups with <3 healthy lifestyle factors but were significantly higher in all 4 of the hypertensive subgroups compared with the normotensive group across stroke subtypes and sex (Tables 2 and S1, available in the online-only Data Supplement). Compared with the normotensive group, the multivariable-adjusted (model 2) hazards ratios (HRs) for total stroke were 1.63 for hypertensive, unaware, untreated group; 2.09 for hypertensive, aware, untreated group; 1.57 for hypertensive, treated, controlled group; and 1.89 for hypertensive, treated, uncontrolled group in men (*P*<0.001 for trend) and 1.56 for hypertensive, unaware, untreated group;

Table 1. General Characteristics of Study Subjects at Baseline

Characteristic	Healthy Lifestyle Factors $\geq 3^*$					Healthy Lifestyle Factors $< 3^*$					P Value for Trend†
	Normal BP	HBP 1	HBP 2	HBP 3	HBP 4	Normal BP	HBP 1	HBP 2	HBP 3	HBP 4	
Men											
No. of subjects	7171	901	762	396	419	4762	1022	871	425	558	
Age at baseline, y	42.2	49.2	48.5	54.2	55.8	44.9	51.7	50.6	55.4	56.0	<0.001
Body mass index, kg/m ²	25.1	26.3	27.4	27.4	28.2	27.3	28.5	29.4	29.9	30.0	<0.001
Diastolic blood pressure, mm Hg	79.3	94.1	98.0	84.6	96.3	80.7	95.1	99.5	83.9	97.8	<0.001
Systolic blood pressure, mm Hg	132.8	157.2	161.2	137.9	161.2	134.2	157.9	162.2	136.9	161.4	<0.001
Serum cholesterol, mmol/L	5.7	6.0	6.0	5.6	5.8	5.9	6.2	6.1	5.8	6.0	<0.001
Education, y	11.4	10.7	11.0	11.1	10.8	9.9	9.6	9.8	10.0	10.1	<0.001
Alcohol consumption, g/wk	66.0	82.1	83.1	70.8	80.1	87.5	111.6	125.3	79.5	102.7	<0.001
Moderate/high physical activity, %	96.3	97.3	97.1	96.7	97.2	80.1	77.7	78.6	72.4	72.4	<0.001
Vegetable consumption ≥ 3 times per wk, %	70.9	68.6	71.7	75.5	75.8	20.9	17.9	19.6	26.7	24.6	<0.001
Ever or current smoker, %	26.1	26.6	25.0	19.9	19.4	53.3	51.7	45.1	38.6	38.1	<0.001
History of diabetes mellitus, %	1.7	1.1	1.4	7.0	7.4	2.3	1.4	2.0	8.2	6.8	<0.001
Women											
No. of subjects	11075	666	920	688	551	3774	399	517	411	398	
Age at baseline, y	42.4	55.1	51.5	54.4	56.5	44.6	56.4	52.7	56.7	58.5	<0.001
Body mass index, kg/m ²	24.6	25.8	26.7	27.9	27.7	27.9	29.3	29.7	30.6	30.9	<0.001
Diastolic blood pressure, mm Hg	76.7	90.1	94.0	82.1	92.2	77.7	91.4	93.9	81.9	92.7	<0.001
Systolic blood pressure, mm Hg	128.1	159.3	163.7	135.5	162.9	129.7	160.2	163.2	135.2	163.2	<0.001
Serum cholesterol, mmol/L	5.6	5.9	5.9	5.6	5.9	5.8	6.0	6.1	5.7	5.9	<0.001
Education, y	11.7	11.3	11.1	11.1	10.9	10.2	10.1	10.0	9.8	9.9	<0.001
Alcohol consumption, g/wk	27.3	26.7	28.3	25.2	23.2	20.6	25.9	27.1	19.8	26.7	<0.001
Moderate/high physical activity, %	93.7	94.2	95.6	93.8	94.8	64.0	60.5	65.0	57.4	49.7	<0.001
Vegetable consumption ≥ 3 times per wk, %	81.9	81.2	86.1	89.1	83.2	30.7	24.5	27.4	34.3	30.7	<0.001
Ever or current smoker, %	15.3	14.1	14.7	12.0	12.9	38.5	32.5	29.6	27.5	24.1	<0.001
History of diabetes mellitus, %	1.2	0.8	1.9	5.4	6.0	1.9	2.2	2.4	10.0	10.1	<0.001

BP indicates blood pressure; HBP 1, hypertensive unaware and untreated; HBP 2, hypertensive aware but untreated; HBP 3, hypertensive treated and controlled; HBP 4, hypertensive treated and uncontrolled. Normotensive (normal BP) was defined as systolic blood pressure < 160 mm Hg, diastolic blood pressure < 95 mm Hg, and without antihypertensive drug treatment.

*Values represent mean or percentage; all of the data except age (adjusted for study year only) were adjusted for age and study year. Healthy lifestyle factors are defined as moderate or high level of physical activity, never smoking, alcohol consumption 0 or 1–209 g/wk in men, 1–139 g/wk in women, body mass index < 25 kg/m², and vegetable consumption ≥ 3 times per wk.

†P value for trend presents a P value for trend across all 10 categories.

1.86 for hypertensive, aware, untreated group; 2.25 for hypertensive, treated, controlled group; and 3.19 for hypertensive, treated, uncontrolled group in women ($P < 0.001$ for trend). Similar results were found for ischemic and hemorrhagic stroke in both men and women.

The multivariable-adjusted (model 2) risks of total and ischemic stroke were higher in all of the hypertensive subgroups compared with the normotensive group within men and women with different lifestyle factors (< 3 and ≥ 3), even in hypertensive and controlled subgroups (Tables 3 and S2). The risks of stroke were decreased in people who adhered to ≥ 3 healthy lifestyle factors compared with those who adhered to < 3 healthy lifestyle factors within different hypertensive status across stroke subtypes and sex (Tables 3 and S2, the Figure, and Figures S1 and S2). For example, compared with normotensive people who had ≥ 3 healthy lifestyle factors (reference group), hypertensive, aware, and untreated people who had ≥ 3 healthy lifestyle

factors had lower multivariable-adjusted (model 2) HRs of total stroke (HR, 1.80 [95% CI, 1.28–2.53] in men; HR, 2.24 [95% CI, 1.64–3.06] in women) than the corresponding group who had < 3 healthy lifestyle factors (HR, 2.86 [95% CI, 2.21–3.70] in men; HR, 2.41 [95% CI, 1.70–3.43] in women).

Compared with hypertensive people who did not use antihypertensive drugs and had ≥ 3 healthy lifestyle factors, hypertensive people who used antihypertensive drugs and had < 3 healthy lifestyle factors had higher multivariable-adjusted (model 2) HRs of total (HR, 1.39 [95% CI, 1.04–1.86] in men; HR, 2.27 [95% CI, 1.71–3.01] in women), ischemic (HR, 1.42 [95% CI, 1.03–1.97] in men; HR, 2.31 [95% CI, 1.69–3.16] in women), and hemorrhagic stroke (HR, 2.21 [95% CI, 1.16–4.23] in women only; Tables 4 and S3). Hypertensive men who did not use antihypertensive drugs and had < 3 healthy lifestyle factors had increased risks of total (HR, 1.53 [95% CI, 1.11–2.11]) and ischemic (HR, 1.57 [95% CI, 1.09–2.25]) stroke compared with hypertensive

Table 2. Hazard Ratios for Total Stroke by Lifestyle Factors and Hypertensive Status

Characteristic	No. of Subjects	No. of Cases	Person-Years	Hazard Ratios (95% CI)*	
				Model 1†	Model 2‡
Lifestyle factors					
Men					
Healthy lifestyle factors ≥ 3	9649	318	131 301	1.00	1.00
Healthy lifestyle factors < 3	7638	462	102 538	1.49 (1.29–1.72)	1.43 (1.24–1.65)
Women					
Healthy lifestyle factors ≥ 3	13 900	354	190 917	1.00	1.00
Healthy lifestyle factors < 3	5499	76	78 479	1.89 (1.37–2.60)	1.84 (1.33–2.55)
Hypertensive status					
Men					
Normotensive	11 933	350	164 178	1.00	1.00
Hypertensive, unaware, untreated	1923	151	28 042	1.66 (1.37–2.01)	1.63 (1.34–1.97)
Hypertensive, aware, untreated	1633	135	21 913	2.12 (1.73–2.58)	2.09 (1.71–2.56)
Hypertensive, treated, controlled	821	52	8325	1.59 (1.18–2.14)	1.57 (1.17–2.11)
Hypertensive, treated, uncontrolled	977	92	11 381	1.91 (1.51–2.42)	1.89 (1.49–2.39)
Women					
Normotensive	14 849	316	208 521	1.00	1.00
Hypertensive, unaware, untreated	1065	81	15 911	1.56 (1.22–2.01)	1.56 (1.21–2.00)
Hypertensive, aware, untreated	1437	95	20 329	1.87 (1.48–2.36)	1.86 (1.47–2.34)
Hypertensive, treated, controlled	1099	80	12 449	2.26 (1.75–2.90)	2.25 (1.75–2.90)
Hypertensive, treated, uncontrolled	949	126	12 185	3.21 (2.59–3.99)	3.19 (2.57–3.96)

*Normotensive was defined as systolic blood pressure < 160 mmHg, diastolic blood pressure < 95 mmHg and without antihypertensive drug treatment.

†Model 1 was adjusted for age and study year.

‡Model 2 was adjusted for age, study year, education, and family history of stroke.

men who used antihypertensive drugs and had ≥ 3 healthy lifestyle factors. The risks of total or ischemic stroke in women or hemorrhagic stroke in both men and women showed no difference between hypertensive people who did not use antihypertensive drugs and had < 3 healthy lifestyle factors and hypertensive people who used antihypertensive drugs and had ≥ 3 healthy lifestyle factors.

Further adjustment for total cholesterol and history of diabetes mellitus affected these results only slightly (data not shown). Exclusion of the participants who were subsequently diagnosed with stroke ($n=107$) or died ($n=181$) during the first 2 years of follow-up after baseline survey did not appreciably change the above results (data not shown). In additional analyses using the defined hypertension as BP $\geq 140/90$ mmHg, the results changed slightly (Tables S4 and S5).

Discussion

We found that stroke risk was significantly lower in the groups with ≥ 3 healthy lifestyle factors compared with the groups with < 3 healthy lifestyle factors and higher in unaware untreated, aware untreated, aware treated and controlled, and aware treated and uncontrolled hypertensive people than in normotensive people. The risks of stroke were decreased in people who adhered to ≥ 3 healthy lifestyle factors compared with those who adhered to < 3 healthy lifestyle factors within

different strata of hypertension status and antihypertensive drug treatments.

High BP has been found as the most important determinant of stroke risk in all ethnic groups.^{19–23} The association between BP and stroke mortality is strong and direct, and the absolute risk of stroke mortality associated with high BP increases with age.²⁰ Our results support above findings and also extend this association among people with or without a healthy lifestyle (≥ 3 or < 3 healthy lifestyle factors).

Prospective cohorts studies have indicated that a healthy lifestyle consisting of never smoking, normal BMI, moderate alcohol consumption, regular physical activity, and healthy diet score was associated with a reduced risk of total and ischemic stroke, and this association is a graded inverse association between the number of healthy lifestyle indicators and the risks of total, ischemic, and hemorrhagic stroke.^{6–8} However, to our knowledge, no studies have assessed whether there are differences in stroke risk among hypertensive patients using antihypertensive drug treatment versus those engaging in a healthy lifestyle. The present study found that compared with treated hypertensive participants with < 3 healthy factors, untreated hypertensive participants with ≥ 3 healthy factors have lower risks of total and ischemic stroke in both men and women and of hemorrhagic stroke in women. However, patients with drug-treated hypertension might be more likely to have severe hypertension and other chronic diseases (eg, coronary heart disease and heart failure) and

Table 3. Hazard Ratios for Total Stroke in Normotensive Individuals and in Different Categories of Hypertensive Individuals by Different Levels of Lifestyle Factors

Characteristic*	No. of Subjects	No. of Cases	Person-Years	Hazard Ratios (95% CI)	
				Model 1†	Model 2‡
Men					
Healthy lifestyle factors ≥3					
Normotensive	7171	166	98 870	1.00	1.00
Hypertensive, unaware, untreated	901	60	13 383	1.77 (1.31–2.38)	1.74 (1.29–2.34)
Hypertensive, aware, untreated	762	42	10 190	1.81 (1.29–2.54)	1.80 (1.28–2.53)
Hypertensive, treated, controlled	396	20	3994	1.54 (0.96–2.45)	1.51 (0.94–2.40)
Hypertensive, treated, uncontrolled	419	30	4864	1.70 (1.15–2.52)	1.68 (1.13–2.49)
Healthy lifestyle factors <3					
Normotensive	4762	184	65 308	1.39 (1.12–1.71)	1.33 (1.08–1.64)
Hypertensive, unaware, untreated	1022	91	14 660	2.09 (1.62–2.71)	1.99 (1.54–2.59)
Hypertensive, aware, untreated	871	93	11 723	2.99 (2.32–3.86)	2.86 (2.21–3.70)
Hypertensive, treated, controlled	425	32	4331	2.17 (1.48–3.18)	2.09 (1.42–3.07)
Hypertensive, treated, uncontrolled	558	62	6517	2.67 (1.98–3.59)	2.56 (1.90–3.45)
Women					
Healthy lifestyle factors ≥3					
Normotensive	11 075	171	154 177	1.00	1.00
Hypertensive, unaware, untreated	666	40	9646	1.75 (1.23–2.49)	1.75 (1.23–2.49)
Hypertensive, aware, untreated	920	53	12 732	2.25 (1.65–3.08)	2.24 (1.64–3.06)
Hypertensive, treated, controlled	688	37	7426	2.46 (1.72–3.54)	2.46 (1.71–3.53)
Hypertensive, treated, uncontrolled	551	53	6937	3.32 (2.42–4.56)	3.33 (2.43–4.56)
Healthy lifestyle factors <3					
Normotensive	3774	145	54 344	1.87 (1.49–2.33)	1.86 (1.48–2.32)
Hypertensive, unaware, untreated	399	41	6265	2.43 (1.71–3.45)	2.41 (1.70–3.43)
Hypertensive, aware, untreated	517	42	7598	2.66 (1.89–3.75)	2.65 (1.88–3.73)
Hypertensive, treated, controlled	411	43	5023	3.50 (2.48–4.94)	3.50 (2.48–4.94)
Hypertensive, treated, uncontrolled	398	73	5248	5.16 (3.88–6.86)	5.13 (3.85–6.85)

*Normotensive was defined as systolic blood pressure <160 mmHg, diastolic blood pressure <95 mmHg and without antihypertensive drug treatment.
 †Model 1 was adjusted for age and study year.
 ‡Model 2 was adjusted for age, study year, education, and family history of stroke.

might be less likely to adhere to healthy lifestyle than hypertensive patients with a healthy lifestyle; thus, in the present study it cannot be concluded that a healthy lifestyle may be more effective in preventing stroke than antihypertensive

treatment alone in hypertensive patients. In addition, the information on changes in BP levels, antihypertensive treatment status, and lifestyle factors status during follow-up was not available in the present study, and all of these factors

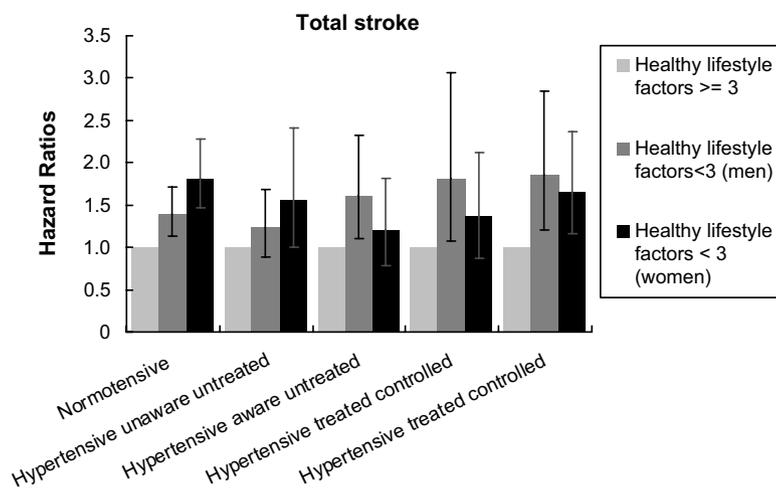


Figure. Hazard ratios for total stroke in normotensive individuals* and in different categories of hypertensive individuals by different levels of lifestyle factors. Data were adjusted for age, study year, education, and family history of stroke.

Table 4. Hazard Ratios for Total Stroke by Different Lifestyle Factors and Hypertensive Subgroups

Characteristic*	No. of Subjects	No. of Cases	Hazard Ratios (95% CI)	
			Model 1†	Model 2‡
Healthy lifestyle vs antihypertensive drug treatment (medication)				
Men				
Hypertensive, untreated, healthy lifestyle factors ≥ 3	1663	102	1.00	1.00
Hypertensive, treated, healthy lifestyle factors < 3	983	94	1.38 (1.03–1.84)	1.39 (1.04–1.86)
Women				
Hypertensive, untreated, healthy lifestyle factors ≥ 3	1586	93	1.00	1.00
Hypertensive, treated, healthy lifestyle factors < 3	809	116	2.23 (1.69–2.95)	2.27 (1.71–3.01)
Healthy lifestyle+medication VS nonhealthy lifestyle+no medication				
Men				
Hypertensive, treated, healthy lifestyle factors ≥ 3	815	50	1.00	1.00
Hypertensive, untreated, healthy lifestyle factors < 3	1893	184	1.56 (1.14–2.15)	1.53 (1.11–2.11)
Women				
Hypertensive, treated, healthy lifestyle factors ≥ 3	1239	90	1.00	1.00
Hypertensive, untreated, healthy lifestyle factors < 3	916	83	0.91 (0.67–1.23)	0.91 (0.67–1.23)

*Hypertension was defined as systolic blood pressure ≥ 160 mmHg, diastolic blood pressure ≥ 95 mmHg, or reported having taken antihypertensive drugs during the preceding 7 d.

†Model 1 was adjusted for age and study year.

‡Model 2 was adjusted for age, study year, education, and family history of stroke.

might be associated with stroke risk. More studies with above available information are needed to assess the effect of lifestyle intervention and antihypertensive treatment with stroke risk among hypertensive patients.

Although mechanisms showing that healthy lifestyles might provide more significant effects than antihypertensive treatment in reducing the risk of stroke are not clear, several putative mechanisms can be proposed. It is well known that risk factors for stroke include old age, high BP, smoking, diabetes mellitus, high cholesterol, and so forth.^{21,24–27} Single pharmacological antihypertensive treatment among hypertensive patients can lower high BP but does not directly affect causes of risk factors for stroke. However, the protective effects of healthy lifestyle on stroke risk may directly decrease high BP²⁸ and also improve other risk factors, such as total and low-density lipoprotein cholesterol,²⁹ diabetes mellitus,³⁰ smoking habits,^{7,30} and some inflammatory biomarkers (such as C-reactive protein).³¹ Further studies should be conducted to replicate these findings.

There are several strengths in our study. First, our study was composed of a large number of both men and women from a relatively homogeneous population. Second, the mean follow-up was long enough to ascertain a large number of stroke events. Third, the computerized register linkage assured that there were no losses of follow-up. Several limitations should be considered. First, information on BP and self-reported physical activity, smoking, and vegetable and alcohol consumptions was recorded only once at baseline. We have no data on possible changes in BP level and above lifestyle factors during the follow-up. Second, only vegetable consumption alone was included in our analysis, because dietary patterns based on the food frequency questionnaires could not be derived from the data available in our study. Third, each healthy lifestyle factor

was weighted the same, which implies that each of them was equally important. This may lead to heterogeneity among people being classified in the same category. Fourth, we cannot completely exclude either the effects of residual confounding because of measurement errors in assessment of confounding factors, some unmeasured lifestyle, or health-related covariates (eg, stress and depression) that may be associated with stroke risk. Finally, the regional guideline defined hypertension as BP $\geq 160/95$ mmHg, which may partly suggest the low rates of intervention and well-controlled treatment. In additional analyses using the defined hypertension as BP $\geq 140/90$ mmHg, the protective effect of a healthy lifestyle on the risks of total, ischemic, and hemorrhagic stroke was still found in different strata of hypertension status (Tables S4 and S5).

Perspectives

Our study demonstrates that a healthy lifestyle significantly decreases the risks of total, ischemic, and hemorrhagic stroke in both men and women in different strata of hypertension status and antihypertensive drug treatment.

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Disclosures

None.

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Novelty and Significance

What Is New?

- The present study is the first one to assess the single and joint relationships between healthy lifestyle and antihypertensive treatment with stroke risk.

What Is Relevant?

- The present study gives an important message for the primary prevention of stroke.

Summary

The present study demonstrates that a healthy lifestyle significantly decreases the risks of total, ischemic, and hemorrhagic

stroke in both men and women in different strata of hypertension status and antihypertensive drug treatment. Our study disentangles the effect of healthy lifestyle from hypertension to further demonstrate the importance of promoting healthy lifestyle in the primary prevention of stroke.

Online Supplement

Lifestyle Factors and Antihypertensive Treatment on the Risks of Ischemic and Hemorrhagic Stroke

Zhang et al. Lifestyle, treatment and stroke

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Tables: S1-S5

Figures: S1-S2

Table S1. Hazard ratios for ischemic and hemorrhagic stroke by lifestyle factors and hypertensive status*

Characteristic	No. of subjects	No. of cases	Person-years	Hazard ratios (95% confidence intervals)	
				Model 1†	Model 2‡
Lifestyle factors					
<i>Ischemic Stroke</i>					
Men					
Healthy lifestyle factors ≥ 3	9649	248	131,301	1.00	1.00
Healthy lifestyle factors < 3	7638	375	102,538	1.54 (1.31-1.81)	1.46 (1.24-1.72)
Women					
Healthy lifestyle factors ≥ 3	13900	276	190,917	1.00	1.00
Healthy lifestyle factors < 3	5499	268	78,479	1.64 (1.39-1.95)	1.64 (1.38-1.94)
<i>Hemorrhagic Stroke</i>					
Men					
Healthy lifestyle factors ≥ 3	9649	70	131,301	1.00	1.00
Healthy lifestyle factors < 3	7638	87	102,538	1.35 (0.98-1.85)	1.37 (0.99-1.89)
Women					
Healthy lifestyle factors ≥ 3	13900	78	190,917	1.00	1.00
Healthy lifestyle factors < 3	5499	76	78,479	1.89 (1.37-2.60)	1.84 (1.33-2.55)
Hypertensive status					
<i>Ischemic Stroke</i>					
Men					
Normotensive	11933	278	164,178	1.00	1.00

Hypertensive, unaware, untreated	1923	121	28,042	1.59 (1.28-1.97)	1.54 (1.24-1.91)
Hypertensive, aware, untreated	1633	109	21,913	2.10 (1.68-2.62)	2.07 (1.66-2.59)
Hypertensive, treated, controlled	821	41	8,325	1.51 (1.08-2.11)	1.50 (1.07-2.09)
Hypertensive, treated, uncontrolled	977	74	11,381	1.81 (1.39-2.36)	1.79 (1.38-2.33)
Women					
Normotensive	14849	236	208,521	1.00	1.00
Hypertensive, unaware, untreated	1065	64	15,911	1.53 (1.16-2.04)	1.53 (1.15-2.03)
Hypertensive, aware, untreated	1437	74	20,329	1.86 (1.43-2.42)	1.85 (1.42-2.41)
Hypertensive, treated, controlled	1099	64	12,449	2.28 (1.72-3.03)	2.28 (1.72-3.03)
Hypertensive, treated, uncontrolled	949	106	12,185	3.38 (2.66-4.29)	3.37 (2.65-4.28)
<i>Hemorrhagic Stroke</i>					
Men					
Normotensive	11933	72	164,178	1.00	1.00
Hypertensive, unaware, untreated	1923	30	28,042	1.82 (1.18-2.80)	1.85 (1.20-2.85)
Hypertensive, aware, untreated	1633	26	21,913	2.14 (1.36-3.36)	2.14 (1.36-3.36)
Hypertensive, treated, controlled	821	11	8,325	1.91 (1.00-3.65)	1.88 (0.98-3.60)
Hypertensive, treated, uncontrolled	977	18	11,381	2.18 (1.28-3.72)	2.16 (1.27-3.68)
Women					
Normotensive	14849	80	208,521	1.00	1.00
Hypertensive, unaware, untreated	1065	17	15,911	1.67 (0.97-2.88)	1.66 (0.96-2.87)
Hypertensive, aware, untreated	1437	21	20,329	1.93 (1.18-3.15)	1.90 (1.16-3.11)
Hypertensive, treated, controlled	1099	16	12,449	2.28 (1.30-3.99)	2.28 (1.30-3.99)

Hypertensive, treated, uncontrolled	949	20	12,185	2.62 (1.56-4.38)	2.59 (1.55-4.35)
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*Normotensive was defined as systolic blood pressure <160 mmHg, diastolic blood pressure <95 mmHg and without antihypertensive drug treatment.

†Model 1 adjusted for age and study year.

‡Model 2 adjusted for age, study year, education, and family history of stroke.

Table S2. Hazard ratios for ischemic and hemorrhagic stroke in normotensive individuals* and in different categories of hypertensive individuals by different levels of lifestyle factors

Characteristic	No. of subjects	No. of cases	Person-years	Hazard ratios (95% confidence intervals)	
				Model 1†	Model 2‡
Ischemic Stroke					
<i>Men</i>					
Healthy lifestyle factors ≥ 3					
Normotensive	7171	128	98,870	1.00	1.00
Hypertensive, unaware, untreated	901	50	13,383	1.76 (1.27-2.46)	1.72 (1.23-2.40)
Hypertensive, aware, untreated	762	31	10,190	1.69 (1.14-2.50)	1.69 (1.14-2.50)
Hypertensive, treated, controlled	396	16	3,994	1.52 (0.90-2.56)	1.48 (0.88-2.50)
Hypertensive, treated, uncontrolled	419	25	4,864	1.59 (1.02-2.49)	1.58 (1.01-2.47)
Healthy lifestyle factors < 3					
Normotensive	4762	150	65,308	1.44 (1.14-1.83)	1.37 (1.08-1.73)
Hypertensive, unaware, untreated	1022	72	14,660	2.02 (1.51-2.70)	1.88 (1.40-2.53)
Hypertensive, aware, untreated	871	78	11,723	3.14 (2.37-4.17)	2.95 (2.20-3.92)
Hypertensive, treated, controlled	425	25	4,331	2.09 (1.35-3.22)	1.99 (1.29-3.08)
Hypertensive, treated, uncontrolled	558	50	6,517	2.63 (1.89-3.67)	2.50 (1.79-3.49)
<i>Women</i>					
Healthy lifestyle factors ≥ 3					
Normotensive	11075	129	154,177	1.00	1.00
Hypertensive, unaware, untreated	666	32	9,646	1.70 (1.15-2.52)	1.70 (1.15-2.52)

Hypertensive, aware, untreated	920	41	12,732	2.18 (1.53-3.11)	2.18 (1.53-3.11)
Hypertensive, treated, controlled	688	31	7,426	2.53 (1.70-3.77)	2.53 (1.70-3.77)
Hypertensive, treated, uncontrolled	551	43	6,937	3.36 (2.37-4.77)	3.37 (2.37-4.78)
Healthy lifestyle factors <3					
Normotensive	3774	107	54,344	1.76 (1.36-2.28)	1.76 (1.36-2.29)
Hypertensive, unaware, untreated	399	32	6,265	2.29 (1.54-3.40)	2.29 (1.54-3.40)
Hypertensive, aware, untreated	517	33	7,598	2.59 (1.76-3.81)	2.59 (1.75-3.81)
Hypertensive, treated, controlled	411	33	5,023	3.33 (2.26-4.90)	3.34 (2.26-4.93)
Hypertensive, treated, uncontrolled	398	64	5,248	5.33 (3.90-7.29)	5.34 (3.89-7.73)
Hemorrhagic Stroke					
<i>Men</i>					
Healthy lifestyle factors ≥ 3					
Normotensive	7157	38	98,870	1.00	1.00
Hypertensive, unaware, untreated	898	10	13,383	1.60 (0.82-3.15)	1.63 (0.83-3.21)
Hypertensive, aware, untreated	759	11	10,190	2.23 (1.14-4.37)	2.21 (1.13-4.34)
Hypertensive, treated, controlled	387	4	3,994	1.60 (0.56-4.52)	1.58 (0.56-4.48)
Hypertensive, treated, uncontrolled	412	5	4,864	1.84 (0.77-4.42)	1.81 (0.75-4.34)
Healthy lifestyle factors <3					
Normotensive	4750	34	65,308	1.19 (0.75-1.89)	1.21 (0.76-1.93)
Hypertensive, unaware, untreated	1016	19	14,660	2.26 (1.29-3.97)	2.35 (1.34-4.13)
Hypertensive, aware, untreated	865	15	11,723	2.39 (1.31-4.36)	2.44 (1.33-4.47)
Hypertensive, treated, controlled	412	7	4,331	2.50 (1.10-5.68)	2.48 (1.09-5.66)

Hypertensive, treated, uncontrolled	542	12	6,517	2.77 (1.43-5.39)	2.80 (1.44-5.44)
<i>Women</i>					
Healthy lifestyle factors ≥ 3					
Normotensive	11046	42	154,177	1.00	1.00
Hypertensive, unaware, untreated	659	8	9,646	1.89 (0.87-4.10)	1.91 (0.88-4.13)
Hypertensive, aware, untreated	915	12	12,732	2.52 (1.31-4.83)	2.48 (1.29-4.76)
Hypertensive, treated, controlled	672	6	7,426	2.11 (0.88-5.04)	2.11 (0.88-5.04)
Hypertensive, treated, uncontrolled	540	10	6,937	3.38 (1.66-6.87)	3.38 (1.66-6.88)
Healthy lifestyle factors < 3					
Normotensive	3741	38	54,344	2.20 (1.41-3.42)	2.15 (1.38-3.36)
Hypertensive, unaware, untreated	391	9	6,265	2.96 (1.41-6.21)	2.90 (1.37-6.11)
Hypertensive, aware, untreated	507	9	7,598	2.90 (1.39-6.02)	2.86 (1.37-5.96)
Hypertensive, treated, controlled	395	10	5,023	4.58 (2.24-9.36)	4.55 (2.22-9.33)
Hypertensive, treated, uncontrolled	367	9	5,248	4.02 (1.96-8.23)	3.95 (1.92-8.12)

*Normotensive was defined as systolic blood pressure < 160 mmHg, diastolic blood pressure < 95 mmHg and without antihypertensive drug treatment.

†Model 1 adjusted for age and study year. ‡Model 2 adjusted for age, study year, education, and family history of stroke.

Table S3. Hazard ratios for ischemic and hemorrhagic stroke by different lifestyle factors and hypertensive* subgroups.

Characteristic	No. of subjects	No. of cases	Hazard ratios (95% confidence intervals)	
			Model 1†	Model 2‡
Ischemic Stroke				
<i>Healthy lifestyle VS Medication</i>				
Men				
Hypertensive, untreated, healthy lifestyle factors ≥ 3	1663	81	1.00	1.00
Hypertensive, treated, healthy lifestyle factors < 3	983	75	1.43 (1.03-1.97)	1.42 (1.03-1.97)
Women				
Hypertensive, untreated, healthy lifestyle factors ≥ 3	1586	73	1.00	1.00
Hypertensive, treated, healthy lifestyle factors < 3	809	97	2.30 (1.69-3.13)	2.31 (1.69-3.16)
<i>Healthy lifestyle + medication VS Non-healthy lifestyle + No medication</i>				
Men				
Hypertensive, treated, healthy lifestyle factors ≥ 3	815	41	1.00	1.00
Hypertensive, untreated, healthy lifestyle factors < 3	1893	150	1.64 (1.15-2.35)	1.57 (1.09-2.25)
Women				
Hypertensive, treated, healthy lifestyle factors ≥ 3	1239	74	1.00	1.00
Hypertensive, untreated, healthy lifestyle factors < 3	916	65	0.85 (0.61-1.18)	0.85 (0.61-1.20)
Hemorrhagic Stroke				
<i>Healthy lifestyle VS Medication</i>				
Men				

Hypertensive, untreated, healthy lifestyle factors ≥ 3	1663	21	1.00	1.00
Hypertensive, treated, healthy lifestyle factors < 3	983	19	1.29 (0.68-2.42)	1.37 (0.72-2.58)
Women				
Hypertensive, untreated, healthy lifestyle factors ≥ 3	1586	20	1.00	1.00
Hypertensive, treated, healthy lifestyle factors < 3	809	19	2.08 (1.09-3.94)	2.21(1.16-4.23)
<i>Healthy lifestyle + medication VS Non-healthy lifestyle + No medication</i>				
Men				
Hypertensive, treated, healthy lifestyle factors ≥ 3	815	9	1.00	1.00
Hypertensive, untreated, healthy lifestyle factors < 3	1893	34	1.38 (0.67-2.84)	1.52 (0.73-3.17)
Women				
Hypertensive, treated, healthy lifestyle factors ≥ 3	1239	16	1.00	1.00
Hypertensive, untreated, healthy lifestyle factors < 3	916	18	1.18 (0.60-2.32)	1.13 (0.57-2.25)

*Hypertension was defined as systolic blood pressure ≥ 160 mmHg, diastolic blood pressure ≥ 95 mmHg, or reported having taken antihypertensive drugs during the preceding 7 days.

†Model 1 adjusted for age and study year.

‡Model 2 adjusted for age, study year, education, and family history of stroke.

Table S4. Hazard ratios for total, ischemic and hemorrhagic stroke by hypertensive status*

Characteristic	No. of subjects	No. of cases	Person-years	Hazard ratios (95% confidence intervals)	
				Model 1†	Model 2‡
<i>Total Stroke</i>					
Men					
Normotensive	7,490	160	100,638	1.00	1.00
Hypertensive, unaware, untreated	5,250	298	76,927	1.71 (1.41-2.08)	1.69 (1.39-2.05)
Hypertensive, aware, untreated	2,749	178	36,568	2.25 (1.81-2.79)	2.22 (1.79-2.76)
Hypertensive, treated, controlled	298	18	3,076	1.97 (1.21-3.21)	1.91 (1.17-3.12)
Hypertensive, treated, uncontrolled	1,500	126	16,630	2.21 (1.74-2.81)	2.18 (1.71-2.77)
Women					
Normotensive	11,364	182	158,101	1.00	1.00
Hypertensive, unaware, untreated	3,283	172	49,341	1.41 (1.13-1.75)	1.40 (1.12-1.74)
Hypertensive, aware, untreated	2,704	138	37,319	1.82 (1.45-2.29)	1.81 (1.44-2.27)
Hypertensive, treated, controlled	413	25	4,388	2.46 (1.61-3.76)	2.45 (1.60-3.75)
Hypertensive, treated, uncontrolled	1,635	181	20,247	3.15 (2.53-3.94)	3.14 (2.51-3.92)
<i>Ischemic Stroke</i>					
Men					
Normotensive	7,490	129	100,638	1.00	1.00
Hypertensive, unaware, untreated	5,250	235	76,927	1.63 (1.31-2.02)	1.59 (1.28-1.98)
Hypertensive, aware, untreated	2,749	144	36,568	2.21 (1.74-2.81)	2.18 (1.72-2.77)
Hypertensive, treated, controlled	298	16	3,076	2.09 (1.24-3.52)	2.03 (1.20-3.42)

Hypertensive, treated, uncontrolled	1,500	98	16,630	2.03 (1.55-2.65)	2.00 (1.52-2.62)
Women					
Normotensive	11,364	130	158,101	1.00	1.00
Hypertensive, unaware, untreated	3,283	134	49,341	1.41 (1.10-1.82)	1.41 (1.09-1.81)
Hypertensive, aware, untreated	2,704	110	37,319	1.91 (1.47-2.48)	1.90 (1.47-2.47)
Hypertensive, treated, controlled	413	24	4,388	3.02 (1.94-4.71)	3.02 (1.94-4.71)
Hypertensive, treated, uncontrolled	1,635	148	20,247	3.27 (2.54-4.20)	3.26 (2.53-4.20)
<i>Hemorrhagic Stroke</i>					
Men					
Normotensive	7,490	31	100,638	1.00	1.00
Hypertensive, unaware, untreated	5,250	63	76,927	2.10 (1.36-3.25)	2.13 (1.38-3.29)
Hypertensive, aware, untreated	2,749	34	36,568	2.42 (1.48-3.95)	2.40 (1.47-3.93)
Hypertensive, treated, controlled	298	2	3,076	1.33 (0.32-5.58)	1.30 (0.31-5.46)
Hypertensive, treated, uncontrolled	1,500	27	16,630	3.04 (1.77-5.20)	3.00 (1.75-5.15)
Women					
Normotensive	11,364	52	158,101	1.00	1.00
Hypertensive, unaware, untreated	3,283	38	49,341	1.41 (0.90-2.20)	1.40 (0.89-2.18)
Hypertensive, aware, untreated	2,704	28	37,319	1.58 (0.98-2.54)	1.56 (0.97-2.51)
Hypertensive, treated, controlled	413	2	4,388	0.92 (0.22-3.81)	0.91 (0.22-3.79)
Hypertensive, treated, uncontrolled	1,635	34	20,247	2.87 (1.78-4.63)	2.84 (1.76-4.59)

*Normotensive was defined as systolic blood pressure <140 mmHg, diastolic blood pressure <90 mmHg and without antihypertensive drug treatment.

†Model 1 adjusted for age and study year.

‡Model 2 adjusted for age, study year, education, and family history of stroke.

Table S5. Hazard ratios for stroke in normotensive individuals* and in different categories of hypertensive individuals by different levels of lifestyle factors

Characteristic	No. of subjects	No. of cases	Person-years	Hazard ratios (95% confidence intervals)	
				Model 1†	Model 2‡
Total Stroke					
<i>Men</i>					
Healthy lifestyle factors ≥ 3					
Normotensive	4,720	77	63,846	1.00	1.00
Hypertensive, unaware, untreated	2,729	131	40,169	1.94 (1.46-2.57)	1.91 (1.44-2.54)
Hypertensive, aware, untreated	1,358	60	18,429	2.00 (1.43-2.81)	2.00 (1.43-2.80)
Hypertensive, treated, controlled	144	9	1,477	2.74 (1.37-5.47)	2.65 (1.32-5.29)
Hypertensive, treated, uncontrolled	671	41	7,380	1.98 (1.35-2.91)	1.95 (1.33-2.87)
Healthy lifestyle factors < 3					
Normotensive	2,770	83	36,793	1.54 (1.13-2.10)	1.48 (1.08-2.02)
Hypertensive, unaware, untreated	2,521	167	36,758	2.26 (1.72-2.97)	2.15 (1.64-2.84)
Hypertensive, aware, untreated	1,364	118	18,139	3.41 (2.56-4.55)	3.25 (2.43-4.35)
Hypertensive, treated, controlled	154	9	1,599	2.17 (1.08-4.33)	2.06 (1.03-4.13)
Hypertensive, treated, uncontrolled	829	85	9,249	3.32 (2.42-4.55)	3.19 (2.33-4.37)
<i>Women</i>					
Healthy lifestyle factors ≥ 3					
Normotensive	8,683	99	120,162	1.00	1.00
Hypertensive, unaware, untreated	2,178	91	31,990	1.70 (1.27-2.27)	1.70 (1.27-2.28)

Hypertensive, aware, untreated	1,800	74	24,402	2.14 (1.58-2.91)	2.14 (1.57-2.90)
Hypertensive, treated, controlled	267	10	2,684	2.38 (1.24-4.58)	2.38 (1.24-4.59)
Hypertensive, treated, uncontrolled	972	80	11,678	3.57 (2.62-4.85)	3.57 (2.62-4.86)
Healthy lifestyle factors <3					
Normotensive	2,681	83	37,939	2.20 (1.64-2.94)	2.19 (1.63-2.93)
Hypertensive, unaware, untreated	1,105	81	17,351	2.26 (1.66-3.06)	2.24 (1.66-3.04)
Hypertensive, aware, untreated	904	64	12,917	3.00 (2.18-4.14)	2.99 (2.16-4.13)
Hypertensive, treated, controlled	146	15	1,703	4.60 (2.65-7.97)	4.59 (2.64-7.97)
Hypertensive, treated, uncontrolled	663	101	8,568	5.19 (3.87-6.97)	5.18 (3.85-6.97)
Ischemic Stroke					
<i>Men</i>					
Healthy lifestyle factors ≥ 3					
Normotensive	4,720	58	63,846	1.00	1.00
Hypertensive, unaware, untreated	2,729	103	40,169	1.96 (1.42-2.71)	1.93 (1.39-2.66)
Hypertensive, aware, untreated	1,358	47	18,429	2.04 (1.39-3.00)	2.04 (1.39-3.00)
Hypertensive, treated, controlled	144	7	1,477	2.72 (1.24-5.98)	2.63 (1.20-5.78)
Hypertensive, treated, uncontrolled	671	32	7,380	1.93 (1.25-2.99)	1.90 (1.23-2.95)
Healthy lifestyle factors <3					
Normotensive	2,770	71	36,793	1.72 (1.22-2.44)	1.63 (1.15-2.31)
Hypertensive, unaware, untreated	2,521	132	36,758	2.27 (1.67-3.11)	2.13 (1.56-2.92)
Hypertensive, aware, untreated	1,364	97	18,139	3.61 (2.60-5.00)	3.39 (2.44-4.71)
Hypertensive, treated, controlled	154	9	1,599	2.73 (1.35-5.53)	2.58 (1.27-5.23)

Hypertensive, treated, uncontrolled	829	66	9,249	3.23 (2.26-4.63)	3.07 (2.14-4.40)
<i>Women</i>					
Healthy lifestyle factors ≥ 3					
Normotensive	8,683	72	120,162	1.00	1.00
Hypertensive, unaware, untreated	2,178	71	31,990	1.67 (1.19-2.34)	1.67 (1.19-2.34)
Hypertensive, aware, untreated	1,800	59	24,402	2.19 (1.55-3.11)	2.19 (1.55-3.11)
Hypertensive, treated, controlled	267	9	2,684	2.69 (1.34-5.41)	2.69 (1.34-5.42)
Hypertensive, treated, uncontrolled	972	66	11,678	3.65 (2.58-5.16)	3.66 (2.58-5.18)
Healthy lifestyle factors < 3					
Normotensive	2,681	58	37,939	2.05 (1.45-2.90)	2.05 (1.45-2.91)
Hypertensive, unaware, untreated	1,105	63	17,351	2.17 (1.53-3.08)	2.17 (1.52-3.09)
Hypertensive, aware, untreated	904	51	12,917	3.03 (2.10-4.37)	3.03 (2.10-4.38)
Hypertensive, treated, controlled	146	15	1,703	5.63 (3.21-9.94)	5.69 (3.23-10.04)
Hypertensive, treated, uncontrolled	663	82	8,568	5.13 (3.67-7.17)	5.15 (3.67-7.21)
Hemorrhagic Stroke					
<i>Men</i>					
Healthy lifestyle factors ≥ 3					
Normotensive	4,720	19	63,846	1.00	1.00
Hypertensive, unaware, untreated	2,729	28	40,169	1.89 (1.05-3.89)	1.91 (1.06-3.43)
Hypertensive, aware, untreated	1,358	13	18,429	1.92 (0.95-3.90)	1.90 (0.94-3.87)
Hypertensive, treated, controlled	144	2	1,477	2.88 (0.67-12.44)	2.83 (0.65-12.24)
Hypertensive, treated, uncontrolled	671	8	7,380	2.00 (0.86-4.65)	1.97 (0.85-4.60)

Healthy lifestyle factors <3

Normotensive	2,770	12	36,793	0.97 (0.47-1.99)	0.98 (0.48-2.03)
Hypertensive, unaware, untreated	2,521	35	36,758	2.27 (1.29-3.99)	2.34 (1.32-4.14)
Hypertensive, aware, untreated	1,364	21	18,139	2.81 (1.50-5.27)	2.85 (1.52-5.36)
Hypertensive, treated, controlled	154	0	1,599	0	0
Hypertensive, treated, uncontrolled	829	19	9,249	3.81 (1.98-7.35)	3.84 (1.99-7.42)

*Women*Healthy lifestyle factors ≥ 3

Normotensive	8,683	27	120,162	1.00	1.00
Hypertensive, unaware, untreated	2,178	20	31,990	1.78 (0.98-3.23)	1.78 (0.98-3.24)
Hypertensive, aware, untreated	1,800	15	24,402	1.97 (1.03-3.74)	1.95 (1.02-3.72)
Hypertensive, treated, controlled	267	1	2,684	1.17 (0.16-8.68)	1.17 (0.16-8.70)
Hypertensive, treated, uncontrolled	972	15	11,678	3.42 (1.76-6.63)	3.41 (1.75-6.62)

Healthy lifestyle factors <3

Normotensive	2,681	25	37,939	2.62 (1.52-4.51)	2.57 (1.48-4.46)
Hypertensive, unaware, untreated	1,105	18	17,351	2.55 (1.36-4.77)	2.48 (1.32-4.67)
Hypertensive, aware, untreated	904	13	12,917	2.88 (1.46-5.68)	2.83 (1.43-5.60)
Hypertensive, treated, controlled	146	1	1,703	1.60 (0.21-11.08)	1.57 (0.21-11.71)
Hypertensive, treated, uncontrolled	663	19	8,568	5.27 (2.80-9.92)	5.20 (2.75-9.84)

*Normotensive was defined as systolic blood pressure <140 mmHg, diastolic blood pressure <90 mmHg and without antihypertensive drug treatment.

†Model 1 adjusted for age and study year. ‡Model 2 adjusted for age, study year, education, and family history of stroke.

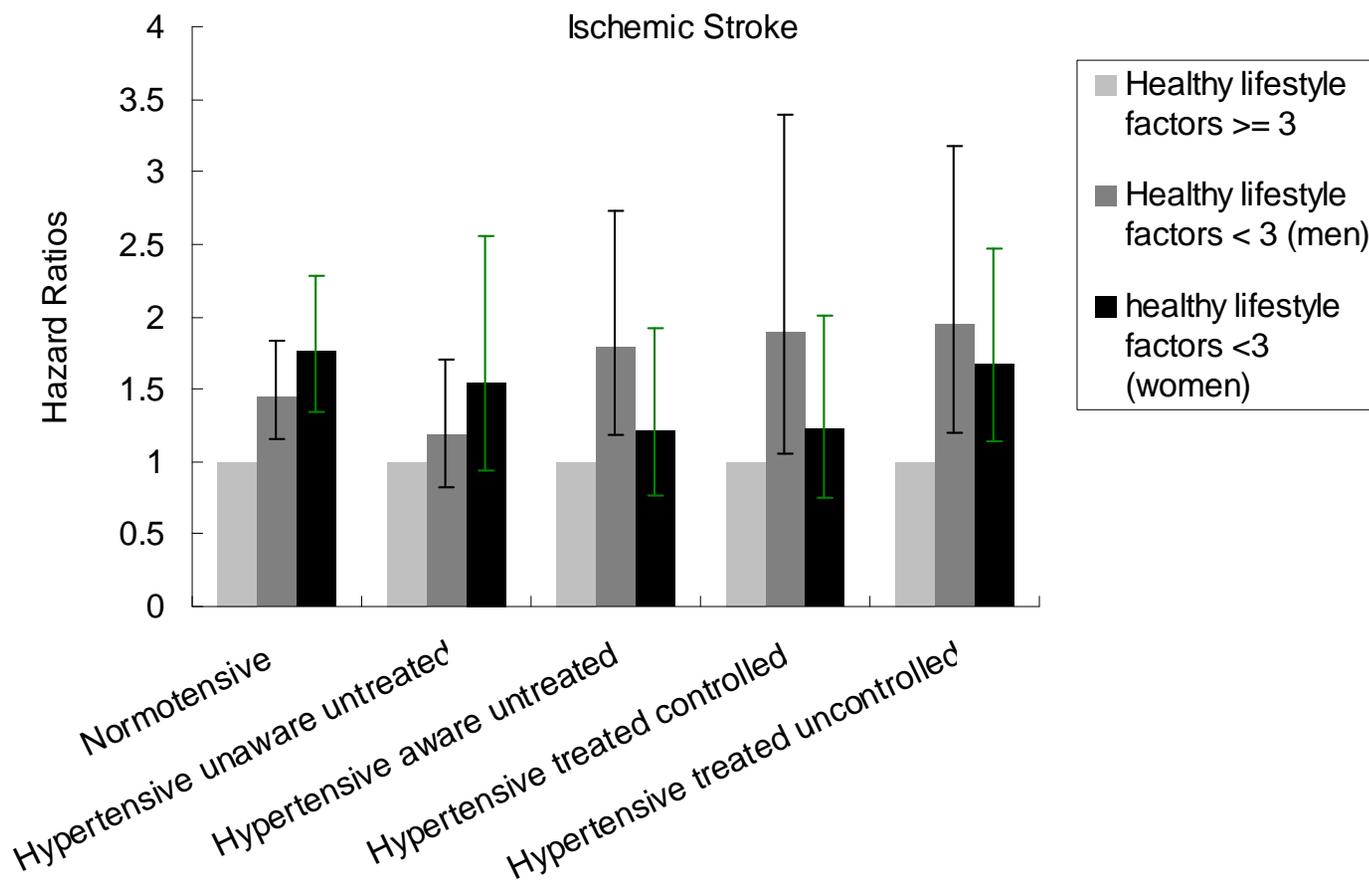


Figure S1. Hazard ratios for ischemic stroke in normotensive individuals* and in different categories of hypertensive individuals by different levels of lifestyle factors. Adjusted for age, study year, education, and family history of stroke.

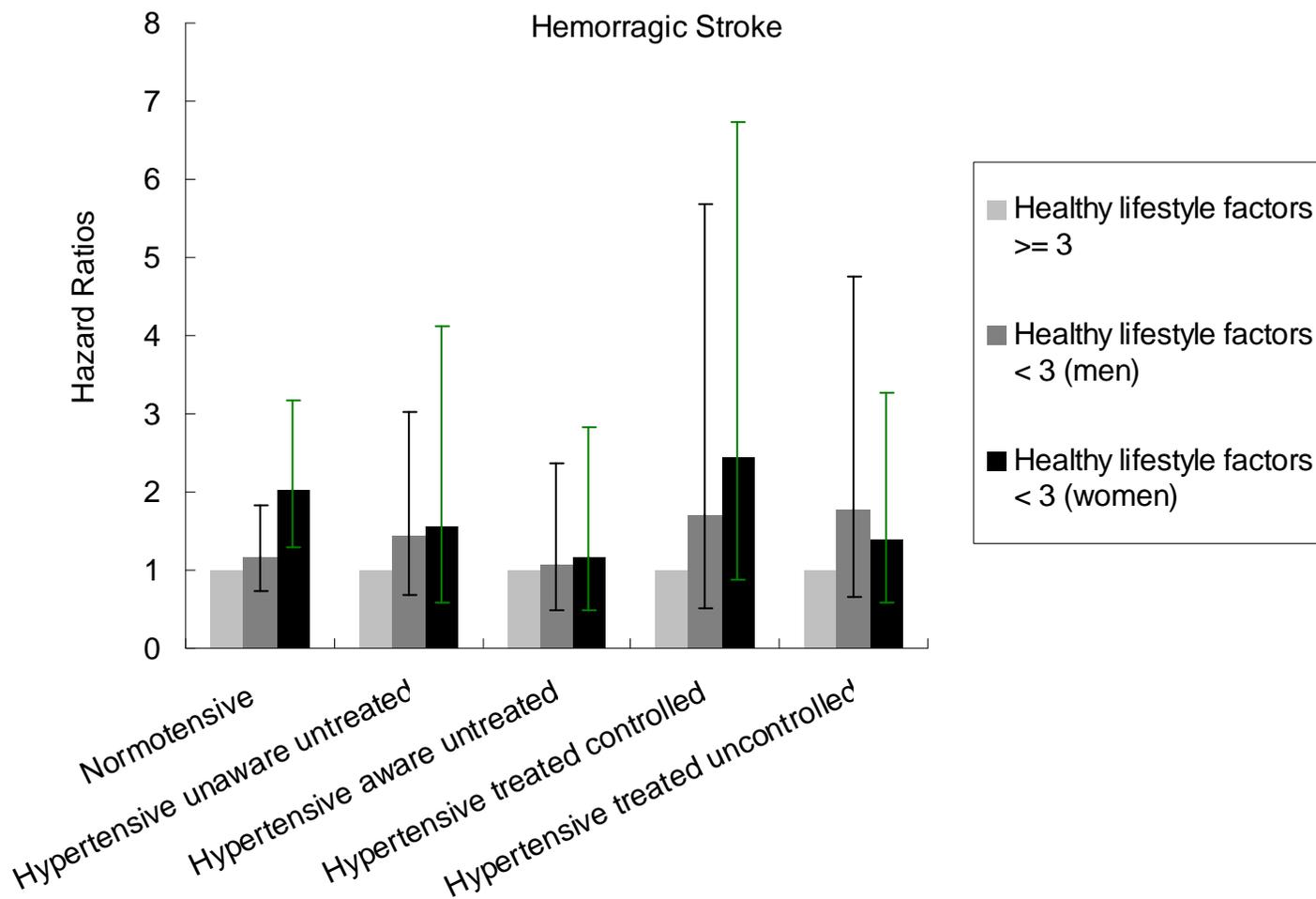


Figure S2. Hazard ratios for hemorrhagic stroke in normotensive individuals* and in different categories of hypertensive individuals by different levels of lifestyle factors. Adjusted for age, study year, education, and family history of stroke.