

Association between the serum uric acid-to-high-density lipoprotein cholesterol ratio and hypertension: a cross-sectional study using NHANES and CHARLS data

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Abstract

Background

Hypertension is a highly prevalent cardiovascular disease associated with metabolic and vascular risks. This study was designed to investigate the association between the serum uric acid to high-density lipoprotein cholesterol ratio (UHR) and hypertension risk, and to establish and validate a hypertension risk prediction nomogram.

Methods

Data were obtained from the National Health and Nutrition Examination Survey (NHANES) and the China Health and Retirement Longitudinal Study (CHARLS). Subsequently, serum uric acid and high-density lipoprotein cholesterol levels were extracted, and the UHR was calculated. Following this, baseline characteristics were summarized and compared. Furthermore, Extreme Gradient Boosting (XGBoost) was applied to evaluate feature importance. Then, logistic regression models were constructed with three progressive adjustment strategies to explore the independent association between UHR and hypertension risk. Additionally, stratified analyses were conducted to assess the stability of the UHR-hypertension association across subgroups. Finally, a nomogram was established and evaluated.

Results

First, baseline analyses revealed that UHR was significantly associated with hypertension in both cohorts. Meanwhile, XGBoost feature importance analysis indicated that UHR contributed stably to hypertension prediction in both NHANES and CHARLS datasets. More importantly, multivariate logistic regression demonstrated that elevated UHR was independently and positively associated with increased hypertension risk in a graded manner, and the association remained robust after full covariate adjustment. Subsequently, stratified analyses confirmed that the positive association was consistent across most age, smoking, and comorbidity subgroups, with only minor effect modification detected in some subgroups. Ultimately, the constructed nomogram showed favorable calibration, clinical net benefit, and discriminative performance in both databases.

Conclusion

The UHR is an independent and stable predictive factor for hypertension. The UHR-integrated nomogram shows reliable performance in hypertension risk stratification and may serve as a practical tool for early screening and individualized clinical assessment of hypertension.

1 Background

Hypertension is a common chronic cardiovascular disorder characterized by persistently elevated blood pressure. It is a major risk factor for coronary heart disease, heart failure, stroke, and kidney failure[1]. Hypertension is also a major global public health problem, and its burden continues to rise with population ageing[2, 3]. In China, hypertension remains highly prevalent, and treatment and control rates are still suboptimal[4]. In 2019, the number of hypertensive patients aged 30–79 worldwide exceeded 1.2 billion; In China, recent national monitoring data also suggests that the prevalence of hypertension remains high, and the treatment and control rates are still unsatisfactory[5]. Therefore, the identification of accessible, low-cost, and reproducible risk markers is of practical significance for the early screening and stratified management of hypertension. Hypertension often coexists with obesity, diabetes, smoking, and other unhealthy lifestyle factors[6]. Recent national data from China indicate that prevalence remains high whereas treatment and control rates are still suboptimal. Therefore, accessible, low-cost, and reproducible biomarkers are still needed for early screening and risk stratification[7].

The National Health and Nutrition Examination Survey (NHANES) is a nationwide health survey that includes health and laboratory examinations for participants of all ages, aiming to assess the nutritional and physical health of the non-institutionalized U.S. population[8]. The China Health and Retirement Longitudinal Study (CHARLS) is a nationally representative longitudinal survey of the middle-aged and elderly populations of China, which evaluates the social, economic, and health circumstances of individuals aged 45 years or older, providing an important platform for exploring risk factors for chronic diseases in the Chinese population[9]. Using these two large databases helps improve population coverage and the generalizability of the findings. UHR has recently been proposed as a simple combined metabolic marker and has shown potential value in conditions such as metabolic syndrome and diabetic kidney disease[10, 11]. Hypertension is closely linked to inflammation, endothelial dysfunction, and metabolic imbalance [12]. Recent studies have shown that higher UHR is associated with poor blood pressure control and vascular dysfunction, suggesting that it may capture risk information beyond single markers[13]. UHR integrates two metabolic signals, namely increased uric acid and reduced HDL-C, and may therefore capture oxidative stress, inflammatory activation, and endothelial dysfunction more comprehensively than a single marker[13–15]. This provides a biologically plausible rationale for evaluating the association between UHR and hypertension across different populations. Against this background, we aimed to evaluate the association between UHR and hypertension in the US NHANES and Chinese CHARLS populations and to develop a UHR-based nomogram to test whether UHR adds value to hypertension risk stratification across populations.

2 Methods

Database and study cohort

Data from the National Health and Nutrition Examination Survey (NHANES) database (<https://www.cdc.gov/nchs/nhanes/index.html>) spanning the period from 1999 to 2018 were included in this study (access date: January 16, 2026). Inclusion criteria were as follows: hypertensive patients were screened from the NHANES database using the questionnaire code (BPQ020: Ever told you had high

blood pressure?). Serum uric acid levels of patients were retrieved using the code (LBXSUA: Uric acid (mg/dL)), and direct high-density lipoprotein cholesterol levels were obtained via the code (LBDHDD: Direct HDL-Cholesterol (mg/dL)). The serum uric acid to high-density lipoprotein cholesterol ratio (UHR) was calculated as serum uric acid divided by high-density lipoprotein cholesterol. Exclusion criteria included age < 18 years, missing outcome data, missing covariate data, and missing information on serum uric acid and high-density lipoprotein cholesterol. A total of 16,056 subjects were finally enrolled (Fig. 1a). Data from the China Health and Retirement Longitudinal Study (CHARLS) database (<http://charls.pku.edu.cn/>) from the 2011 survey were included in the study (access date: January 16, 2026). All participants had provided written informed consent prior to enrollment. Inclusion criteria were as follows: hypertensive patients were screened from the questionnaire dataset by searching for the relevant question using the questionnaire code (DA007: Have you been diagnosed with [conditions listed below, read one by one] by a doctor?). Serum uric acid levels of patients were retrieved using the code (newua: Uric Acid (mg/dL)), and high-density lipoprotein cholesterol levels were obtained via the code (newhdl: High Density Lipoprotein Cholesterol (mg/dL)). Exclusion criteria included age < 45 years, missing outcome data, missing covariate data, and missing information on serum uric acid and high-density lipoprotein cholesterol. A total of 10,686 subjects were finally enrolled (Fig. 1b).

The baseline characteristics of patients from the NHANES and CHARLS databases included the following variables: hypertension (yes/no), serum uric acid (continuous variable, mg/dL), high-density lipoprotein cholesterol (continuous variable, mg/dL), UHR (quartiles, Q1-Q4 with increasing numerical levels), age (divided into low, middle, and high age groups using tertile classification), gender (male/female), marital status (married/unmarried), education level (junior high school or below/junior high school or above), smoking status (yes/no), diabetes mellitus (yes/no), asthma (yes/no), heart disease (yes/no), stroke (yes/no), cancer (yes/no), creatinine (continuous variable, mg/dL), glycosylated hemoglobin (continuous variable, %), hemoglobin (continuous variable, g/dL), hematocrit (continuous variable, %), low-density lipoprotein (continuous variable, mg/dL), blood urea nitrogen (continuous variable, mg/dL), and total cholesterol (continuous variable, mg/dL) (Table 1).

Table 1
Information of covariates and their corresponding variable codes

Variable	Variable Definition	NHANES Code	CHARLS Code	Year
Hypertension (Outcome)	Categorical Variable	BPQ020	da007_1_	NHANES:1999–2018; CHARLS:2011
Serum Uric Acid	Continuous Variable	LBXSUA	newua	NHANES:1999–2018; CHARLS:2011
High-Density Lipoprotein Cholesterol	Continuous Variable	LBDHDD	newhdl	NHANES:1999–2018; CHARLS:2011
UHR (Exposure)	Categorical Variable	-	-	NHANES:1999–2018; CHARLS:2011
Age	Categorical Variable	RIDAGEYR	ba002_1	NHANES:1999–2018; CHARLS:2011
Gender	Categorical Variable	RIAGENDR	rgender	NHANES:1999–2018; CHARLS:2011
Marital Status	Categorical Variable	DMDMARTL	be001	NHANES:1999–2018; CHARLS:2011
Education	Categorical Variable	DMDEDUC2	bd001	NHANES:1999–2018; CHARLS:2011
Smoking	Categorical Variable	SMQ020	da059	NHANES:1999–2018; CHARLS:2011
Diabetes Mellitus	Categorical Variable	DIQ010	da007_3_	NHANES:1999–2018; CHARLS:2011
Asthma	Categorical Variable	MCQ010	da007_14_	NHANES:1999–2018; CHARLS:2011
Heart Disease	Categorical Variable	MCQ160E	da007_7_	NHANES:1999–2018; CHARLS:2011
Stroke	Categorical Variable	MCQ160F	da007_8_	NHANES:1999–2018; CHARLS:2011
Cancer	Categorical Variable	MCQ220	da007_4_	NHANES:1999–2018; CHARLS:2011
Creatinine	Continuous Variable	LBXSCR	newcrea	NHANES:1999–2018; CHARLS:2011
Glycated Hemoglobin (HbA1c)	Continuous Variable	LBXGH	newhba1c	NHANES:1999–2018; CHARLS:2011
Hemoglobin	Continuous Variable	LBXHGB	qc1_vb004	NHANES:1999–2018; CHARLS:2011

Variable	Variable Definition	NHANES Code	CHARLS Code	Year
Hematocrit	Continuous Variable	LBXHCT	qc1_vb005	NHANES:1999–2018; CHARLS:2011
Low-Density Lipoprotein (LDL) Cholesterol	Continuous Variable	LBDLDL	newldl	NHANES:1999–2018; CHARLS:2011
Blood Urea Nitrogen (BUN)	Continuous Variable	LBXSBU	newbun	NHANES:1999–2018; CHARLS:2011
Total Cholesterol	Continuous Variable	LBXTC	newcho	NHANES:1999–2018; CHARLS:2011

Statistical analysis

Statistical analyses were performed using R software (v 4.2.2). Baseline statistics were performed using the tableone package (version 0.13.2)[16]. For the description of baseline characteristics, categorical variables were presented as percentages, and analyses were conducted using the chi-square test (for categorical variables) and t-test (for continuous variables). An eXtreme Gradient Boosting (XGBoost) model was constructed using the xgboost package (version 1.7.7.1)[17], and the contribution of exposure factors to hypertension prediction was systematically evaluated based on the feature importance scoring system of Gain values. To further investigate the influencing factors of hypertension, the glmnet package (version 4.1-8) [18] was utilized to construct logistic regression models for exploring the relationship between exposure factors and the disease, with adjusted odds ratios (ORs) and 95% confidence intervals (CIs) calculated. Three models were established: Model 1 was adjusted only for exposure factors; Model 2 was further adjusted for age, gender, and education level on the basis of Model 1; and Model 3 incorporated all confounding factors in addition to the adjustments in Model 2. Finally, the rms package (version 6.5.0)[19] was used to draw a nomogram. Calibration curves were generated using the regplot package (version 1.1)[20], decision curve analysis (DCA) curves were plotted with the rmda package (version 1.6)[21], and Receiver Operating Characteristic (ROC) curves were constructed using the pROC package (version 1.18.5)[22]. An area under the curve (AUC) > 0.7 was considered to indicate a certain diagnostic ability. Two-tailed tests with $p < 0.05$ were regarded as statistically significant.

3 Results

Patient characteristics

To clarify the associations between hypertension and various potential variables, statistical analyses of baseline data from the NHANES and CHARLS databases were performed in this study. In the NHANES database, significant correlations with hypertension were identified for the UHR, age, marital status, educational level, smoking status, diabetes mellitus, asthma, stroke, cancer, heart disease, and other

demographic and clinical characteristics, as well as laboratory indicators including creatinine, hemoglobin, glycosylated hemoglobin, hematocrit, low-density lipoprotein, total cholesterol, and blood urea nitrogen ($p < 0.05$), while no statistically significant association was detected for gender alone (Table 2). For the CHARLS database, the analysis results revealed that UHR, age, gender, marital status, smoking status, diabetes mellitus, stroke, heart disease, and other demographic and clinical characteristics, together with laboratory indicators such as creatinine, hemoglobin, glycosylated hemoglobin, hematocrit, low-density lipoprotein, and total cholesterol, were significantly associated with hypertension ($p < 0.05$). In contrast, the associations of educational level, asthma, cancer, and blood urea nitrogen with hypertension did not achieve statistical significance (Table 3). Consistent findings from the two databases indicated that UHR, age, marital status, smoking status, diabetes mellitus, stroke, heart disease, and multiple metabolism-related laboratory indicators (e.g., creatinine, hemoglobin, glycosylated hemoglobin) were all potential influencing factors closely linked to hypertension. Population differences were only observed in the associations of gender, educational level, certain diseases (asthma, cancer), and the laboratory indicator (blood urea nitrogen) with hypertension, which may partly reflect differences in age eligibility between the two databases (NHANES included individuals aged ≥ 18 years, while CHARLS enrolled those aged ≥ 45 years).

Table 2
Baseline characteristics of participants in the NHANES cohort

n	Level	No	Yes	p
		10399	5657	
UHR (%)	Q1	3143 (30.2)	1072 (18.9)	< 0.001
	Q2	2712 (26.1)	1345 (23.8)	
	Q3	2459 (23.6)	1586 (28.0)	
	Q4	2085 (20.1)	1654 (29.2)	
Age (%)	Low	4375 (42.1)	538 (9.5)	< 0.001
	Middle	3767 (36.2)	1804 (31.9)	
	High	2257 (21.7)	3315 (58.6)	
Sex (%)	Female	5416 (52.1)	2961 (52.3)	0.765
	Male	4983 (47.9)	2696 (47.7)	
Marital Status (%)	Unmarried	5042 (48.5)	2624 (46.4)	0.011
	Married	5357 (51.5)	3033 (53.6)	
Education (%)	Low Education	1042 (10.0)	669 (11.8)	< 0.001
	High Education	9357 (90.0)	4988 (88.2)	
Smoking (%)	No	6068 (58.4)	2855 (50.5)	< 0.001
	Yes	4331 (41.6)	2802 (49.5)	
Diabetes (%)	No	9744 (93.7)	4260 (75.3)	< 0.001
	Yes	655 (6.3)	1397 (24.7)	
Asthma (%)	No	9049 (87.0)	4723 (83.5)	< 0.001
	Yes	1350 (13.0)	934 (16.5)	
Heart Disease (%)	No	10198 (98.1)	5159 (91.2)	< 0.001
	Yes	201 (1.9)	498 (8.8)	

n	Level	No	Yes	p
		10399	5657	
Stroke (%)	No	10245 (98.5)	5212 (92.1)	< 0.001
	Yes	154 (1.5)	445 (7.9)	
Cancer (%)	No	9768 (93.9)	4827 (85.3)	< 0.001
	Yes	631 (6.1)	830 (14.7)	
Creatinine (mean (SD))	-	0.83 (0.20)	0.93 (0.26)	< 0.001
Glycosylated Hemoglobin (mean (SD))	-	5.56 (0.94)	6.07 (1.22)	< 0.001
Hemoglobin (mean (SD))	-	14.20 (1.52)	13.99 (1.59)	< 0.001
Hematocrit (mean (SD))	-	41.94 (4.24)	41.49 (4.47)	< 0.001
Low-Density Lipoprotein-Cholesterol (mean (SD))	-	114.92 (35.19)	111.01 (36.37)	< 0.001
Blood Urea Nitrogen (BUN) (mean (SD))	-	12.35 (4.37)	14.95 (6.14)	< 0.001
Total Cholesterol (mean (SD))	-	192.50 (40.46)	190.25 (41.86)	0.001

Table 3
Baseline characteristics of participants in the CHARLS cohort

n	Level	No	Yes	p
		7913	2773	
UHR (%)	Q1	2211 (27.9)	476 (17.2)	< 0.001
	Q2	2085 (26.3)	598 (21.6)	
	Q3	1948 (24.6)	740 (26.7)	
	Q4	1669 (21.1)	959 (34.6)	
Age (%)	High	2192 (27.7)	1118 (40.3)	< 0.001
	Low	2955 (37.3)	634 (22.9)	
	Middle	2766 (35.0)	1021 (36.8)	
Sex (%)	Female	4100 (51.8)	1536 (55.4)	0.001
	Male	3813 (48.2)	1237 (44.6)	
Education (%)	High Education	824 (10.4)	298 (10.7)	0.648
	Low Education	7089 (89.6)	2475 (89.3)	
Marital Status (%)	Married	7025 (88.8)	2381 (85.9)	< 0.001
	Unmarried	888 (11.2)	392 (14.1)	
Smoking (%)	No	4696 (59.3)	1750 (63.1)	0.001
	Yes	3217 (40.7)	1023 (36.9)	
Diabetes (%)	No	7637 (96.5)	2423 (87.4)	< 0.001
	Yes	276 (3.5)	350 (12.6)	
Asthma (%)	No	7628 (96.4)	2657 (95.8)	0.184
	Yes	285 (3.6)	116 (4.2)	
Heart Disease (%)	No	7267 (91.8)	2097 (75.6)	< 0.001
	Yes	646 (8.2)	676 (24.4)	
XGBoost feature importance analysis				

n	Level	No	Yes	p
		7913	2773	
Stroke (%)	No	7819 (98.8)	2607 (94.0)	< 0.001
	Yes	94 (1.2)	166 (6.0)	
Cancer (%)	No	7833 (99.0)	2743 (98.9)	0.835
	Yes	80 (1.0)	30 (1.1)	
Creatinine (mean (SD))	-	0.77 (0.18)	0.81 (0.21)	< 0.001
Glycosylated Hemoglobin (mean (SD))	-	5.23 (0.77)	5.39 (0.92)	< 0.001
Hemoglobin (mean (SD))	-	14.34 (2.21)	14.60 (2.25)	< 0.001
Hematocrit (mean (SD))	-	41.59 (6.11)	42.08 (5.89)	< 0.001
Low-Density Lipoprotein-Cholesterol (mean (SD))	-	115.44 (34.17)	118.79 (36.31)	< 0.001
Blood Urea Nitrogen (BUN) (mean (SD))	-	15.72 (4.47)	15.87 (4.53)	0.113
Total Cholesterol (mean (SD))	-	191.93 (37.74)	196.79 (38.87)	< 0.001
XGBoost feature importance analysis				

To systematically evaluate the predictive efficacy of UHR and other potential variables for the risk of hypertension, the XGBoost model was employed in this study to conduct feature importance analysis, aiming to clarify the priority of predictive contributions of each variable. The analysis results from the NHANES database revealed that demographic characteristics (age), metabolism-related laboratory indicators (e.g., creatinine, glycosylated hemoglobin, low-density lipoprotein cholesterol), and comorbidity status (diabetes mellitus) were all core predictive factors for hypertension, with age ranking first in terms of predictive importance. UHR ranked 9th among all variables in predictive importance, exhibiting a clear contribution (Gain = 0.044), and its predictive value was significantly superior to smoking status, marital status, educational level, as well as multiple comorbidities such as stroke, heart disease, asthma, and cancer (Fig. 2a). For the CHARLS database, the results indicated that comorbidity status (heart disease) and metabolic/hematological indicators (e.g., total cholesterol, hemoglobin, blood urea nitrogen, creatinine, hematocrit) occupied important positions among the predictive factors. UHR ranked 8th in predictive importance with a contribution of 0.081, which was significantly superior to demographic characteristics including diabetes mellitus, age, stroke, and gender, as well as smoking status and comorbidities such as asthma and cancer (Fig. 2b). Consistent findings from both databases

confirmed that UHR exerted a stable and clear contribution to hypertension risk prediction, and its predictive value was superior to multiple traditional demographic characteristics and comorbid factors. These results further support the potential clinical application value of UHR as an indicator for hypertension risk prediction.

Risk association and stratified analysis

To investigate the association between the exposure factor UHR and the risk of hypertension, three progressively adjusted regression models were constructed, and risk association analysis was performed based on UHR quartiles. Results from both databases showed that a significant positive correlation existed between UHR levels and the risk of hypertension: compared with the lowest UHR quartile (Q1), the risk of hypertension in the Q2, Q3, and Q4 groups gradually increased with the elevation of UHR levels. In the analysis of the NHANES database, from Model 1 (without adjusting for covariates) to Model 2 (adjusted for age, gender, and educational level), and further to Model 3 (additionally incorporating smoking status, marital status, diabetes mellitus, other comorbidities (asthma, heart disease, stroke, cancer), and multiple hematological and biochemical indicators), the positive association between UHR and hypertension remained significant with robust effect magnitude. The association strength in Model 2 was further enhanced compared with Model 1, and even after comprehensive adjustment for confounding factors, the risk of hypertension in the high UHR group (Q4) was still significantly higher than that in the Q1 group (Table 4). The analysis results from the CHARLS database were highly consistent with those from the NHANES database: the association between elevated UHR quartiles and increased hypertension risk was statistically significant in all three models, the risk estimates in Model 2 were slightly higher than those in Model 1, and the association was not attenuated after incorporating comprehensive confounding factors such as smoking status and marital status. The high UHR levels (Q3 and Q4) still maintained robust risk predictive value for hypertension (Table 5). In summary, consistent findings from both databases confirmed that a stable and significant positive association existed between UHR and hypertension risk, which was not significantly affected by confounding factors including demographic characteristics, lifestyle factors, comorbidities, and other hematological and biochemical indicators. Moreover, the risk showed an increasing trend with the elevation of UHR levels, suggesting that UHR may be an independent associated factor for increased hypertension risk.

Table 4
Risk association analysis between UHR and hypertension across three models
in the NHANES cohort

Different Model	Different Levels of UHR	OR	pvalue
Model 1	UHR Q2	1.386818056	3.47109E-06
	UHR Q3	1.872684587	1.88028E-21
	UHR Q4	2.484829393	1.93276E-27
Model 2	UHR Q2	1.628205113	9.06861E-09
	UHR Q3	2.44739552	5.74369E-24
	UHR Q4	3.842329147	1.53369E-32
Model 3	UHR Q2	1.745596937	1.77832E-09
	UHR Q3	2.635485487	3.40082E-21
	UHR Q4	3.946286252	1.15189E-27

Table 5
Risk association analysis between UHR and hypertension across three
models in the CHARLS cohort

Different Model	Different Levels of UHR	OR	pvalue
Model 1	UHR Q2	1.3322	0.0000289
	UHR Q3	1.7645	1.3E-17
	UHR Q4	2.669	6.83E-52
Model 2	UHR Q2	1.3944	0.00000183
	UHR Q3	1.9044	3.61E-21
	UHR Q4	3.0813	4.34E-61
Model 3	UHR Q2	1.3832	0.00000815
	UHR Q3	1.7855	9.26E-16
	UHR Q4	2.5941	7.59E-38

To further verify the population applicability and potential modification effect of the positive association between UHR and hypertension, stratified analysis was conducted based on the NHANES and CHARLS databases, with key characteristics including age, smoking status, and comorbidities such as diabetes mellitus, asthma, heart disease, and stroke, to examine the consistency of this association across different population subgroups. The core results from both databases were highly consistent: in the total population, a significant positive correlation was observed between UHR levels and hypertension risk,

with the risk of hypertension continuously increasing with the gradient elevation of UHR quartiles (from Q1 to Q4) (all $p < 0.001$). Stratified analysis revealed that this positive association remained stable and significant across different age groups (low, middle, high), smoking status subgroups (smokers/non-smokers), and healthy population subgroups without diabetes mellitus, asthma, heart disease, or stroke (all $p < 0.05$). Among these, the modification effects of age, heart disease, and stroke on the association were not statistically significant (most interaction $p > 0.05$), indicating that the association between UHR and hypertension had good population generalizability. Differences among subgroups were mainly reflected in potential modifying factors: in the NHANES database, the interaction effect of smoking status was statistically significant ($p = 0.043$), but the positive trend of the association was not reversed; in the CHARLS database, the interaction effect of diabetes mellitus status was statistically significant ($p = 0.008$), with only the Q3 and Q4 UHR groups showing a significant increase in hypertension risk, suggesting that diabetes mellitus may modify the strength of this association. In addition, in the asthma subgroup of the CHARLS database, the risk estimate of the Q4 group was significantly higher (OR = 5.53, $p < 0.001$), but the interaction effect was not statistically significant ($p = 0.205$), which did not affect the overall consistency of the association (Figs. 3a-b). In summary, the positive association between UHR and hypertension was robust and consistent across most population subgroups, with only a potential modification effect on the association strength observed in the context of diabetes mellitus. These findings further confirm the reliability of UHR as an associated factor for hypertension risk, and its associative value is applicable across different age groups, smoking statuses, and most comorbidity subgroups, providing a basis for population stratification in subsequent clinical applications.

Nomogram construction and evaluation

To improve the identification and risk stratification of hypertension status, we developed a UHR-based nomogram and evaluated its discrimination, calibration, and potential net benefit in both datasets. The present study took UHR, demographic characteristics (age, gender, educational level, marital status), lifestyle factors (smoking status), comorbidities (diabetes mellitus, asthma, stroke, cancer, heart disease), and laboratory indicators (creatinine, hemoglobin, glycosylated hemoglobin, hematocrit, low-density lipoprotein, total cholesterol, blood urea nitrogen) as predictive variables, with hypertension as the outcome variable. Nomogram prediction models were constructed respectively, and systematic evaluations were performed from three aspects: calibration, clinical net benefit, and discriminative ability. For the nomograms constructed from both databases, the total score was obtained by summing the scores of individual indicators. Specifically, for the nomogram derived from the NHANES database, a total score of 1,040 corresponded to a predicted probability of hypertension of 43.3%, while for that from the CHARLS database, a total score of 620 was associated with a predicted probability of 46.7%. The model evaluation results showed high consistency: in the calibration curves, the predicted probabilities of the nomograms from both databases exhibited a high degree of overlap with the reference line (slope approaching 1), indicating good goodness of fit of the models and strong consistency between the predicted values and actual outcomes. In the DCA, the model curves maintained a certain distance from the two extreme curves ("All" and "None") with net benefit values greater than 0, demonstrating that the models had good clinical practical value and could bring positive benefits to clinical decision-making. In

the ROC curves, the AUC of the nomogram from the NHANES database was 0.794, and that from the CHARLS database was 0.718, confirming that the models possessed good discriminative ability and could effectively identify high-risk individuals for hypertension (Figs. 4a-b). In summary, the nomogram prediction models constructed based on the two databases performed well in terms of goodness of fit, clinical net benefit, and discriminative ability, with consistent results across databases. These findings suggest that the models may serve as useful tools for hypertension screening and risk stratification.

4 Discussion

Hypertension remains a major global cardiovascular risk factor and continues to impose a substantial health burden[23, 24]. Using NHANES and CHARLS, we found a stable positive association between UHR and hypertension, and the UHR-based nomogram showed acceptable discrimination and calibration in both datasets. These findings suggest that UHR may serve as a simple candidate marker for hypertension screening and risk stratification. Our findings support an independent association between UHR and hypertension, but this association should not be interpreted as causal. A more cautious interpretation is that UHR may serve as a candidate marker for hypertension risk stratification, pending confirmation in prospective studies.

This study found that higher UHR was associated with hypertension in both US and Chinese populations. The association remained after adjustment for demographic characteristics, lifestyle factors, comorbidities, and metabolic indicators. This pattern is consistent with previous reports in US women and Iranian adults[13, 25]. Notably, this study found a significant association between gender and hypertension in the CHARLS database, whereas no significant association was observed in NHANES. One possible explanation is the older age structure of CHARLS. This may also be consistent with earlier sex-stratified findings[13].

Uric acid (UA), an end product of purine metabolism, may contribute to hypertension by inducing oxidative stress, reducing endothelial nitric oxide bioavailability, and activating the renin-angiotensin system[26]. Lower HDL cholesterol reflects metabolic dysregulation and reduced anti-inflammatory protection[27]. By combining elevated uric acid with reduced HDL cholesterol, UHR may better reflect the metabolic-inflammatory profile linked to hypertension[28]. Zhou et al. [29] reported that UHR was associated with insulin resistance. A study in Iran also linked UHR to metabolic syndrome and related risk stratification[30]. These observations are consistent with evidence that metabolic disturbance is a core driver of hypertension[31, 32]. Higher UHR has also been linked to inflammatory conditions. Kurtkulagi et al.[33] reported that UHR was associated with Hashimoto's thyroiditis. Recent population studies also reported positive associations between UHR and hypertension in women[25]. Higher UHR was also associated with poor blood pressure control in patients with hypertension[34]. UA induces hypertension initially by triggering renal vasoconstriction, ischemia, and oxidative stress, which are followed by the activation of immune mechanisms that cause persistent inflammation in target organs and drive the increase in blood pressure[26, 35]. Although the exact mechanism remains unclear, a pathway involving metabolic dysfunction, low-grade inflammation, and vascular impairment is

biologically plausible. In our study, the correlations between UHR and metabolic markers such as creatinine, glycated hemoglobin, and low-density lipoprotein cholesterol also support this interpretation.

The potential value of UHR for hypertension risk stratification is supported by multiple lines of evidence, and its advantages are further highlighted when compared with other metabolic indicators. In this study, XGBoost analysis showed that UHR ranked 9th in the NHANES database and 8th in the CHARLS database, respectively, with higher feature importance than smoking status, marital status, and several comorbidities such as stroke and asthma. These findings are in line with previous studies linking higher UHR with hypertension, frailty, and mortality[13, 36]. Because uric acid and HDL-C are routinely measured, UHR may be easy to apply in large datasets and clinical practice. The nomogram constructed in this study showed acceptable performance in both databases. Calibration and decision curve analyses suggested potential clinical utility, although further validation is needed before clinical application. This is in line with the broader view that hypertension risk stratification should integrate multiple dimensions rather than rely on a single marker[37].

The subgroup analyses provide additional information on possible heterogeneity in the UHR-hypertension association. This study found that the association between UHR and hypertension was stable in people of different ages, smoking statuses, and individuals without diabetes, stroke, or heart disease. Only diabetes exerted a modifying effect: in the CHARLS database, hypertension risk was significantly elevated only in the UHR Q3 and Q4 groups among diabetic patients. This is consistent with findings that UHR is more strongly associated with mortality in the diabetic subgroup, which may reflect a heavier metabolic burden in this subgroup[38]. Across age groups, the direction of the association was similar, suggesting that UHR may be relevant in both younger and older adults. However, these data do not directly support different blood pressure treatment targets based on UHR[37]. Education level and other socioeconomic factors may still influence exposure profiles, access to care, and treatment adherence, and they deserve fuller evaluation in future analyses[39]. Interestingly, this study also found an interactive effect of smoking status in the NHANES database and a significantly higher risk in the UHR Q4 group of the asthma subgroup in the CHARLS database. These findings suggest that lifestyle and comorbidity profiles may influence the strength of the association, although the results should be interpreted cautiously[32]. Lifestyle factors such as diet and physical activity may still be relevant because they can influence uric acid, HDL-C, and inflammatory status, but this hypothesis requires direct testing[31, 36].

A main strength of this study is the use of two independent databases with a broad set of covariates. The findings also support a stable positive association between UHR and hypertension across the two populations. The association was broadly consistent across most subgroups, with some heterogeneity by diabetes and smoking. UHR integrates information from UA and HDL cholesterol and may reflect a pathway involving metabolic disturbance, inflammation, and vascular dysfunction. Because both components are routinely measured, UHR may be a practical candidate marker for hypertension screening and risk stratification.

However, this study has several limitations. First, the analysis was cross-sectional, so causal or temporal inferences cannot be made. Second, hypertension status partly relied on questionnaire data, which may have introduced misclassification. Third, differences in UHR across distinct hypertension phenotypes were not explored. Fourth, residual confounding from medication use, diet, kidney function, and socioeconomic factors may remain. Fifth, the nomogram still needs prospective and independent external validation before clinical use. Future studies should test temporal associations, identify clinically useful UHR thresholds, examine different hypertension phenotypes, and validate the nomogram in independent cohorts.

5 Conclusions

In conclusion, this cross-sectional study based on NHANES and CHARLS data demonstrated that the serum uric acid-to-high-density lipoprotein cholesterol ratio (UHR) was positively and independently associated with hypertension risk in both U.S. and Chinese populations. The association remained stable after adjustment for demographic characteristics, lifestyle factors, comorbidities, and laboratory indicators, and was generally consistent across most population subgroups. XGBoost analysis further supported the predictive contribution of UHR, while the UHR-integrated nomogram showed acceptable discrimination, calibration, and clinical net benefit in both cohorts. These findings suggest that UHR may serve as an accessible and practical candidate marker for hypertension screening and risk stratification. However, because of the cross-sectional design, causal relationships cannot be inferred, and prospective studies are still needed to validate its clinical utility.

Abbreviations

Abbreviation	Full term
AUC	area under the curve
CHARLS	China Health and Retirement Longitudinal Study
CI	confidence interval
DCA	decision curve analysis
HDL-C	high-density lipoprotein cholesterol
NHANES	National Health and Nutrition Examination Survey
OR	odds ratio
ROC	receiver operating characteristic
UA	uric acid
UHR	serum uric acid-to-high-density lipoprotein cholesterol ratio
XGBoost	eXtreme Gradient Boosting

Declarations

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Data Availability Statement

The datasets ANALYZED for this study can be found in the National Health and Nutrition Examination Survey (NHANES) database [<https://www.cdc.gov/nchs/nhanes/index.html>] and the China Health and Retirement Longitudinal Study (CHARLS) database [<http://charls.pku.edu.cn/>].

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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Author Contributions

Lei Shen and Jing-Yuan Tian: Conceptualization, Data curation, Validation, Visualization, Writing—original draft, Writing—review & editing. Mei-Hui Sun: Data curation, Validation, Visualization, Writing—review & editing. Hai-Shan Zhao: Validation, Writing—review & editing. Lei Shen: Visualization, Writing—review & editing. Hui-Ying Wang: Conceptualization, Supervision, Writing—review & editing. Da-Yong Gao: Conceptualization, Project administration, Supervision, Writing—review & editing. This work currently described has not been published, is not being considered for publication elsewhere, and its publication was approved by all authors.

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Figures

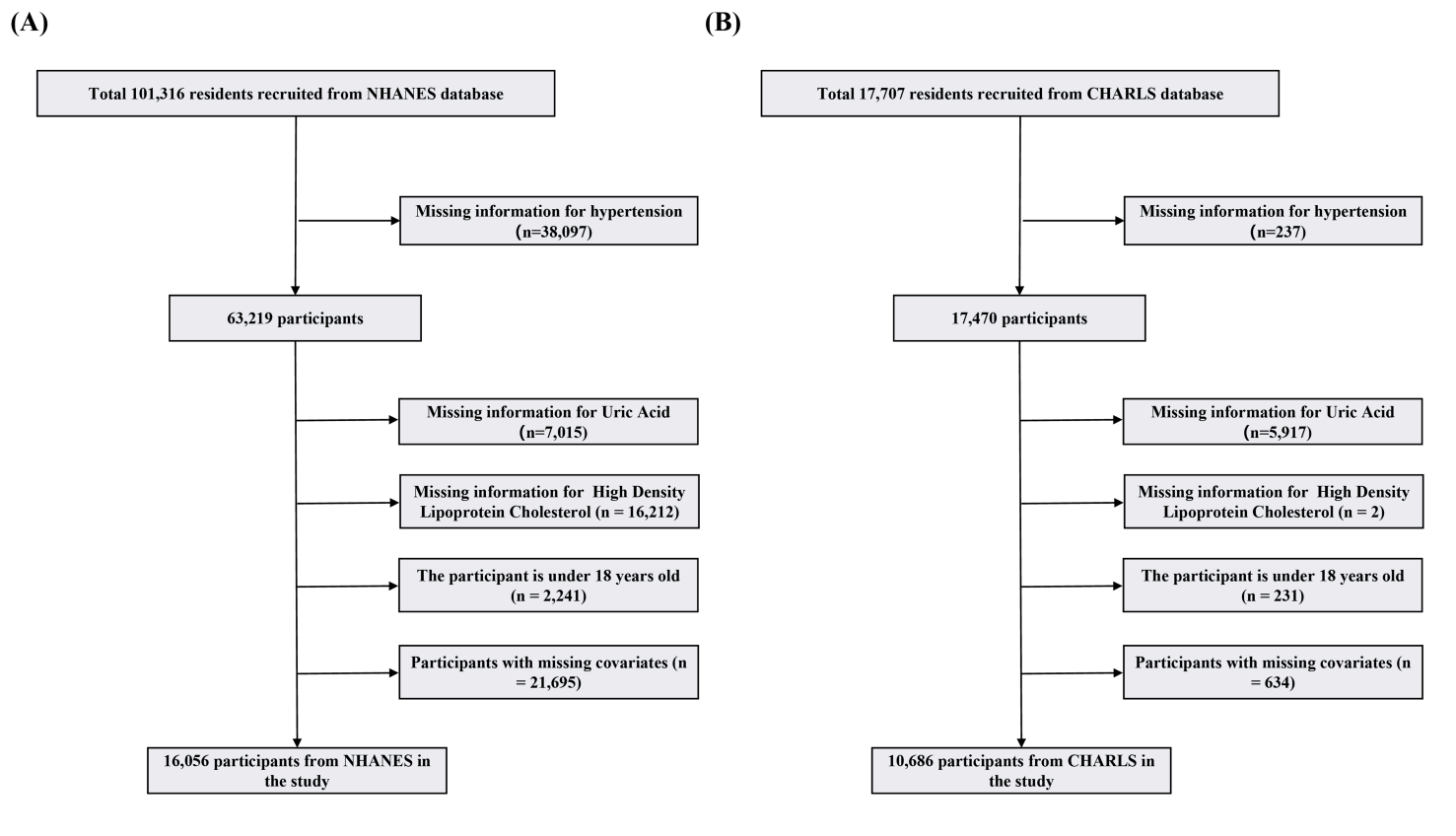


Figure 1

Flow diagrams of participant enrollment and exclusion. **(a)** Enrollment and exclusion flowchart for the NHANES database. **(b)** Enrollment and exclusion flowchart for the CHARLS database.

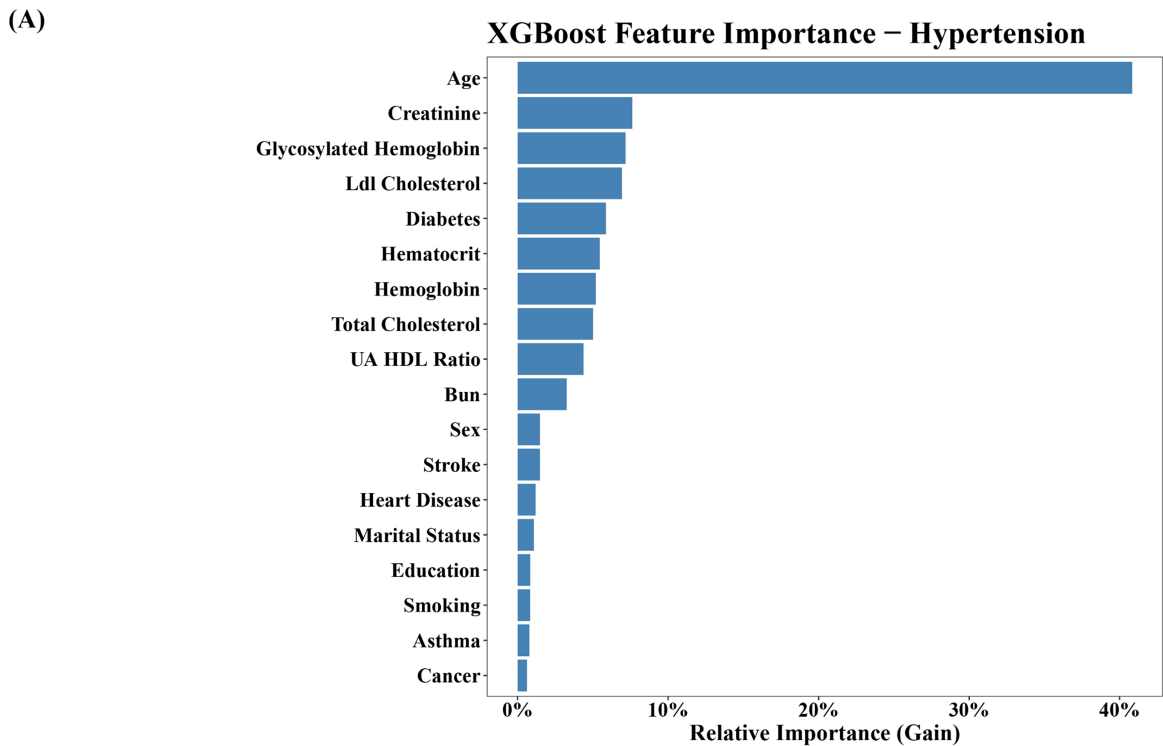
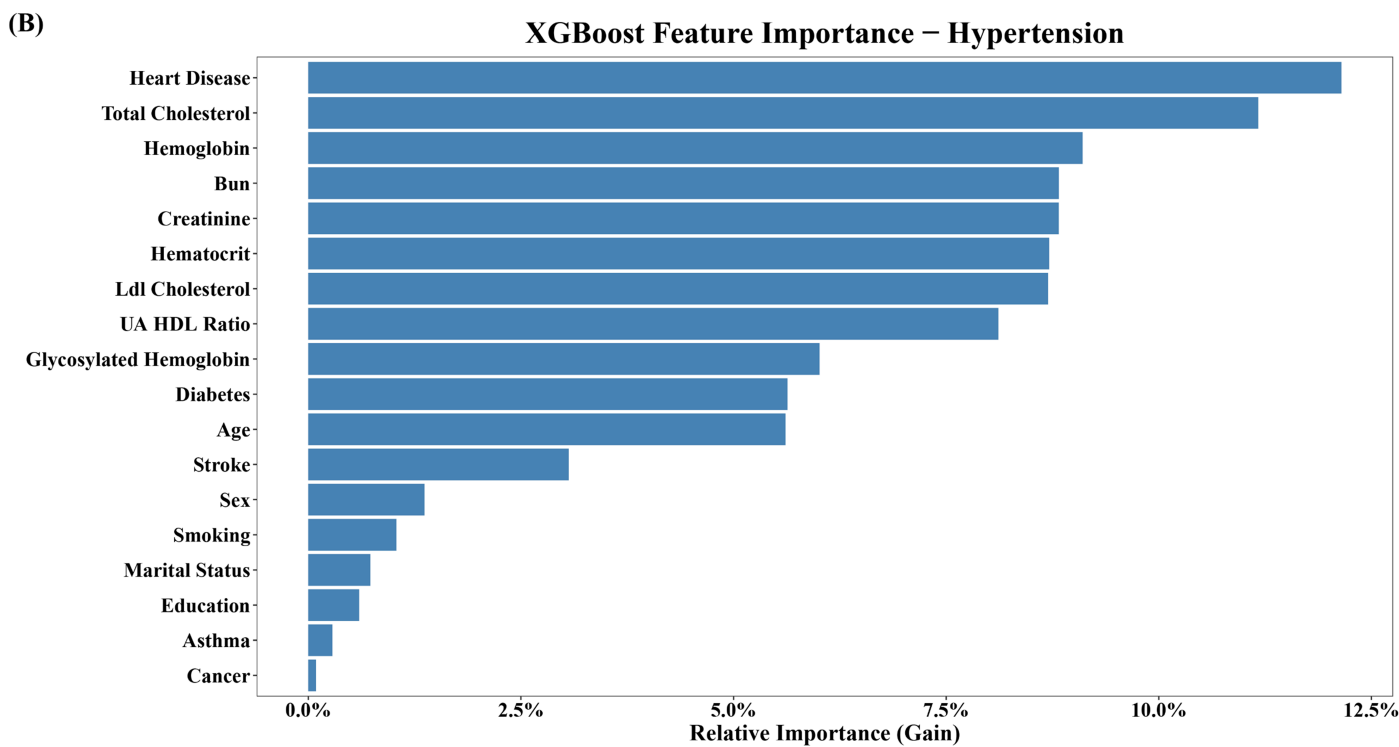
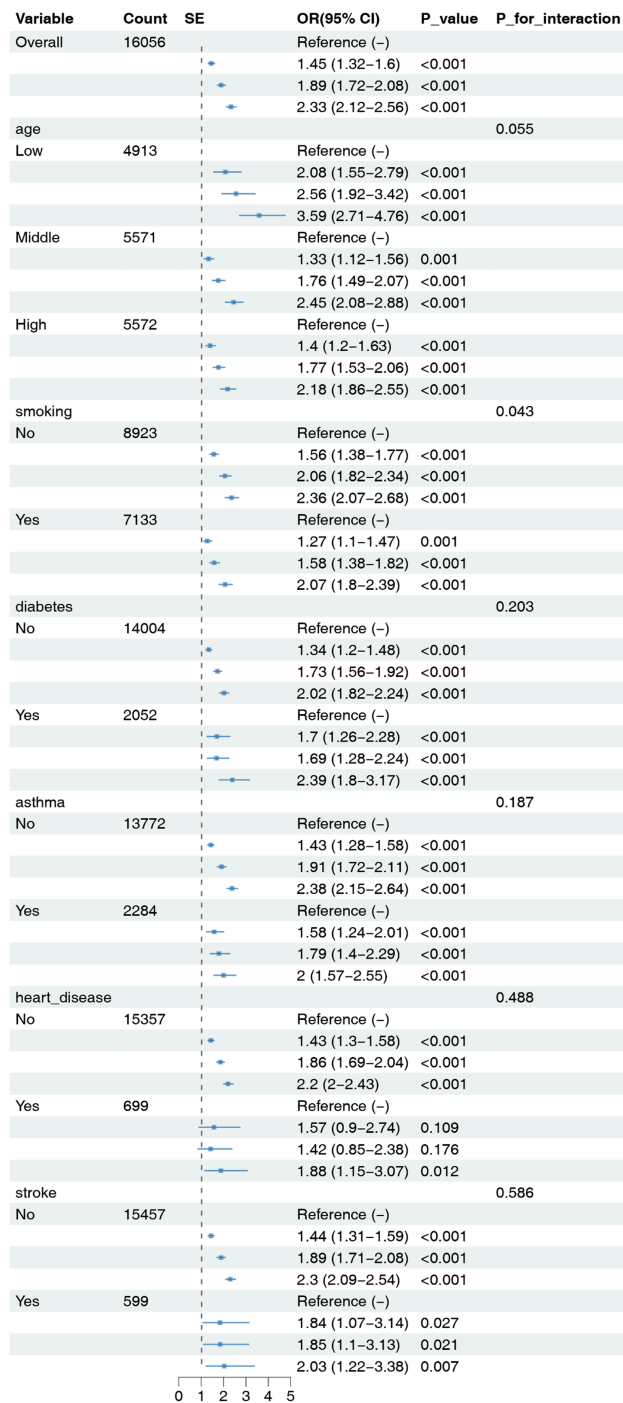


Figure 2

XGBoost feature importance. **(a)**Relative importance ranking of each variable in the hypertension prediction model based on the NHANES database. **(b)**Relative importance ranking of each variable in the hypertension prediction model based on the CHARLS database.

(A)



(B)

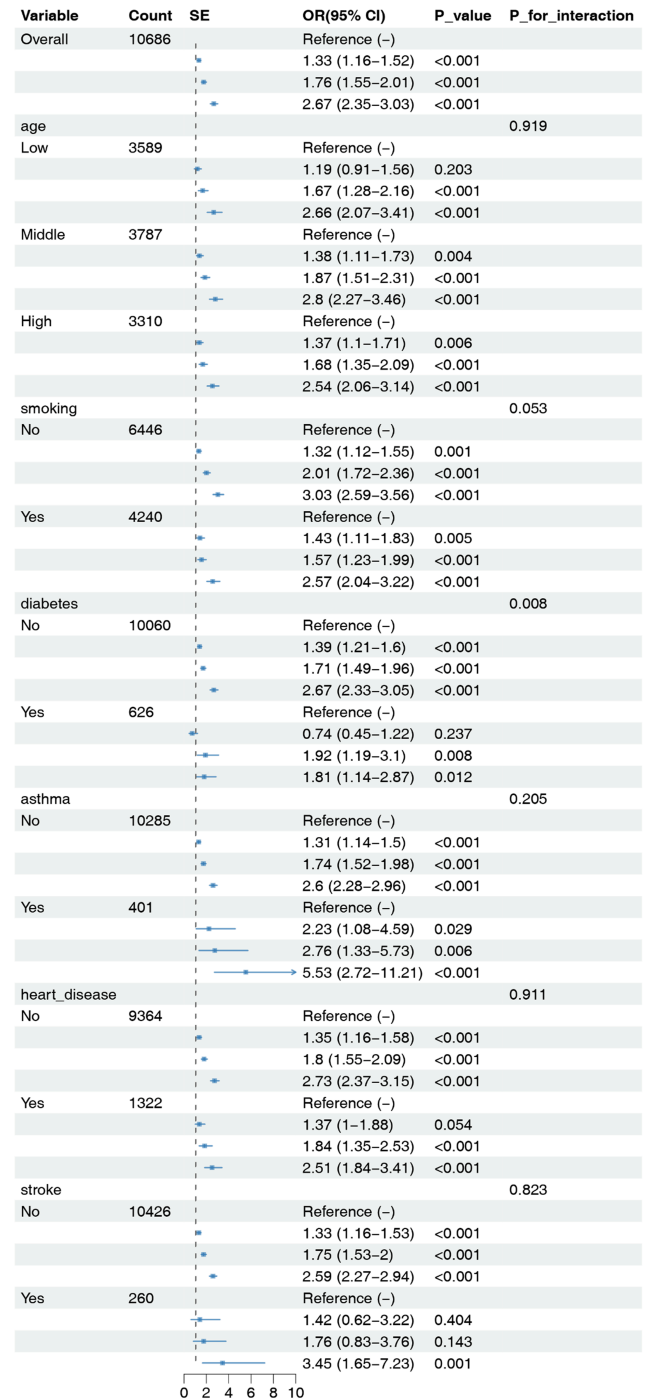


Figure 3

Stratified analysis of risk. (a)Forest plot of stratified analysis between UHR and hypertension in the NHANES database. (b)Forest plot of stratified analysis between UHR and hypertension in the CHARLS database.

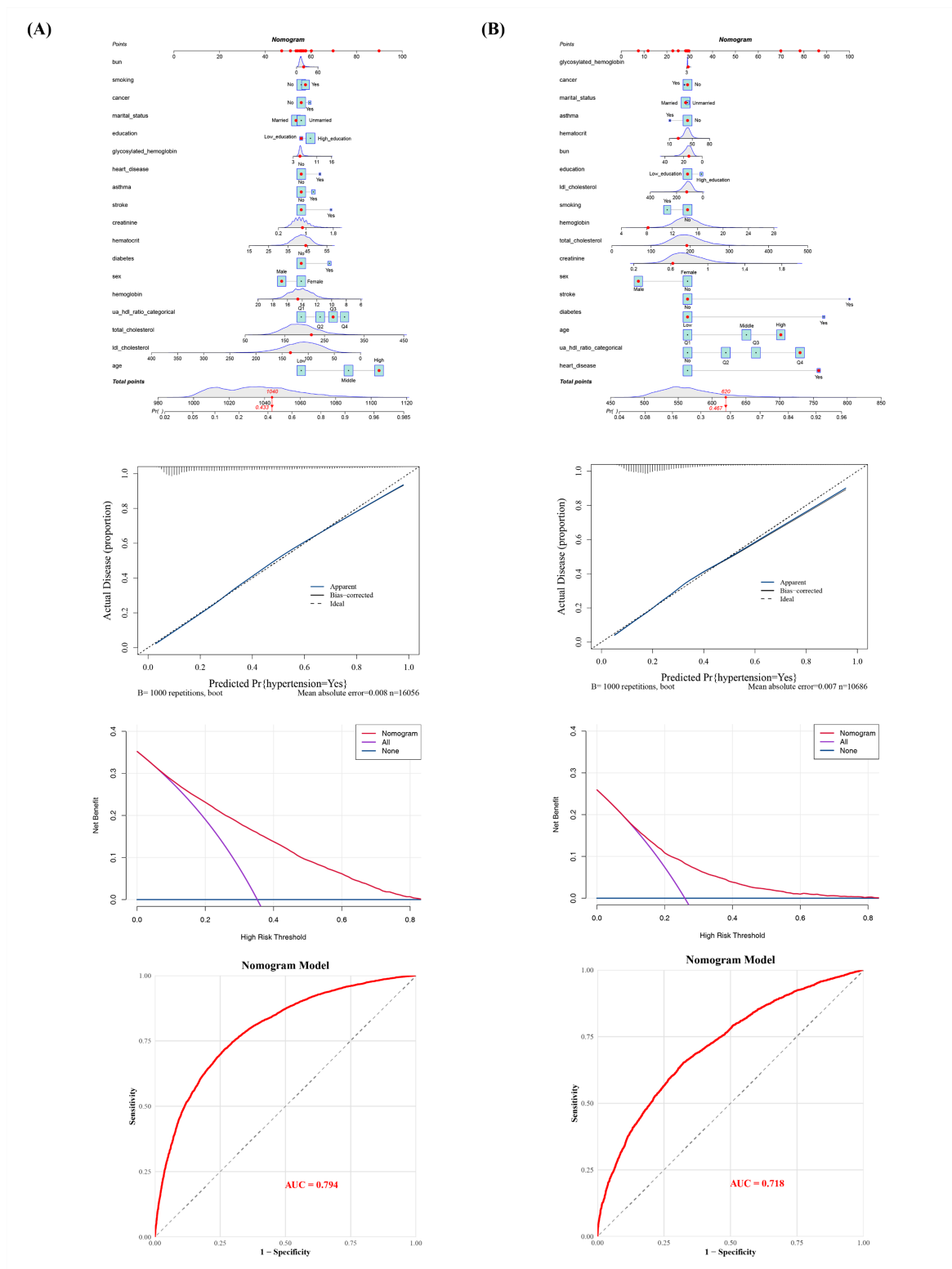


Figure 4

Construction and evaluation of nomogram. **(a-b)** Nomogram construction and model evaluation for the NHANES and CHARLS databases, respectively. In the nomograms, red dots indicate the score of each variable under specific conditions; vertical lines sum the individual scores to obtain the total score, and the probability of the target event (hypertension) is predicted on the bottom horizontal axis. Calibration curves: The black dashed line represents perfect prediction. The blue solid line represents the entire

cohort, and the black solid line represents the observed nomogram performance after bias correction via Bootstrapping (1000 repetitions). DCA curves: The horizontal axis denotes the risk threshold, and the vertical axis denotes the net benefit (benefit minus harm). The lines in the figure represent the net benefit at each risk threshold; the blue line parallel to the horizontal axis indicates all samples are considered negative (no intervention applied to anyone, resulting in a net benefit of 0), the slanted purple line indicates all samples are considered positive (intervention applied to everyone), and the red line represents the decision curve of the Nomogram. ROC curves: The red curve represents the model performance at different thresholds, and the diagonal line serves as the reference line (representing random classification).