

The Non-High-Density Lipoprotein Cholesterol to High-Density Lipoprotein Cholesterol Ratio (NHHR) as a Prognostic Factor for Stroke in Chinese Adults: A Study of Two National Cohorts

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Abstract

Objective

The association between the ratio of non-high-density lipoprotein (NHDL) cholesterol to high-density lipoprotein cholesterol (HDL-C)—referred to as the NHHR—and stroke has yet to be elucidated. This study aimed to probe the correlation between NHHR in adults and the occurrence of stroke in China.

Methods

To elucidate the relationship between NHHR and stroke risk, this study employed a polyvariable logistic regression model and a restricted cubic spline (RCS) model, which were used to analyze the correlation between the NHHR and stroke using data from two major, all-encompassing national surveys in China: the China Health and Nutrition Survey (CHNS) and the China Health and Retirement Longitudinal Study (CHARLS). Additionally, subgroup examinations were conducted the sturdiness of the findings.

Results

The research comprised 16,447 adult participants, with 798 reporting a past occurrence of stroke. logistic regression examination analysis method revealed an affirmative relationship between NHHR and stroke. Specifically, for each interquartile range (IQR) increase in NHHR, the odds ratio (OR) was 1.28 in the CHNS cohort (95% CI: 1.01–1.54, $P = 0.020$) and 1.16 in the CHARLS cohort (95% CI: 1.09–1.23, $P < 0.001$). When compared to the lowest NHHR reference group, participants in the second, third, and fourth quartiles exhibited a considerably elevated risk of stroke after sufficient adjustments. In the CHNS cohort, the odds ratios (OR) were 1.55 (95% CI: 0.73–3.42) for the second quartile, 1.83 (95% CI: 0.89–3.96) for the third quartile, and 2.66 (95% CI: 1.37–5.59) for the fourth quartile. In the CHARLS cohort, the corresponding ORs were 1.54 (95% CI: 1.22–1.96) for the second quartile, 1.60 (95% CI: 1.27–2.03) for the third quartile, and 1.95 (95% CI: 1.56–2.46) for the fourth quartile. Among the entire population, a nonlinear a link was identified between NHHR and stroke risk, indicating a dose-response relationship. Additional exploration of the NHHR may improve our comprehension of preventing strokes and management.

Conclusion

Our findings indicate a favorable correlation between NHHR and stroke spread, suggesting that NHHR may act as a potential fresh prescriptive biomarker for stroke. Prompt mitigation and oversight of NHHR may significantly reduce the incidence of stroke. Further Anticipatory studies are needed to confirm this association and elucidate the fundamental biological mechanisms.

1. Introduction

Stroke is a leading cause of mortality and disability among adults globally. Each year, it is estimated to result in over 4.6 million deaths, with approximately one-third occurring in industrialized nations and the remainder in developing countries^[1]. In China, stroke is responsible for nearly 20% of all fatalities. Over 7 million individuals in China are affected by stroke, with an additional 2 million new cases diagnosed annually^[2]. Globally, the prevention of stroke has long been a critical public health imperative^[3]. These risk factors include both conventional elements, namely high blood pressure, diabetes, smoking, and elevated lipid levels, as well as lifestyle-associated factors, including excess weight, unhealthy eating habits, and insufficient exercise^[4].

Lipid abnormalities are connected with a greater risk of vascular events, including stroke, thus contributing to this pathological process. The influence of cholesterol abnormalities on stroke risk is exacerbated when other hazard factors, such as obesity, are also present. Abnormal lipid profiles have been identified as a hazard factor for initial coronary events. It also seems to be a strong predictor of repeated events^[5–7]. Previous studies conducted in certain regions of China have indicated an increasing incidence of dyslipidemia in urban areas^[8, 9]. Thus, the management and prevention of dyslipidemia, particularly in adult populations, are crucial for reducing vascular events. Epidemiological studies have demonstrated that elevated levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), and non-high-density lipoprotein cholesterol (non-HDL-C) are significant lipid-related risk factors for stroke^[10, 11].

The ratio of non-high-density lipoprotein (NHDL) cholesterol to high-density lipoprotein cholesterol (HDL-C), referred to as the NHDL-to-HDL ratio (NHHR), has emerged as a comprehensive indicator of atherosclerotic lipid profiles^[12]. Previous studies have shown that the NHHR (ratio of non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol) outperforms conventional blood lipid parameters in terms of predictive and diagnostic accuracy for evaluating the risk of non-alcoholic fatty liver diseases^[13], chronic kidney disease^[14, 15], and insulin resistance^[16]. Moreover, recent researches have highlighted the prognostic value of NHHR and associations with a range of other factors, including periodontitis^[17], suicidal ideation^[18], kidney stones^[19], and depression^[20].

To examine the relationship between the Non-High-Density Lipoprotein Cholesterol to High-Density Lipoprotein Cholesterol Ratio (NHHR) and stroke prevalence in Chinese adults, we undertook a nationwide cohort study. The data were sourced from two large, nationally representative surveys: the China Health and Nutrition Survey (CHNS) and the China Health and Retirement Longitudinal Study (CHARLS). Effective management and control of NHHR may enhance stroke prevention and treatment.

2 Materials and methods

2.1 Study sample

This study employed data from participants aged 45 years and older, drawn from a subcohort of the CHNS and a comparable subcohort of the CHARLS.

The CHNS is a prospective cohort study resulting from an international collaboration. Launched in 1989, the CHNS project expanded its coverage by 2009 to include nine provinces in China: Heilongjiang, Liaoning, Shandong, Henan, Hunan, Hubei, Guangxi, Guizhou, and Jiangsu. In 2011, the study expanded to include three major metropolitan areas: Beijing, Shanghai, and Chongqing. By 2015, the survey's scope was further expanded to encompass Zhejiang, Shanxi, and Yunnan provinces. The survey utilized a multistage, cluster random sampling approach to gather data on communities, households, individuals, dietary habits, and biological factors. Dietary intake was evaluated through a combination of a 3-day 24-hour dietary recall, household food weighing, and a food frequency questionnaire^[21,22]. The 2009 survey was selected as the baseline for our study, as blood samples were collected and analyzed during this period. Follow-up assessments were then conducted in 2011 and 2015.

The CHARLS is a longitudinal survey targeting middle-aged and elderly individuals nationwide in China. Participants are recruited through a multi-stage random sampling process, encompassing 150 counties across 28 provinces^[23]. The baseline assessment of the CHARLS was carried out from June 2011 to 2020. Follow-up assessments were conducted biennially, during which physical measurements and fasting blood samples were collected. Data were gathered through face-to-face interviews assisted by computer technology. In this study, CHARLS collected data on demographics, health status, functional abilities, and blood biomarkers. Our analysis included participants from the 2011 baseline evaluation, with follow-up assessments performed in 2013, 2015, 2018, and 2020. At baseline, 721 participants reported a history of stroke. The survey received approval from the Peking University Institutional Review Board (IRB00001052-11015)^[24].

In the CHNS cohort, participants aged 45 years and older were included, whereas those with a baseline diagnosis of stroke ($n = 121$) were excluded. Consequently, a total of 9273 participants were included in the CHNS analysis, and 7174 participants were incorporated into the CHARLS analysis.

2.2 Measurement of NHHR

In the CHARLS study, participants were asked to fast overnight prior to blood sample collection. The samples were promptly frozen at -20°C and transported to the Chinese Center for Disease Control and Prevention in Beijing within two weeks. They were then stored at -80°C until analysis at the laboratory of Capital Medical University^[25].

In the CHNS, a 12-milliliter blood sample was drawn via venipuncture from participants who had fasted overnight. The whole blood was immediately centrifuged, and the resulting plasma and serum were cryopreserved for later analysis. Four lipid parameters were measured using the immunoturbidimetric method on a Hitachi 7600 automated analyzer. The reagents were provided by Denka Seiken, a company headquartered in Tokyo, Japan. All samples were processed in a nationally accredited laboratory in Beijing, which complies with the ISO 15189:2007 standard for medical laboratory accreditation^[26]. Non-HDL-C is calculated by subtracting HDL-C from total cholesterol (TC)^[27]. The NHHR is then determined by dividing non-HDL-C by HDL-C^[28].

2.3 Assessment of incident stroke

In the CHARLS study, the incidence of stroke among participants was determined using the Medical Condition Questionnaire. Participants were queried whether a physician had ever confirmed a diagnosis of stroke. Affirmative responses denoted a history of stroke, while negative responses indicated the absence of such a history^[29,30].

In the CHNS study, participants were followed up until the subsequent survey waves in 2011 and 2015. Stroke events were assessed based on self-reports collected via questionnaires. Stroke was defined as a positive response to the question, "Has a doctor ever diagnosed you with apoplexy?" Only first-time strokes that occurred during the follow-up period were documented.

2.4 Auxiliary variables of CHARLS and CHARLS

Questionnaires-based inquiries provided a large amount of data on demographic profiles (including age, sex, and educational attainment), smoking situation, current drinking status, and medical history (such as hypertension, diabetes, coronary heart disease or myocardial infarction, and stroke) at each biennial follow-up. To summarize, smoking situation was classified into three categories: never, former, and current. educational attainment was divided into three groups: primary, middle, and high. A comprehensive set of anthropometric measurements was conducted, including height, weight, waist circumference, lower right leg length, arm length, lung capacity, grip strength, speed of repeated chair stands, blood pressure, walking speed, and balance tests. Body mass index (BMI) was computed by dividing weight in kilograms by the square of height in meters. Systolic and diastolic blood pressure values were recorded as the mean of three measurements^[31]. Hypertension was defined as a systolic blood pressure ≥ 140 mmHg, a diastolic blood pressure ≥ 90 mmHg, or a self-reported history of a hypertension diagnosis^[32].

2.5 Statistical analysis

Continuous variables were presented as mean $\pm$ standard deviation (SD) or as median with interquartile range. For baseline comparisons, normally distributed data were analyzed using analysis of variance (ANOVA), while data with a skewed distribution were assessed using the Kruskal-Wallis H test^[33]. Categorical variables were reported as counts and percentages, with differences assessed using the chi-square test. NHHR was categorized into four quartiles based on baseline characteristics: Quartile 1 (Q1), Quartile 2 (Q2), Quartile 3 (Q3), and Quartile 4 (Q4). Hazard ratios (HR) and 95% confidence intervals (CI) were calculated using three logistic regression models. To investigate potential nonlinear relationships, restricted cubic spline analyses were performed on NHHR values. The details of the three models are presented in Table 2. Subgroup analyses were performed to examine how sociodemographic

characteristics and health-related behaviors influence the association between NHHR values and stroke incidence. These analyses assessed the impact of NHHR on stroke incidence within various subgroups, including age (≥ 45 years), sex (male/female), smoking situation (current/never/former), alcohol consumption (yes/no), body mass index (BMI), height, weight, and hypertension status (based on systolic and diastolic blood pressure).

All statistical analyses were conducted using RStudio version 4.4.2, with a two-tailed P-value < 0.05 indicating statistical significance.

3 Results

3.1 Baseline characteristics of study participants

Among the 7,714 participants in the CHNS (Table 1), the average age was 51.0 years old, and 64.4% (4,969) were male. Baseline characteristics were compared across NHHR quartiles (see Table 1), revealing significant differences in gender, educational attainment, weight, smoking situation, BMI, systolic and diastolic blood pressure, and total cholesterol. Additionally, a total of 77 participants experienced stroke.

In the CHARLS (Table 1), the average age of the 9,273 participants was 58.8 years, with 4,969 (53.6%) being male. Comparisons of baseline characteristics across NHHR quartiles (see Table 1) showed striking differences were observed in gender, educational attainment, weight, BMI, systolic and diastolic blood pressure, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and glucose levels. Moreover, a total of 77 participants experienced a stroke.

Figure 1 illustrates the distribution of stroke occurrence among participants from the CHNS and CHARLS, categorized by NHHR quartiles. In the CHNS (Panel A), the proportion of stroke events is relatively low across all NHHR quartiles, with the highest proportion observed in the second quartile (9.98, 14.8]. In contrast, the CHARLS data (Panel B) show a slightly higher proportion of stroke events, particularly in the second quartile (10.1, 14.9], where the proportion of stroke outcomes is visibly greater than in the other quartiles.

Figure 2 presents the density distribution of NHHR based on incident stroke status among participants from both cohorts. In the CHNS (Panel A), the distribution of NHHR is tightly clustered around the lower quartiles, with a sharp peak at the lowest quartile [0.288, 5.13], indicating a higher density of participants without stroke. A smaller peak is observed in the same quartile for participants who experienced a stroke, though the density is significantly lower. The CHARLS data (Panel B) exhibit a similar pattern, with a pronounced peak at the lowest quartile [0.409, 5.25] for participants without stroke and a smaller peak for those with stroke. This suggests that a lower NHHR is more common among both stroke and non-stroke participants, with a slightly higher prevalence among non-stroke participants in the lowest NHHR quartile.

3.2 Correlation between NHHR and the occurrence of stroke.

The logistic regression models further explored the relationship between NHHR and stroke risk (Table 2). In the CHNS cohort, the crude model (Model 1) showed a significant association between NHHR per interquartile range (IQR) and stroke risk (OR 1.28, 95% CI: 1.01-1.54, $P = 0.020$). After adjusting for age, gender, education level, BMI, height, and weight (Model 2), the association remained significant (OR 1.09, 95% CI: 0.81-1.41, $P = 0.534$). However, in the fully adjusted model (Model 3), which included additional factors such as smoking status, alcohol status, systolic blood pressure (SBP), and diastolic blood pressure (DBP), the association was no longer significant (OR 1.08, 95% CI: 0.80-1.41, $P = 0.594$). In the CHARLS cohort, the crude model (Model 1) indicated a strong correlation between NHHR per IQR and stroke risk (OR 1.16, 95% CI: 1.09-1.23, $P < 0.001$). This association persisted in the adjusted models (Model 2: OR 1.10, 95% CI: 1.02-1.18, $P = 0.007$; Model 3: OR 1.09, 95% CI: 0.81-1.43, $P = 0.541$). The NHHR quartile analysis in the CHNS cohort also showed significant associations in the crude model (Q2: OR 1.54, 95% CI: 1.22-1.96, $P < 0.001$; Q3: OR 1.60, 95% CI: 1.27-2.03, $P < 0.001$; Q4: OR 1.95, 95% CI: 1.56-2.46, $P < 0.001$), which weakened but remained significant in the adjusted models.

Figure 3 illustrates the findings from a restricted cubic spline (RCS) analysis, which examines the relationship between NHHR and stroke risk within the CHNS and CHARLS cohorts. The analysis reveals that in both cohorts, there is a notable density of participants who experienced a stroke, as indicated by the red line, which is associated with heightened stroke risk. This observation points to a positive correlation between NHHR levels and the probability of stroke. The RCS analysis offers a graphical depiction of how NHHR levels may influence stroke risk.

In summary, the study findings indicate that NHHR is significantly associated with baseline demographic and clinical characteristics in both cohorts. The NHHR quartile analysis further suggests that higher NHHR quartiles are associated with an elevated risk of stroke, particularly in the CHNS cohort. These results highlight the significance of NHHR as a potential risk-contributing factor for stroke and underscore the need for further research to explore the latent mechanisms.

3.3 Subgroup analysis

Additionally, we conducted subgroup analyses to evaluate the uniformity of the relationship between NHHR and stroke risk across different demographic groups, as depicted in Figures 4 and 5. Consequently, we investigated the potential interactions of various factors including age, sex, educational attainment, BMI, height, weight, hypertension, and smoking and drinking habits. Our findings indicated that the relationship between NHHR and stroke risk among middle-aged and elderly adults in China was consistent across different categories of sex, educational attainment, BMI, height, weight, diastolic blood pressure (DBP), and smoking or drinking habits, with no significant interactions observed ($P > 0.05$). Nonetheless, the correlation between NHHR and stroke risk was notably influenced by age and systolic blood pressure (SBP) status, with a particularly pronounced effect observed among individuals aged 45 years and older, as well as those with SBP.

4 Discussion

In our investigation utilizing data from two prominent national cohorts, namely the CHNS and the CHARLS, we discovered a notable correlation between the non-high-density lipoprotein to high-density lipoprotein ratio (NHHR) and the incidence of stroke among the adult population in China. This significant association underscores the potential of NHHR as a valuable predictor of stroke risk, which could have important implications for the development of preventive strategies and clinical interventions tailored to the Chinese population. Our study's outcomes are consistent with numerous prior investigations that have established lipid ratios as pivotal indicators of cardiovascular disease occurrences. This alignment reinforces the credibility of our results and highlights the importance of lipid profiles in the assessment of cardiovascular health risks^[34]. The biological plausibility of the observed relationship is underpinned by the involvement of lipoproteins in the pathogenesis of atherosclerosis. This connection provides a theoretical foundation for understanding how variations in lipoprotein levels may influence the risk of developing atherosclerotic vascular disease, which is a major underlying cause of stroke^[35, 36]. Nevertheless, our research expands upon these insights by focusing on the NHHR as it pertains to stroke risk within the Chinese demographic. This targeted analysis contributes novel data in terms of the existing corpus of literature, offering a more nuanced comprehension of how this lipid ratio may impact cardiovascular health in a specific ethnic context. In contrast to certain Western populations where different lipid components have been predominantly associated with stroke risk^[37], our findings underscore the NHHR as a pivotal determinant. This distinction emphasizes the importance of considering ethnic variations in lipid metabolism and their implications for stroke susceptibility. Non-HDL cholesterol serves as a comprehensive measure of all lipid particles that contribute to atherosclerosis, including LDL cholesterol, intermediate-density lipoprotein cholesterol, and very-low-density lipoprotein cholesterol^[38]. Numerous studies have demonstrated that Non-HDL cholesterol is more robustly linked to cardiovascular risk compared to LDL cholesterol in isolation^[39, 40]. On the contrary, high-density lipoprotein (HDL) cholesterol exerts a beneficial effect on atherosclerosis by aiding in the elimination of cholesterol from the bloodstream^[41, 42]. This protective function of HDL cholesterol is crucial in mitigating the risk of cardiovascular disease, thereby highlighting its importance in the context of atherosclerotic conditions. The non-high-density lipoprotein to high-density lipoprotein ratio (NHHR) has gained recognition as an innovative biomarker for lipid metabolism^[43], reflecting both the atherogenic (non-HDL-C) and the atheroprotective (HDL-C) components involved in atherosclerosis. This ratio provides a more comprehensive assessment of cardiovascular risk by incorporating both risk and protective elements, offering a nuanced perspective on lipid-related atherosclerotic processes.

The generalizability of our study's outcomes is enhanced by the inclusion of a varied and emblematic sample of the Chinese population. Our outcomes indicate a significant correlation between the NHHR and the incidence of stroke, implying that the NHHR could potentially serve as an innovative predictive indicator for stroke risk, in alignment with previous studies such as^[44]. This potential novel marker could contribute to more effective stroke prevention and management strategies.

5 Limitations

This research is not without its limitations. To begin with, the reliance on self-reported diagnoses of stroke might lead to bias. Additionally, the nature of the national cohort data precludes us from definitively establishing causal relationships. Furthermore, the applicability of our findings may be confined primarily to the Chinese demographic. Nevertheless, despite these constraints, our investigation offers significant contributions to the understanding of NHHR's predictive role in stroke risk assessment.

6 Conclusion

Our research has established a substantial correlation between the ratio of NHHR and the likelihood of stroke among Chinese adults. The findings highlight NHHR's significance as a prospective biomarker for predicting stroke, emphasizing its utility in clinical settings for assessing and categorizing risk levels. Subsequent studies should concentrate on deciphering the biological pathways that connect NHHR with stroke, and also investigate NHHR's applicability in the formulation of tailored preventive measures.

Declarations

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here:

CHARLS:<https://charls.pku.edu.cn/>; CHNS:<http://www.cpc.unc.edu/projects/china>; and the availability of data and materials publicly available.

Ethics approval and consent to participate

This study utilized de-identified public data from the China Health and Retirement Longitudinal Study and the CHNS. All original cohort studies were conducted in accordance with the Declaration of Helsinki and obtained ethics approval from their respective institutional review boards. Informed consent was waived for secondary analyses of anonymized data per local regulations.

Author contributions

Concept and design: Liying Xie, Feng Xu, Jianfang Hu, Haihong Wang, Weimin Wu and Qing Liu. Acquisition, analysis, and interpretation: Liying Xie, Feng Xu. Drafting of the article: Feng Xu, Jianfang Hu, Haihong Wang and Weimin Wu. Statistical analysis: Feng Xu, Jianfang Hu, Haihong Wang, Weimin Wu and Qing Liu. Supervision: Jianfang Hu and Qing Liu.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Ethics approval and consent to participate

Ethical approval and consent was not specifically for this study as we used summary data that is publicly available.

ADM statement :

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

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Tables

Table1 Characteristics of the participants at baseline

		CHNS				CHARLS			
	level	Included	Excluded	Stroke	P value	Included	Excluded	Stroke	P value
sex	female	3831 (53.4)	3798 (53.5)	33 (42.9)	0.080	4814 (51.9)	4465 (52.2)	349 (48.4)	0.054
	male	3343 (46.6)	3299 (46.5)	44 (57.1)		4459 (48.1)	4087 (47.8)	372 (51.6)	
age, M (SD), y		51.0 (14.0)	50.9 (14.0)	64.9 (9.7)	<0.001	58.8 (9.4)	58.7 (9.4)	61.0 (8.8)	<0.001
education	high	323 (4.5)	320 (4.5)	3 (3.9)	<0.001	150 (1.6)	144 (1.7)	6 (0.8)	0.047
	middle	3677 (51.3)	3655 (51.5)	22 (28.6)		2765 (29.8)	2569 (30.0)	196 (27.2)	
	primary	3174 (44.2)	3122 (44.0)	52 (67.5)		6358 (68.6)	5839 (68.3)	519 (72.0)	
SBP, M (SD)		125.0 (18.8)	124.8 (18.6)	146.8 (23.5)	<0.001	130.1 (21.4)	129.4 (21.0)	138.7 (24.1)	<0.001
DBP, M (SD)		80.8 (11.3)	80.7 (11.2)	88.9 (12.4)	<0.001	75.7 (12.1)	75.4 (12.0)	79.1 (13.0)	<0.001
height, M (SD)		160.9 (8.6)	160.9 (8.5)	160.1 (9.3)	0.418	157.9 (8.6)	157.9 (8.6)	158.2 (8.6)	0.438
weight, M (SD)		60.9 (11.3)	60.8 (11.3)	63.4 (11.5)	0.048	58.5 (11.3)	58.3 (11.2)	61.0 (12.0)	<0.001
smoking	current	2009 (28.0)	1991 (28.1)	18 (23.4)	0.151	2772 (29.9)	2547 (29.8)	225 (31.2)	<0.001
	never	4950 (69.0)	4896 (69.0)	54 (70.1)		5790 (62.4)	5379 (62.9)	411 (57.0)	
	quit	215 (3.0)	210 (3.0)	5 (6.5)		711 (7.7)	626 (7.3)	85 (11.8)	
alcohol	no	4808 (67.0)	4754 (67.0)	54 (70.1)	0.644	6063 (65.4)	5598 (65.5)	465 (64.5)	0.630
	yes	2009 (28.0)	1991 (28.1)	18 (23.4)		3210 (34.6)	2954 (34.5)	256 (35.5)	
BMI, M (SD),kg/m2		23.4 (3.4)	23.4 (3.4)	24.6 (3.5)	0.003	23.4 (3.8)	23.3 (3.8)	24.3 (3.9)	<0.001
TC, M (SD)		188.8 (38.5)	188.7 (38.5)	199.8 (37.0)	0.012	193.2 (38.5)	192.8 (38.5)	198.3 (38.5)	<0.001
TG, M (SD)		147.9 (122.1)	147.7 (122.3)	164.1 (96.5)	0.239	51.3 (15.3)	51.5 (15.4)	49.0 (14.9)	<0.001
Ldlc, M (SD)		115.9 (38.0)	115.8 (38.1)	123.0 (34.4)	0.099	116.1 (34.7)	115.8 (34.6)	120.3 (35.9)	0.001
Hdlc, M (SD)		55.1 (14.4)	55.2 (14.3)	54.7 (16.4)	0.780	51.3 (15.3)	51.5 (15.4)	49.0 (14.9)	<0.001
Glu, M (SD)		5.4 (1.5)	5.4 (1.5)	5.5 (1.4)	0.451	109.5 (34.3)	108.9 (33.2)	116.9 (45.0)	<0.001
NHHR (quartile)	Q1	1794 (25.0)	1783 (25.1)	11 (14.3)	0.031	2319 (25.0)	2197 (25.7)	122 (16.9)	<0.001
	Q2	1793 (25.0)	1776 (25.0)	17 (22.1)		2318 (25.0)	2135 (25.0)	183 (25.4)	
	Q3	1794 (25.0)	1774 (25.0)	20 (26.0)		2318 (25.0)	2129 (24.9)	189 (26.2)	
	Q4	1793 (25.0)	1764 (24.9)	29 (37.7)		2318 (25.0)	2091 (24.5)	227 (31.5)	
NHHR_per_IQR		1.8 (0.8)	1.8 (0.8)	2.0 (0.9)	0.023	1.8 (1.0)	1.8 (1.0)	2.0 (0.9)	<0.001

M, mean; SD, standard deviation; SBP, systolic blood pressure; DBP, diastolic blood pressure;BMI, body mass index; TC,total cholesterol; TG, triglyceride; hdlc, high-density lipoprotein cholesterol;ldlc, low-density lipoprotein cholesterol;Glu,glucose;NHHR, Non-high-density lipoprotein to high-density lipoprotein ratio; Q1, the 5th of the NHHR; Q2, the 35th of the NHHR; Q3, the 65th of the NHHR; Q4, the 95th of the NHHR;IQR, interquartile range;p-value for Chi-square tests (categorical variables) or independent sample ttests (continuous variables).

TABLE2:Longitudinal association between NHHR and stroke risk ,adjusted for various demographic and clinical characteristics

A:CHNS cohort

CHNS	Model 1		Model 2		Model 3	
	OR(95% CI)	p	OR(95% CI)	p	OR(95% CI)	p
MHHR per IQR	1.28 [1.01, 1.54]	0.020	1.09 [0.81,1.41]	0.534	1.08 [0.80, 1.41]	0.594
NHHR (quartile)						
Q1	Ref		Ref		Ref	
Q2	1.55 [0.73, 3.42]	0.258	1.48 [0.69, 3.29]	0.320	1.42 [0.66, 3.20]	0.376
Q3	1.83 [0.89, 3.96]	0.110	1.55 [0.73, 3.43]	0.261	1.57 [0.74, 3.50]	0.255
Q4	2.66 [1.37, 5.59]	0.006	1.78 [0.86, 3.91]	0.131	1.69 [0.81, 3.75]	0.179
P for trend		0.020		0.534		0.594

B:CHARLS cohort

CHARLS	Model 1		Model 2		Model 3	
	OR(95% CI)	p	OR(95% CI)	p	OR(95% CI)	p
NHHR per IQR	1.16[1.09,1.23]	<0.001	1.10 [1.02, 1.18]	0.007	1.09 [0.81, 1.43]	0.541
NHHR (quartile)						
Q1	Ref		Ref		Ref	
Q2	1.54 [1.22, 1.96]	<0.001	1.50 [1.16, 1.95]	0.002	1.42 [0.66, 3.19]	0.380
Q3	1.60 [1.27, 2.03]	<0.001	1.42 [1.10, 1.86]	0.008	1.60 [0.75, 3.59]	0.232
Q4	1.95 [1.56, 2.46]	<0.001	1.68 [1.30, 2.18]	<0.001	1.73 [0.83, 3.85]	0.160
P for trend		<0.001		<0.001		<0.001

Model 1 was crude model.

Model 2 was adjusted for age, gender, education level, body mass index (BMI), height, weight .

Model 3 was adjusted for age, gender, education level, body mass index (BMI), height, weight, smoking status, alcohol status, SBP and DBP.

NHHR, Non-high-density lipoprotein to high-density lipoprotein ratio; Q1, the 5th of the NHHR; Q2, the 35th of the NHHR; Q3, the 65th of the NHHR; Q4, the 95th of the NHHR;IQR, interquartile range; CHARLS, China Health and Retirement Longitudinal Study; SBP, systolic blood pressure; DBP, diastolic blood pressure

Figures

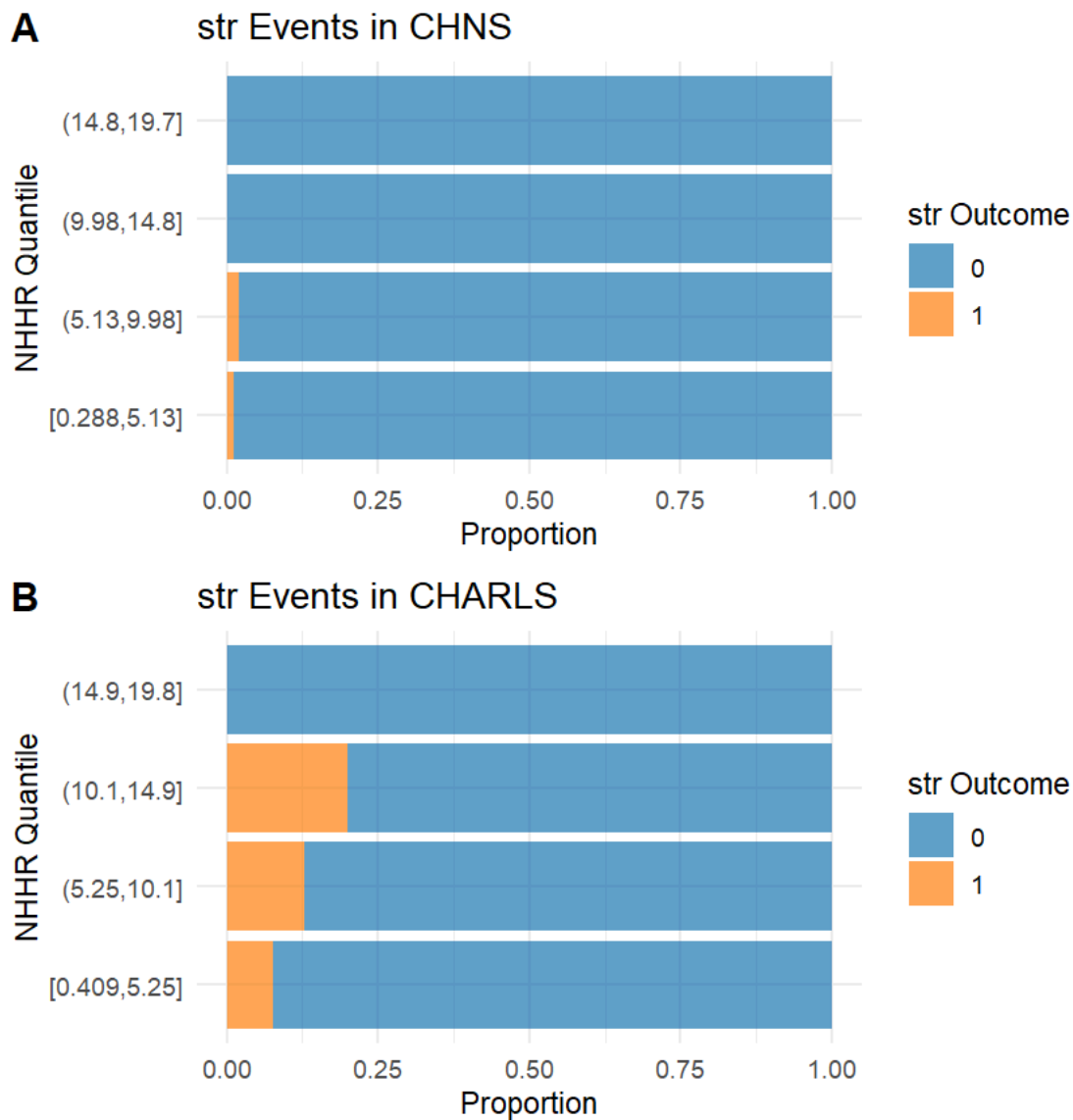
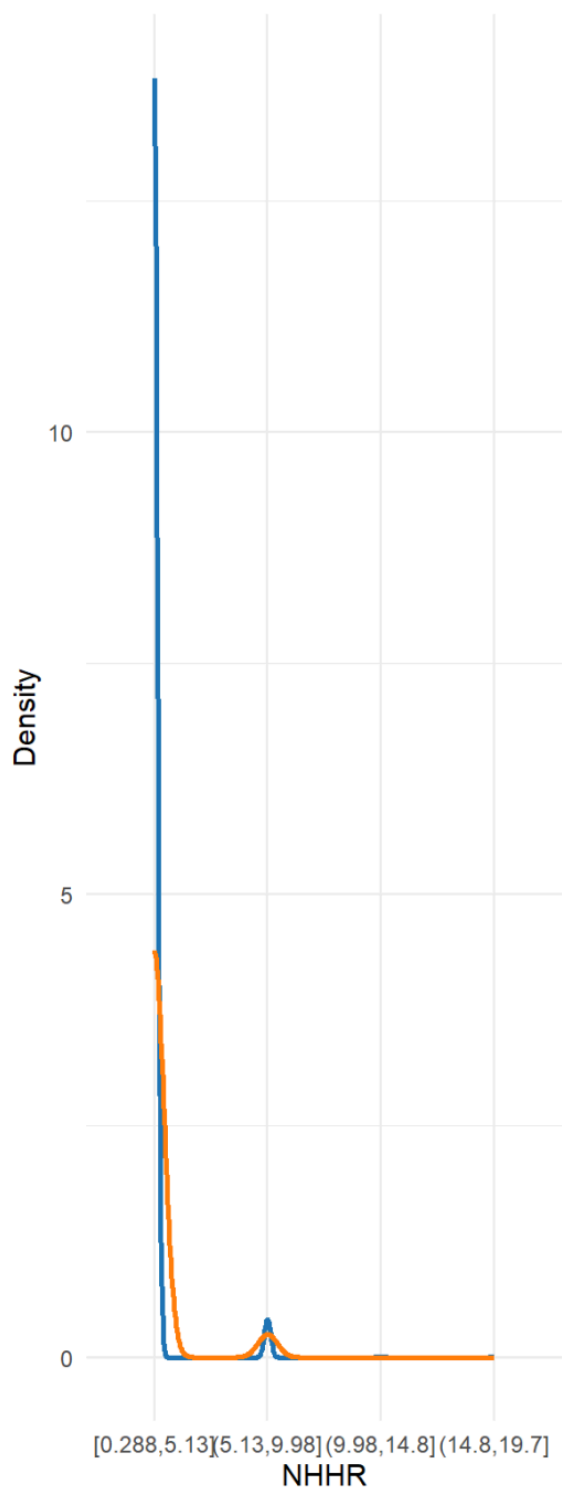


Figure 1

The distribution of stroke occurrence based on NHHR among participants from CHNS and CHARLS.

STR,stroke;NHHR, Non-high-density lipoprotein to high-density lipoprotein ratio; CHNS indicates China Health and Nutrition Survey; and CHARLS, China Health and Retirement Longitudinal Study

A STR Event Distribution in CHNS



B STR Event Distribution in CHARLS

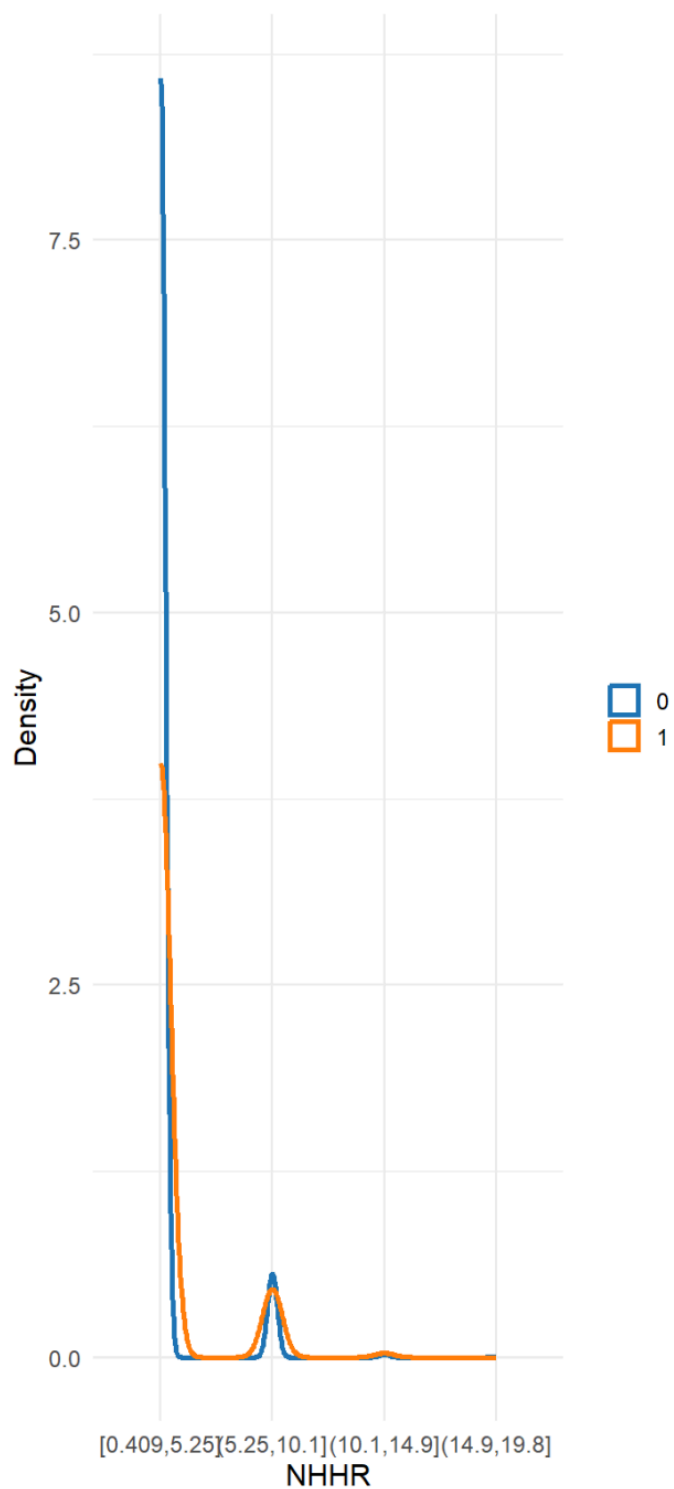


Figure 2

The distribution of NHHR based on incident stroke status among participants from CHNS and CHARLS .

STR,stroke;NHHR, Non-high-density lipoprotein to high-density lipoprotein ratio; CHNS indicates China Health and Nutrition Survey; and CHARLS, China Health and Retirement Longitudinal Study.

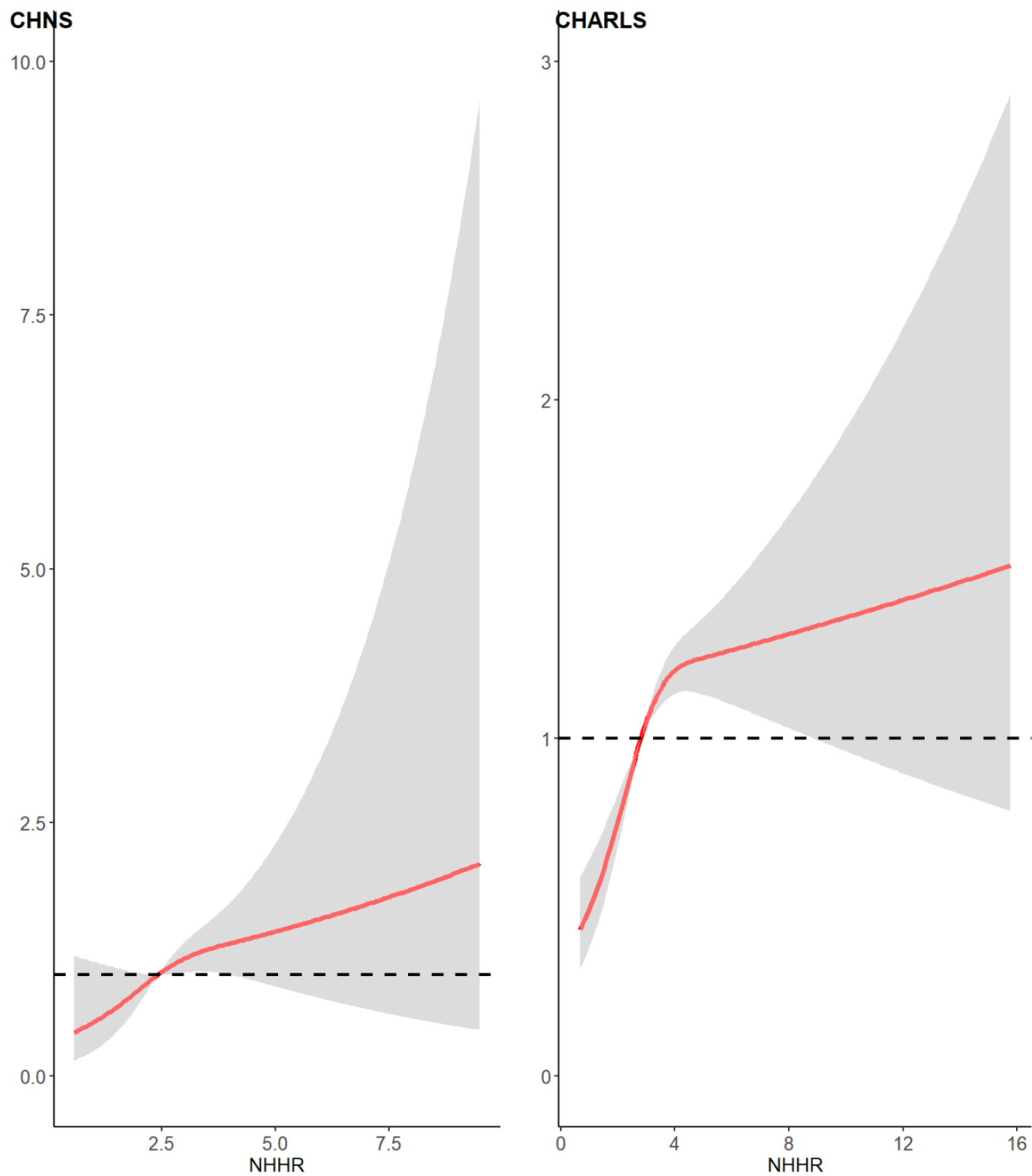


Figure 3
Dose–response relationship of the discordance between NHHR with stroke onset.

NHHR, Non-high-density lipoprotein to high-density lipoprotein ratio; CHNS, China Health and Nutrition Survey; CHARLS, China Health and Retirement Longitudinal Study;

Forest Plot of Logistic Regression Model

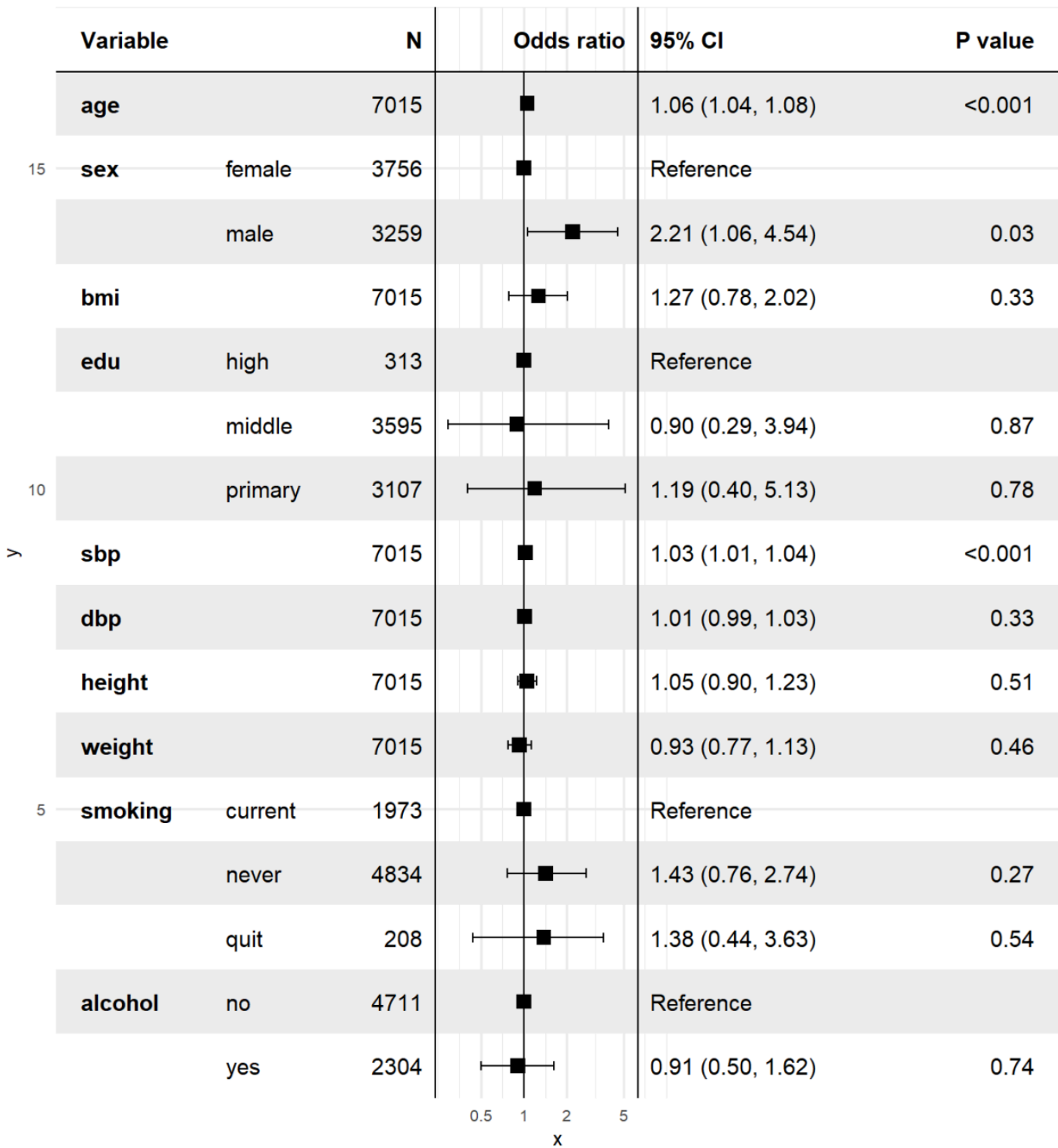


Figure 4

Forest plot from CHNS of analysis of the association of NHHR with the risk of stroke.

OR, odds ratio; CI, confidence intervals; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; CHNS, China Health and Nutrition Survey.

p-value for Chi-square tests (categorical variables) or independent sample t-tests (continuous variables)

Forest Plot of Logistic Regression Model

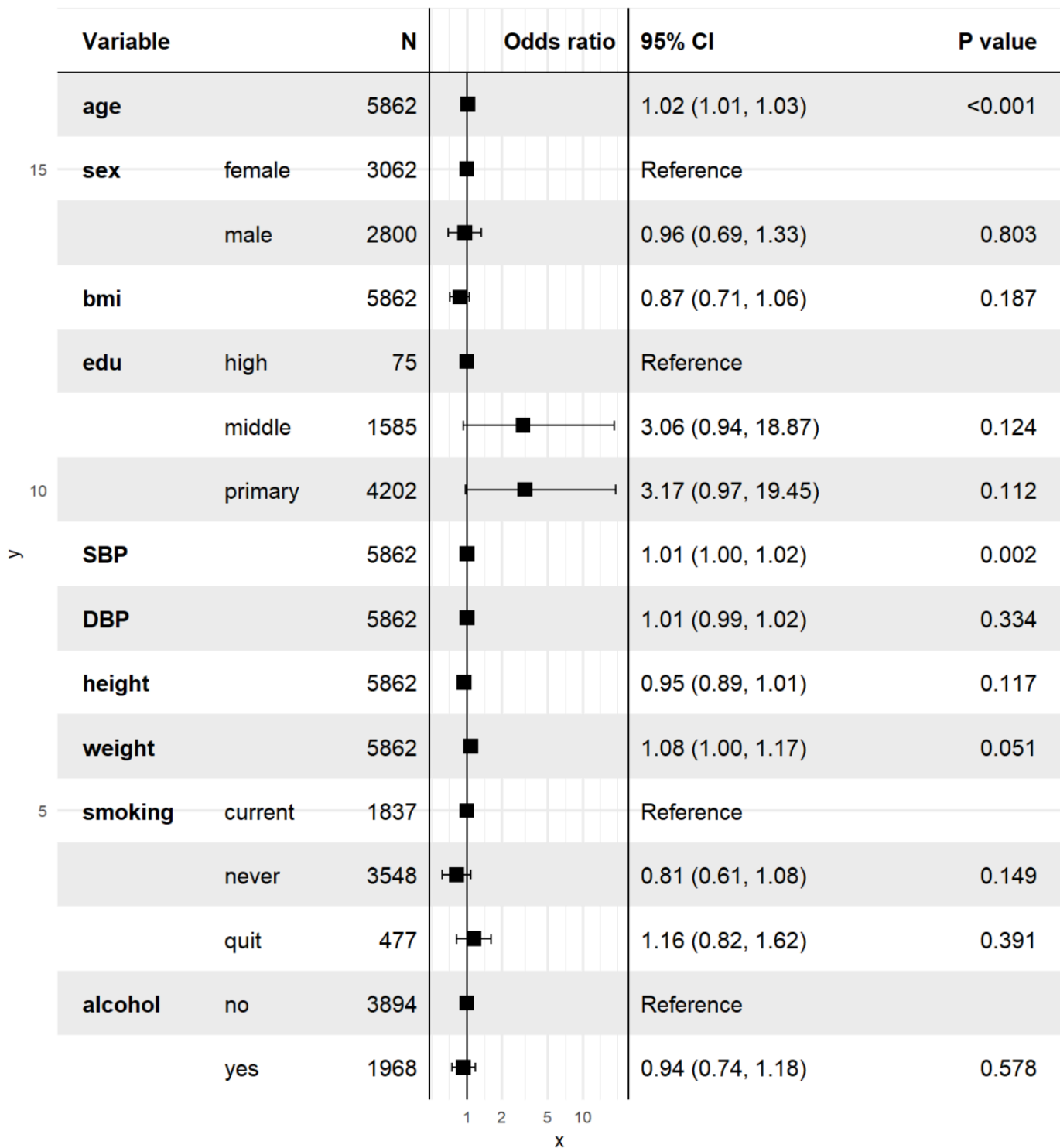


Figure 5

Forest plot from CHARLS of analysis of the association of NHHR with the risk of stroke.

OR, odds ratio; CI, confidence intervals; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; CHARLS, China Health and Retirement Longitudinal Study.

p-value for Chi-square tests (categorical variables) or independent sample ttests (continuous variables).