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Distribution Differences of Risk Factors for Coronary Heart Disease and Stroke in China: Findings from the China National Stroke Screening Survey

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Keywords: Coronary heart disease, Stroke, Cardiovascular diseases, Risk factors, Heterogeneity

Abstract

Objectives: This study aimed to explore the distribution differences of common risk factors between coronary heart disease (CHD) and stroke in China.

Setting: The China National Stroke Screening Survey is a cluster sampling survey based on a nationwide general community population, adopting multi-stage stratified sampling method and covering all 31 provinces in China mainland.

Participants: Total number of 725 707 people aged 40 and above were included in the study.

Primary and secondary outcome measures: The basic demographic information, lifestyle behavior, physical examination, traditional risk factors, family history of cardiovascular disease

(CVD) and CVD events were collected. Risk factors of CHD and stroke were explored and analyzed in the whole investigated population to identify the common risk factors. Multivariate logistic regression analysis was used to analyze the distribution difference of risk factors between CHD and stroke.

Results: There were 13 variables associated with CHD and stroke, in which 11 variables revealed differences in the distribution between CHD and stroke. Family history of stroke (OR: 2.30; 95% CI, 2.15-2.45), male (OR: 1.92; 95% CI, 1.80-2.05), rural areas (OR: 1.70; 95% CI,1.60-1.80), transient ischemic attack (OR: 1.41; 95% CI, 1.30-1.54) and hypertension (OR: 1.28; 95% CI, 1.19-1.38) indicated significantly stronger association with stroke, while family history of CHD (OR: 0.25; 95% CI, 0.23-0.27), atrial fibrillation (OR: 0.60; 95% CI, 0.51-0.71), diabetes (OR: 0.76; 95% CI, 0.71-0.81), dyslipidemia (OR: 0.76; 95% CI, 0.72-0.81), smoking (OR: 0.79; 95% CI, 0.73-0.85) and overweight/obesity (OR: 0.90; 95% CI, 0.86-0.93) had closer relationship with CHD.

Conclusions: The distribution of risk factors for CHD and stroke were substantial differences. More specific prevention and control measures should be formulated according to the distribution differences of risk factors related to CVD.

Strengths and limitations of this study

The China National Stroke Screening Survey is a nationwide cross-sectional study based on general community population.

CHD and stroke had many common risk factors, while the distribution of specific risk factors between CHD and stroke were substantial differences.

More specific prevention and control measures should be formulated according to the distribution differences of risk factors related to CVD.

1 Introduction

Cardiovascular disease (CVD) is the leading cause of death in China and worldwide[1,2]. Previous studies have shown the significant regional and ethnic differences in the incidence and mortality of CVD[3-6]. For example, coronary heart disease (CHD) is the leading cause of death in most Western countries, while stroke is more common in China[4-6]. The distributional differences of specific risk factors for different CVD types may be an important reason for this phenomenon. To clarify the relationship between different risk factors and the first manifestation of CVD can help us better understand the pathophysiological mechanism of different CVD, as well as the potential benefits of controlling these risk factors.

Many previous studies have considered the CHD and stroke as a whole to explore common risk factors of both[7-9]. Only a few studies investigated the differences of risk factors between CHD and stroke in a same cohort[10-14], some of which just enrolled male or female populations[10,11], or only reported the difference of a single risk factor[12], or conducted based on a small sample size[14]. There is still lack of large sample size, representative population-based research about whether differences exist in the distribution of risk factors between CHD and stroke. The China National Stroke Screening Survey (CNSSS) is a nationwide cross-sectional study based on general community population. By analyzing the data collected from the CNSSS, this study aimed to explore the specific common risk factors of CHD and stroke and whether there are differences in the distribution of these specific risk factors between CHD and stroke.

2 Materials and Methods

2.1 Study design

The CNSSS is a cluster sampling survey based on a nationwide general community population, adopting multi-stage stratified sampling method and covering all 31 provinces in China mainland. The initial stages of CNSSS had been described in our previous publications[15-19].

In the first stage, a certain number of prefecture-level cities were selected by each province according to the different proportion of the Sixth National Population Census of China in 2010. In the second stage, one urban street and one rural town were selected from each prefecture-level city, respectively. In the third stage, residents aged 40 and above were selected as a group in a given number of urban streets and rural towns, and the response rate of each place was required to be no less than 85%. Ultimately, 828 764 subjects from 256 streets and towns participated in the survey, each of whom signed a written informed consent.

2.2 Data collection

A questionnaire survey which conducted by trained staff was performed based on the population aged 40 and above in the sampled communities and towns by adopting the unified epidemiological survey scale of CVD. The project developed a data reporting information platform, in which the information of the paper questionnaire was reported uniformly by trained staff of each sub-center. The following variables were analyzed for the present study: (1) basic demographic information: sex, age and place of residence; (2) lifestyle behavior: smoking, alcohol consumption, and exercise; (3) physical examination: blood pressure, height, weight, body mass index (BMI); (4) traditional risk factors: hypertension, diabetes, dyslipidemia, atrial fibrillation (AF), transient ischemic attack (TIA), family history of CHD or stroke; (5) CVD events: CHD, stroke.

2.3 Definition of cardiovascular diseases and risk factors

The diagnosis of CHD and stroke were confirmed by professional doctors, based on self-reported history and medical records. Blood pressure, fasting blood sugar, fasting blood lipids and BMI were measured on site for all survey subjects[19,20]. Hypertension was diagnosed by self-reported history of hypertension, or current use of anti-hypertensive drugs within 2 weeks, or elevated blood pressure (systolic pressure ≥ 140mmhg or diastolic pressure ≥ 90mmhg) in the on-site measurement[16]. Diabetes was diagnosed by self-report history of diabetes, or current use of hypoglycemic drugs, or fasting blood glucose ≥ 7.0mmol/l in the on-site measurement[17]. Dyslipidemia was diagnosed by self-reported history of dyslipidemia, or current use of lipid-lowering drugs, or the detection of one or more of the following status (total cholesterol ≥ 240 mg/dl, triglycerides ≥ 200 mg/dl, HDL < 40 mg/dl) in the on-site measurement[17]. AF was diagnosed by self-reported history of AF, or previous electrocardiogram support, or the detection of AF indicated in electrocardiogram in the on-site measurement[18]. Body mass index was calculated as weight in kilograms divided by height in meters squared. Overweight was defined as 24≤ BMI <28, and obesity was defined as BMI ≥ 28[16]. Smoking was defined as one cigarette per day for at least three consecutive months. Regular drinking was defined as drinking at least 3 times per week with the consumption of alcohol more than 100 g. Lack of exercise was defined as weekly exercise less than 3 times the intensity of moderate and above exercise ≥ 30 minutes. Exercise lack is defined as moderate or higher intensity exercise no less than 3 times per week, no less than 30 minutes each time.

2.4 Quality control

The National Health and Family Planning Commission had established a special project office responsible for the quality control, organization and coordination of the project. Firstly, this study conducted a unified training for all personnel involved in questionnaire survey, physical examination and data entry. The training course was divided into two steps below: the provincial training was responsible by the project office, and the training of participating units in the province was managed by provincial units. Secondly, the data reporting information platform could realize automatic control of the system, systematic checking of necessary items, and questionnaires with unfinished or incomplete items could not be submitted successfully. Thirdly, epidemiologists and statistical experts were organized by the project office to analyze the data reported by the sub-centers, who were responsible for checking abnormal data and returning to the sub-centers for one-by-one review.

2.5 Patient and public involvement

Patients were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

2.6 Statistical analysis

The statistical analysis was carried out in two steps. Firstly, Risk factors of CHD and stroke were explored and analyzed in the whole investigated population to identify the common risk factors. Secondly, people with both CHD and stroke were excluded, as well as those neither with CHD nor with stroke, we just took the samples only with CHD and the samples only with stroke as our analysis population, then taking CVD as dependent variables (stroke was defined as 1, whereas CHD was defined as 0) and the common risk factors as independent variables, multivariate logistic regression analysis was carried out to study the distribution difference of the common risk factors between CHD and stroke.

Descriptive analysis was performed for baseline information. Categorical variables were expressed as n (%), and continuous variables were presented in the form of mean ± standard deviation. □2 test and t test were used for univariate analysis of categorical variables and continuous variables, and the differences were statistically significant with $P<0.1$. Binary Logistic regression was utilized for multivariate analysis, the odd ratio (OR) and 95% confidence interval (CI) were calculated by backward stepwise regression, and the difference was statistically significant with $P < 0.05$. SPSS19.0 was used for all statistical analyses (SPSS Inc., Chicago, Illinois, USA).

3 Results

3.1 Basic information

A total of 828 764 permanent residents in general communities aged 40 and above completed the survey from May 2014 to April 2015. Of these, we excluded data from project areas with a response rate less than 85%, incomplete baseline information and abnormal data. Finally, 725 707 people were included in the study. The average age was 57.23±11.40 years, with males accounting for 46.73% and the rural population accounting for 52.55% of the total. All variables had sex difference except BMI. To be specific, the rates of smoking and drinking of males were significantly higher than those of females, whereas there was an opposite relationship in other variables. Furthermore, except hypertension, all variables revealed geographical difference. The proportion of smoking and drinking in rural areas was higher than that in urban areas, and the proportion of other variables in urban areas were higher than that in rural areas (Table 1).

Table 1. General Characteristics of the CNSSS

Characteristics	Total, n (%)	Sex, n (%)		Region, n (%)		*P* value for sex	*P* value for region
		female	male	urban	rural		
Age, y	57.23±11.40	57.40±11.38	57.03±11.41	57.26±11.50	57.20±11.30	< 0.001	0.029
40~	224173(30.89)	115964(30.00)	108209(31.91)	106788(31.01)	117385(30.88)	< 0.001	< 0.001
50~	213000(29.35)	115023(29.76)	97977(28.89)	101240(29.40)	111760(29.41)		
60~	172780(23.81)	93393(24.16)	79387(23.41)	79411(23.06)	93369(24.56)		
70~	86475(11.92)	46161(11.94)	40314(11.89)	42716(12.41)	43759(11.51)		
80~	29279(4.03)	16018(4.14)	13261(3.91)	14188(4.12)	15091(3.97)		
Height, cm	162.96±8.12	158.26±6.31	168.31±6.48	163.95±7.91	162.06±8.20	< 0.001	< 0.001
Weight, kg	63.63±10.04	59.94±8.87	67.83±9.63	64.69±9.99	62.66±9.96	< 0.001	< 0.001
BMI, kg/m^2	23.91±3.04	23.92±3.20	23.90±2.85	24.02±3.00	23.81±3.07	0.130	< 0.001
< 18.5	16308(2.25)	10052(2.60)	6256(1.84)	6913(2.01)	9395(2.47)	< 0.001	< 0.001
18.5~24	380043(52.37)	201371(52.09)	178672(52.68)	174900(50.79)	205143(53.99)		
24~28	264385(36.43)	136843(35.40)	127542(37.61)	131176(38.09)	133209(35.03)		
≥28	64971(8.95)	38293(9.91)	26678(7.87)	31354(9.11)	33617(8.84)		
Smoking	47997(6.61)	4163(1.08)	43834(12.92)	20223(5.87)	27774(7.30)	< 0.001	< 0.001
Regular drinking	24939(3.44)	2148(0.56)	22791(6.72)	11574(3.36)	13365(3.52)	< 0.001	0.001
Lack of exercise	59712(8.23)	33104(8.56)	26608(7.85)	31722(9.21)	27990(7.36)	< 0.001	< 0.001
Hypertension	121281(16.71)	65681(16.99)	55600(16.39)	57538(16.71)	63743(16.77)	< 0.001	0.955
Diabetes	39752(5.48)	22283(5.76)	17469(5.15)	21770(6.32)	17982(4.73)	< 0.001	< 0.001
Dyslipidemia	113159(15.59)	62817(16.25)	50342(14.84)	56793(16.55)	56186(14.78)	< 0.001	< 0.001
AF	2783(0.38)	1636(0.42)	1147(0.34)	1433(0.42)	1350(0.35)	< 0.001	< 0.001
TIA	13284(1.83)	8199(2.12)	5085(1.50)	6707(1.95)	6577(1.72)	< 0.001	< 0.001
Family history of CHD	13077(1.80)	7947(2.06)	5130(1.51)	8070(2.34)	5007(1.31)	< 0.001	< 0.001
Family history of stroke	30103(4.15)	16987(4.39)	13116(3.87)	15553(4.52)	14550(3.82)	< 0.001	< 0.001

CNSSS, China National Stroke Screening Survey; BMI, body mass index; AF, atrial fibrillation; TIA, transient ischemic attack; CHD, coronary heart disease

3.2 Common risk factors of CHD and stroke

In the univariate factor analysis, all 14 variables were associated with CHD and stroke (Table 2). After adjusting for other risk factors, 13 variables (except alcohol consumption) were associated with CHD and stroke. There was a negative correlation of males and rural population with CHD, while hypertension, family history of CHD, dyslipidemia, AF, TIA, smoking, diabetes, family history of stroke, age, lack of exercise, overweight/obesity and alcohol consumption were positively correlated with CHD. Besides, all the 13 risk factors were positively correlated with stroke (Table 3). According to the odds ratio (OR) value from high to low, Figure 1 showed the distribution of risk factors of CHD and stroke.

Table 2. Univariate analysis of risk factors for CHD and stroke

Characteristics	CHD, n (%)				Stroke, n (%)			
	Yes	No	χ^2	*P* value	Yes	No	χ^2	*P* value
Total	10654	715053			15989	709718		
Sex (male)	4125(28.72)	335023(46.85)	279.078	< 0.001	8110(50.72)	331038(46.64)	104.502	< 0.001
Region (rural)	4379(41.10)	376985(52.72)	568.386	< 0.001	8515(53.26)	372849(52.53)	3.256	0.071
Age			4657.234	< 0.001			6926.216	< 0.001
40~	687(6.45)	223486(31.25)			913(5.71)	223260(31.46)		
50~	2324(21.81)	210676(29.46)			3539(22.13)	209461(29.51)		
60~	4209(39.51)	168571(23.57)			6644(41.55)	166136(23.41)		
70~	2767(25.97)	83708(11.71)			3915(24.49)	82560(11.63)		
80~	667(6.26)	28612(4.00)			978(6.12)	28301(3.99)		
BMI			2767.767	< 0.001			2261.651	< 0.001
< 18.5	207(1.94)	16101(2.25)			322(2.01)	15986(2.25)		
18.5~24	3420(32.10)	376623(52.67)			5875(36.74)	374168(52.72)		
24~28	4588(43.06)	259797(36.33)			6841(42.79)	257544(36.29)		
≥28	2439(22.89)	62532(8.75)			2951(18.46)	62020(8.74)		
Smoking	2628(24.67)	45369(6.34)	5705.550	< 0.001	4416(27.62)	43581(6.14)	11679.211	< 0.001
Regular drinking	1551(14.56)	23388(3.27)	4030.177	< 0.001	2484(17.81)	22455(3.16)	7212.358	< 0.001
Lack of exercise	4269(40.07)	55443(7.75)	14518.060	< 0.001	6013(37.61)	53699(7.57)	18687.903	< 0.001
Hypertension	8614(80.85)	112667(15.76)	31958.204	< 0.001	13182(82.44)	108099(15.23)	50750.234	< 0.001
Diabetes	3565(33.46)	36187(5.06)	16353.881	< 0.001	4118(25.75)	35634(5.02)	12983.573	< 0.001
Dyslipidemia	6883(64.60)	106276(14.86)	19734.787	< 0.001	8982(56.18)	104177(14.68)	20458.912	< 0.001
AF	397(3.73)	2386(0.33)	3162.834	< 0.001	387(2.42)	2396(0.34)	1775.677	< 0.001
TIA	1409(13.23)	11875(1.66)	7812.480	< 0.001	2504(15.66)	10780(1.52)	17402.607	< 0.001
Family history of CHD	2762(25.92)	10315(1.44)	35557.668	< 0.001	1808(11.31)	11269(1.59)	8348.822	< 0.001
Family history of stroke	3061(28.73)	27042(3.78)	16434.360	< 0.001	6069(37.96)	24034(3.39)	47002.257	< 0.001

CHD, coronary heart disease; BMI, body mass index; AF, atrial fibrillation; TIA, transient ischemic attack

Table 3. Multivariate logistic regression analysis of risk factors for CHD and stroke

Characteristics	CHD		Stroke	
	OR (95%*CI*)	*P* value	*OR* (95%*CI*)	*P* value
Sex (male)	0.63(0.59-0.66)	< 0.001	1.18(1.14-1.23)	< 0.001
Region (rural)	0.73(0.70-0.76)	< 0.001	1.17(1.13-1.21)	< 0.001
Age	1.54(1.51-1.57)	< 0.001	1.52(1.50-1.55)	< 0.001
BMI	1.16(1.13-1.20)	< 0.001	1.03(1.00-1.05)	0.034
Smoking	1.79(1.68-1.90)	< 0.001	1.45(1.39-1.52)	< 0.001
Lack of exercise	1.37(1.31-1.43)	< 0.001	1.35(1.30-1.40)	< 0.001
Hypertension	5.83(5.49-6.18)	< 0.001	9.09(8.65-9.55)	< 0.001
Diabetes	1.76(1.68-1.84)	< 0.001	1.30(1.25-1.36)	< 0.001
Dyslipidemia	2.03(1.94-2.13)	< 0.001	1.44(1.38-1.49)	< 0.001
AF	1.98(1.76-2.24)	< 0.001	1.28(1.13-1.44)	< 0.001
TIA	1.97(1.85-2.11)	< 0.001	2.92(2.77-3.08)	< 0.001
Family history of CHD	4.89(4.63-5.17)	< 0.001	1.09(1.03-1.16)	0.004
Family history of stroke	1.60(1.52-1.68)	< 0.001	4.33(4.16-4.50)	< 0.001
Regular drinking	1.10(1.03-1.18)	0.007	……	……

CHD, coronary heart disease; BMI, body mass index; AF, atrial fibrillation; TIA, transient ischemic attack

3.3 Distribution differences of common risk factors between CHD and stroke

After the exclusion of 1,988 patients with both CHD and stroke, there were 8,666 patients with CHD and 14,001 patients with stroke separately. In multivariate logistic regression analysis, CVD was taken as the dependent variable (stroke was defined as 1, whereas CHD was defined as 0) and the 13 common risk factors were taken as independent variables. The results showed that 11 of 13 risk factors (except age and lack of exercise) revealed differences in the distribution between CHD and stroke (Table 4). The risk factors with OR>1 were more frequently detected in stroke patients, and others with OR<1 may be more frequently detected in CHD patients. The family history of stroke, male, rural area, TIA and hypertension were more closely associated with stroke, while the family history of CHD, AF, diabetes, dyslipidemia, smoking and overweight/obesity indicated stronger relationship with CHD. Figure 2 displayed the distribution differences of risk factors for stroke and CHD.

Table 4. Multivariate logistic regression analysis of common risk factors distribution between CHD and stroke

Characteristics	*OR*	95%*CI*	*P* value
Family history of stroke	2.30	2.15-2.45	< 0.001
Sex (male)	1.92	1.80-2.05	< 0.001
Region (rural)	1.70	1.60-1.80	< 0.001
TIA	1.41	1.30-1.54	< 0.001
Hypertension	1.28	1.19-1.38	< 0.001
BMI	0.90	0.86-0.93	< 0.001
Smoking	0.79	0.73-0.85	< 0.001

Dyslipidemia	0.76	0.72-0.81	< 0.001
Diabetes	0.76	0.71-0.81	< 0.001
AF	0.60	0.51-0.71	< 0.001
Family history of CHD	0.25	0.23-0.27	< 0.001

CHD, coronary heart disease; TIA, transient ischemic attack; BMI, body mass index; AF, atrial fibrillation

Subgroup analysis by gender and region showed that the distribution differences of risk factors between CHD and stroke also existed in different gender and region groups (Figure 3). The risk factors that were more closely related to stroke were the same across different genders or regions (Table 5, Table 6). Smoking and lack of exercise were more closely related to CHD than stroke in the female population, but not in the male population (Table 5). AF and lack of exercise were more closely related to CHD than stroke in rural area, but not in urban area (Table 6).

Table 5. Subgroup Analysis of Distribution Differences by gender

Characteristics	Women		Men	
	OR (95%*CI*)	*P* value	*OR* (95%*CI*)	*P* value
Family history of stroke	2.19(2.01-2.39)	< 0.001	2.44(2.20-2.71)	< 0.001
Region (rural)	1.61(1.49-1.73)	< 0.001	1.84(1.68-2.01)	< 0.001
TIA	1.35(1.21-1.51)	< 0.001	1.52(1.32-1.76)	< 0.001
Hypertension	1.20(1.08-1.32)	< 0.001	1.39(1.25-1.56)	< 0.001
BMI	0.91(0.86-0.95)	< 0.001	0.88(0.83-0.93)	< 0.001
Diabetes	0.76(0.70-0.83)	< 0.001	0.75(0.68-0.83)	< 0.001
Dyslipidemia	0.81(0.75-0.88)	< 0.001	0.71(0.65-0.77)	< 0.001
AF	0.73(0.59-0.91)	0.005	0.47(0.36-0.61)	< 0.001
Family history of CHD	0.25(0.23-0.28)	< 0.001	0.24(0.21-0.27)	< 0.001
Smoking	0.47(0.41-0.55)	< 0.001	……	……
Lack of exercise	0.92(0.85-0.99)	0.036	……	……

TIA, transient ischemic attack; BMI, body mass index; AF, atrial fibrillation; CHD, coronary heart disease

Table 6. Subgroup Analysis of Distribution Differences by region

Characteristics	Rural		Urban	
	OR (95%*CI*)	*P* value	*OR* (95%*CI*)	*P* value
Sex (male)	2.51(2.27-2.79)	< 0.001	1.56(1.43-1.70)	< 0.001
Family history of stroke	2.10(1.91-2.32)	< 0.001	2.44(2.23-2.66)	< 0.001
TIA	1.31(1.15-1.48)	< 0.001	1.51(1.34-1.70)	< 0.001
Hypertension	1.24(1.11-1.39)	< 0.001	1.32(1.19-1.45)	< 0.001
BMI	0.92(0.87-0.97)	0.002	0.87(0.83-0.92)	< 0.001
Dyslipidemia	0.77(0.71-0.84)	< 0.001	0.75(0.69-0.82)	< 0.001
Diabetes	0.73(0.66-0.80)	< 0.001	0.78(0.72-0.85)	< 0.001
Family history of CHD	0.21(0.18-0.23)	< 0.001	0.28(0.25-0.32)	< 0.001
Lack of exercise	0.88(0.81-0.96)	0.004	……	……
Smoking	0.55(0.49-0.61)	< 0.001	……	……
AF	0.38(0.30-0.48)	< 0.001	……	……

TIA, transient ischemic attack; BMI, body mass index; CHD, coronary heart disease; AF, atrial fibrillation

4 Discussion

The China National Stroke Screening Survey is a large sample size, nationwide community population-based cluster sampling survey, which can reflect the distribution of CVD and risk factors in real world. This study showed that CHD and stroke had many common risk factors, while the distribution of these risk factors between CHD and stroke were substantial differences.

4.1 Necessity of comprehensive screening and prevention of CVD in China

As revealed in the present study, there were substantial similarities in the association of risk factors with CHD and stroke, including hypertension, diabetes, dyslipidemia, AF, TIA, smoking, overweight/obesity, lack of exercise, family history of CVD, age, sex and region. An enormous amount of studies has confirmed that these traditional risk factors are related to CVD[7, 21], although the pathophysiological mechanisms leading to CVD are not identical. At present, China has a large number of high-risk groups of CVD, including 244.5 million hypertension, 113.9 million diabetes, 358.3 million dyslipidemia, and 7.7 million atrial fibrillation[22-25]. In order to reduce the disease burden caused by CVD, the Chinese government launched the screening and prevention programs for CHD and stroke[19, 26], respectively. Since CHD and stroke have many common risk factors, we believe that it is necessary to carry out comprehensive screening and prevention of CVD. We found that hypertension is the most important risk factor for both CHD and stroke. Although the latest survey shows that the awareness rate, treatment rate and control rate of hypertension in China have been improved, but compared with the developed countries is still very low[21, 22]. These results suggest that interventions for hypertension are still a top priority for CVD prevention in China.

4.2 Heterogeneity of risk factor distribution

The distribution of most risk factors involved in this study was significantly different between CHD and stroke. Family history of CVD was the most different risk factor for CHD and stroke among all risk factors. Men were more closely associated with stroke, while women were more closely associated with CHD. Geographically, stroke was more likely in rural population and CHD more likely in urban population. Among the risk factors that can be intervened, AF, dyslipidemia, diabetes, smoking, overweight/obesity were more closely related to CHD, while TIA and hypertension were more closely related to stroke.

The heterogeneity of the relationship between specific risk factors and different types of CVD may be related to the pathophysiological mechanisms of these risk factors in different types of CVD. As expected, we found that hypertension is more related to stroke, while dyslipidemia is more related to CHD, which is consistent with previous studies[11, 13, 14]. The possible reasons are that hypertension increases the risk of ischemic stroke and hemorrhagic stroke at the same time, while dyslipidemia shows the opposite effect[21]. On the pathophysiological mechanism, the strong association between hypertension and stroke might be explained by the relationship between hypertension and cerebral small vessel disease or atrial fibrillation[13, 27]. Conversely, the relationship of different lipid subtypes with ischemic and hemorrhagic stroke are different. Hypercholesterolemia increases the risk of ischemic stroke but reduces the risk of hemorrhagic stroke. Higher level of low-density lipoprotein cholesterol seems to be associated with lower risk of hemorrhagic stroke, however high-density lipoprotein cholesterol level seems to be positively associated with risk of intracerebral hemorrhage[28, 29]. In addition, diabetes and smoking were associated with ischemic stroke, but not predictive of hemorrhagic stroke[11]. This may be the reason why they are more closely related to CHD. Contrary to

expectations, atrial fibrillation is more closely associated with CHD than stroke. The possible reason is that CHD increases the risk of atrial fibrillation, while stroke does not increase the risk of atrial fibrillation[30, 31].

Elucidating the underlying mechanism for the heterogeneity of specific risk factors distribution on CVD types requires further work. Only a few studies focused on the differences of risk factors between CHD and stroke in a same cohort in the past[10-13]. There was a great heterogeneity among these studies, for example, the Women's Health Initiative Observational Study included only female and sample size is small[11], the Physicians' Health Study included only male[10], the Rotterdam study just compared gender differences in one area of the population[12], the EPIC-Norfolk Study included only three risk factors (LDL-c, systolic blood pressure and smoking)[13]. Findings in our study were consistent with those reported in EPIC-Norfolk Study and Women's Health Initiative Observational Study. The EPIC-Norfolk Study suggested that hypertension was intimately associated with stroke, and dyslipidemia showed stronger relationship with CHD[13]. Meanwhile, Women's Health Initiative Observational Study revealed that BMI, smoking, diabetes, family history of CHD and hypercholesterolemia were associated with CHD, while hypertension was related to stroke[11]. Unlike our results, the Physicians' Health Study indicated no difference in the distribution of risk factors such as hypertension, hypercholesterolemia, diabetes, smoking and physical exercise between CHD and stroke[10]. Contrary to our results, the Rotterdam study showed that females were more likely to have stroke, while males had higher risk of CHD[12]. The reason for this huge difference may be the different race, age and occupation backgrounds included in different studies. Besides, the geographical environment and climate of different countries may also play an important role[32]. Different countries should formulate corresponding prevention and control measures for CVD according to the prevalence and distribution of risk factors in their own countries.

4.3 Implications

Our results could suggest that differences may exist in the efficacy of improving specific risk factors across CVD types. The heterogeneity in the association between particular risk factors and specific CVD types demonstrated in the current study could improve the selection of high-risk patients for population-based screening programs. For example, for women with a family history of CHD, more attention should be paid to the prevention of CHD, and for men with a family history of stroke, more stroke should be prevented. In addition, the results of this study are helpful for clinical studies to select appropriate endpoint indicators. The specific types of CVD events may vary depending on the risk factors for clinical intervention. In the study of lipid lowering, the risk of CHD should be paid more attention, while the study of blood pressure lowering should pay more attention to the risk of stroke.

There are several limitations in this study. Firstly, the judgment of CVD events was mainly based on self-reported history. In order to reduce the recall bias, each CVD event should be confirmed by a specialist in cardiology or neurology to make the diagnosis as accurate as possible. Secondly, this study was a cross-sectional survey that can only indicate the correlation between risk factors and CVD, without the ability to reflect the causal relationship. However, this study has a large sample size and is based on a nationwide cluster sampling survey, which can explain the relationship between specific risk factors and CVD types to a certain extent.

5 Conclusion

Although CHD and stroke had many common risk factors, the distribution of these risk factors between CHD and stroke were substantial differences. More specific prevention and control

measures should be formulated according to the distribution differences of risk factors related to CVD.

6 Contributorship statement

LD W and YM X contributed to research design and the revision of this manuscript; YP L contributed to research design, data collection and writing of this manuscript; L Y, Y S, YS L, J L and SH S contributed to data collection and processing; AR W, L Z, Y G, CS T contributed to data collection and the revision of the manuscript; all authors read and approved the final manuscript.

7 Competing interests

None.

8 Funding

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9 Data sharing

No additional data available.

10 Acknowledgments

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11 Ethics Approval

The study was approved by the ethics committee of the First Affiliated Hospital of Zhengzhou University (2021-KY-0067-001).

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Figure Legends

Figure 1. The rank of common risk factors of CHD and stroke based on OR value.

The solid line indicates that the ranking of risk factors goes down, while the dotted line indicates that the ranking goes up.

Abbreviation: CHD = coronary heart disease; AF = atrial fibrillation; TIA = transient ischemic attack; BMI = body mass index.

Figure 2. The forest plots of distribution differences of common risk factors between CHD and stroke.

Abbreviation: TIA = transient ischemic attack; BMI = body mass index; AF = atrial fibrillation; CHD = coronary heart disease.

Figure 3. Subgroup analysis of distribution differences based on sex and region.

Abbreviation: TIA = transient ischemic attack; BMI = body mass index; AF = atrial fibrillation; CHD = coronary heart disease.

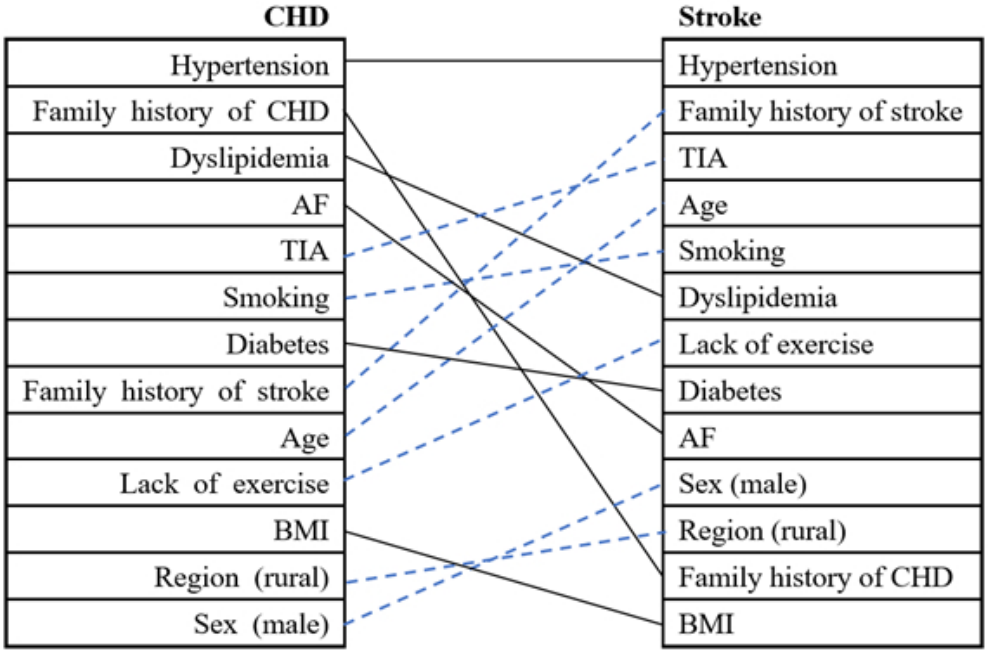


Figure 1. The rank of common risk factors of CHD and stroke based on OR value

101x67mm (144 x 144 DPI)

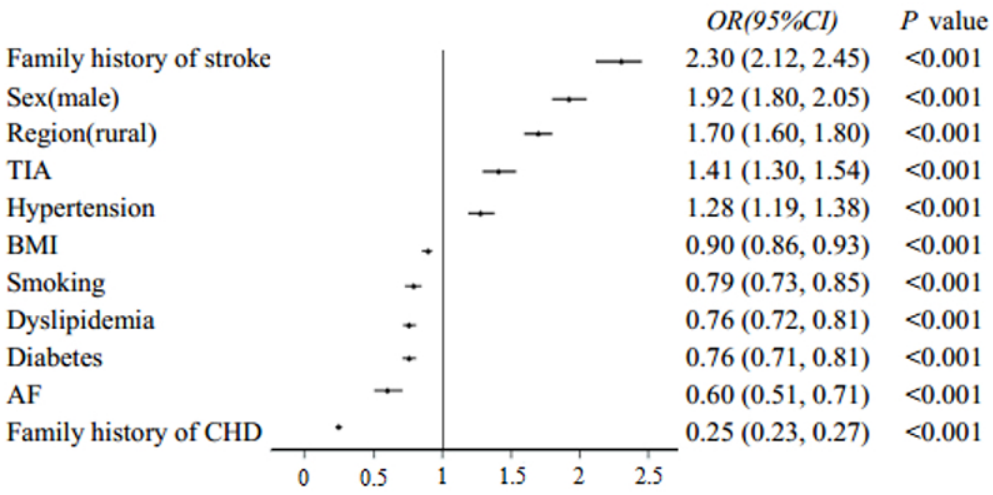
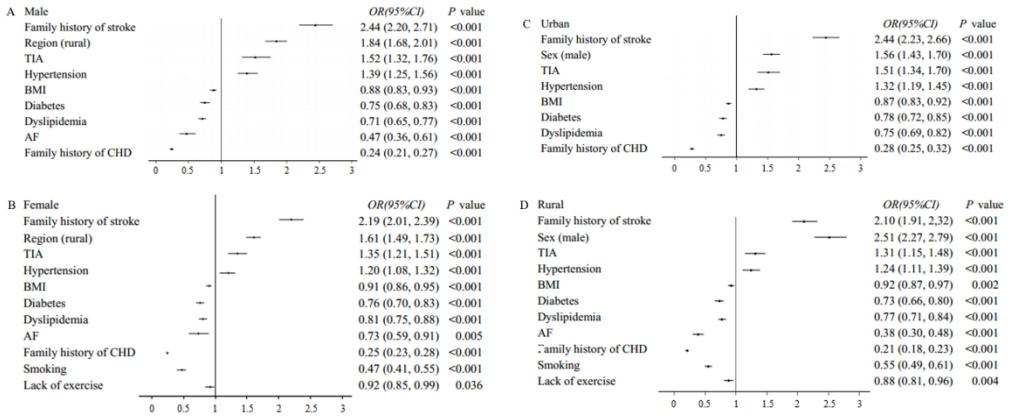


Figure 2. The forest plots of distribution differences of common risk factors between CHD and stroke

141x69mm (144 x 144 DPI)



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Distribution of Risk Factors Differ from Coronary Heart Disease and Stroke in China: A National Population Survey

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Keywords: Coronary heart disease, Stroke, Cardiovascular diseases, Risk factors, Heterogeneity

Abstract

Objectives: This study aimed to explore the distribution differences of common risk factors between coronary heart disease (CHD) and stroke in China.

Setting: The China National Stroke Screening Survey is a cluster sampling survey based on a nationwide general community population, adopting multi-stage stratified sampling method and covering all 31 provinces in China mainland.

Participants: A total number of 725 707 people aged 40 years and above were included in the study.

Primary and secondary outcome measures: The basic demographic information, lifestyle behavior, physical examination, traditional risk factors, family history of cardiovascular disease

(CVD) and CVD events were collected. Risk factors of CHD and stroke were explored and analyzed in the whole investigated population to identify the common risk factors. Multivariate logistic regression analysis was used to analyze the distribution difference of risk factors between CHD and stroke.

Results: There were 13 variables associated with CHD and stroke, in which 11 variables revealed differences in the distribution between CHD and stroke. Family history of stroke (OR: 2.30; 95% CI, 2.15-2.45), male (OR: 1.92; 95% CI, 1.80-2.05), rural areas (OR: 1.70; 95% CI,1.60-1.80), transient ischemic attack (OR: 1.41; 95% CI, 1.30-1.54) and hypertension (OR: 1.28; 95% CI, 1.19-1.38) indicated significantly stronger association with stroke, while family history of CHD (OR: 0.25; 95% CI, 0.23-0.27), atrial fibrillation (OR: 0.60; 95% CI, 0.51-0.71), diabetes (OR: 0.76; 95% CI, 0.71-0.81), dyslipidemia (OR: 0.76; 95% CI, 0.72-0.81), smoking (OR: 0.79; 95% CI, 0.73-0.85) and overweight/obesity (OR: 0.90; 95% CI, 0.86-0.93) had closer relationship with CHD.

Conclusions: The distribution of risk factors for CHD and stroke were substantial differences. More specific prevention and control measures should be formulated according to the distribution differences of risk factors related to CVD.

Strengths and limitations of this study

- The China National Stroke Screening Survey is a nationwide cross-sectional study based on general community population.
- CHD and stroke had many common risk factors, while the distribution of specific risk factors between CHD and stroke were substantial differences.
- More specific prevention and control measures should be formulated according to the distribution differences of risk factors related to CVD.

1 Introduction

Cardiovascular disease (CVD) is the leading cause of death in China and worldwide[1,2]. Previous studies have shown the significant regional and ethnic differences in the incidence and mortality of CVD[3-6]. For example, coronary heart disease (CHD) is the leading cause of death in most Western countries, while stroke is more common in China[4-6]. The distributional differences of specific risk factors for different CVD types may be an important reason for this phenomenon. To clarify the relationship between different risk factors and the first manifestation of CVD can help us better understand the pathophysiological mechanism of different CVD, as well as the potential benefits of controlling these risk factors.

Many previous studies have considered the CHD and stroke as a whole to explore common risk factors of both[7-9]. Only a few studies investigated the differences of risk factors between CHD and stroke in a same cohort[10-14], some of which just enrolled male or female populations[10,11], or only reported the difference of a single risk factor[12], or conducted based on a small sample size[14]. There is still lack of large sample size, representative population-based research about whether differences exist in the distribution of risk factors between CHD and stroke. The China National Stroke Screening Survey (CNSSS) is a nationwide cross-sectional study based on general community population. By analyzing the data collected from the CNSSS, this study aimed to explore the specific common risk factors of CHD and stroke and whether there are differences in the distribution of these specific risk factors between CHD and stroke.

2 Materials and Methods

2.1 Study design

The CNSSS is a cluster sampling survey based on a nationwide general community population, adopting multi-stage stratified sampling method and covering all 31 provinces in China mainland. The initial stages of CNSSS had been described in our previous publications[15-19].

The CNSSS used a third-stage stratified cluster sampling method. In the first stage, 128 prefecture-level cities were selected by 31 provinces according to the different proportion of the Sixth National Population Census of China in 2010. In the second stage, one urban street and one rural town were selected from each prefecture-level city, respectively. In the third stage, an urban community and a rural village were selected from each urban street and rural town. All residents aged 40 years or older were surveyed during the primary screening, and the response rate of each place was required to be no less than 85%. Ultimately, 828 764 subjects from 256 communities and villages participated in the survey, each of whom signed a written informed consent.

2.2 Data collection

A questionnaire survey which conducted by trained staff was performed based on the population aged 40 and above in the sampled communities and towns by adopting the unified epidemiological survey scale of CVD. The project developed a data reporting information platform, in which the information of the paper questionnaire was reported uniformly by trained staff of each sub-center. The following variables were analyzed for the present study: (1) basic demographic information: sex, age and place of residence; (2) lifestyle behavior: smoking, alcohol consumption, and exercise; (3) physical examination: blood pressure, height, weight, body mass index (BMI); (4) traditional risk factors: hypertension, diabetes, dyslipidemia, atrial fibrillation (AF), transient ischemic attack (TIA), family history of CHD or stroke; (5) CVD events: CHD, stroke.

2.3 Definition of cardiovascular diseases and risk factors

Stroke was diagnosed by a combination of self-reported history, medical records and the judgment of professional doctors according to WHO criteria. The diagnosis of CHD included history of angina pectoris, myocardial infarction, as well as previous history of coronary artery bypass grafting or stent implantation, and be confirmed by a specialist. Blood pressure, fasting blood sugar, fasting blood lipids and BMI were measured on site for all survey subjects[19,20]. Hypertension was diagnosed by self-reported history of hypertension, or current use of anti-hypertensive drugs within 2 weeks, or elevated blood pressure (systolic pressure ≥ 140mmhg or diastolic pressure ≥ 90mmhg) in the on-site measurement[16]. Diabetes was diagnosed by self-report history of diabetes, or current use of hypoglycemic drugs, or fasting blood glucose ≥ 7.0mmol/l in the on-site measurement[17]. Dyslipidemia was diagnosed by self-reported history of dyslipidemia, or current use of lipid-lowering drugs, or the detection of one or more of the following status (total cholesterol ≥ 240 mg/dl, triglycerides ≥ 200 mg/dl, HDL < 40 mg/dl) in the on-site measurement[17]. AF was diagnosed by self-reported history of AF, or previous electrocardiogram support, or the detection of AF indicated in electrocardiogram in the on-site measurement[18]. Body mass index was calculated as weight in kilograms divided by height in meters squared. Overweight was defined as 24≤ BMI <28, and obesity was defined as BMI ≥ 28[16]. Smoking was defined as one cigarette per day for at least three consecutive months. Regular drinking was defined as drinking at least 3 times per week with the consumption of alcohol more than 100 g. Lack of exercise was defined as weekly exercise less than 3 times the intensity of moderate and above exercise ≥ 30 minutes. Exercise lack is defined as moderate or higher intensity exercise no less than 3 times per week, no less than 30 minutes each time.

2.4 Quality control

The National Health and Family Planning Commission had established a special project office responsible for the quality control, organization and coordination of the project. Firstly, this study conducted a unified training for all personnel involved in questionnaire survey, physical examination and data entry. The training course was divided into two steps below: the provincial training was responsible by the project office, and the training of participating units in the province was managed by provincial units. In the on-site survey, each sub-center had a trained staff, usually a neurologist, responsible for the review and reporting of data. Secondly, the data reporting information platform could realize automatic control of the system, systematic checking of necessary items, and questionnaires with unfinished or incomplete items could not be submitted successfully. Thirdly, epidemiologists and statistical experts were organized by the project office to analyze the data reported by the sub-centers, who were responsible for checking abnormal data and returning to the sub-centers for one-by-one review.

2.5 Patient and public involvement

Patients were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

2.6 Statistical analysis

The statistical analysis was carried out in two steps. Firstly, Risk factors of CHD and stroke were explored and analyzed in the whole investigated population to identify the common risk factors. Secondly, people with both CHD and stroke were excluded, as well as those neither with CHD nor with stroke, we just took the samples only with CHD and the samples only with stroke as our analysis population, then taking CVD as dependent variables (stroke was defined as 1, whereas CHD was defined as 0) and the common risk factors as independent variables, multivariate logistic regression analysis was carried out to study the distribution difference of the common risk factors between CHD and stroke.

Descriptive analysis was performed for baseline information. Categorical variables were expressed as n (%), and continuous variables were presented in the form of mean ± standard deviation. 2 test and t test were used for univariate analysis of categorical variables and continuous variables, and the differences were statistically significant with $P<0.1$. Binary Logistic regression was utilized for multivariate analysis, the odd ratio (OR) and 95% confidence interval (CI) were calculated by backward stepwise regression, and the difference was statistically significant with $P < 0.05$. SPSS19.0 was used for all statistical analyses (SPSS Inc., Chicago, Illinois, USA).

3 Results

3.1 Basic information

A total of 828 764 permanent residents in general communities aged 40 and above completed the survey from May 2014 to April 2015. Of these, we excluded data from project areas with a response rate less than 85%, incomplete baseline information and abnormal data. Finally, 725 707 people were included in the study. The average age was 57.23±11.40 years, with males accounting for 46.73% and the rural population accounting for 52.55% of the total. All variables had sex difference except BMI. To be specific, the rates of smoking and drinking of males were significantly higher than those of females, whereas there was an opposite relationship in other variables. Furthermore, except

hypertension, all variables revealed geographical difference. The proportion of smoking and drinking in rural areas was higher than that in urban areas, and the proportion of other variables in urban areas were higher than that in rural areas (Table 1).

Table 1. General Characteristics of the CNSSS

Characteristics	Total, n (%)	Sex, n (%)		Region, n (%)		*P* value for sex	*P* value for region
		female	male	urban	rural		
Age, y	57.23±11.40	57.40±11.38	57.03±11.41	57.26±11.50	57.20±11.30	< 0.001	0.029
40~	224173(30.89)	115964(30.00)	108209(31.91)	106788(31.01)	117385(30.83)	< 0.001	< 0.001
50~	213000(29.35)	115023(29.76)	97977(28.89)	101240(29.40)	111760(29.21)		
60~	172780(23.81)	93393(24.16)	79387(23.41)	79411(23.06)	93369(24.41)		
70~	86475(11.92)	46161(11.94)	40314(11.89)	42716(12.41)	43759(11.44)		
80~	29279(4.03)	16018(4.14)	13261(3.91)	14188(4.12)	15091(3.94)		
Height, cm	162.96±8.12	158.26±6.31	168.31±6.48	163.95±7.91	162.06±8.20	< 0.001	< 0.001
Weight, kg	63.63±10.04	59.94±8.87	67.83±9.63	64.69±9.99	62.66±9.96	< 0.001	< 0.001
BMI, kg/m^2	23.91±3.04	23.92±3.20	23.90±2.85	24.02±3.00	23.81±3.07	0.130	< 0.001
< 18.5	16308(2.25)	10052(2.60)	6256(1.84)	6913(2.01)	9395(2.46)	< 0.001	< 0.001
18.5~24	380043(52.37)	201371(52.09)	178672(52.68)	174900(50.79)	205143(53.59)		
24~28	264385(36.43)	136843(35.40)	127542(37.61)	131176(38.09)	133209(34.83)		
≥28	64971(8.95)	38293(9.91)	26678(7.87)	31354(9.11)	33617(8.82)		
Smoking	47997(6.61)	4163(1.08)	43834(12.92)	20223(5.87)	27774(7.26)	< 0.001	< 0.001
Regular drinking	24939(3.44)	2148(0.56)	22791(6.72)	11574(3.36)	13365(3.50)	< 0.001	0.001
Lack of exercise	59712(8.23)	33104(8.56)	26608(7.85)	31722(9.21)	27990(7.34)	< 0.001	< 0.001
Hypertension	121281(16.71)	65681(16.99)	55600(16.39)	57538(16.71)	63743(16.71)	< 0.001	0.955
Diabetes	39752(5.48)	22283(5.76)	17469(5.15)	21770(6.32)	17982(4.71)	< 0.001	< 0.001
Dyslipidemia	113159(15.59)	62817(16.25)	50342(14.84)	56793(16.55)	56186(14.73)	< 0.001	< 0.001
AF	2783(0.38)	1636(0.42)	1147(0.34)	1433(0.42)	1350(0.35)	< 0.001	< 0.001
TIA	13284(1.83)	8199(2.12)	5085(1.50)	6707(1.95)	6577(1.72)	< 0.001	< 0.001
Family history of CHD	13077(1.80)	7947(2.06)	5130(1.51)	8070(2.34)	5007(1.31)	< 0.001	< 0.001
Family history of stroke	30103(4.15)	16987(4.39)	13116(3.87)	15553(4.52)	14550(3.82)	< 0.001	< 0.001

CNSSS, China National Stroke Screening Survey; BMI, body mass index; AF, atrial fibrillation; TIA, transient ischemic attack; CHD, coronary heart disease

3.2 Common risk factors of CHD and stroke

In the univariate factor analysis, all 14 variables were associated with CHD and stroke (Table 2). After adjusting for other risk factors, 13 variables (except alcohol consumption) were associated with CHD and stroke. There was a negative correlation of males and rural population with CHD, while hypertension, family history of CHD, dyslipidemia, AF, TIA, smoking, diabetes, family history of stroke, age, lack of exercise, overweight/obesity and alcohol consumption were positively correlated with CHD. Besides, all the 13 risk factors were positively correlated with stroke (Table 3). According to the odds ratio (OR) value from high to low, Figure 1 showed the distribution of risk factors of CHD and stroke.

Table 2. Univariate analysis of risk factors for CHD and stroke

Characteristics	CHD, n (%)				Stroke, n (%)			
	Yes	No	χ^2	*P* value	Yes	No	χ^2	*P* value
Total	10654	715053			15989	709718		
Sex (male)	4125(28.72)	335023(46.85)	279.078	< 0.001	8110(50.72)	331038(46.64)	104.502	< 0.001
Region (rural)	4379(41.10)	376985(52.72)	568.386	< 0.001	8515(53.26)	372849(52.53)	3.256	0.071
Age			4657.234	< 0.001			6926.216	< 0.001
40~	687(6.45)	223486(31.25)			913(5.71)	223260(31.46)		
50~	2324(21.81)	210676(29.46)			3539(22.13)	209461(29.51)		
60~	4209(39.51)	168571(23.57)			6644(41.55)	166136(23.41)		
70~	2767(25.97)	83708(11.71)			3915(24.49)	82560(11.63)		
80~	667(6.26)	28612(4.00)			978(6.12)	28301(3.99)		
BMI			2767.767	< 0.001			2261.651	< 0.001
< 18.5	207(1.94)	16101(2.25)			322(2.01)	15986(2.25)		
18.5~24	3420(32.10)	376623(52.67)			5875(36.74)	374168(52.72)		
24~28	4588(43.06)	259797(36.33)			6841(42.79)	257544(36.29)		
≥28	2439(22.89)	62532(8.75)			2951(18.46)	62020(8.74)		
Smoking	2628(24.67)	45369(6.34)	5705.550	< 0.001	4416(27.62)	43581(6.14)	11679.211	< 0.001
Regular drinking	1551(14.56)	23388(3.27)	4030.177	< 0.001	2484(17.81)	22455(3.16)	7212.358	< 0.001
Lack of exercise	4269(40.07)	55443(7.75)	14518.060	< 0.001	6013(37.61)	53699(7.57)	18687.903	< 0.001
Hypertension	8614(80.85)	112667(15.76)	31958.204	< 0.001	13182(82.44)	108099(15.23)	50750.234	< 0.001
Diabetes	3565(33.46)	36187(5.06)	16353.881	< 0.001	4118(25.75)	35634(5.02)	12983.573	< 0.001
Dyslipidemia	6883(64.60)	106276(14.86)	19734.787	< 0.001	8982(56.18)	104177(14.68)	20458.912	< 0.001
AF	397(3.73)	2386(0.33)	3162.834	< 0.001	387(2.42)	2396(0.34)	1775.677	< 0.001
TIA	1409(13.23)	11875(1.66)	7812.480	< 0.001	2504(15.66)	10780(1.52)	17402.607	< 0.001
Family history of CHD	2762(25.92)	10315(1.44)	35557.668	< 0.001	1808(11.31)	11269(1.59)	8348.822	< 0.001
Family history of stroke	3061(28.73)	27042(3.78)	16434.360	< 0.001	6069(37.96)	24034(3.39)	47002.257	< 0.001

CHD, coronary heart disease; BMI, body mass index; AF, atrial fibrillation; TIA, transient ischemic attack

Table 3. Multivariate logistic regression analysis of risk factors for CHD and stroke

Characteristics	CHD		Stroke	
	OR (95%*CI*)	*P* value	*OR* (95%*CI*)	*P* value
Sex (male)	0.63(0.59-0.66)	< 0.001	1.18(1.14-1.23)	< 0.001
Region (rural)	0.73(0.70-0.76)	< 0.001	1.17(1.13-1.21)	< 0.001
Age	1.54(1.51-1.57)	< 0.001	1.52(1.50-1.55)	< 0.001
BMI	1.16(1.13-1.20)	< 0.001	1.03(1.00-1.05)	0.034
Smoking	1.79(1.68-1.90)	< 0.001	1.45(1.39-1.52)	< 0.001
Lack of exercise	1.37(1.31-1.43)	< 0.001	1.35(1.30-1.40)	< 0.001
Hypertension	5.83(5.49-6.18)	< 0.001	9.09(8.65-9.55)	< 0.001
Diabetes	1.76(1.68-1.84)	< 0.001	1.30(1.25-1.36)	< 0.001
Dyslipidemia	2.03(1.94-2.13)	< 0.001	1.44(1.38-1.49)	< 0.001
AF	1.98(1.76-2.24)	< 0.001	1.28(1.13-1.44)	< 0.001
TIA	1.97(1.85-2.11)	< 0.001	2.92(2.77-3.08)	< 0.001
Family history of CHD	4.89(4.63-5.17)	< 0.001	1.09(1.03-1.16)	0.004
Family history of stroke	1.60(1.52-1.68)	< 0.001	4.33(4.16-4.50)	< 0.001
Regular drinking	1.10(1.03-1.18)	0.007	……	……

CHD, coronary heart disease; BMI, body mass index; AF, atrial fibrillation; TIA, transient ischemic attack

3.3 Distribution differences of common risk factors between CHD and stroke

After the exclusion of 1,988 patients with both CHD and stroke, there were 8,666 patients with CHD and 14,001 patients with stroke separately. In multivariate logistic regression analysis, CVD was taken as the dependent variable (stroke was defined as 1, whereas CHD was defined as 0) and the 13 common risk factors were taken as independent variables. The results showed that 11 of 13 risk factors (except age and lack of exercise) revealed differences in the distribution between CHD and stroke (Table 4). The risk factors with OR>1 were more frequently detected in stroke patients, and others with OR<1 may be more frequently detected in CHD patients. The family history of stroke, male, rural area, TIA and hypertension were more closely associated with stroke, while the family history of CHD, AF, diabetes, dyslipidemia, smoking and overweight/obesity indicated stronger relationship with CHD. Figure 2 displayed the distribution differences of risk factors for stroke and CHD.

Table 4. Multivariate logistic regression analysis of common risk factors distribution between CHD and stroke

Characteristics	*OR*	95%*CI*	*P* value
Family history of stroke	2.30	2.15-2.45	< 0.001
Sex (male)	1.92	1.80-2.05	< 0.001
Region (rural)	1.70	1.60-1.80	< 0.001
TIA	1.41	1.30-1.54	< 0.001
Hypertension	1.28	1.19-1.38	< 0.001
BMI	0.90	0.86-0.93	< 0.001
Smoking	0.79	0.73-0.85	< 0.001

Dyslipidemia	0.76	0.72-0.81	< 0.001
Diabetes	0.76	0.71-0.81	< 0.001
AF	0.60	0.51-0.71	< 0.001
Family history of CHD	0.25	0.23-0.27	< 0.001

CHD, coronary heart disease; TIA, transient ischemic attack; BMI, body mass index; AF, atrial fibrillation

Subgroup analysis by gender and region showed that the distribution differences of risk factors between CHD and stroke also existed in different gender and region groups (Figure 3). The risk factors that were more closely related to stroke were the same across different genders or regions (Table 5, Table 6). Smoking and lack of exercise were more closely related to CHD than stroke in the female population, but not in the male population (Table 5). AF and lack of exercise were more closely related to CHD than stroke in rural area, but not in urban area (Table 6).

Table 5. Subgroup Analysis of Distribution Differences by gender

Characteristics	Women		Men	
	OR (95%*CI*)	*P* value	*OR* (95%*CI*)	*P* value
Family history of stroke	2.19(2.01-2.39)	< 0.001	2.44(2.20-2.71)	< 0.001
Region (rural)	1.61(1.49-1.73)	< 0.001	1.84(1.68-2.01)	< 0.001
TIA	1.35(1.21-1.51)	< 0.001	1.52(1.32-1.76)	< 0.001
Hypertension	1.20(1.08-1.32)	< 0.001	1.39(1.25-1.56)	< 0.001
BMI	0.91(0.86-0.95)	< 0.001	0.88(0.83-0.93)	< 0.001
Diabetes	0.76(0.70-0.83)	< 0.001	0.75(0.68-0.83)	< 0.001
Dyslipidemia	0.81(0.75-0.88)	< 0.001	0.71(0.65-0.77)	< 0.001
AF	0.73(0.59-0.91)	0.005	0.47(0.36-0.61)	< 0.001
Family history of CHD	0.25(0.23-0.28)	< 0.001	0.24(0.21-0.27)	< 0.001
Smoking	0.47(0.41-0.55)	< 0.001	……	……
Lack of exercise	0.92(0.85-0.99)	0.036	……	……

TIA, transient ischemic attack; BMI, body mass index; AF, atrial fibrillation; CHD, coronary heart disease

Table 6. Subgroup Analysis of Distribution Differences by region

Characteristics	Rural		Urban	
	OR (95%*CI*)	*P* value	*OR* (95%*CI*)	*P* value
Sex (male)	2.51(2.27-2.79)	< 0.001	1.56(1.43-1.70)	< 0.001
Family history of stroke	2.10(1.91-2.32)	< 0.001	2.44(2.23-2.66)	< 0.001
TIA	1.31(1.15-1.48)	< 0.001	1.51(1.34-1.70)	< 0.001
Hypertension	1.24(1.11-1.39)	< 0.001	1.32(1.19-1.45)	< 0.001
BMI	0.92(0.87-0.97)	0.002	0.87(0.83-0.92)	< 0.001
Dyslipidemia	0.77(0.71-0.84)	< 0.001	0.75(0.69-0.82)	< 0.001
Diabetes	0.73(0.66-0.80)	< 0.001	0.78(0.72-0.85)	< 0.001
Family history of CHD	0.21(0.18-0.23)	< 0.001	0.28(0.25-0.32)	< 0.001
Lack of exercise	0.88(0.81-0.96)	0.004	……	……
Smoking	0.55(0.49-0.61)	< 0.001	……	……
AF	0.38(0.30-0.48)	< 0.001	……	……

TIA, transient ischemic attack; BMI, body mass index; CHD, coronary heart disease; AF, atrial fibrillation

4 Discussion

The China National Stroke Screening Survey is a large sample size, nationwide community population-based cluster sampling survey, which can reflect the distribution of CVD and risk factors in real world. This study showed that CHD and stroke had many common risk factors, while the distribution of these risk factors between CHD and stroke were substantial differences.

4.1 Necessity of comprehensive screening and prevention of CVD in China

As revealed in the present study, there were substantial similarities in the association of risk factors with CHD and stroke, including hypertension, diabetes, dyslipidemia, AF, TIA, smoking, overweight/obesity, lack of exercise, family history of CVD, age, sex and region. An enormous amount of studies has confirmed that these traditional risk factors are related to CVD[7,21], although the pathophysiological mechanisms leading to CVD are not identical. At present, China has a large number of high-risk groups of CVD, including 244.5 million hypertension, 113.9 million diabetes, 358.3 million dyslipidemia, and 7.7 million atrial fibrillation[22-25]. In order to reduce the disease burden caused by CVD, the Chinese government launched the screening and prevention programs for CHD and stroke[19,26], respectively. Since CHD and stroke have many common risk factors, we believe that it is necessary to carry out comprehensive screening and prevention of CVD. We found that hypertension is the most important risk factor for both CHD and stroke. Although the latest survey shows that the awareness rate, treatment rate and control rate of hypertension in China have been improved, but compared with the developed countries is still very low[21,22]. These results suggest that interventions for hypertension are still a top priority for CVD prevention in China.

4.2 Heterogeneity of risk factor distribution

The distribution of most risk factors involved in this study was significantly different between CHD and stroke. Family history of CVD was the most different risk factor for CHD and stroke among all risk factors. Men were more closely associated with stroke, while women were more closely associated with CHD. Geographically, stroke was more likely in rural population and CHD more likely in urban population. Among the risk factors that can be intervened, AF, dyslipidemia, diabetes, smoking, overweight/obesity were more closely related to CHD, while TIA and hypertension were more closely related to stroke.

The heterogeneity of the relationship between specific risk factors and different types of CVD may be related to the pathophysiological mechanisms of these risk factors in different types of CVD. As expected, we found that hypertension is more related to stroke, while dyslipidemia is more related to CHD, which is consistent with previous studies[11,13,14]. The possible reasons are that hypertension increases the risk of ischemic stroke and hemorrhagic stroke at the same time, while dyslipidemia shows the opposite effect[21]. On the pathophysiological mechanism, the strong association between hypertension and stroke might be explained by the relationship between hypertension and cerebral small vessel disease or atrial fibrillation[13,27]. Conversely, the relationship of different lipid subtypes with ischemic and hemorrhagic stroke are different. Hypercholesterolemia increases the risk of ischemic stroke but reduces the risk of hemorrhagic stroke. Higher level of low-density lipoprotein cholesterol seems to be associated with lower risk of hemorrhagic stroke, however high-density lipoprotein cholesterol level seems to be positively associated with risk of intracerebral hemorrhage[28,29]. In addition, diabetes and smoking were associated with ischemic stroke, but not predictive of hemorrhagic stroke[11]. This may be the reason why they are more closely related to

CHD. Contrary to expectations, atrial fibrillation is more closely associated with CHD than stroke. The possible reason is that CHD increases the risk of atrial fibrillation, while stroke does not increase the risk of atrial fibrillation[30,31].

Elucidating the underlying mechanism for the heterogeneity of specific risk factors distribution on CVD types requires further work. Only a few studies focused on the differences of risk factors between CHD and stroke in a same cohort in the past[10-13]. There was a great heterogeneity among these studies, for example, the Women's Health Initiative Observational Study included only female and sample size is small[11], the Physicians' Health Study included only male[10], the Rotterdam study just compared gender differences in one area of the population[12], the EPIC-Norfolk Study included only three risk factors (LDL-c, systolic blood pressure and smoking) [13]. Findings in our study were consistent with those reported in EPIC-Norfolk Study and Women's Health Initiative Observational Study. The EPIC-Norfolk Study suggested that hypertension was intimately associated with stroke, and dyslipidemia showed stronger relationship with CHD[13]. Meanwhile, Women's Health Initiative Observational Study revealed that BMI, smoking, diabetes, family history of CHD and hypercholesterolemia were associated with CHD, while hypertension was related to stroke[11]. Unlike our results, the Physicians' Health Study indicated no difference in the distribution of risk factors such as hypertension, hypercholesterolemia, diabetes, smoking and physical exercise between CHD and stroke[10]. Contrary to our results, the Rotterdam study showed that females were more likely to have stroke, while males had higher risk of CHD[12]. The reason for this huge difference may be the different race, age and occupation backgrounds included in different studies. Besides, the geographical environment and climate of different countries may also play an important role[32]. Different countries should formulate corresponding prevention and control measures for CVD according to the prevalence and distribution of risk factors in their own countries.

4.3 Implications

Our results could suggest that differences may exist in the efficacy of improving specific risk factors across CVD types. The heterogeneity in the association between particular risk factors and specific CVD types demonstrated in the current study could improve the selection of high-risk patients for population-based screening programs. For example, for women with a family history of CHD, more attention should be paid to the prevention of CHD, and for men with a family history of stroke, more stroke should be prevented. In addition, the results of this study are helpful for clinical studies to select appropriate endpoint indicators. Heterogeneity in the definitions of composite endpoints may lead to different results and conclusions on the efficacy of study interventions and could lead to over- or underestimation of the effect on specific CVD types. The specific types of CVD events may vary depending on the risk factors for clinical intervention. In the study of lipid lowering, the risk of CHD should be paid more attention, while the study of blood pressure lowering should pay more attention to the risk of stroke.

There are several limitations in this study. Firstly, the judgment of CVD events was mainly based on self-reported history. In order to reduce the recall bias, each CVD event should be confirmed by a specialist in cardiology or neurology to make the diagnosis as accurate as possible. Secondly, this study was a cross-sectional survey that can only indicate the correlation between risk factors and CVD, without the ability to reflect the causal relationship. However, this study has a large sample size and is based on a nationwide cluster sampling survey, which can explain the relationship between specific risk factors and CVD types to a certain extent.

5 Conclusion

Although CHD and stroke had many common risk factors, the distribution of these risk factors between CHD and stroke were substantial differences. More specific prevention and control measures should be formulated according to the distribution differences of risk factors related to CVD.

6 Contributorship statement

LD W and YM X contributed to research design and the revision of this manuscript; YP L contributed to research design, data collection and writing of this manuscript; L Y, Y S, YS L, J L and SH S contributed to data collection and processing; AR W, L Z, Y G, CS T contributed to data collection and the revision of the manuscript; all authors read and approved the final manuscript.

7 Competing interests

None.

8 Funding

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9 Data sharing

The data are available upon reasonable request from the corresponding authors.

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11 Ethics Approval

The study was approved by the ethics committee of the First Affiliated Hospital of Zhengzhou University (2021-KY-0067-001).

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Figure Legends

Figure 1. The rank of common risk factors of CHD and stroke based on OR value.

The solid line indicates that the ranking of risk factors goes down, while the dotted line indicates that the ranking goes up.

Abbreviation: CHD = coronary heart disease; AF = atrial fibrillation; TIA = transient ischemic attack; BMI = body mass index.

Figure 2. The forest plots of distribution differences of common risk factors between CHD and stroke.

Abbreviation: TIA = transient ischemic attack; BMI = body mass index; AF = atrial fibrillation; CHD = coronary heart disease. The risk factors with OR>1 indicates a closer association with stroke, and others with OR<1 indicates a closer association with CHD.

Figure 3. Subgroup analysis of distribution differences based on sex and region.

Abbreviation: TIA = transient ischemic attack; BMI = body mass index; AF = atrial fibrillation; CHD = coronary heart disease. The risk factors with OR>1 indicates a closer association with stroke, and others with OR<1 indicates a closer association with CHD.

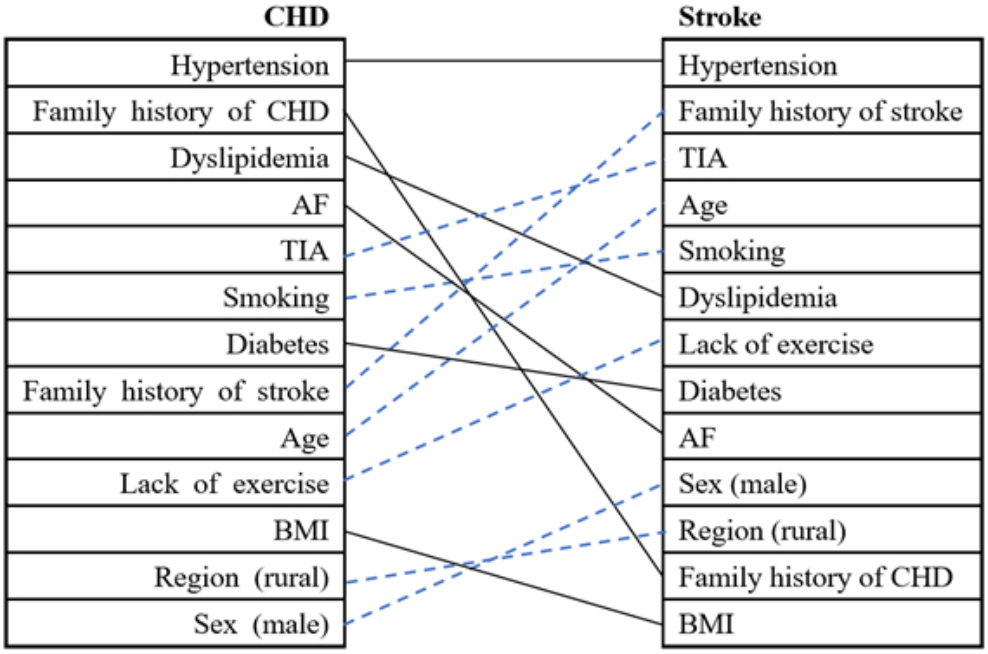


Figure 1. The rank of common risk factors of CHD and stroke based on OR value

101x67mm (144 x 144 DPI)

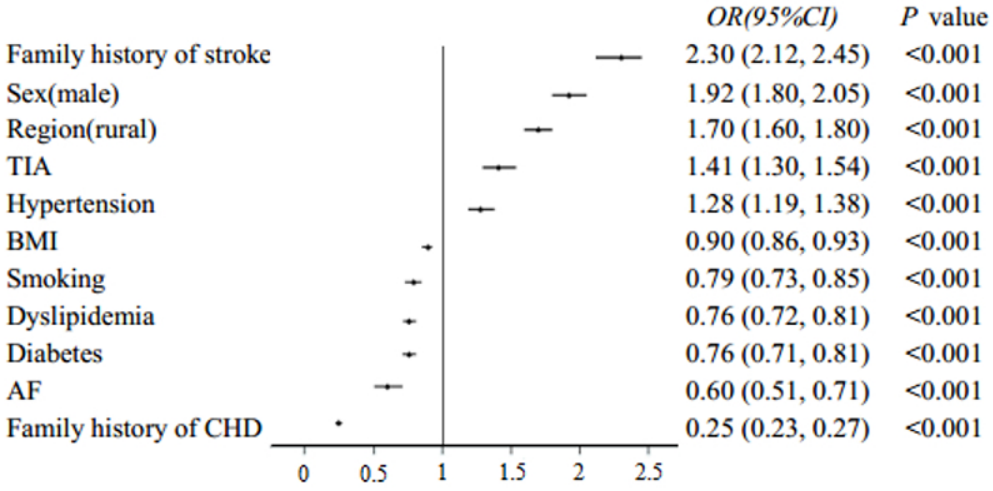
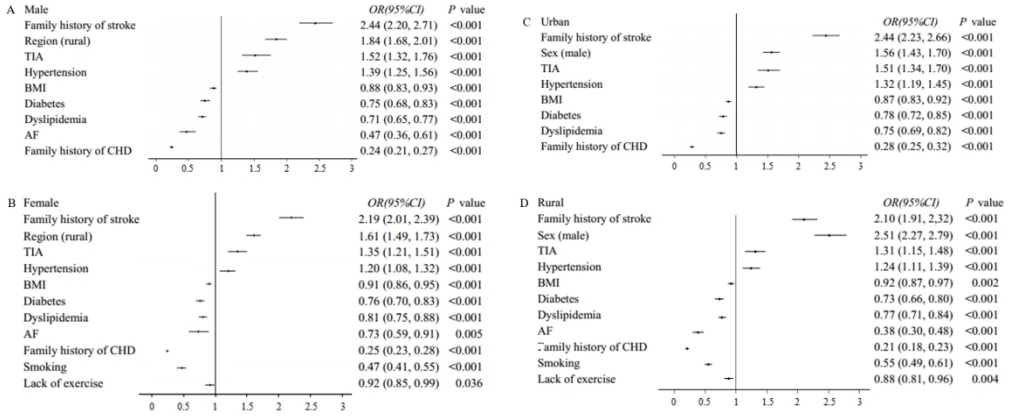


Figure 2. The forest plots of distribution differences of common risk factors between CHD and stroke

141x69mm (144 x 144 DPI)



367x150mm (144 x 144 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Lines 45-47
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Lines 56-63
Objectives	3	State specific objectives, including any prespecified hypotheses	Lines 71-73
Methods			
Study design	4	Present key elements of study design early in the paper	Lines 76-78
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Lines 88-96
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Lines 79-86
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Lines 98-118
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Lines 98-118
Bias	9	Describe any efforts to address potential sources of bias	Lines 120-131
Study size	10	Explain how the study size was arrived at	Lines 79-85

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Lines 144-147
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Lines 136-150
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Lines 153-156
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Lines 156-162
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	Line 163
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Lines 166-191
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Lines 192-202
Discussion			
Key results	18	Summarise key results with reference to study objectives	Lines 204-207
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Lines 281-287
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Lines 208-287
Generalisability	21	Discuss the generalisability (external validity) of the study results	Lines 283-285
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Lines 301-304

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.