


# BMJ Open Prevalence of stroke and associated risk factors: a population-based cross-sectional study from the Qinghai-Tibet Plateau of China

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## ABSTRACT

**Background and objectives** The epidemiology of stroke at high altitudes has not been extensively studied, especially at heights of 4000 m and above. Thus, stroke prevention and treatment at high altitudes are challenging. We conducted a cross-sectional study to estimate the prevalence of stroke, the detection rate of individuals at high risk of stroke and the risk factors for stroke in the Qinghai-Tibet Plateau in China, a high altitude plateau that inhabits approximately 15 million people.

**Design** A population-based cross-sectional study in the Qinghai-Tibet Plateau.

**Setting** Data were collected from participants through face-to-face screening using a primary screening table. The table relied on the China National Stroke Screening and Prevention Project.

**Participants** A total of 10 700 residents aged ≥40 years and living on the Qinghai-Tibet Plateau for more than 6 months participated from January 2019 to December 2021.

**Main outcome measures** The primary screening table included basic demographic information, medical history information, personal lifestyle habits and physical examination information.

**Results** A total of 10 056 people were included in the analysis. The prevalence of stroke was 2.3% (95% CI 2.0% to 2.6%), and the detection rate of individuals at high risk of stroke was 26.2% (95% CI 25.3% to 27.0%). The prevalence of stroke and the detection rate of individuals at high risk of stroke increased with altitude ( $p<0.01$ ), and the prevalence of stroke at high altitudes was almost 2.2 times that at mid-altitudes ( $p<0.01$ ). After full adjustments, age, residence, hypertension, family history of stroke and smoking were significantly associated with stroke ( $p<0.05$ ).

**Conclusions** The prevalence of stroke, the related risk factors and the detection rate of high-risk individuals were clarified. The prevalence rates of hypertension, overweight or obesity and diabetes in the Qinghai-Tibet Plateau were all higher than the Chinese average. Higher-altitude exposure may be an independent risk factor for stroke.

## INTRODUCTION

Stroke is one of the main threats to human health and is the second most deadly disease globally, causing enormous burdens, crises

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This cross-sectional study had a large sample size based on the population (n=10 056).
- ⇒ This study used randomised multistage stratified cluster sampling to obtain data and adopted complex weighting calculations to analyse the data to increase the reliability of the results.
- ⇒ A nomogram was constructed to predict the occurrence of the outcomes.
- ⇒ Our study obtained information through inquiries and surveys, which may cause recall bias.
- ⇒ Our study did not follow individuals prospectively to collect data on mortality or cause of death or to examine the cerebral arterial disease.

and challenges for human beings.<sup>1 2</sup> The National Death Cause System showed that deaths caused by cerebrovascular disease accounted for 22.33% of the total national deaths.<sup>3-5</sup> In addition, stroke is China's most significant cause of death and disability.<sup>6 7</sup> As China rapidly enters an ageing society, the incidence of stroke is also rising, per the seventh federal current population survey. There are more than 2 million new stroke cases in China every year.<sup>8 9</sup> This will bring heavy economic and social burdens to China and the world. The prevalence of stroke increases with hypertension, diabetes, dyslipidaemia, atrial fibrillation, family history of stroke, smoking, lack of exercise, overweight or obesity.<sup>10</sup> Some environmental factors, such as high-altitude residence, are also associated with stroke.<sup>11</sup> The plateau has thin air (approximately 60–70% of the air density at sea level), low-oxygen levels (35–40% lower than the oxygen content at sea level) and low-pressure levels (only half of the pressure at sea level).<sup>12 13</sup> Due to the differences in regional climates and local traditional lifestyles, the prevalence of stroke and stroke risk factors varies.<sup>14 15</sup> At least 5.7% of the population worldwide lives at altitudes above

1500 m. Some studies have found<sup>16 17</sup> that the morbidity and mortality of stroke among residents in plateau areas are lower than those among residents in plain areas. Conversely, an Indian study<sup>18</sup> found that higher altitudes were associated with higher stroke rates. China has a vast territory, very different environments and noticeable climate differences, which lead to regional differences in the prevalence of stroke. A study reported that the stroke prevalence in the Northeast was almost three times higher than in the Southwest.<sup>11 19</sup> However, stroke epidemiology at high altitudes has not been extensively studied, especially in areas with 4000 m and over.<sup>20</sup> Therefore, a household survey was conducted to explore the prevalence of stroke, the detection rate of individuals at high risk of stroke and the risk factors for stroke among residents living in the Tibetan Plateau of China (2000–4500 m). The results could provide epidemiological data for the primary prevention of stroke in plateau areas.

## METHODS

### Study design

This study analysed data from the National Health and Family Planning Commission's public welfare project—The China National Stroke Screening and Prevention Project (CNSSPP).<sup>21</sup> The main aims of the study were as follows: (1) to determine the prevalence of stroke, the detection rate of individuals at high risk of stroke and the prevalence of risk factors among people over 40 years old living in the Qinghai-Tibet Plateau in China and (2) to determine associated risk factors for stroke and develop a model to predict the occurrence of the outcomes.

The survey adopted a cross-sectional observation method to obtain epidemiological data. Epidemiological data included general data, demographic information, medical history, physical examination data, laboratory examination data and other information. This research adhered to the principles of voluntariness, confidentiality and benefit and harmlessness and was submitted for review and approval by the hospital's Ethics Committee (the People's Hospital of Qinghai province). According to the research results on related risk factors associated with stroke at home and abroad, eight risk factors, including hypertension, atrial fibrillation (AF), smoking, dyslipidaemia, diabetes, lack of exercise, obesity or overweight and family history of stroke (FHS), were selected to design a preliminary screening scale.<sup>1</sup> In the preliminary screening work, trained and qualified community doctors conducted face-to-face interviews to confirm the screened population's medical history and preliminary examinations according to the items on the primary screening table.

### Participants, data collection and measurement

The CNSSPP constructed risk assessment scales for stroke, which have been shown to have excellent validity and reliability compared with the modified Framingham Stroke Profile and can be used as a tool for stroke risk

assessment.<sup>22</sup> From January 2019 to December 2021, cluster sampling selected 10 700 residents aged  $\geq 40$  years who had lived on the Tibetan Plateau of China for more than 6 months. The data were cleaned, and unqualified data were removed. Among the selected 644 participants with an incomplete stroke history or incomplete risk factor questionnaires were excluded. A total of 10 056 participants were ultimately enrolled as research subjects for analysis. Screening content included primary demographic (name, age, sex, nationality), medical history (history of stroke, hypertension, dyslipidaemia, family history of diabetes, AF, FHS), personal lifestyle (smoking status, exercise habits) and medical information (blood pressure, pulse, height, weight, body mass index (BMI)).

This study trained all project and study participants, including screeners, administrators and quality controllers. A third-party quality control method was applied. Quality control was divided into three parts: the first involved the automatic control of the system, the second involved real-time data quality control and the third involved quality control spot checks conducted by the quality control expert group.

### Assessment criteria

Based on the WHO criteria, stroke, also called a 'cerebrovascular accident', involves a group of diseases caused by the sudden rupture of a blood vessel in the brain or by a blockage that prevents blood from flowing to the brain, causing damage to brain tissue.<sup>23</sup> According to the CNSSPP protocol,<sup>21</sup> the eight risk factors related to stroke were defined as follows. Hypertension was defined as a systolic blood pressure  $\geq 140$  mm Hg or a diastolic blood pressure  $\geq 90$  mm Hg and a history of hypertension or the use of antihypertensive drugs in the past 2 weeks (blood pressure was measured after participants had rested in a sitting position for 5–15 min and after interference factors, such as room temperature, medications, mood and body position, were excluded).<sup>24</sup> Diabetes was defined as a fasting blood glucose level  $\geq 7.0$  mmol/L (fasted for at least 8 hours), an oral glucose tolerance test 2-hour blood glucose level  $\geq 11.1$  mmol/L or a glycosylated haemoglobin (HbA1c) level  $\geq 6.5\%$ ; significant hyperglycaemia or hyperglycaemic crisis symptoms; or a random blood glucose level  $\geq 11.1$  mmol/L. If it was uncertain whether a participant had a history of hyperglycaemia, multiple tests were performed to analyse the first three criteria (according to the American Diabetes Association 2010 guidelines).<sup>25 26</sup> Participants who were diagnosed with diabetes received treatment (diagnosed by a secondary or higher hospital). Dyslipidaemia was defined as a triglyceride level  $\geq 2.26$  mmol/L, a total cholesterol level  $\geq 6.22$  mmol/L, a low-density lipoprotein cholesterol level  $\geq 4.14$  mmol/L or a high-density lipoprotein cholesterol level  $< 1.04$  mmol/L.<sup>27</sup> AF was defined as the disappearance of regular atrial electrical activity followed by rapid and disordered fibrillation waves. The main clinical manifestations were absolute irregularity of the vibration and pulse rhythm, absolute irregularity

determined by heart auscultation, change in the intensity of the first heart sound, the disappearance of the P wave with a pulse rate less than the heart rate, the presence of an f wave on an ECG and the absolute difference between the R-R interval. Participants with a history of paroxysmal AF require diagnostic support from hospitals at or above the county level.<sup>28</sup> BMI  $\geq 26$  was defined as overweight or obesity (BMI=weight kg/body height m<sup>2</sup>).<sup>29</sup> Physical inactivity was defined as little or light physical activity performed less than three times a week, with less than 30 min of exercise per session for 1 year or over. Industrial and agricultural work was considered physical exercise.<sup>29</sup> FHS was limited to at least one first-degree relative with stroke history. First-degree relatives included parents, children and siblings (of the same parents). Smoking was defined as continuous or cumulative smoking for 6 months or more in a lifetime, having smoked in the 30 days prior to the survey and having smoked at least one cigarette per day during the survey.<sup>30</sup> In this study, participants with three or more of the eight risk factors mentioned above were included in the group of individuals at high risk of stroke. The altitude of the community screening point was divided into low-altitude (2000–2500 m), mid-altitude (>2500–3000 m) and high-altitude residence (>3000–4500 m).<sup>31</sup>

### Sample size estimates and statistical analysis

According to China's sixth national population census, 354692 inhabitants aged 40 years or over were in the six communities in 2010. The CNSSPP stipulates that screening should be performed with a minimum of 1% of local people over.<sup>19 32</sup> Therefore, the sample size was anticipated to be 10640 (accounting for 3% of the target population). This study used the sample size formula  $n = t\alpha^2 pq/d^2$  ( $t=1.96$ ,  $\alpha=95\%$  for both sides,  $q=1-p$ ). The study showed a stroke prevalence ( $p$ ) of 2.32% in adults aged  $\geq 40$  years.<sup>8</sup> The allowable error ( $d$ ) was 0.3%. The final sample size was determined to be 9673 by the formula described above. The sample size was increased by 10% to avoid non-compliance and information loss, and the total sample size was determined to be 10640 people. In this study, there were a total of 10700 participants.

According to the report, the cerebrovascular disease big data platform was used to enter data. The Brain Prevention Committee of the National Health and Health Commission returned these data after being cleaned. IBM SPSS V.22.0 was used to organise and analyse the data. The number of participants, composition ratios, rates and other indicators were used, and the  $\chi^2$  test and logistic regression analysis were used. The national population in the 2010 China Statistical Yearbook Standardisation was used to compare the line rate. All tests were two-sided, and statistical significance was defined as a  $p$  value  $< 0.05$ . We used R V.4.2.0 software to create the nomogram diagram and calculate the c-index.

### Participant and public involvement

No participants were involved in developing the research question or outcome measures or in the recruitment or conduct of the study. The results will be disseminated to study participants through news media.

## RESULTS

### Demographic characteristics of the screened population

A total of 10056 participants (including 223 patients who had a stroke and 2630 individuals at high risk of stroke) were enrolled in the follow-up analysis as the research subjects by cleaning unqualified data. The response rate was 94.0% (10056/10700), as shown in [table 1](#).

There were 4467 (44.4%) men and 5589 (55.6%) women in this study of 10056 (mean age, 60.8 $\pm$ 11.6 years) participants. The results using this male-to-female ratio were similar to those of stroke screening in China.<sup>8</sup> Regarding age distribution, people aged 50–59 years accounted for the highest proportion of participants with stroke (30.9%) compared with the other age groups. In terms of regional distribution, the low-altitude group represented approximately 30.3% of the sample, the middle-altitude group represented almost 48.4% of the sample and the high-altitude group represented approximately 21.2% of the sample. In terms of ethnicity distribution, Han nationality accounted for the highest proportion (65.7%), similar to the sixth census results.

### Prevalence analysis

#### Prevalence of stroke and the detection rate of individuals at high risk of stroke

[Table 1](#) shows that the prevalence of stroke was 2.32%. There was no significant difference in stroke prevalence between men and women ( $p=0.062$ ). The prevalence of stroke increased with age and altitude ( $p<0.001$ ). Among the ethnicity groups, the prevalence of stroke was significantly higher in Tibetan individuals than in Han and Hui individuals (3.63% vs 1.98% vs 2.08%,  $p<0.001$ ).

A total of 2630 high-risk individuals were detected in this study, and the detection rate was significantly higher than that of the national high-risk group (19.8%).<sup>8</sup> It is worth noting that among the high-risk individuals, the detection rate of men (30.5%) was significantly higher than that of women (22.7%). Among the different altitudes, the high-risk detection rate in the middle-altitude area was slightly higher than that in the low-altitude and high-altitude areas (30.0% vs 24.2% vs 20.4%,  $p<0.001$ ). In addition, there were significant differences in the detection rates among different ethnic groups ( $p<0.001$ ). The detection rates of the Han, Tibetan, Hui and other ethnic groups were 28.1%, 20.8%, 23.3% and 30.5%, respectively, as shown in [table 1](#).

### Prevalence of general risk factors

As shown in [table 2](#), the overall screened population was analysed concerning eight stroke risk factors, including hypertension, dyslipidaemia, diabetes, AF, smoking,



**Table 1** Characteristics of the participants and the prevalence of stroke and individuals at high risk of stroke

Category	Subcategory	Survey population (n, (%))	Participants with stroke, % (95% CI) (n=233)	Participants at high risk of stroke, % (95% CI) (n=2630)
Overall		10056 (100)	2.32 (2.02 to 2.61)	26.2 (25.3 to 27.0)
ASR			2.11 (1.81 to 2.41)	23.8 (27.2 to 29.1)
Sex	Male	4467 (44.4)	2.64 (2.17 to 3.11)	30.5 (29.1 to 31.8)
	Female	5589 (55.6)	2.06 (1.69 to 2.43)	22.7 (21.6 to 23.8)
	P value	<0.001	0.062	<0.001
Age (years)	40–49	1896 (18.9)	0.90 (0.47 to 1.32)	20.1 (18.3 to 21.9)
	50–59	3105 (30.9)	1.55 (1.11 to 1.98)	26.5 (25.0 to 28.1)
	60–69	2549 (25.3)	2.43 (1.83 to 3.03)	27.4 (25.7 to 29.1)
	70–79	1859 (18.5)	3.93 (3.04 to 4.81)	28.1 (26.0 to 30.1)
	≥80	647 (6.4)	5.10 (3.40 to 6.80)	31.7 (28.1 to 35.3)
	P value	<0.001	<0.001	<0.001
Residence	Low-altitude	3051 (30.3)	1.67 (1.21 to 2.13)	24.2 (22.7 to 25.7)
	Mid-altitude	4869 (48.4)	2.14 (1.73 to 2.54)	30.0 (28.6 to 31.2)
	High-altitude	2136 (21.2)	3.65 (2.86 to 4.44)	20.4 (18.7 to 22.1)
	P value	<0.001	<0.001	<0.001
Ethnicity	Han	6610 (65.7)	1.98 (1.65 to 2.32)	28.1 (27.0 to 29.1)
	Tibetan	2260 (22.5)	3.63 (2.86 to 4.40)	20.8 (19.2 to 22.5)
	Hui	802 (8.0)	1.50 (0.66 to 2.34)	23.3 (20.4 to 26.2)
	Others	384 (3.8)	2.08 (0.65 to 3.51)	30.5 (25.9 to 35.1)
	P value	<0.001	<0.001	<0.001

P values were calculated with the Rao-Scott- $\chi^2$  test and were intragroup comparisons of the surveyed population/participants with stroke/participants at high risk of stroke were calculated with the Rao-Scott- $\chi^2$  test. ASR, age-standardised rates for the Chinese population 2010.

overweight or obesity, lack of exercise and FHS. The data showed that in the risk factor analysis of the participants with stroke, the top three risk factors were hypertension, overweight or obesity and dyslipidaemia, which was similar to the results of the participants at high risk of stroke.

### Hypertension

The crude prevalence of hypertension was 48.7%, and the age-standardised prevalence was 41.8%. Moreover, the prevalence of hypertension increases with age. In terms of sex, there was no significant difference in the prevalence between men and women. In terms of different altitudes, the prevalence of hypertension at middle altitudes was higher than that at low and high altitudes (55.1% vs 46.0% vs 38.0%). The prevalence of hypertension in different ethnic groups also varied. The prevalence was higher in Han individuals than in Tibetan and Hui individuals, as shown in table 3.

### Diabetes

As shown in table 3, the crude prevalence of diabetes was 15.4%, and the age-standardised prevalence was 12.0%. The prevalence of diabetes increased with age between 40 and 79 years. Men were slightly higher than those

women (17.3% vs 13.8%). Consistent with hypertension, the prevalence of diabetes was also higher at middle altitudes. However, the prevalence of diabetes was highest in the Hui population.

### Dyslipidaemia

The crude prevalence of dyslipidaemia was 42.8% and 44.6% after age normalisation. The prevalence was higher in people aged 50–69 years. There was no significant difference between men and women. Consistent with hypertension, the prevalence was higher in the middle-altitude areas and the Han nationality group, as shown in table 3.

### AF

This study suggested that the crude prevalence of AF was 3.7%, and the age-standardised prevalence was 2.3%. These findings were consistent with the results of the population study in China. Moreover, the prevalence of AF increased with increasing age and altitude. The prevalence was 17.5% in people aged ≥80 years and 14.6% at high altitudes. The Tibetan population had the highest prevalence of 13.8%, as shown in table 3.

### Smoking

This study found that the crude smoking rate in the plateau area was 13.2%. The age-standardised smoking

**Table 2** Proportion of participants with stroke and those at high risk of stroke by risk factors

Category	Subcategory	Surveyed population (n, (%))	Participants with stroke (n, (%))	Participants at high risk of stroke (n, (%))
Total		10 056 (100)	233 (2.3)	2630 (26.2)
Hypertension	Yes	4893 (48.7)	186 (79.8)	2261 (86.0)
	No	5163 (51.3)	47 (20.2)	369 (14.0)
P value		<0.001	<0.001	<0.001
Dyslipidaemia	Yes	4299 (42.8)	102 (43.8)	1890 (71.9)
	No	5757 (57.2)	131 (56.2)	740 (28.1)
P value		<0.001	0.8	<0.001
Diabetes	Yes	1545 (15.4)	46 (19.7)	878 (33.4)
	No	8511 (84.6)	187 (80.3)	1752 (66.6)
P value		<0.001	0.075	<0.001
Atrial fibrillation	Yes	376 (3.7)	21 (9.0)	274 (10.4)
	No	9680 (96.3)	212 (91.0)	2356 (89.6)
P value		<0.001	<0.001	<0.001
FHS	Yes	368 (3.7)	16 (6.9)	266 (10.1)
	No	9688 (96.3)	217 (93.1)	2364 (89.9)
P value		<0.001	0.014	<0.001
Smoking	Yes	1154 (11.5)	35 (15.0)	621 (23.6)
	No	8902 (88.5)	198 (85.0)	2009 (76.4)
P value		<0.001	0.106	<0.001
Lack of exercise	Yes	2160 (21.5)	52 (22.3)	936 (35.6)
	No	7896 (78.5)	181 (77.7)	1694 (64.4)
P value		<0.001	0.815	<0.001
Overweight or obesity	Yes	3961 (39.4)	103 (44.2)	1326 (50.4)
	No	6095 (60.6)	130 (55.8)	1304 (49.6)
P value		<0.001	0.146	<0.001

P values, intragroup comparisons of the surveyed population/participants with stroke/participants at high risk of stroke, were calculated with the Rao-Scott- $\chi^2$  test.  
FHS, family history of stroke.

rate was 15.0%, which was lower than that of the whole population (25.2%). The smoking rate decreased with age, and the smoking rate of men was significantly higher than that of women (28.4% vs 1.0%). In terms of regional distribution, the smoking rate was the highest in the middle-altitude area, similar to those of hypertension, diabetes and dyslipidaemia. The smoking rate of the Han nationality group was higher than that of the Tibetan and Hui nationality groups, as shown in [table 3](#).

### Overweight or obesity

The crude prevalence of overweight or obesity was 43.0%, and the standardised prevalence was 40.8%. Consistent with that diabetes, the prevalence of overweight or obesity increased with age between the ages of 40 and 79 years. Men scored significantly higher than women. Consistent with AF, the prevalence was higher in high-altitude areas and the Tibetan group, as shown in [table 3](#).

### Lack of exercise

The gross inactivity rate was 29.4%, and the normalised inactivity rate was 33.7%. Physical inactivity increased significantly with age. There was no significant difference in exercise habits between men and women. Consistent with the overweight and obesity rates, people at high altitudes and Tibetan individuals were less likely to exercise, as shown in [table 3](#).

### FHS

The rate of FHS decreased with age in people aged 60 years or older. The rate was highest in the middle-altitude area and the Han population. There was no significant difference in sex, as shown in [table 3](#).

### Stroke-associated risk factors

Univariate logistic regression was performed for sex, age, ethnicity, region, hypertension, diabetes, dyslipidaemia, AF, FHS, overweight or obesity, smoking history and



**Table 3** Prevalence of risk factors of stroke

Category	Subcategory	Hypertension, % (95% CI)	Dyslipidaemia, % (95% CI)	Diabetes, % (95% CI)	Atrial fibrillation, % (95% CI)	Smoking, % (95% CI)	Overweight or obesity, % (95% CI)	Lack of exercise, % (95% CI)	FHS, % (95% CI)
Overall		48.7 (47.7 to 49.6)	42.8 (41.8 to 43.7)	15.4 (14.7 to 16.1)	3.7 (3.4 to 4.1)	13.2 (12.5 to 13.8)	43.0 (42.0 to 44.0)	29.4 (28.5 to 30.3)	3.7 (3.3 to 4.0)
ASR		41.8 (40.1 to 43.0)	44.6 (43.3 to 45.8)	12.0 (11.3 to 12.7)	2.3 (2.0 to 2.6)	15.0 (14.1 to 15.9)	40.8 (39.6 to 42.1)	33.7 (32.6 to 34)	4.3 (3.8 to 4.8)
Age (years)	40–49	31.5 (29.4 to 33.6)*	43.9 (41.6 to 46.1)*	7.4 (6.3 to 8.6)*	1.3 (0.8 to 1.8)*	17.0 (15.3 to 18.7)*	38.2 (36.0 to 40.4)*	39.5 (37.3 to 41.7)*	4.8 (3.8 to 5.8)*
	50–59	47.8 (46.0 to 49.6)	50.5 (48.7 to 52.3)	12.0 (10.8 to 13.1)	1.5 (1.1 to 1.9)	15.3 (14.0 to 16.6)	41.1 (39.4 to 42.9)	32.7 (31.0 to 34.3)	5.5 (4.7 to 6.3)
	60–69	53.5 (51.5 to 55.4)	48.5 (46.5 to 50.4)	20.2 (18.6 to 21.8)	1.5 (1.1 to 2.0)	13.3 (12.1 to 14.6)	42.9 (41.0 to 44.8)	26.7 (25.0 to 28.4)	3.3 (2.6 to 4.0)
	70–79	57.6 (55.4 to 59.9)	30.0 (27.9 to 32.1)	21.5 (19.6 to 23.4)	8.2 (7.0 to 9.5)	7.6 (6.4 to 8.8)	49.5 (47.3 to 51.8)	20.7 (18.9 to 22.6)	1.0 (0.5 to 1.4)
	≥80	58.4 (54.6 to 62.2)	16.4 (13.5 to 19.2)	18.1 (15.1 to 21.1)	17.5 (14.5 to 20.4)	7.3 (5.3 to 9.3)	48.2 (44.4 to 52.1)	20.4 (17.3 to 23.5)	0.6 (0 to 1.2)
Sex	Male	48.7 (47.2 to 50.1)	42.5 (41.1 to 44.0)	17.3 (16.2 to 18.4)	3.8 (3.3 to 4.4)	28.4 (27.1 to 29.7)*	45.8 (44.4 to 47.3)*	29.3 (27.9 to 30.6)	3.5 (3.0 to 4.1)
	Female	48.6 (47.3 to 50.0)	42.9 (41.6 to 44.2)	13.8 (12.9 to 14.7)	3.7 (3.2 to 4.2)	1.0 (0.7 to 1.2)	40.8 (39.5 to 42.1)	24.3 (22.3 to 24.5)	3.8 (3.3 to 4.3)
Residence	Low-altitude	46.0 (44.2 to 47.7)*	41.7 (40.0 to 43.5)*	26.0 (24.4 to 27.5)*	0.9 (0.6 to 1.3)*	9.9 (8.8 to 11.0)*	49.7 (47.9 to 51.4)*	29.6 (28.0 to 31.2)†	2.7 (2.1 to 3.3)*
	Mid-altitude	55.1 (53.7 to 56.5)	60.2 (58.8 to 61.6)	13.2 (12.4 to 14.2)	0.8 (0.5 to 1.0)	18.2 (17.1 to 19.3)	30.9 (29.6 to 32.2)	26.9 (25.6 to 28.0)	5.4 (4.8 to 6.1)
	High-altitude	38.0 (35.9 to 40.0)	4.4 (3.6 to 5.3)	5.1 (4.1 to 6.0)	14.6 (13.1 to 16.1)	6.4 (5.4 to 7.5)	61.2 (59.1 to 63.3)	31.6 (29.7 to 33.6)	1.0 (0.6 to 1.4)
Ethnicity	Han	52.1 (50.9 to 53.3)*	54.4 (53.2 to 55.6)*	17.5 (16.6 to 18.4)*	0.9 (0.6 to 1.1)*	16.3 (15.4 to 17.2)*	35.1 (34.0 to 36.2)*	27.7 (26.7 to 28.8)*	4.8 (4.3 to 5.4)*
	Tibetan	39.0 (37.0 to 41.0)	9.8 (8.8 to 10.8)	5.5 (4.5 to 6.4)	13.8 (12.3 to 15.0)	7.0 (5.9 to 8.0)	60.6 (58.6 to 62.6)	31.5 (29.6 to 33.0)	1.1 (0.6 to 1.5)
	Hui	45.6 (42.2 to 49.1)	46.4 (42.9 to 49.8)	26.2 (23.1 to 29.2)	0.2 (0.0 to 0.6)	2.0 (1.0 to 3.0)	57.0 (53.6 to 60.4)	35.7 (32.3 to 39.0)	1.5 (0.7 to 2.3)
	Other	52.6 (47.6 to 57.6)	46.9 (41.9 to 51.9)	14.1 (10.6 to 17.5)	0.8 (0.0 to 1.7)	18.8 (14.8 to 22.7)	47.9 (42.9 to 52.9)	32.6 (27.9 to 37.2)	2.9 (1.2 to 4.5)

P values, intragroup comparison in different factors, were calculated with the Rao-Scott- $\chi^2$  test.

\*Significant at p<0.001.

†Significant at p<0.05.

ASR, age-standardised rate; FHS, family history of stroke.

**Table 4** ORs for stroke by univariate analysis and multivariate regression models

Category	Subcategory	Univariate analysis			Multivariable analysis		
		B	OR (95% CI)	P value	B	OR (95% CI)	P value
Sex	Male		1.00 (reference)			1.00 (reference)	
	Female	-0.26	0.77 (0.58 to 1.01)	0.053	-0.13	0.87 (0.65 to 1.16)	0.37
Age (years)	40–49		1.00 (reference)			1.00 (reference)	
	50–59	0.55	1.74 (1.02 to 3.11)	0.05	0.40	1.49 (0.87 to 2.70)	0.15
	60–69	1.01	2.76 (1.64 to 4.88)	<0.01	0.92	2.50 (1.47 to 4.48)	<0.01
	70–79	1.51	4.52 (2.72 to 7.94)	<0.01	1.24	3.44 (2.01 to 6.19)	<0.01
	≥80	1.78	5.94 (3.33 to 10.98)	<0.01	1.44	4.20 (2.25 to 8.10)	<0.01
Ethnicity	Han		1.00 (reference)			1.00 (reference)	
	Tibetan	-0.29	1.86 (1.40 to 2.46)	<0.01	-0.74	1.68 (0.50 to 4.13)	0.32
	Hui	0.62	0.75 (0.39 to 1.31)	0.35	0.52	0.93 (0.47 to 1.67)	0.82
	Others	0.51	1.05 (0.47 to 2.03)	0.89	0.04	0.96 (0.43 to 1.88)	0.92
Residence	Low-altitude		1.00 (reference)			1.00 (reference)	
	Mid-altitude	0.25	1.28 (0.92 to 1.81)	0.15	0.41	1.51 (1.04 to 2.22)	0.03
	High-altitude	0.80	2.23 (1.56 to 3.20)	<0.01	0.42	1.52 (0.57 to 5.34)	0.45
Hypertension	No		1.00 (reference)			1.00 (reference)	
	Yes	1.46	4.30 (3.15 to 6.00)	<0.01	1.33	3.78 (2.73 to 5.33)	<0.01
Diabetes	No		1.00 (reference)			1.00 (reference)	
	Yes	0.31	1.37 (0.97 to 1.88)	0.06	0.28	1.32 (0.92 to 1.86)	0.12
Dyslipidaemia	No		1.00 (reference)			1.00 (reference)	
	Yes	0.04	1.04 (0.80 to 1.36)	0.75			
Atrial fibrillation	No		1.00 (reference)			1.00 (reference)	
	Yes	0.97	2.64 (1.62 to 4.09)	<0.01	0.10	1.11 (0.65 to 1.83)	0.67
FHS	No		1.00 (reference)			1.00 (reference)	
	Yes	0.69	1.98 (1.14 to 3.23)	<0.01	0.84	2.30 (1.30 to 3.84)	<0.01
Smoking	No		1.00 (reference)			1.00 (reference)	
	Yes	0.32	1.38 (0.94 to 1.95)	0.09	0.33	1.50 (1.01 to 2.16)	0.03
Lack of exercise	No		1.00 (reference)			1.00 (reference)	
	Yes	0.05	1.05 (0.76 to 1.43)	0.75			
Overweight or obesity	No		1.00 (reference)			1.00 (reference)	
	Yes	0.20	1.23 (0.94 to 1.59)	0.13	0.05	1.05 (0.80 to 1.38)	0.73

Factors with a univariate p value<0.2 were included in multivariate logistic regression.  
FHS, family history of stroke .

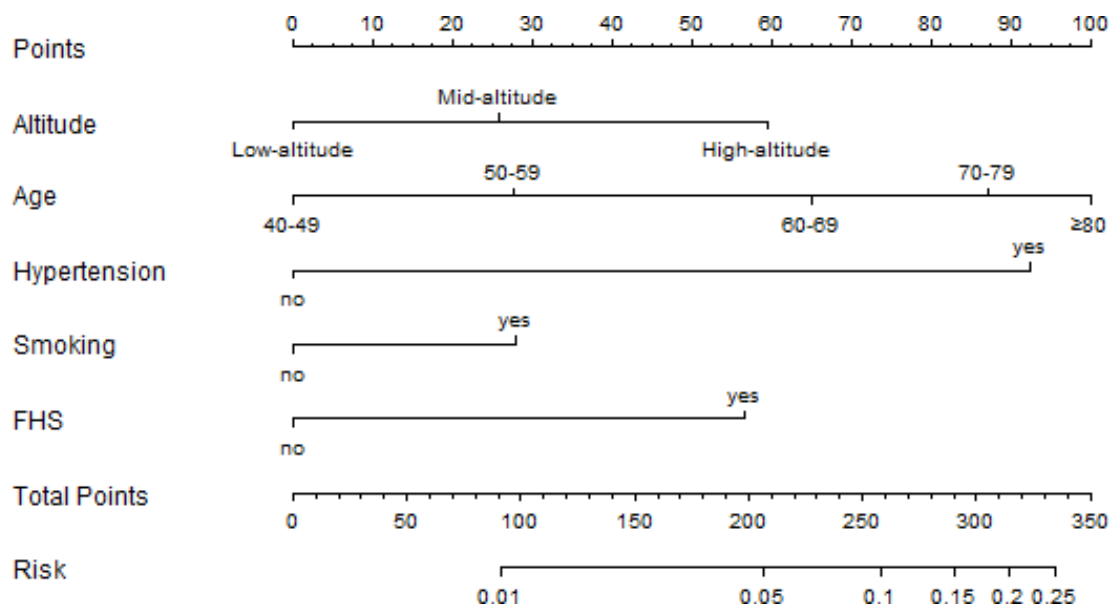
physical inactivity. Factors with a univariate p value of <0.2 (sex, age, ethnicity, region, hypertension, diabetes, AF, FHS, overweight or obesity and smoking history) were then included in multivariate logistic regression. The results showed that age, region, hypertension, FHS and smoking history were closely related to stroke ( $p<0.05$ ). Stroke risk increases with age and altitude. People with high blood pressure, an FHS and a history of smoking on the Qinghai-Tibet Plateau are more likely to suffer a stroke. However, sex, ethnicity, diabetes, AF, dyslipidaemia, overweight or obesity and physical inactivity were not significantly associated with stroke, as shown in [table 4](#).

### Stroke prediction model

Based on the logistic regression analysis results, a nomogram was developed using data for all participants based on five standard parameters. Each predictor was given one point in the visual interface of the nomogram. The total points were calculated as a linear combination of the points of each predictor ranging from 0% to 100% to determine the associated stroke risk, as shown in [figure 1](#).

### DISCUSSION

Based on the CNSSPP, this study used a cross-sectional survey method to analyse the prevalence of stroke, the



**Figure 1** Nomogram predicting risk for stroke. Factors include altitude, age, family history of stroke (FHS), hypertension and smoking. After the scores of all factors were calculated and the total score was added, the total score corresponding obtained the risk value of stroke to the risk score.

detection rate of individuals at high risk of stroke and the related risk factors in the Qinghai-Tibet Plateau of China. A total of 56.2% of the population aged 50–69 years was screened; this proportion was more significant than the proportion of the population screened in the sixth census (40.7%). The above result may be related to the fact that the economy of the Qinghai-Tibet Plateau region is lagging. Most young people work in other locations and missed screening.<sup>33</sup> This study's population living at an altitude of 3000–4500 m (21.2%) was more extensive than that reported in the sixth census (8.3%) because this study focuses on improving the epidemiological data of stroke in high-altitude areas.

China has a vast area and a complex geographical environment, and the prevalence of stroke varies among different regions.<sup>19</sup> The China 2019 Stroke Report showed that the national average prevalence of stroke in adults aged 40 years and older was 2.23%.<sup>8</sup> Moreover, a cross-sectional survey with a sample size of 16 892 in southwestern China showed that the prevalence of stroke was 3.1% in individuals over 40 years of age.<sup>32</sup> In addition, a cross-sectional survey with a sample size of 144 722 in northern China showed that the standardised stroke prevalence in participants over 60 years was 4.94%.<sup>34</sup> This study showed that the prevalence of stroke in residents aged 40 years and above in the plateau area above 3000 m was 3.65%. A lower prevalence than those reported in the northern regions may be related to the 20-year age difference in the inclusion criteria. The prevalence of stroke in the plateau area above 3000 m was significantly higher than the national average level and the level in southwestern China. This may be due to the particular geographical environment of the plateau region, dietary differences and potential differences in vascular risk factors. Some studies have found that different degrees of

vascular remodelling can occur at altitudes of 2000–3500 m. Regenerated blood vessels have a protective effect on the body, resulting in a lower risk of stroke and better outcomes than in areas of low altitude and altitudes >3500 m.<sup>35–38</sup> Therefore, this study further confirms that primary stroke prevention should be strengthened for people above an altitude of 3000 m.

This study found that hypertension, dyslipidaemia and overweight and obesity were the top three risk factors from the eight risk factors examined. Hypertension is one of the most common risk factors for cerebrovascular disease and the leading risk for premature death worldwide. The prevalence of hypertension (48.7%) in the Qinghai-Tibet Plateau region was higher than the national average (37.2%),<sup>39</sup> and the prevalence is higher than those of elderly Han nationality individuals living in high-altitude areas. This may be an essential factor for the high prevalence of stroke in high-altitude areas. The importance of controlling hypertension has been thoroughly emphasised.

Several medical studies have confirmed that being overweight and obese increases the risk of stroke. A 2018 meta-analysis of 44 prospective cohort studies involving 4.43 million participants showed a J-shaped dose-response relationship between BMI and stroke risk, with a 1.10-fold increase in stroke risk for each 5-unit increase in BMI.<sup>40</sup> In this survey, we found that the prevalence of overweight or obesity in the plateau area (44.2%) was significantly higher than that at the national level (32.3%).<sup>41</sup> Furthermore, the prevalence was higher in men than in women, contrary to the findings of the WHO.<sup>29</sup> It was also found that the prevalence of overweight or obesity was higher in participants living in high-altitude regions and Tibetan individuals than in participants not living in high-altitude regions and non-Tibetan individuals. Dyslipidaemia is



one of the most critical risk factors for the development of atherosclerosis and a significant independent risk factor for stroke. The prevalence of dyslipidaemia (42.8%) in the Qinghai-Tibet Plateau region was significantly higher than the national average (11.2%). High-altitude residents are prone to hypertension, overweight or obesity and dyslipidaemia. This is because people like to drink alcohol and eat high-fat foods, such as beef, mutton and animal offal, to keep warm to resist the cold climate and low-calorie, hypoxic environment.<sup>42–44</sup>

Studies have found that smoking cessation can reduce stroke incidence and improve stroke prognosis and recurrence. A 2018 foreign study showed that quitting smoking within 6 months of a stroke or transient ischaemic attack significantly reduced the incidence of recurrent stroke, myocardial infarction or death within 4.8 years.<sup>45</sup> We found that smoking was more closely associated with stroke in plateau areas than in other areas.<sup>19 30</sup> Therefore, we can hypothesise that smoking bans in the Qinghai-Tibet Plateau are more effective in preventing stroke.

According to the 2017 International Diabetes Federation report on Global Diabetes Overview, China has 114.4 million adults (aged 20–79 years) with diabetes, of whom 34.1 million are over 65 years old. Thus, it is the country with the most significant number of patients with diabetes globally and the fastest-growing prevalence rate. The prevalence of diabetes (19.7%) in this study was significantly higher than that reported in previous studies (10.9%).<sup>46</sup> This may be due to the cold and hypoxic conditions of the high-altitude areas. These conditions stimulate epinephrine secretion and increase the number of red blood cells, which in turn increases the HbA1c level.<sup>47</sup> Therefore, residents in plateau areas need to monitor blood glucose changes to promote the primary prevention of stroke.

Studies have found that participants with AF have a fivefold higher risk of developing cerebral infarction.<sup>48</sup> This study found a higher risk of AF in the high-altitude area, which may be related to the higher incidence of pulmonary hypertension and congenital heart disease in the high-altitude hypoxic environment.<sup>49 50</sup> In addition to controlling blood pressure, blood lipids and body weight, heart health needs special attention at high altitudes. Finally, this survey developed a prediction model according to the correlations among the risk factors, which provides more intuitive data to support the prevention of high-altitude stroke.

This study has some limitations. First, several other risk factors (such as alcohol intake, air pollutants and dietary habits) have also been shown to contribute to stroke risk.<sup>51</sup> We could not include these risk factors in the current analysis due to the lack of information in this survey. Second, part of the information in this study was obtained through inquiries and surveys, which may lead to recall bias and result differences. In addition, this survey only sampled residents aged ≥40 years, so our current results cannot be generalised to all age groups in the Qinghai-Tibet Plateau.

## CONCLUSIONS

This study provides epidemiological data on stroke in the Qinghai-Tibet Plateau for the first time. We clarified the prevalence of stroke, the detection rate of individuals at high risk of stroke and the related risk factors. The prevalence of stroke and the detection rate of individuals at high risk of stroke in the Qinghai-Tibet Plateau were all higher than the Chinese average. Moreover, high-altitude exposure may be an independent risk factor for stroke in the Qinghai-Tibet Plateau. This study suggests that it is necessary to accurately prevent and treat stroke according to altitude and risk factors.

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**Patient consent for publication** Not applicable.

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**Data availability statement** Data are available upon reasonable request.

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