Journal of the American Heart Association

ORIGINAL RESEARCH

Risk Factors for Incident Stroke and Its Subtypes in China: A Prospective Study

Wenwei Qi, PhD; Jing Ma, PhD; Tianjia Guan, PhD; Dongsheng Zhao, PhD; Ameen Abu-Hanna, PhD; Martijn Schut, PhD; Baohua Chao, BD; Longde Wang, MD; Yuanli Liu, PhD

BACKGROUND: Managing risk factors is crucial to prevent stroke. However, few cohort studies have evaluated socioeconomic factors together with conventional factors affecting incident stroke and its subtypes in China.

METHODS AND RESULTS: A 2014 to 2016 prospective study from the China National Stroke Screening and Intervention Program comprised 437 318 adults aged ≥40 years without stroke at baseline. There were 2429 cases of first-ever stroke during a median follow-up period of 2.1 years, including 2206 ischemic strokes and 237 hemorrhagic strokes. The multivariable Cox regression analysis indicated that age 50 to 59 years (versus 40–49 years), primary school or no formal education (versus middle school), having >1 child (versus 1 child), living in Northeast, Central, East, or North China (versus Southwest China), physical inactivity, hypertension, diabetes mellitus, and obesity were positively associated with the risk of total and ischemic stroke, whereas age 60 to 69 years and living with spouse or children (versus living alone) were negatively associated with the risk of total and ischemic stroke. Men, vegetable-based diet, underweight, physical inactivity, hypertension, living in a high-income region, having Urban Resident Basic Medical Insurance, and New Rural Cooperative Medical System were positively associated with the risk of hemorrhagic stroke, whereas age 60 to 69 years was negatively associated with the risk of hemorrhagic stroke.

CONCLUSIONS: We identified socioeconomic factors that complement traditional risk factors for incident stroke and its subtypes, allowing targeting these factors to reduce stroke burden.

Key Words: primary prevention ■ prospective study ■ risk factors ■ socioeconomic status ■ stroke

Stroke is a leading cause of death and disability, making stroke prevention a global health priority.[1,2] Although the incidence of stroke has remained stable and mortality has decreased over the past 2 decades, the number of incident strokes, disability-adjusted life-years lost because of stroke, and stroke-related survivors and deaths are increasing.[3,4] The total cost of hospitalization because of stroke in China was 85.5 billion Renminbi (≈12.2 billion [US dollar]) in 2016.[5]

Reducing stroke incidence ensures the quality of life for adults and has a positive impact on individuals, families, and society. Managing risk factors is crucial to prevent stroke, and primary stroke prevention approaches should be multifactorial. Previous studies have shown that stroke risk factors include family history of stroke (FHS), physiological components (eg, adiposity, hypertension, dyslipidemia, diabetes mellitus, atrial fibrillation [AF]), and lifestyle behaviors (eg, smoking, physical inactivity, poor diet, and high alcohol consumption).[6–8] However, few cohort studies have evaluated the correlation between socioeconomic status (SES) (different age populations, geographic and economic region, education level, living status, family size, social healthcare insurance status, marital status, and occupation), lifestyle behaviors (plant or meat-based diet and the consumption of vegetables and fruits), and incident stroke, especially hemorrhagic stroke. The distribution of stroke risk factors is changing worldwide, and analyzing this distribution is crucial to allocate resources

Correspondence to: Yuanli Liu, PhD, School of Health Policy and Management, Chinese Academy of Medical Sciences and Peking, Union Medical College, No. 9, Dongdansantiao Street, Dongcheng District, Beijing, 100730 People's Republic of China. E-mail: liuyl_fpo@126.com

For Sources of Funding and Disclosures, see page 18.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- We not only verified the effect of traditional risk factors on incident stroke and its subtypes, but also found interesting changes compared with previous studies, such as age, body mass index, and diet pattern.
- This study firstly introduced new socioeconomic status factors and explored the association of socioeconomic status with incident and stroke and its subtypes across China, such as living status, number of children, and healthcare insurance.

What Are the Clinical Implications?

- Provide new evidence for the primary prevention of stroke and improve the stroke risk predictive model.
- Hypertension control and proper physical activity may benefit most to prevent stroke among the whole population.
- Support the need for stroke risk reduction programs and policies that incorporate conventional and socioenvironmental components.

Nonstandard Abbreviations and Acronyms

CNSSI	China National Stroke Screening and Intervention program
NRCMS	New Rural Cooperative Medical System
SES	socioeconomic status
UEBMI	Urban Employee Basic Medical Insurance
URBMI	Urban Resident Basic Medical Insurance

of prevention strategies to manage these factors.[9] Epidemiological transition, industrialization, and urbanization in China may influence stroke risk factors, and consequently affect stroke incidence.

To investigate stroke epidemiology and improve public awareness of stroke in China, the Ministry of Health of the Peoples' Republic of China established the National Stroke Screening and Intervention (CNSSI) program in 2011, supported by the China Stroke Data Center, a nationwide stroke screening platform.[10]

In this study, we determined the distribution of incident stroke and its subtypes and evaluated the risk factors for stroke and its subtypes in a 2014 to 2016 prospective study of Chinese adults to provide evidence to improve primary stroke prevention in the future.

METHODS

The data and study materials supporting the conclusions of this article are available from the China Stroke Data Center but restrictions are applied to the availability of these data, which were used under license for the current study, and so are not publicly available. However, more details on analytical methods and the study results are available from the corresponding author upon reasonable request.

Materials

The design, methods, and participants of the CNSSI program were detailed previously.[11] Briefly, the study population was derived from the CNSSI program involving of Chinese residents aged ≥40 years from 31 provinces except Tibet in mainland China, including 437 318 adults (235 169 women and 202 149 men) without stroke at baseline from 2014 to 2016.

A 2-stage stratified cluster sampling method was adopted for screening. All participants were screened using a structured face-to-face questionnaire to obtain information on demographic characteristics (age and sex), SES (marital status, education level, social healthcare insurance status, living condition, and number of siblings or children), and traditional risk factors (overweight, hypertension, dyslipidemia, diabetes mellitus, AF, transient ischemic attacks [TIA], FHS, physical inactivity, and smoking). The interviewers were neurologists or physicians from community hospitals. Detailed information on lifestyle (alcohol drinking history, diet, and the consumption of vegetables and fruits), related diseases, and clinical examinations were also obtained from individuals who suffered stroke or were at a high risk for stroke. The CNSSI program performs stroke screening nationwide each year and follow-up interventions on screened populations every 2 years. The quality of data collection and measurements was maintained by implementing standardized protocols and training. The staff involved in the survey were trained in the CNSSI program and evaluated through theoretical and practical tests. All interview data were checked against resident health records to ensure reliability and validity and were entered electronically into a data terminal with direct access to the CNSSI database.

Ethics Approval

The study was performed according to the Declaration of Helsinki and was approved by the research ethics committee of the institutional review board of Xuanwu Hospital affiliated to Capital Medical University, located in Beijing, China. All participants were informed about the study and signed informed consent.

Definitions

The history of stroke and its subtypes was obtained by a combination of self-reporting and assessments by a neurologist or physician using neuroimaging examinations (computed tomography and magnetic resonance imaging) according to the World Health Organization criteria.[12,13] The stroke subtype was classified according to *International Classification of Diseases, Tenth Revision (ICD-10)* codes as ischemic stroke with I63 or hemorrhagic stroke (intracerebral hemorrhage with I61 and subarachnoid hemorrhage with I60). TIA was defined as G45.[13] The participants with TIA were not included in the stroke group.

Economic regions were trisected according to the per capita disposable income of households in 2015.[14] Low-income regions included Sichuan, Henan, Guangxi, Guizhou, Yunnan, Gansu, Shaanxi, Ningxia, Qinghai, and Xinjiang. Middle-income regions comprised Shanxi, Hebei, Jilin, Heilongjiang, Anhui, Hubei, Hunan, Jiangxi, Chongqing, and Hainan, whereas high-income regions included Beijing, Tianjin, Shanghai, Zhejiang, Jiangsu, Shandong, Fujian, Guangdong, Liaoning, and Inner Mongolia. Current smoking was defined as continuous or cumulative smoking for >6 months. Former smoking was defined as continuous smoking for >6 months but no smoking at the time of the survey. Passive smoking was defined as exposure to smoke from smokers for at least 15 minutes per day and >1 day per week among non-smokers. Heavy alcohol consumption was defined as the intake of alcoholic beverages ≥3 times per week and ≥100 mL per drinking episode. Light to moderate alcohol consumption was defined as the intake of alcoholic beverages <3 times per week or <100 mL per drinking episode. Vegetable and fruit consumption were classified according to the following frequency tertiles (days per week): ≤2, 3 to 4, and ≥5. Physical activity was defined as regular physical exercise performed for >1 year, >2 times per week, and at least 30 minutes each time, or heavy physical labor. Body mass index (BMI) was calculated as body weight (kg) divided by the square of height (m). Overweight (BMI of 24.0–27.9 kg/m^2) and obesity (BMI ≥28 kg/m^2) were defined according to the guidelines established for Chinese adults.[15] Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, self-reported hypertension, or the use of antihypertension medications. Diabetes mellitus was defined as fasting plasma glucose level ≥7.0 mmol/L, self-reported diabetes mellitus, the use of oral hypoglycemic agents, or insulin injections. Dyslipidemia was defined on the basis of ≥1 of the following criteria: triglycerides ≥2.26 mmol/L, total cholesterol ≥6.22 mmol/L, high-density lipoprotein cholesterol <1.04 mmol/L, low-density lipoprotein cholesterol ≥4.14 mmol/L, self-reported dyslipidemia, or the use of anti-dyslipidemia medications.[16] AF was defined as self-reported history of persistent AF or ECG results. FHS was defined as the occurrence of stroke in ≥1 of the participant's parents or siblings. Social healthcare insurance status was categorized as Urban Employee Basic Medical Insurance (UEBMI), Urban Resident Basic Medical Insurance (URBMI), New Rural Cooperative Medical System (NRCMS), or other insurance systems.

Statistical Analysis

For baseline characteristics, continuous and categorical variables were reported as means (SD) or frequencies (percentages), respectively. Continuous variables were compared between groups using t tests or nonparametric tests when appropriate, and categorical variables were analyzed using the χ^2 test.

For incident stroke and its subtypes, Cox proportional hazards regression models were constructed to estimate univariate (unadjusted) and multivariate (adjusted) hazard ratios and 95% CIs between different influencing factors and stroke. We also stratified the Cox proportional model by time intervals for time-dependent variables according to the proportional hazard assumption. Person-years at risk were calculated as the time difference between baseline and the diagnosis of stroke, death, loss to follow-up, or the end of the study, whichever came first. Censoring events included death, loss to follow-up, and participants without any type of stroke during follow-up. To avoid the competing risks of different types of stroke, we made analysis stratified by stroke subtype. Possible risk factors for incident stroke and its subtypes were selected according to literature reviews, clinical plausibility, and variables considered significant in the univariate analyses, including 27 risk factors for all stroke and ischemic stroke and 26 risk factors for hemorrhagic stroke. The collinearity between independent variables was tested using the variance inflation factor.

Population attributable risk percent (PAR%) was calculated using a semiparametric method to determine the adjusted PAR% and 95% CIs[17] and corresponded to the estimated percentage of incident stroke in this population during follow-up that would not have occurred if all participants had been in the low-risk group. We used a single binary variable and compared the participants in the low-risk group with all other participants for each modifiable factor, according to the method proposed by Chen et al.[17]

Statistical analyses were performed with R software version 3.6.1 (https://www.r-project.org/). Statistical tests of hypotheses were 2-sided, and statistical significance was defined as P<0.05.

RESULTS

Baseline Characteristics

The baseline characteristics of the study population stratified by sex are presented in Table 1. The mean age of the participants with first-ever stroke was 57.0±11.2 years (56.80±11.23 years in men and 57.13±11.20 years in women). Of the total sample, 235 169 (53.8%) subjects were women, 237 632 (54.3%) subjects lived in rural areas, 121 296 (27.7%) resided in East China, 154 464 (35.3%) lived in high-income regions, 12 148 (2.8%) lived alone, 75 573 (17.3%) had >3 children, 81 068 (18.5%) had >5 siblings, 177 951 (40.7%) had primary school or no formal education, 127 283 (29.1%) were covered by UEBMI, 98 404 (22.5%) had URBMI, 202 212 (46.2%) had NRCMS, 123 083 (28.1%) were physically inactive, 60 330 (13.8%) were current smokers, and 41 357 (9.4%) were current drinkers. The percentage of subjects who consumed vegetables ≤2, 3 to 4, and ≥5 days per week was 6.5%, 24.9%, and 64.6%, respectively. The percentage of participants who consumed fruits ≤2, 3 to 4, and ≥5 days per week was 25.3%, 36.0%, and 33.2%, respectively. Moreover, 346 944 (79.3%) subjects had a balanced intake of vegetables and meat, 32 037 (7.3%) preferred meat-based diets, and 46 785 (10.7%) preferred vegetable-based diets. The mean BMI was 23.94±3.15. The number of participants with BMI <24 and ≥28 kg/m^2 was 236 770 (54.4%) and 39 402 (9.0%), respectively. The prevalence of hypertension, dyslipidemia, diabetes mellitus, AF, and TIA was 24.5%, 18.8%, 7.3%, 1.8%, and 1.5%, respectively. The number of patients with FHS or a family history of coronary heart disease (CHD), hypertension, dyslipidemia, or diabetes mellitus was 29 694 (6.8%), 15 717 (3.6%), 46 441 (10.6%), 8131 (1.9%), and 14 864 (3.4%), respectively.

Follow-Up Characteristics

Incident stroke cases were included in the analyses from 2014 to 2016 (median of 2.1 years), by which time 3801 (0.9%) participants died and 7864 (1.8%) were lost to follow-up. During 0.9 million person-years of follow-up, there were 2429 (0.56%) incident first-ever strokes, of which 93.5% cases were confirmed by neuroimaging (computed tomography or magnetic resonance imaging), including 2206 (90.8%) cases of ischemic stroke and 237 (9.8%) cases of hemorrhagic stroke. Fourteen participants had both types of stroke during the study period. The overall crude incidence of first-ever total, ischemic, and hemorrhagic stroke was 260.6, 238.0, and 25.6 per 100 000 person-years, respectively.

Association of Risk Factors With Total Stroke and Its Subtypes

In the univariable Cox proportional hazard regression analysis, the potential predictors of first-ever total stroke included age, BMI, hypertension, dyslipidemia, diabetes mellitus, AF, TIA, family history (stroke, hypertension, dyslipidemia, diabetes mellitus, and CHD), physical inactivity, smoking and drinking status, consumption of vegetables, fruits, and milk, balanced diet, geographic and economic regions, education level, marital status, number of siblings or children, and living status.

After including these variables and sex into the multivariable Cox proportional hazard regression model, the factors positively associated with the risk of incident first-ever total stroke were age 50 to 59 years (compared with age 40–49 years), primary school or no formal education (compared with middle school), living in Northeast, Central, East, and North China (compared with living in Southwest China), having >1 child (compared with having 1 child), fruit consumption ≤4 days per week (compared with ≥5 days per week), a plant-based diet (compared with a balanced diet), smoking (former, current, and passive) (compared with no smoking), former alcohol drinking (compared with no alcohol drinking), BMI ≥28.0 (compared with BMI of 18.5–24.0), physical inactivity, hypertension, diabetes mellitus, and family history (stroke, CHD, and hypertension). The factors negatively associated with stroke risk were age 60 to 69 years (compared with age 40–49 years), vegetable consumption 3 to 4 days per week (compared with ≥5 days per week), and living with spouse or children (compared with living alone). However, dyslipidemia, AF, and TIA were not significantly associated with stroke in the multivariable Cox proportional hazard regression model (Table 2 and Figure 1).

Stroke Subtypes

The risk factors for first-ever ischemic stroke and total stroke were the same in the univariate analysis. After including these factors and sex into the multivariable Cox regression model, the risk factors for first-ever total stroke and ischemic stroke remained the same (Table 3 and Figure 2).

The potential predictors of first-ever hemorrhagic stroke in the univariate analysis were sex, age, BMI, hypertension, dyslipidemia, diabetes mellitus, TIA, family history (stroke, hypertension, dyslipidemia, diabetes mellitus, or CHD), physical inactivity, smoking and drinking status, vegetable consumption, balanced diet, economic regions, geographic regions, education level, marital status, healthcare insurance, and number of siblings or children.

After including these variables into the multivariable Cox regression model, age 60 to 69 years

Table 1. Baseline Characteristics of Participants Aged ≥40 Years Without Previous Stroke Stratified by Sex

Characteristic	Men	Women	Total
Participants, n (%)	202 149 (46.2)	235 169 (53.8)	437 318
Age and socioeconomic factors			
Age (y), mean (SD)	56.80 (11.2)	57.13 (11.2)	56.98 (11.2)
Age groups (y), n (%)			
40–49	65 356 (32.3)	71 420 (30.4)	136 776 (31.3)
50–59	58 709 (29.0)	71 213 (30.3)	129 922 (29.7)
60–69	47 911 (23.7)	56 929 (24.2)	104 840 (24.0)
70–79	23 121 (11.4)	26 768 (11.4)	49 889 (11.4)
≥80	7052 (3.5)	8839 (3.8)	15 891 (3.6)
Number of siblings, mean (SD)	3.68 (1.57)	3.73 (1.58)	3.71 (1.58)
Number of siblings, n (%)			
0	1495 (0.7)	1897 (0.8)	3392 (0.8)
1	6291 (3.1)	6534 (2.8)	12 825 (2.9)
2	21 872 (10.8)	24 036 (10.2)	45 908 (10.5)
3	36 471 (18.0)	41 609 (17.7)	78 080 (17.9)
4	31 531 (15.6)	36 736 (15.6)	68 267 (15.6)
≥5	37 081 (18.3)	43 987 (18.7)	81 068 (18.5)
Number of children, mean (SD)	2.03 (1.07)	2.10 (1.10)	2.06 (1.09)
Number of children, n (%)			
0	1632 (0.8)	617 (0.3)	2249 (0.5)
1	43 774 (21.7)	49 416 (21.0)	93 190 (21.3)
2	55 747 (27.6)	62 739 (26.7)	118 486 (27.1)
≥3	33 572 (16.6)	42 001 (17.9)	75 573 (17.3)
Living status, n (%)			
Living alone	5015 (2.5)	7133 (3.0)	12 148 (2.8)
Living with spouse only	67 864 (33.6)	75 994 (32.3)	143 858 (32.9)
Living with children only	5020 (2.5)	10 231 (4.4)	15 251 (3.5)
Living with spouse and children	87 204 (43.1)	101 064 (43.0)	188 268 (43.1)
Other	987 (0.5)	941 (0.4)	1928 (0.4)
Living in rural areas, n (%)	110 709 (54.8)	126 923 (54.0)	237 632 (54.3)
Geographic region of China, n (%)			
Northeast	22 539 (11.1)	25 487 (10.8)	48 026 (11.0)
North	43 540 (21.5)	51 230 (21.8)	94 770 (21.7)
East	56 655 (28.0)	64 641 (27.5)	121 296 (27.7)
South	7247 (3.6)	8568 (3.6)	15 815 (3.6)
Central	26 965 (13.3)	33 319 (14.2)	60 284 (13.8)
Northwest	19 692 (9.7)	22 113 (9.4)	41 805 (9.6)
Southwest	25 511 (12.6)	29 811 (12.7)	55 322 (12.7)
Economic region, n (%)			
Low-income	51 180 (25.3)	61 178 (26.0)	112 358 (25.7)
Middle-income	79 333 (39.2)	91 163 (38.8)	170 496 (39.0)
High-income	71 636 (35.4)	82 828 (35.2)	154 464 (35.3)
Social healthcare insurance, n (%)			
Urban Employee Basic Medical Insurance	60 756 (30.1)	66 527 (28.3)	127 283 (29.1)
Urban Resident Basic Medical Insurance	43 335 (21.4)	55 069 (23.4)	98 404 (22.5)
New Rural Cooperative Medical System	93 432 (46.2)	108 780 (46.3)	202 212 (46.2)
Other	3248 (1.6)	3602 (1.5)	6850 (1.6)

(*Continued*)

Table 1. Continued

Characteristic	Men	Women	Total
Education, n (%)			
Primary school or no formal education	72 857 (36.0)	105 094 (44.7)	177 951 (40.7)
Middle school	81 349 (40.2)	83 911 (35.7)	165 260 (37.8)
High school or higher	45 421 (22.5)	43 878 (18.7)	89 299 (20.4)
Lifestyle factors			
Smoking status, n (%)			
Never	133 126 (65.9)	217 804 (92.6)	350 930 (80.2)
Former smoker	6645 (3.3)	605 (0.3)	7250 (1.7)
Current smoker	56 075 (27.7)	4255 (1.8)	60 330 (13.8)
Passive smoker	2037 (1.0)	8387 (3.6)	10 424 (2.4)
Alcohol consumption, n (%)			
Never	157 586 (78.0)	226 615 (96.4)	384 201 (87.9)
Former drinker	2835 (1.4)	513 (0.2)	3348 (0.8)
Current (light-moderate)	32 339 (16.0)	3658 (1.6)	35 997 (8.2)
Current (heavy)	5105 (2.5)	255 (0.1)	5360 (1.2)
Physical inactivity, n (%)	54 321 (26.9)	68 762 (29.2)	123 083 (28.1)
Dietary pattern			
Vegetables, n (%)			
≥5 d/wk	128 949 (63.8)	153 515 (65.3)	282 464 (64.6)
3–4 d/wk	51 327 (25.4)	57 460 (24.4)	108 787 (24.9)
≤2 d/wk	13 543 (6.7)	14 676 (6.2)	28 219 (6.5)
Fruits, n (%)			
≥5 d/wk	64 263 (31.8)	80 964 (34.4)	145 227 (33.2)
3–4 d/wk	72 676 (36.0)	84 576 (36.0)	157 252 (36.0)
≤2 d/wk	54 189 (26.8)	56 437 (24.0)	110 626 (25.3)
Diet, n (%)			
Balanced intake of vegetables and meat	160 713 (79.5)	186 231 (79.2)	346 944 (79.3)
Meat-based diet	16 451 (8.1)	15 586 (6.6)	32 037 (7.3)
Vegetable-based diet	19 091 (9.4)	27 694 (11.8)	46 785 (10.7)
Family history of disease			
Stroke, n (%)			
No	175 332 (86.7)	203 821 (86.7)	379 153 (86.7)
Yes	12 737 (6.3)	16 957 (7.2)	29 694 (6.8)
Unknown	9315 (4.6)	9814 (4.2)	19 129 (4.4)
Coronary heart disease, n (%)			
No	178 720 (88.4)	208 420 (88.6)	387 140 (88.5)
Yes	6536 (3.2)	9181 (3.9)	15 717 (3.6)
Unknown	10 629 (5.3)	11 451 (4.9)	22 080 (5.0)
Hypertension, n (%)			
No	164 418 (81.3)	192 037 (81.7)	356 455 (81.5)
Yes	20 855 (10.3)	25 586 (10.9)	46 441 (10.6)
Unknown	10 622 (5.3)	11 437 (4.9)	22 059 (5.0)
Dyslipidemia, n (%)			
No	173 418 (85.8)	202 820 (86.2)	376 238 (86.0)
Yes	3333 (1.6)	4798 (2.0)	8131 (1.9)
Unknown	19 138 (9.5)	21 448 (9.1)	40 586 (9.3)
Diabetes mellitus, n (%)			
No	177 597 (87.9)	208 049 (88.5)	385 646 (88.2)

(*Continued*)

Table 1. Continued

Characteristic	Men	Women	Total
Yes	6522 (3.2)	8342 (3.5)	14 864 (3.4)
Unknown	11 766 (5.8)	12 670 (5.4)	24 436 (5.6)
Medical history and health status			
Hypertension, n (%)	47 156 (23.3)	59 918 (25.5)	107 074 (24.5)
Dyslipidemia, n (%)	35 186 (17.4)	47 109 (20.0)	82 295 (18.8)
Diabetes mellitus, n (%)	13 891 (6.9)	18 248 (7.8)	32 139 (7.3)
Atrial fibrillation, n (%)	3138 (1.6)	4804 (2.0)	7942 (1.8)
Transient ischemic attacks, n (%)	2390 (1.2)	4176 (1.8)	6566 (1.5)
BMI, kg/m^2 (mean [SD])	23.94 (2.97)	23.94 (3.30)	23.94 (3.15)
BMI, n (%)			
<18.5	3607 (1.8)	5991 (2.5)	9598 (2.2)
18.5–24	106 049 (52.5)	122 131 (51.9)	228 180 (52.2)
24–28	76 531 (37.9)	83 445 (35.5)	159 976 (36.6)
≥28	15 951 (7.9)	23 591 (10.0)	39 542 (9.0)

BMI indicates body mass index.

(compared with age 40–49 years) was negatively associated with the risk of first-ever hemorrhagic stroke, whereas being male, passive smoking, former drinking, physical inactivity, hypertension, BMI <18.5, FHS, family history of hypertension, living in high-income regions, URBMI, and NRCMS were positively associated with the risk of first-ever hemorrhagic stroke (Table 4 and Figure 3).

Sensitivity Analyses

We examined the potential confounding effect of SES by adding occupation to the model and stratified the Cox proportional model by time intervals for the time-varying variables to test the robustness of the findings. Sensitivity analysis did not substantially alter the risk estimates (data not shown).

Population-Attributable Risk

The PAR% of each modifiable factor is shown in Table 5. The PAR% (95% CI) of hypertension for total stroke and ischemic stroke was 27.3% (22.7%–31.6%) and 26.0% (22.1%–30.5%), respectively, corresponding to the highest PAR% among all modifiable risk factors, followed by physical inactivity, smoking, level of education, and other factors, suggesting that >25% of incident first-ever strokes in this population during follow-up could have been prevented if all participants had been in the non-hypertension group. The PAR% (95% CI) of hypertension and physical inactivity was higher for hemorrhagic stroke, corresponding to 40.7% (29.0%–54.5%), and 24.2% (13.8%–33.2%), respectively.

Discussion

This study found that conventional risk factors, such as hypertension, smoking, and physical inactivity, were associated with an increased risk of incident stroke and its subtypes. However, variations in traditional risk factors did not explain all the variance in the risk of incident stroke. Furthermore, SES, including education level, geographic and economic region, social health-care insurance status, living condition, and number of children, were predictors of incident stroke and its subtypes. SES usually dictates health behaviors, access to medical care, and stress level, suggesting that these indicators should be targeted for preventing and controlling stroke.

Men were more likely to develop hemorrhagic stroke, which agrees with data from Ji County in Tianjin, where stroke incidence increased significantly among middle-aged men.[18] This phenomenon may be because of sex hormones or job strain,[19,20] but needs to be further studied.

Physical inactivity was a significant risk factor for all types of stroke, and the PAR% of physical inactivity was the second highest among all modifiable risk factors. A Japanese study showed that moderate levels of physical activity might be optimal for preventing stroke.[21] This finding may be attributable to the fact that moderate exercise strengthens muscles, increases energy consumption and bone density, and reduces blood pressure, lipids, and psychological stress.[22]

Current smoking increased the risk of total and ischemic stroke compared with non-smoking, which might be because smoking elevates the levels of homocysteine and fibrinogen,[23] and passive smoking may lead to carotid atherosclerosis.[24] Therefore, passive

Table 2. Multivariable-Adjusted Hazard Ratios (95% CIs) for Incident First-Ever Total Stroke by Risk Factors Among 437 318 Participants

	No. of Events	Incidence Rate (No./100 000 PYs)	Univariate	Multivariate
			HR (95% CI)	HR (95% CI)
Total	2429	260.9		
Conventional factors				
Age, y				
40–49	162	55.4	1	1
50–59	575	207.0	4.48 (3.85–5.22)	2.84 (2.25–3.58)
60–69	977	438.9	0.34 (0.30–0.39)	0.45 (0.37–0.54)
70–79	593	564.2	0.97 (0.87–1.07)	0.95 (0.83–1.09)
≥80	122	370.6	0.97 (0.90–1.05)	0.93 (0.84–1.03)
Dietary pattern				
Vegetable ≥5 d/w	1871	310.1	1	1
Vegetable 3–4 d/w	375	161.2	0.79 (0.70–0.90)	0.69 (0.58–0.81)
Vegetable ≤2 d/w	134	223.8	1.50 (1.35–1.68)	0.98 (0.85–1.13)
Fruit ≥5 d/w	692	223.2	1	1
Fruit 3–4 d/w	774	228.4	1.37 (1.28–1.47)	1.18 (1.06–1.31)
Fruit ≤2 d/w	820	350.9	1.20 (1.11–1.28)	1.24 (1.12–1.38)
Balanced intake of vegetables and meat	1735	234.4	1	1
Meat-based diet	117	171.4	0.71 (0.59–0.86)	0.90 (0.70–1.15)
Vegetable-based diet	577	576.9	2.48 (2.26–2.72)	1.44 (1.26–1.66)
Alcohol consumption				
Never	1925	234.9	1	1
Former drinker	145	2065.3	8.54 (7.21–10.11)	2.66 (2.03–3.47)
Current (light-moderate)	295	382.9	1.61 (1.43–1.82)	1.03 (0.86–1.23)
Current (heavy)	64	560.7	2.38 (1.86–3.05)	1.27 (0.90–1.80)
Smoking status				
Never	1660	221.5	1	1
Former smoker	178	1156.4	5.18 (4.44–6.05)	2.38 (1.90–2.98)
Current smoker	512	398.9	1.80 (1.63–1.99)	1.33 (1.13–1.56)
Passive smoker	79	356.8	1.63 (1.30–2.04)	1.77 (1.30–2.40)
BMI, kg/m^2				
<18.5	1024	211.2	1.94 (1.75–2.16)	0.90 (0.60–1.34)
18.5 to 23.9	38	187.5	1	1
24.0 to 27.9	962	281.9	1.41 (1.19–1.68)	1.03 (0.91–1.16)
28.0 to ≥28	405	479.6	0.89 (0.71–1.10)	1.20 (1.02–1.41)
Physical inactivity	1003	383.3	1.74 (1.61–1.89)	1.52 (1.37–1.70)
Hypertension	1431	630.4	4.48 (4.13–4.85)	1.97 (1.74–2.23)
Diabetes mellitus	469	688.4	3.06 (2.77–3.38)	1.35 (1.17–1.56)
Family history of stroke	634	1001.8	4.75 (4.33–5.20)	2.13 (1.85–2.46)
Family history of coronary heart disease	303	902.0	3.70 (3.28–4.17)	1.26 (1.05–1.51)
Family history of hypertension	755	765.7	3.77 (3.45–4.11)	1.49 (1.29–1.73)
Socioeconomic factors				
Geographic region of China				
Southwest	97	83.9	1	1
Northeast	324	303.7	3.61 (2.88–4.53)	3.37 (2.12–5.37)
North	455	227.7	2.76 (2.22–3.44)	2.23 (1.40–3.53)
East	875	338.9	4.13 (3.34–5.09)	2.93 (1.84–4.67)
South	72	199.5	1.63 (1.19–2.24)	1.25 (0.71–2.23)

(*Continued*)

Table 2. Continued

	No. of Events	Incidence Rate (No./100 000 PYs)	Univariate	Multivariate
			HR (95% CI)	HR (95% CI)
Central	404	319.4	3.85 (3.09–4.81)	2.82 (1.85–4.32)
Northwest	202	229.3	2.60 (2.04–3.32)	1.34 (0.85–2.12)
Education				
Primary school or no formal education	1305	346.2	1.65 (1.51–1.80)	1.24 (1.08–1.41)
Middle school	734	208.2	1	1
High school or higher	388	201.9	0.97 (0.86–1.10)	1.06 (0.90–1.24)
Living status				
Living alone	155	602.3	1	1
Living with spouse only	953	307.5	0.51 (0.43–0.60)	0.74 (0.59–0.92)
Living with children only	137	423.2	0.68 (0.54–0.86)	0.73 (0.56–0.96)
Living with spouse and children	851	212.5	0.35 (0.29–0.41)	0.63 (0.49–0.80)
Other	18	436.5	0.72 (0.44–1.17)	1.22 (0.68–2.17)
Number of children				
0	12	245.5	1.41 (0.79–2.50)	0.74 (0.35–1.56)
1	353	174.7	1	1
2	639	252.1	1.41 (1.24–1.61)	1.20 (1.03–1.40)
≥3	673	416.4	2.29 (2.01–2.61)	1.29 (1.08–1.53)

The multivariable model was adjusted for sex, marital status, dyslipidemia, atrial fibrillation, transient ischemic attack, diabetes mellitus family history, dyslipidemia family history, milk intake, number of siblings, and economic region at baseline. BMI indicates body mass index; HRs, hazard ratios; and PYs, person-years.

smoking should also be considered in policy making. Former smoking or former alcohol drinking was positively associated with the risk of stroke, which might be attributable to the fact that smoking or drinking was discontinued because of illness, or a longer period of smoking and drinking cessation was necessary to produce significant effects. The stroke screening survey conducted between 2013 and 2015 in Shenzhen showed that quitting smoking for >20 years virtually eliminated the stroke risk associated with smoking.[25] Therefore, former smokers or drinkers who quit these habits because of illness should be included in the group of current smokers or drinkers, and former drinking and smoking should be classified according to the time elapsed since cessation to avoid bias in future studies.

Consuming fruits ≤4 days per week was positively associated with the risk of total and ischemic stroke compared with consuming fruits ≥5 days per week. This result was consistent with a previous study published in the New England Journal of Medicine, wherein fruit consumption was significantly and inversely associated with the risk of ischemic heart disease and other cerebrovascular diseases.[26] However, consuming vegetables 3 to 4 days per week was negatively associated with stroke risk compared with ≥5 days per week, which might be because a vegetarian diet was positively associated with the risk of total and ischemic stroke, compared with a balanced diet. This result may be because of the fact that the increased consumption of fruits and moderate consumption of vegetables can lower blood pressure, improve microvascular function, and have favorable effects on other risk factors for cardiovascular disease (CVD), including waist circumference, inflammation, thrombotic effects, and oxidative stress.[27] Moreover, vegetables and fruits are rich in potassium, magnesium, folate, fibers, and antioxidants, which are significantly linked with a decreased risk of stroke.[28] However, high vegetable consumption might decrease the intake of dietary protein and vitamin D, and the latter has been shown to decrease the risk of stroke.[29] Our results suggest that specific nutritional deficiencies in Chinese vegetarian diets may be associated with stroke risk; however, additional studies are necessary to confirm this conclusion.

Hypertension remains the leading modifiable predictor of stroke worldwide.[9] Our findings indicated that the PAR% of hypertension was the highest among all modifiable risk factors. Furthermore, diabetes mellitus was a significant risk factor for total and ischemic stroke, which was consistent with a previous study conducted in Japan.[30] This result may be because individuals with diabetes mellitus are more susceptible to the consequences of cerebral small-vessel disease.[31]

Obesity was positively associated with the risk of total and ischemic stroke, which agrees with a previous

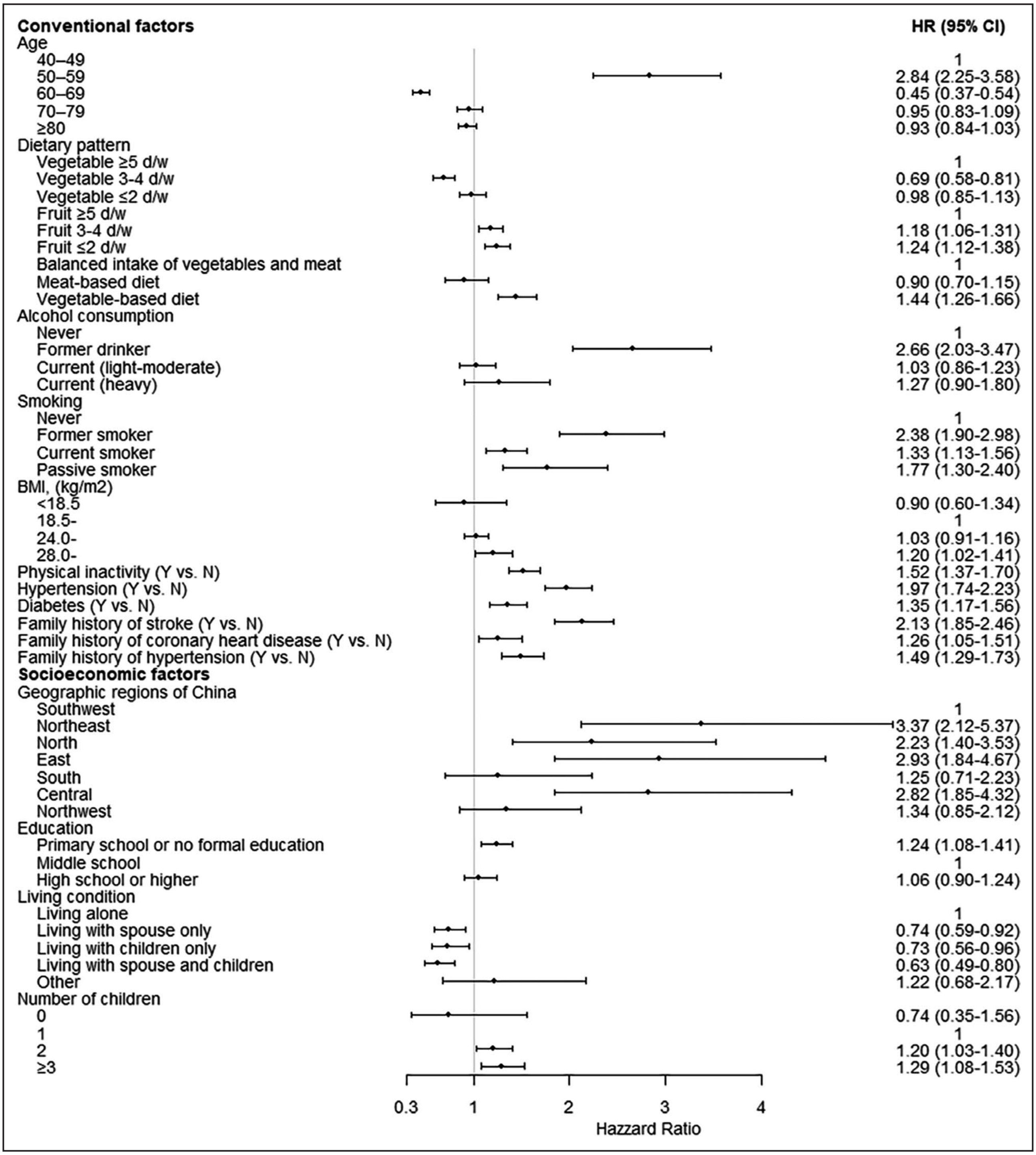

Figure 1. Multivariable-adjusted hazard ratioss (95% CIs) for incident first-ever total stroke by risk factors.
BMI indicates body mass index; and HR, hazard ratio.

study.[32] Underweight was positively associated with the risk of hemorrhagic stroke. In a cohort of Korean men, there was a J-shaped association between BMI and hemorrhagic stroke and a linear association between BMI and ischemic stroke.[33] Our findings indicate that BMI was differentially associated with ischemic and hemorrhagic stroke and underscore the need to keep normal weight.

FHS was an independent risk factor for stroke, which agrees with a previous study.[11] FHS represents shared environmental and genetic factors. The

Table 3. Multivariable-Adjusted HRs (95% CIs) for Incident First-Ever Ischemic Stroke by Risk Factors Among 437 318 Participants

	No. of Events	Incidence Rate (No./100 000 PYs)	Univariate	Multivariate
			HR (95% CI)	HR (95% CI)
Total	2206	237.00		
Conventional factors				
Age, y				
40–49	140	47.85	1	1
50–59	522	187.95	4.58 (3.89–5.39)	3.05 (2.39–3.90)
60–69	897	402.99	0.33 (0.28–0.38)	0.44 (0.36–0.53)
70–79	538	511.90	0.98 (0.88–1.09)	0.97 (0.83–1.12)
≥80	109	331.14	0.97 (0.90–1.06)	0.94 (0.84–1.04)
Dietary pattern				
Vegetable ≥5 d/w	1702	282.10	1	1
Vegetable 3–4 d/w	335	144.03	0.81 (0.71–0.92)	0.67 (0.56–0.80)
Vegetable ≤2 d/w	126	210.45	1.55 (1.38–1.73)	0.98 (0.84–1.14)
Fruit ≥5 d/w	627	202.20	1	1
Fruit 3–4 d/w	692	204.16	1.39 (1.29–1.50)	1.22 (1.09–1.36)
Fruit ≤2 d/w	757	323.95	1.22 (1.13–1.31)	1.24 (1.11–1.37)
Balanced intake of vegetables and meat	1574	212.62	1	1
Meat-based diet	104	152.32	0.70 (0.57–0.85)	0.84 (0.65–1.10)
Vegetarian-based diet	528	527.92	2.50 (2.26–2.76)	1.44 (1.25–1.67)
Alcohol consumption				
Never	1753	213.90	1	1
Former drinker	124	1766.22	8.01 (6.68–9.62)	2.68 (2.02–3.54)
Current (light-moderate)	267	346.57	1.60 (1.41–1.82)	1.02 (0.84–1.23)
Current (heavy)	62	543.18	2.53 (1.97–3.26)	1.36 (0.96–1.93)
Smoking				
Never	1505	200.83	1	1
Former smoker	154	1000.49	4.94 (4.19–5.83)	2.37 (1.87–3.01)
Current smoker	481	374.78	1.87 (1.68–2.07)	1.44 (1.22–1.70)
Passive smoker	66	298.12	1.50 (1.17–1.92)	1.49 (1.05–2.12)
BMI, kg/m^2				
<18.5	32	157.93	0.80 (0.56–1.13)	0.78 (0.50–1.22)
18.5 to 23.9	929	191.58	1	1
24.0 to 27.9	872	255.51	1.35 (1.23–1.48)	1.02 (0.90–1.16)
28.0 to ≥28	373	441.68	2.34 (2.08–2.64)	1.19 (1.00–1.41)
Physical inactivity	890	340.16	1.68 (1.54–1.83)	1.49 (1.33–1.67)
Hypertension	1292	569.15	4.41 (4.05–4.80)	1.90 (1.66–2.16)
Diabetes mellitus	446	654.61	3.24 (2.92–3.59)	1.46 (1.26–1.70)
Family history of stroke	579	914.90	4.79 (4.35–5.26)	2.08 (1.79–2.42)
Family history of coronary heart disease	284	845.40	3.84 (3.39–4.35)	1.31 (1.08–1.58)
Family history of hypertension	685	694.72	3.76 (3.44–4.12)	1.43 (1.22–1.66)
Socioeconomic factors				
Geographic region of China				
Southwest	76	65.72	1	1
Northeast	292	273.67	4.15 (3.22–5.34)	4.11 (2.41–7.00)
North	425	212.73	3.29 (2.58–4.21)	2.88 (1.69–4.89)

(Continued)

Table 3. Continued

	No. of Events	Incidence Rate (No./100 000 PYs)	Univariate	Multivariate
			HR (95% CI)	HR (95% CI)
East	804	311.43	4.84 (3.83–6.13)	3.80 (2.23–6.47)
South	57	157.95	1.65 (1.16–2.35)	1.48 (0.76–2.88)
Central	371	293.32	4.51 (3.53–5.78)	3.50 (2.13–5.75)
Northwest	181	205.49	2.98 (2.28–3.89)	1.69 (0.99–2.88)
Education				
Primary school or no formal education	1173	311.18	1.62 (1.48–1.79)	1.23 (1.07–1.41)
Middle school	670	190.01	1	1
High school or higher	361	187.87	0.99 (0.87–1.12)	1.11 (0.94–1.32)
Living status				
Living alone	142	551.75	1	1
Living with spouse only	868	280.10	0.51 (0.42–0.60)	0.74 (0.59–0.94)
Living with children only	125	386.17	0.68 (0.54–0.87)	0.75 (0.57–1.00)
Living with spouse and children	771	192.49	0.34 (0.29–0.41)	0.63 (0.49–0.81)
Other	18	436.51	0.79 (0.48–1.29)	1.35 (0.75–2.42)
Number of children				
0	11	225.08	1.45 (0.80–2.65)	0.86 (0.40–1.83)
1	313	154.93	1	1
2	592	233.60	1.48 (1.29–1.70)	1.27 (1.08–1.49)
≥3	604	373.68	2.32 (2.03–2.67)	1.32 (1.10–1.58)

The multivariable model was adjusted for sex, marital status, dyslipidemia, atrial fibrillation, transient ischemic attack, diabetes mellitus family history, dyslipidemia family history, milk intake, number of siblings, and economic region at baseline. BMI indicates body mass; HRs, hazard ratios; and PYs, person-years.

causative factors for family history of hypertension and CHD may be the same as those for FHS.

The results of multivariable Cox regression analysis showed that the risk of incident stroke varied across age groups. Age 50 to 59 years was positively associated with stroke risk, whereas age 60 to 69 years was negatively associated with stroke risk, which might be because people aged 50 to 59 years have an overall higher level of stress, whereas individuals aged 60 to 69 years who retired in China have a lower stress level than the working population and are younger than those aged ≥70 years. Previous findings suggest that job strain may be related to early asymptomatic stage atherosclerosis.[20] Moreover, most people aged 50 to 59 years experienced the famine of 1959 to 1961 in China and were exposed to undernutrition in the fetal or neonatal period, and prenatal exposure to famine might be associated with an increased risk of CVD or diabetes mellitus in adulthood.[34]

Wang et al found that stroke incidence and mortality varied significantly across China, with a noticeable north-south geographical gradient.[35] We found that people living in Northeast, Central, East, and North China had increased risk of total and ischemic stroke, and those living in high-income regions had a higher risk of hemorrhagic stroke. However, we didn't find statistically significant differences in the risk of incidence stroke and its subtypes between urban and rural areas of China. Significant variations in the risk of stroke between geographic and economic regions may be partly because of unmeasured factors, including genetic variations, lifestyle, mental stress, or healthcare level.

Primary school or no formal education was positively associated with the risk of total and ischemic stroke, compared with middle school education. Albert et al found that the incidence of CVD decreased as the level of education increased in healthy female health professionals after adjusting for traditional risk factors and CVD biomarkers, suggesting that these variables could not explain the protective effect of education.[36] The effect of education level on stroke risk might be related to other factors such as chronic psychosocial stress, small social networks, working conditions, poverty in early life, medical management, and compliance with medical regimens.[37]

Living with spouse or children was negatively associated with the risk of total and ischemic stroke, compared with those living alone. Living alone is an indicator of social isolation. Previous studies have shown that socially isolated individuals are more likely to live

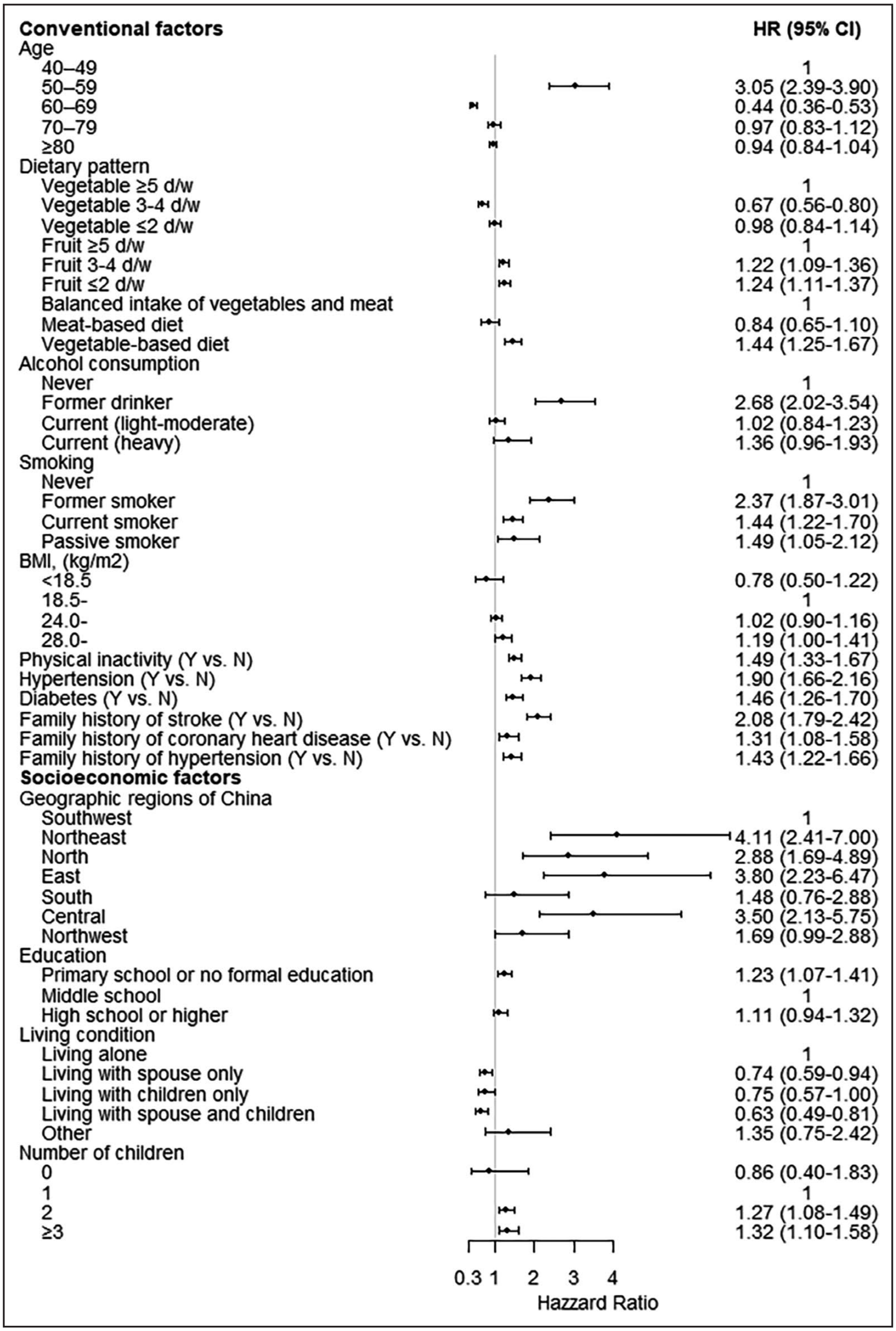

Figure 2. Multivariable-adjusted hazard ratios (95% CIs) for incident first-ever ischemic stroke by risk factors.

BMI indicates body mass index; and HR, hazard ratio.

alone, have poorer mental health and quality of life, and present a higher rate of depression,[38] and individuals with small social networks may be less likely to participate in health-promoting behaviors and follow medical recommendations.[39] Furthermore, having small social networks is associated with psychological stress and may impact the cardiovascular system via physical and mental changes.[40] In this respect, individuals with small

Table 4. Multivariable-Adjusted HRs (95% CIs) for Incident First-Ever Hemorrhagic Stroke by Risk Factors Among 437 318 Participants

	No. of Events	Incidence Rate (No./100 000 PYs)	Univariate	Multivariate
			HR (95% CI)	HR (95% CI)
Total	237	25.5		
Conventional factors				
Sex, men	131	30.4	0.78 (0.65–0.93)	1.76 (1.18–2.63)
Age, y				
40–49	22	7.5	1	1
50–59	59	21.2	4.10 (2.66–6.31)	1.83 (0.87–3.86)
60–69	84	37.7	0.49 (0.33–0.71)	0.47 (0.26–0.85)
70–79	57	54.2	0.98 (0.72–1.33)	0.93 (0.60–1.46)
≥80	15	45.6	0.94 (0.73–1.19)	0.86 (0.62–1.19)
Dietary pattern				
Balanced intake of vegetables and meat	170	23.0	1	1
Meat-based diet	13	19.0	0.80 (0.46–1.41)	1.28 (0.65–2.52)
Vegetable-based diet	54	54.0	2.37 (1.75–3.22)	1.62 (1.05–2.49)
Alcohol consumption				
Never	185	22.6	1	1
Former drinker	21	299.1	12.70 (8.09–19.95)	2.63 (1.16–5.97)
Current (light-moderate)	29	37.6	1.64 (1.11–2.43)	0.96 (0.54–1.69)
Current (heavy)	2	17.5	0.77 (0.19–3.11)	0.34 (0.05–2.50)
Smoking				
Never	166	22.2	1	1
Former smoker	24	155.9	6.97 (4.54–10.69)	2.21 (1.14–4.27)
Current smoker	34	26.5	1.20 (0.83–1.73)	0.60 (0.34–1.07)
Passive smoker	13	58.7	2.70 (1.53–4.75)	3.14 (1.61–6.13)
BMI, kg/m^2				
<18.5	7	34.5	1.60 (0.74–3.44)	2.41 (1.02–5.69)
18.5 to 23.9	100	20.6	1	1
24.0 to 27.9	94	27.5	1.36 (1.03–1.81)	1.01 (0.69–1.50)
28.0 to ≥28	36	42.6	2.11 (1.44–3.09)	1.44 (0.88–2.35)
Physical inactivity	117	44.7	2.40 (1.86–3.10)	1.83 (1.30–2.59)
Hypertension	147	64.8	5.09 (3.92–6.62)	2.84 (1.90–4.24)
Stroke family history	58	59.5	4.27 (3.17–5.75)	2.47 (1.60–3.81)
Hypertension family history	73	74.0	3.67 (2.78–4.85)	2.36 (1.52–3.65)
Socioeconomic factors				
Economic regions				
Low-income	70	29.1	1	1
Middle-income	66	18.6	1.07 (0.86–1.34)	0.92 (0.45–1.89)
High-income	101	30.0	1.43 (1.13–1.80)	1.69 (1.13–2.55)
Social healthcare insurance				
UEBMI	48	17.5	1	1
URBMI	66	31.5	1.83 (1.26–2.65)	2.41 (1.40–4.13)
NRCMS	118	27.6	1.58 (1.13–2.21)	1.91 (1.12–3.25)
Other	5	32.1	1.96 (0.78–4.92)	1.37 (0.32–5.86)

Multivariable model was adjusted for age, marital status, education, diabetes mellitus, dyslipidemia, TIA, diabetes mellitus family history, dyslipidemia family history, coronary heart disease family history, vegetable or fruit intake, geographic region, living condition, numbers of siblings or children at baseline. BMI indicates body mass index; HRs, hazard ratios; NRCMS, New Rural Cooperative Medical Scheme; PYs, person-years; UEBMI, Urban Employee Basic Medical Insurance; and URBMI, Urban Resident Basic Medical Insurance.

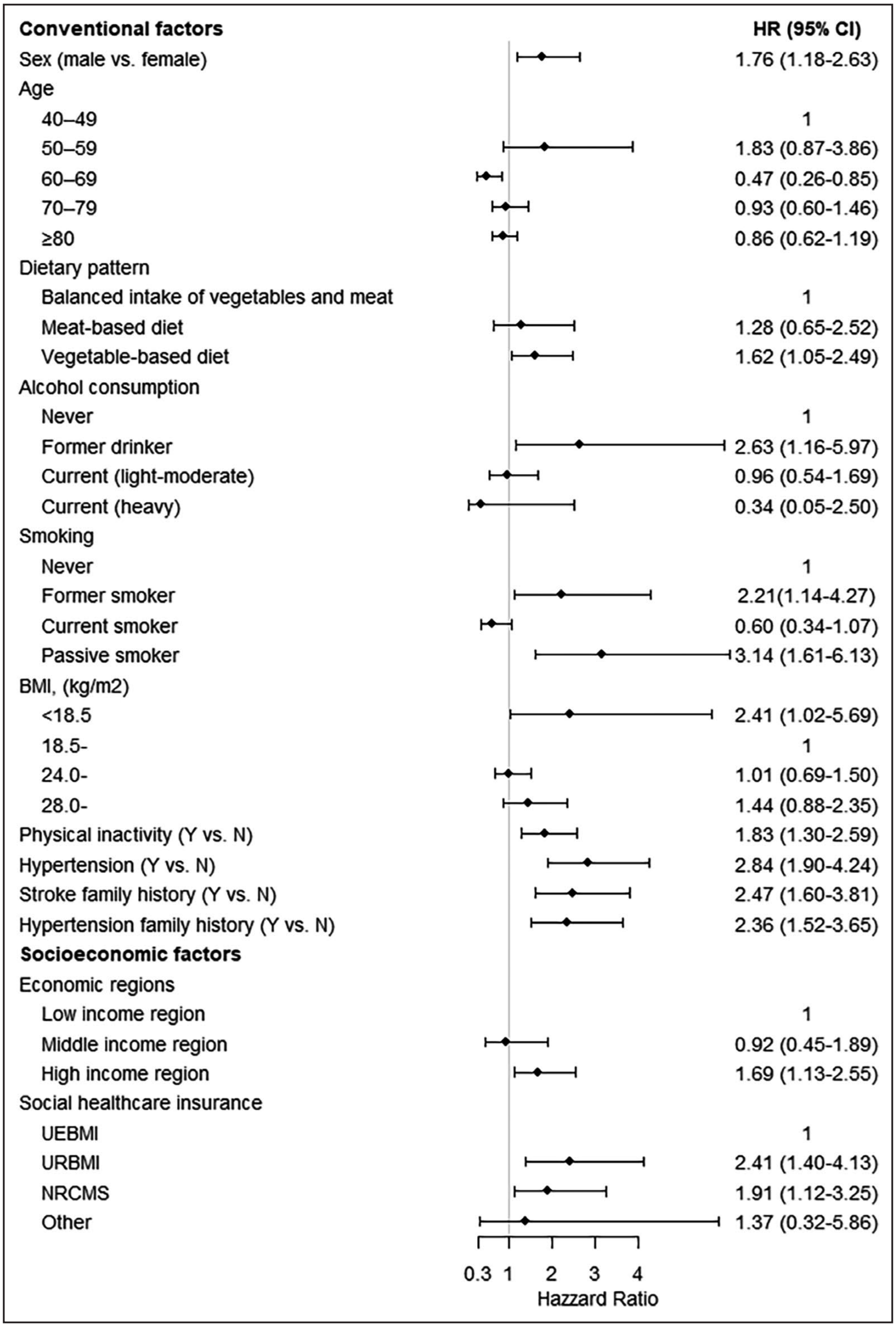

Figure 3. Multivariable-adjusted hazard ratios (95% CIs) for incident first-ever hemorrhagic stroke by risk factors.
BMI indicates body mass index; HR, hazard ratio; NRCMS, New Rural Cooperative Medical Scheme; UEBMI, Urban Employee Basic Medical Insurance; and URBMI, Urban Resident Basic Medical Insurance.

social networks have higher levels of exhaustion, which increases the risk of incident stroke.[41] Depression is also associated with incident stroke[42] potentially through elevated levels of inflammatory markers.[43] Therefore, social support or depression relief might explain the decreased risk of incident stroke among

Table 5. Multivariable-Adjusted PAR% (95% CIs) at the Second Year for Stroke and Its Subtypes by Low-Risk Factors* Among 437 318 Participants

Modifiable Variables	Cases in Low-Risk Group	Incidence Rate (No./100 000 PYs) in Low-Risk Group	PAR% (95% CI)
Total stroke (n case=2429)			
Hypertension	998	141.8	27.3 (22.7 to 31.6)
Diabetes mellitus	1960	227.2	5.1 (2.9 to 7.4)
BMI	1024	211.2	5.4 (−0.1 to 10.1)
Smoking	1650	220.2	10.1 (6.8 to 13.2)
Alcohol consumption	1925	234.9	5.5 (2.9 to 8.1)
Physical inactivity	1426	218.2	14.9 (11.1 to 18.6)
Vegetable consumption	372	159.9	4.4 (0.5 to 8.0)
Fruit consumption	692	223.2	1.7 (−0.8 to 4.1)
Balance intake of vegetables and meat	1735	234.4	5.9 (3.1 to 8.7)
Living condition	1941	261.3	2.8 (1.2 to 4.3)
Education	1122	583.9	9.0 (3.6 to 14.1)
Ischemic stroke (n case=2206)			
Hypertension	914	129.8	26.0 (22.1 to 30.5)
Diabetes mellitus	1760	204.0	6.3 (3.9 to 8.7)
BMI	929	191.6	4.6 (−1.3 to 10.1)
Smoking	1506	201.0	10.3 (6.9 to 13.6)
Alcohol consumption	1753	213.9	5.2 (2.4 to 7.9)
Physical inactivity	1316	201.4	13.3 (9.2 to 17.2)
Vegetable consumption	335	144.0	4.5 (0.5 to 8.4)
Fruit consumption	627	202.2	2.0 (−0.6 to 4.6)
Balance intake of vegetables and meat	1574	212.6	5.9 (2.8 to 8.8)
Living condition	1764	237.5	2.9 (1.3 to 4.5)
Education	1031	536.5	8.2 (2.5 to 13.6)
Hemorrhage stroke (n case=237)			
Hypertension	90	12.8	40.7 (29.0.1 to 50.5)
BMI	100	20.6	7.1 (−8.9 to 20.7)
Smoking	166	22.2	6.1 (−3.7 to 15.0)
Alcohol consumption	185	22.6	7.1 (−1.8 to 13.9)
Physical inactivity	117	44.7	24.2 (13.8 to 33.2)
Balance intake of vegetables and meat	54	54.0	7.2 (−0.5 to 14.1)

Multivariable model for total stroke and ischemic stroke was adjusted for age, education, geographic regions, family histories of stroke, hypertension or coronary heart disease, and numbers of children or siblings at baseline. The multivariable model for hemorrhage stroke was adjusted for sex, economic regions, healthcare insurance, family history of stroke or hypertension at baseline. BMI indicates body mass index; PAR%, population-attributable risk percentage; and PYs, person-years.

*Low-risk factors were non-hypertension, non-diabetes mellitus, non-smoking, non-alcohol drinking, physical activity, BMI of 18.5 to 23.9 kg/m^2, eating fruits ≥5 days/week, eating vegetables 3 to 4 days/week, balanced intake of vegetables and meat, and living with spouse or children.

subjects living with spouse or children. Psychosocial interventions for mental health or social support should be provided to individuals living alone or with others. Further studies are necessary to determine the role of living status in mental health and stroke.

Having >1 child was positively associated with the risk of total stroke and ischemic stroke, compared with having 1 child. A previous study found that the association between the number of children in the household and the risk of cardio-cerebrovascular diseases was similar between adult men and women in China, suggesting that factors associated with childrearing and parenting were more likely to affect the risk of these diseases than factors related to childbearing.[44] Socioeconomic factors, mental stress, behavioral factors related to parenting and childrearing in large families (poor sleep, limited leisure time, physical inactivity, increased intake of cheaper and unhealthier foods) may form the link between parenting and CVD outcomes.[45] Children are part of social networks, and the effects of social networks on the risk of stroke should be further studied.

Previous studies suggest that better healthcare insurance predicts better stroke outcomes.[46,47] However, these studies focused on the effects of healthcare insurance after stroke. Our study demonstrated that the type of healthcare insurance was significantly associated with the incidence of hemorrhagic stroke. People with URBMI and NRCMS were more likely to develop hemorrhagic stroke than those with UEBMI, which may be because healthcare payment methods are indicators of healthcare consumption such as use of local health services or hospitalization. Healthcare consumption seemed to play an important role in the risk of incident hemorrhage stroke because people with URBMI and NRCMS were more likely to have poorer health care than those with UEBMI. Higher reimbursements may lead to better health service usage and health outcomes. URBMI and NRCMS-reimbursed expenses were allocated primarily to catastrophic medical events. Lower reimbursement of medical expenses related to hypertension or diabetes mellitus, which are risk factors for stroke, imposes a heavy financial burden on users of URBMI and NRCMS. Previous studies have indicated that healthcare insurance can reduce disparities in healthcare access and health outcomes.[48,49] It is believed that the fragmentation of social healthcare insurance schemes translates into poor funding of healthcare insurance and inequitable access to financial and health protection.[50] In this respect, users of URBMI and NRCMS have a higher economic burden and less access to health care than users of UEBMI. Therefore, health policies should include strategies to overcome barriers to health care, especially for people with URBMI and NRCMS.

The study has several strengths, including a large population size; different measurements of demographic variables; analysis of lifestyle characteristics, medical records, and SES; completeness of follow-up; and the high proportion of reliable diagnosis of stroke subtypes by neuroimaging. Moreover, this study explored the association between different risk factors and stroke subtypes concomitantly, allowing assessing whether the relationship between the measured indicators and incident stroke was independent of known risk factors.

The study has some limitations. First, only participants aged ≥40 years were evaluated; therefore, the results cannot be generalized to those aged <40 years. Second, there were missing data from 2014 on education, smoking status, alcohol drinking status, physical activity, consumption of vegetables and fruits, diet, and number of children. However, we assumed that these variables were stable in 2 years, and imputed the missing values with information from 2016. Third, dietary information was collected through a self-reported questionnaire, the definition of a vegetable-based diet and former drinking was subjective, and the definition of "former smoker" and "current smoker" was only smoking status at the time of survey, which might generate bias. However, we attempted to reduce the bias by adjusting for available confounders. Fourth, there might be a risk bias if death was considered a possible competing risk in the censoring event. However, it may not have a significant effect on our results because the mortality rate was <10%. Furthermore, other factors may contribute to the development of stroke, including vascular risk factor control, obstructive sleep apnea, working conditions, psychosocial stress, compliance with medical regimens, and air pollution. These should be considered to reduce residual confounding and need to be further investigated.

CONCLUSIONS

This cohort study showed that age 50 to 59 years, primary school or no formal education, consuming fruits ≤4 days per week, plant-based diet, physical inactivity, smoking (former, current, and passive), former drinking, having >1 child, hypertension, diabetes mellitus, obesity, family history (stroke, coronary heart disease, and hypertension), and living in Northeast, Central, East, and North China increased the risk of total stroke, whereas age 60 to 69 years, consuming vegetables 3 to 4 days per week, and living with spouse or children decreased the risk of total stroke. The effects of several risk factors, except for hypertension, family history of stroke and hypertension, alcohol drinking, and diet, were different between stroke subtypes. These findings provide evidence to improve the predictive risk model for stroke and help individuals and policy makers adopt effective strategies for the primary prevention and management of stroke, consequently reducing the risk and burden of stroke.

These results underscore that only targeting traditional risk factors for stroke without incorporating programs and policies that address socioeconomic variables is not enough to reduce stroke burden, and managing health-risk behaviors is crucial to mitigate this problem. Moreover, these data support the need to implement stroke risk reduction programs and policies that incorporate conventional and socioenvironmental components. It is essential to improve stroke awareness among groups with similar socioeconomic characteristics and implement effective socioeconomic policies to reduce inequalities in health care. Therefore, screening people with conventional and socioeconomic risk factors for stroke and designing tailored preventive strategies are crucial.

ARTICLE INFORMATION

Received February 25, 2020; accepted August 24, 2020.

Affiliations

From the School of Health Policy and Management, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China (W.Q., T.G., Y.L.); Tianjin Institute of Cardiology, Second Hospital of Tianjin Medical University, Tianjin, China (W.Q.); Department of Medical Informatics, Amsterdam UMC, Amsterdam, The Netherlands (W.Q., A.A.-H., M.S.); Brigham & Women's Hospital, Harvard Medical School, Boston, MA (J.M.); Information Center, Academy of Military Medical Sciences, Beijing, China (D.Z.); National Health Commission of the People's Republic of China, Beijing, China (B.C.); and School of Public Health, Peking University Health Science Center, Beijing, People's Republic of China (L.W.).

Acknowledgments

We are grateful to the study participants, project staff, and the China National Centre for Disease Control and Prevention and its regional offices for giving access to death and disease registries, the Chinese National Health Insurance System for providing electronic access to all hospital admission data, and China Stroke Data Center members for collecting and sharing the data used in this study.

Sources of Funding

This research was funded by the National Natural Science Foundation of China (Protocol No. 71532014) and the Innovative Engineering Program on global health policy sponsored by Chinese Academy of Medical Sciences (2017-I2M-B&R-17).

Disclosures

None.

REFERENCES

1. Feigin VL, Mensah GA, Norrving B, Murray CJ, Roth GA. Atlas of the global burden of stroke (1990–2013): the GBD 2013 study. *Neuroepidemiology*. 2015;45:230–236.
2. Norrving B, Davis SM, Feigin VL, Mensah GA, Sacco RL, Varghese C. Stroke prevention worldwide-what could make it work? *Neuroepidemiology*. 2015;45:215–220.
3. Hankey GJ. Stroke. *Lancet*. 2017;389:641–654.
4. Wu S, Wu B, Liu M, Chen Z, Wang W, Anderson CS, Sandercock P, Wang Y, Huang Y, Wang L, et al. Stroke in China: advances and challenges in epidemiology, prevention, and management. *Lancet Neurol*. 2019;18:394–405.
5. National Center for Cardiovascular Disease, China. *Report on Cardiovascular Diseases in China (2018)*. Beijing, China: Encyclopedia of China Publishing House; 2019.
6. O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, Rao-Melacini P, Zhang X, Pais P, Agapay S, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. *Lancet*. 2016;388:761–775.
7. Wang J, Wen X, Li W, Li X, Wang Y, Lu W. Risk factors for stroke in the Chinese population: a systematic review and meta-analysis. *Stroke Cerebrovasc Dis*. 2017;26:509–517.
8. Chen Z, Iona A, Parish S, Chen Y, Guo Y, Bragg F, Yang L, Bian Z, Holmes MV, Lewington S, et al. Adiposity and risk of ischaemic and haemorrhagic stroke in 0.5 million Chinese men and women: a prospective cohort study. *Lancet Glob Health*. 2018;6:e630–e640.
9. Avan A, Digaleh H, Di Napoli M, Stranges S, Behrouz R, Shojaeianbabaei G, Amiri A, Tabrizi R, Mokhber N, Spence JD, et al. Socioeconomic status and stroke incidence, prevalence, mortality, and worldwide burden: an ecological analysis from the Global Burden of Disease Study 2017. *BMC Med*. 2019;17:191.
10. Jinghui Y, Huajian M, Mei L, Dan Y, Dongsheng Z. CSDC: a nationwide screening platform for stroke control and prevention in China. *Conf Proc IEEE Eng Med Biol Soc*. 2016;2016:2974–2977.
11. Guan T, Ma J, Li M, Xue T, Lan Z, Guo J, Shen Y, Chao B, Wang L, Liu Y, et al. Rapid transitions in the epidemiology of stroke and its risk factors in China from 2002 to 2013. *Neurology*. 2017;89:53–61.
12. Asplund K, Tuomilehto J, Stegmayr B, Wester PO, Tunstall-Pedoe H. Diagnostic criteria and quality control of the registration of stroke events in the MONICA project. *Acta Med Scand Suppl*. 1988;728:26–39.
13. Stroke—1989. Recommendations on stroke prevention, diagnosis, and therapy. Report of the WHO Task Force on Stroke and other Cerebrovascular Disorders. *Stroke*. 1989;20:1407–1431.
14. National Bureau of Statistics of China. *China Statistical Yearbook 2016*. Beijing: China Statistics Press; 2016. Available at: http://www.stats.gov.cn/tjsj/ndsj/2016/indexch.htm. Accessed June 19, 2019.
15. Chen C, Lu FC. The guidelines for prevention and control of overweight and obesity in Chinese adults. *Biomed Environ Sci*. 2004;17(suppl):1–36.
16. Chinese guidelines on prevention and treatment of dyslipidemia in adults. *Zhonghua Xin Xue Guan Bing Za Zhi*. 2007;35:390–419.
17. Chen L, Lin DY, Zeng D. Attributable fraction functions for censored event times. *Biometrika*. 2010;97:713–726.
18. Li B, Lou Y, Gu H, Long X, Wang T, Wei J, Wang J, Tu J, Ning X. Trends in incidence of stroke and transition of stroke subtypes in rural Tianjin China: a population-based study from 1992 to 2012. *PLoS One*. 2015;10:e0139461.
19. Yeap BB, Hyde Z, Almeida OP, Norman PE, Chubb SA, Jamrozik K, Flicker L, Hankey GJ. Lower testosterone levels predict incident stroke and transient ischemic attack in older men. *J Clin Endocrinol Metab*. 2009;94:2353–2359.
20. Hintsanen M, Kivimaki M, Elovainio M, Pulkki-Raback L, Keskivaara P, Juonala M, Raitakari OT, Keltikangas-Jarvinen L. Job strain and early atherosclerosis: the Cardiovascular Risk in Young Finns study. *Psychosom Med*. 2005;67:740–747.
21. Kubota Y, Iso H, Yamagishi K, Sawada N, Tsugane S. Daily total physical activity and incident stroke: the Japan public health center-based prospective study. *Stroke*. 2017;48:1730–1736.
22. Lancaster GI, Febbraio MA. The immunomodulating role of exercise in metabolic disease. *Trends Immunol*. 2014;35:262–269.
23. Hackshaw A, Morris JK, Boniface S, Tang JL, Milenkovic D. Low cigarette consumption and risk of coronary heart disease and stroke: meta-analysis of 141 cohort studies in 55 study reports. *BMJ*. 2018;360:j5855.
24. Rehill N, Beck CR, Yeo KR, Yeo WW. The effect of chronic tobacco smoking on arterial stiffness. *Br J Clin Pharmacol*. 2006;61:767–773.
25. Gan Y, Wu J, Li L, Zhang S, Yang T, Tan S, Mkandawire N, Zhong Y, Jiang J, Wang Z, et al. Association of smoking with risk of stroke in middle-aged and older Chinese: evidence from the China National Stroke Prevention Project. *Medicine*. 2018;97:e13260.
26. Du H, Li L, Bennett D, Guo Y, Key TJ, Bian Z, Sherliker P, Gao H, Chen Y, Yang L, et al. Fresh fruit consumption and major cardiovascular disease in China. *N Engl J Med*. 2016;374:1332–1343.
27. Hu D, Huang J, Wang Y, Zhang D, Qu Y. Fruits and vegetables consumption and risk of stroke: a meta-analysis of prospective cohort studies. *Stroke*. 2014;45:1613–1619.
28. Dauchet L, Amouyel P, Dallongeville J. Fruit and vegetable consumption and risk of stroke: a meta-analysis of cohort studies. *Neurology*. 2005;65:1193–1197.
29. Larsson SC. Dietary approaches for stroke prevention. *Stroke*. 2017;48:2905–2911.
30. Cui R, Iso H, Yamagishi K, Saito I, Kokubo Y, Inoue M, Tsugane S. Diabetes mellitus and risk of stroke and its subtypes among Japanese: the Japan public health center study. *Stroke*. 2011;42:2611–2614.
31. Chen R, Ovbiagele B, Feng W. Diabetes and stroke: epidemiology, pathophysiology, pharmaceuticals and outcomes. *Am J Med Sci*. 2016;351:380–386.
32. Bazzano LA, Gu D, Whelton MR, Wu X, Chen CS, Duan X, Chen J, Chen JC, He J. Body mass index and risk of stroke among Chinese men and women. *Ann Neurol*. 2010;67:11–20.
33. Song YM, Sung J, Davey Smith G, Ebrahim S. Body mass index and ischemic and hemorrhagic stroke: a prospective study in Korean men. *Stroke*. 2004;35:831–836.

34. Meng R, Yu C, Guo Y, Bian Z, Si J, Nie J, Yang L, Chen Y, Du H, Zhou L, et al. Early famine exposure and adult disease risk based on a 10-year prospective study of Chinese adults. *Heart*. 2020;106:213–220.
35. Wang W, Jiang B, Sun H, Ru X, Sun D, Wang L, Wang L, Jiang Y, Li Y, Wang Y, et al. Prevalence, incidence, and mortality of stroke in China: results from a nationwide population-based survey of 480 687 adults. *Circulation*. 2017;135:759–771.
36. Albert MA, Glynn RJ, Buring J, Ridker PM. Impact of traditional and novel risk factors on the relationship between socioeconomic status and incident cardiovascular events. *Circulation*. 2006;114:2619–2626.
37. Meneton P, Hoertel N, Wiernik E, Lemogne C, Ribet C, Bonenfant S, Menard J, Goldberg M, Zins M. Work environment mediates a large part of social inequalities in the incidence of several common cardiovascular risk factors: findings from the Gazel cohort. *Soc Sci Med*. 2018;216:59–66.
38. Bucholz EM, Strait KM, Dreyer RP, Geda M, Spatz ES, Bueno H, Lichtman JH, D'Onofrio G, Spertus JA, Krumholz HM. Effect of low perceived social support on health outcomes in young patients with acute myocardial infarction: results from the VIRGO (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients) study. *J Am Heart Assoc*. 2014;3:e001252. DOI: 10.1161/JAHA.114.001252.
39. Untas A, Thumma J, Rascle N, Rayner H, Mapes D, Lopes AA, Fukuhara S, Akizawa T, Morgenstern H, Robinson BM, et al. The associations of social support and other psychosocial factors with mortality and quality of life in the dialysis outcomes and practice patterns study. *Clin J Am Soc Nephrol*. 2011;6:142–152.
40. Stuller KA, Jarrett B, DeVries AC. Stress and social isolation increase vulnerability to stroke. *Exp Neurol*. 2012;233:33–39.
41. Kopp MS, Falger PR, Appels A, Szedmak S. Depressive symptomatology and vital exhaustion are differentially related to behavioral risk factors for coronary artery disease. *Psychosom Med*. 1998;60:752–758.
42. Dong JY, Zhang YH, Tong J, Qin LQ. Depression and risk of stroke: a meta-analysis of prospective studies. *Stroke*. 2012;43:32–37.
43. Hurley LL, Tizabi Y. Neuroinflammation, neurodegeneration, and depression. *Neurotox Res*. 2013;23:131–144.
44. Peters SA, Yang L, Guo Y, Chen Y, Bian Z, Millwood IY, Wang S, Yang L, Hu Y, Liu J, et al. Parenthood and the risk of cardiovascular diseases among 0.5 million men and women: findings from the China Kadoorie Biobank. *Int J Epidemiol*. 2017;46:180–189.
45. Alter G, Dribe M, Van Poppel F. Widowhood, family size, and post-reproductive mortality: a comparative analysis of three populations in nineteenth-century Europe. *Demography*. 2007;44:785–806.
46. Umberson D, Pudrovska T, Reczek C. Parenthood, childlessness, and well-being: a life course perspective. *J Marriage Fam*. 2010;72:612–629.
47. Gu HQ, Li ZX, Zhao XQ, Liu LP, Li H, Wang CJ, Yang X, Rao ZZ, Wang CX, Pan YS, et al. Insurance status and 1-year outcomes of stroke and transient ischaemic attack: a registry-based cohort study in China. *BMJ Open*. 2018;8:e021334.
48. Levy H, Meltzer D. The impact of health insurance on health. *Annu Rev Public Health*. 2008;29:399–409.
49. Freeman JD, Kadiyala S, Bell JF, Martin DP. The causal effect of health insurance on utilization and outcomes in adults: a systematic review of US studies. *Med Care*. 2008;46:1023–1032.
50. Meng Q, Fang H, Liu X, Yuan B, Xu J. Consolidating the social health insurance schemes in China: towards an equitable and efficient health system. *Lancet*. 2015;386:1484–1492.