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Non high density lipoprotein to high density lipoprotein cholesterol ratio and type 2 diabetes in Middle aged and Elderly Chinese

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The aim of this study was to assess the potential association between non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) and type 2 diabetes mellitus (T2DM) in a middle-aged and elderly Chinese population using data from the China Health and Retirement Longitudinal Study (CHARLS) from 2011 to 2015. Methods We used data from CHARLS 2011 as baseline data and follow-up data from 2015. NHHR was used as a continuous and categorical variable, and multivariate logistic regression modeling was used to explore its relationship with T2DM. Three models were developed to adjust for the possible effects of 14 factors on the outcomes. Restricted cubic spline was used to check for possible nonlinear associations, and subgroup and interaction analyses were used to assess differences between groups. Results A total of 7847 subjects were enrolled in the study, of whom 948 (12.1%) were diagnosed with T2DM. The last NHHR quartile group (Q4) presented the highest risk of T2DM (OR, 1.115, 95% CI, 1.088–1.141) after accounting for all covariates. Restricted cubic spline regression modeling revealed a nonlinear relationship between NHHR and T2DM (p for nonlinear = 0.001). The results of the subgroup analyses were consistent across the categories, indicating a significant positive correlation. Interaction analyses revealed significant interactions between NHHR and age, gender and marital status. Conclusion In the middle-aged and elderly population in China, there is a strong correlation between elevated NHHR and increased risk of T2DM onset. The relationship between NHHR and T2DM can be further investigated in the future to provide reference for the development of more accurate prediction models.

Keywords Type 2 diabetes mellitus, NHHR, CHARLS, Prospective cohort study

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease characterized by persistent elevations in blood glucose that is associated with genetic, environmental, obesity, and other lifestyle factors[1]. The main features of T2DM include insufficient insulin secretion and insulin resistance. Prolonged illness and improper management can lead to a series of serious complications, such as cardiovascular disease, nephropathy, retinopathy and neuropathy, which seriously affect human health[2–4]. It is estimated that 537 million adults aged 20–79 years will have T2DM in 2021, and the incidence of T2DM is gradually increasing with the aging of the population, improvement of living standards, and changes in diet and lifestyle habits[5]. China has the largest number of diabetic patients in the world, and the annual cost of treating diabetes imposes a huge economic burden on society[6]. Therefore, by identifying high-risk groups and providing early screening and customized interventions, the incidence of T2DM can be reduced and population health improved.

Previous studies have shown that dyslipidemia is a risk factor for T2DM[7]. Lipid parameters, including total cholesterol (TC), triglycerides (TG), low-density lipoproteins (LDL-C), and high-density lipoproteins (HDL-C), have been used individually in previous studies to assess the risk and outcome of T2DM[8,9], but the predictive value of these parameters is limited. In recent years, the non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) has gained increasing attention as an innovative and comprehensive metric for assessing the lipid composition of atherosclerosis and providing broad insights into anti-atherogenic and atherogenic lipid particles[10]. In addition to assessing the severity of atherosclerosis, the NHHR has relevance

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and predictive value for a wide range of diseases (cardiovascular, neurologic, hepatic and renal, etc.)[11–13]. Kim et al.[14] demonstrated that the diagnostic efficacy of NHHR in assessing insulin resistance (IR) and identifying metabolic syndrome surpasses that of traditional lipid markers, demonstrating greater accuracy and clinical value. These studies demonstrate the potential strength of NHHR to predict metabolism-related diseases. Therefore, studying the association between NHHR and T2DM has significant scientific and clinical value. By understanding the association between NHHR and T2DM, the harm of T2DM to individuals and society can be reduced through early screening and intervention in specific populations.

It is worth mentioning that there have been previous studies exploring the correlation between NHHR and T2DM in rural areas of China and cross-sectional studies based on the NHANES database[15,16]. However, the data in this study were obtained from the China Health and Retirement Longitudinal Study (CHARLS) database. CHARLS covers 450 urban and rural communities in 28 provinces in China, which is a much broader and more representative sample. The aim of our study was to conduct a longitudinal prospective analysis of NHHR as a continuous and categorical variable to predict the risk of developing type 2 diabetes mellitus in the Chinese population. By utilizing the rich data resources of CHARLS, we expect to more accurately assess the relationship between NHHR and the risk of type 2 diabetes.

Results
Baseline characteristics
Characteristics of the study population are shown in Table 1. A total of 7847 subjects were enrolled to participate, with a mean age of 58.0 years, 3657 (46.6%) males and 4187 (53.4%) females. 84.1% of the subjects were married, 90.7% had an education level of primary school or below, 93.6% lived in rural areas, 39.0% were smokers, and the vast majority (66.7%) did not consume alcohol. 948 cases (12.1%) developed T2DM in 2015 (Table 1).

Dose–response relationship between NHHR and T2DM
Table 2 shows the association of NHHR and quartiles of NHHR with the risk of T2DM. The risk of T2DM increased progressively with quartiles of NHHR (p indicates trend <0.001). Compared with the first NHHR group (Q1), the last NHHR quartile (Q4) had the highest risk of T2DM after adjusting for age, sex, education level, residence and marital status, smoking status, drinking status, sleep duration, systolic blood pressure, diastolic blood pressure, BMI, heart disease, stroke, and other chronic conditions (OR, 1.115, 95% CI, 1.088–1.141). Analyzed as a continuous variable, NHHR was significantly associated with T2DM (OR = 1.027; 95% CI: 1.013–1.042; $p < 0.001$). Figure 1 shows the dose-response relationship between NHHR and risk of T2DM. Restricted cubic spline regression showed a nonlinear relationship between NHHR and T2DM risk (p for nonlinear = 0.001).

Stratified analysis
To see if there were differences in the effect of NHHR on the risk of developing T2DM between subgroups, we grouped participants by characteristics. The results showed that the effect of NHHR on the risk of T2FM was consistent across subgroups (Fig. 2). There was an interaction between NHHR and age, sex and marriage.

Discussion
Our results suggest that high NHHR is associated with T2DM risk. Subgroup analyses further validated the stability of this positive correlation result, which remained stable when the subgroups were stratified according to age, gender, marital status, education, place of residence, smoking, alcohol consumption sleep duration, and BMI. Based on dose-response relationship analysis, we found a nonlinear relationship between NHHR and T2DM risk.

Consistent with previous findings, our results suggest that dyslipidemia is strongly associated with T2DM risk[7]. Most of the previous studies have focused on conventional lipid parameters (TC, TG, HDL-C, LDL-C) for the treatment of dyslipidemia, while others have suggested that non-HDL-C (all plasma lipoproteins except HDL-C) is an important risk factor for cardiovascular disease[17–19]. The non-HDL-C to HDL-C ratio (NHHR) has been a hot topic in recent years compared to traditional conventional lipid parameters[20]. Numerous studies have shown that NHHR may be an important indicator of various diseases, including cardiovascular disease, neurologic disease, diabetes, and metabolic syndrome[11–13]. In atherosclerosis, NHHR is thought to play an important role in the balance between anti-atherogenic and atherogenic[10]. In the field of diabetes, it has been shown that NHHR has excellent predictive ability for diabetes and has better predictive accuracy compared to conventional lipid parameters[15,16,21]. Han et al.[15]. demonstrated the relevance of the non-HDL-C/HDL-C ratio to T2DM by following 11,487 nondiabetic participants ≥ 18 years of age in rural China. Talk et al.[16] also demonstrated that an increase in NHHR may be associated with an increased likelihood of developing T2DM through a cross-sectional study using data from 10,420 U.S. adults from NHANES 2007–2018. Our findings are consistent with previous studies, further confirming the exact association between NHHR and T2DM and highlighting the status of NHHR as an important predictor. The present study covered 450 urban and rural communities in 28 provinces in China, which is a broader and more representative sample, and a longitudinal prospective analysis was conducted using the most recent data available.

The mechanism of the relationship between NHHR accumulation and T2DM risk is unclear, but this may be related to atherosclerosis. NHHR correlates with lipoprotein particle size, reflecting the balance between anti-atherosclerotic and pro-atherosclerotic particles[15,21]. Elevated NHHR suggests that a decrease in the size of LDL particles and an increase in the proportion of sdLDL promotes the development of atherosclerotic plaques. Second, NHHR levels reflect the risk of cholesterol deposition in peripheral tissues, resulting in increased free fatty acid concentrations and decreased insulin sensitivity[22,23]. Excessive lipid-induced oxidative stress disrupts

| Characteristic (FMI) | Overall | Non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio(NHHR) | | | | |
		Q1[0.40,2.06]	Q2[2.06,2.78]	Q3[2.78,3.72]	Q4[3.72,31.2]	p Value
N (0%)	7847	1962[52.0,66.0]	1962	1961	1962	
Age (0%)	58.0[52.0,65.0]	59.0[52.0,66.0]	59.0[52.0,66.0]	58.0[52.0,64.0]	58.0[52.0,65.0]	0.406
Gender (0.08%)						
Female	4184(53.4)	960(49.0)	1090(55.6)	1059(54.1)	1075(54.8)	<0.001
Male	3657(46.6)	1001(51.0)	871(44.4)	899(45.9)	886(45.2)	
Education (0%)						
Primary-	7120(90.7)	1794(91.4)	1767(90.1)	1797(91.6)	1762(89.8)	0.298
High school	639(8.1)	144(7.3)	172(8.8)	147(7.5)	176(9.0)	
College+	88(1.1)	24(1.2)	23(1.2)	17(0.9)	24(1.2)	
Marital (0%)						
Married	6599(84.1)	1617(82.4)	1647(83.9)	1653(84.3)	1682(85.7)	0.043
Unmarried	1248(15.9)	345(17.6)	315(16.1)	308(15.7)	280(14.3)	
Location (0.01%)						
Urban	500(6.4)	89(4.5)	120(6.1)	135(6.9)	156(8.0)	<0.001
Rural	7345(93.6)	1873(95.5)	1841(93.9)	1826(93.1)	1805(92.0)	
Smoking (0%)						
No	4787(61.0)	1135(57.8)	1219(62.2)	1207(61.6)	1226(62.5)	0.010
Yes	3059(39.0)	827(42.2)	742(37.8)	754(38.4)	736(37.5)	
Drinking (0%)						
Drink but less than once a month	614(7.8)	156(8.0)	153(7.8)	143(7.3)	162(8.3)	<0.001
Drink more than once a month	2001(25.5)	638(32.5)	494(25.2)	454(23.2)	415(21.2)	
None of these	5232(66.7)	1168(59.5)	1315(67.0)	1364(69.6)	1385(70.6)	
Sleep time, hours (1.43%)	6.0[5.0,8.0]	6.0[5.0,8.0]	6.0[5.0,8.0]	7.0[5.0,8.0]	7.0[5.0,8.0]	0.103
Sbp, mmHg (0.98%)	126.7[114.3,141.7]	123.7[111.7,138.3]	124.7[113.0,140.0]	127.7[114.7,143.0]	130.3[118.7,145.0]	<0.001
Dbp, mmHg (1.03%)	74.7[67.0,83.0]	72.7[65.0,81.3]	73.3[66.0,81.7]	75.0[68.0,84.0]	77.0[69.7,85.3]	<0.001
BMI, kg/m² (0%)	23.0[20.8,25.6]	21.4[19.8,23.6]	22.5[20.5,24.7]	23.7[21.4,26.2]	24.8[22.7,27.4]	<0.001
Glucose, mg/dl (0.10%)	101.9[94.1,111.6]	99.2[92.2,108.0]	100.3[92.9,108.7]	101.7[94.7,110.9]	106.6[98.1,120.0]	<0.001
TC, mg/dl (0%)	5.0[4.4,5.6]	4.5[4.0,5.0]	4.8[4.3,5.4]	5.1[4.5,5.6]	5.5[4.9,6.3]	<0.001
Hdl, mg/dl (0%)	1.3[1.1,1.6]	1.7[1.5,1.9]	1.4[1.3,1.6]	1.2[1.1,1.4]	1.0[0.8,1.1]	<0.001
CVD (0.37%)						
No	6975(89.2)	1759(90.3)	1757(89.8)	1756(89.8)	1703(87.0)	0.003
Yes	843(10.8)	189(9.7)	199(10.2)	200(10.2)	255(13.0)	
Stroke (0.22%)						
No	7681(98.1)	1934(98.7)	1924(98.3)	1922(98.3)	1901(97.1)	0.003
Yes	149(1.9)	26(1.3)	33(1.7)	34(1.7)	56(2.9)	
Other chronic diseases (0.27%)						
No	6981(89.2)	1707(87.2)	1740(88.8)	1767(90.3)	1767(90.4)	0.003
Yes	845(10.8)	250(12.8)	219(11.2)	189(9.7)	187(9.6)	
NHHR(mean(SD))	3.1(1.6)	1.6(0.3)	2.4(0.2)	3.2(0.3)	5.0(2.1)	<0.001
NHHR_per_IQR	1.8(1.0)	1.0(0.2)	1.5(0.1)	1.9(0.2)	3.0(1.2)	<0.001

Table 1. The baseline characteristics of participants. FMI, fraction of missing information; Sbp, systolic blood pressure; Dbp, diastolic blood pressure; BMI, body mass index; TC, total cholesterol; Hdl, high-density lipoprotein; CVD, cardiovascular disease. "NHHR per IQR" is a ratio calculated as the amount of change in the NHHR index per IQR (interquartile range).

insulin-related signaling pathways, decreases insulin activity, and increases the risk of T2DM development[24]. In addition, a rise in NHHR represents a decrease in HDL-C levels, which have very potent antidiabetic effects, such as enhancing insulin sensitivity, decreasing levels of oxidative stress and inflammation caused by non-HDL-C, and maintaining β-cell integrity[25,26]. Finally, long-term high NHHR is often accompanied by higher BMI and TC, and more habitual smoking and drinking, which is consistent with our results, and these are also common risk factors for the risk of developing T2DM[27,28].

Our subgroup and interaction analyses showed differences in the relationship between NHHR and T2DM analysis by age, gender and marital status. With age, the body's metabolic functions gradually diminish, including lipid metabolism, which leads to an imbalance in the metabolism of lipid components in the blood, which in turn affects the NHHR[29]. Older adults may be more prone to an elevated NHHR due to a reduced

	Model 1	p	Model 2	p	Model 3	p
NHHR Per IQR	1.049(1.042,1.057)	<0.001	1.037(1.029,1.045)	<0.001	1.027(1.013,1.042)	<0.001
Quartiles of NHHR						
Q1	Ref					
Q2	1.017(0.997,1.038)	0.092	1.004(0.984,1.025)	0.169	1.011(0.988,1.034)	0.364
Q3	1.053(1.032,1.074)	<0.001	1.028(1.007,1.050)	<0.001	1.043(1.019,1.068)	<0.001
Q4	1.135(1.113,1.158)	<0.001	1.125(1.102,1.148)	<0.001	1.115(1.088,1.141)	<0.001
p for trend	<0.001		<0.001		<0.001	

Table 2. Relationship between NHHR and risk of new T2DM in CHARLS. We excluded 1292 subjects who already had T2DM in 2011 and used multivariate logistic regression models to explore the association between NHHR and new-onset T2DM in 2015. Model 1 was crude model. Model 2 was adjusted for age, gender, education, location, and marital status. Model 3 was adjusted for age, gender, education level, location, marital, smoking, drinking, sleep time, SBP, DBP, BMI, stroke, heart disease, and other chronic conditions. NHHR, the non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio; IQR, interquartile range. "NHHR per IQR" is a ratio calculated as the amount of change in the NHHR index per IQR (interquartile range).

metabolic efficiency, increasing the risk of T2DM. In addition, aging is accompanied by a systemic low-grade inflammatory state and increased levels of oxidative stress, both of which are closely associated with elevated NHHR levels and the development of T2DM[30,31]. With respect to gender, although both men and women are more likely to develop T2DM with higher NHHR levels, women are more susceptible than men to the effects of NHHR, which influence the development of T2DM, similar to previous studies[32]. There are a number of possible explanations for this, firstly, estrogen benefits cardiovascular health, regulates insulin sensitivity as well as glucose metabolism, and reduces inflammation as well as levels of oxidative stress in tissues, however this protective effect diminishes with age, leading to an elevated NHHR and adverse outcomes[16,33,34]. Secondly, women are more likely to accumulate fat in the abdomen and hips, leading to increased systemic inflammation, which is also a risk factor for T2DM[16,35]. Finally, women have lower levels of basal fatty acid oxidation and are more likely to have metabolic disturbances compared to men[36]. It is worth mentioning that compared with married ones, single people (including unmarried, divorced, and widowed) are more likely to have elevated NHHR and increased risk of T2DM, which may be related to lifestyle, psychological factors, and behavioral habits.

Given the results of this study, the potential clinical significance is to emphasize the importance of incorporating NHHR into routine health assessments, especially for middle-aged and older populations who are at higher risk for T2DM. Early screening programs that include NHHR can help identify individuals who may benefit from lifestyle modifications or closer monitoring. In addition, healthcare providers should consider the significant interactions between NHHR and age, gender, and marital status when designing personalized prevention strategies. Additional research is needed to further substantiate these findings and develop more robust predictive models that combine NHHR with other relevant biomarkers and health indicators.

As a nationwide population-based prospective cohort study, this study has a wide coverage and a good sample representation. We used NHHR as a continuous variable to explore its dose-response relationship with stroke risk, and made the findings reliable and convincing by developing three models to adjust for the possible effects of 11 factors on the outcome. Subgroup analyses were conducted to explore differences in the correlation between NHHR and T2DM risk across multiple subgroups.

There are some limitations of this study. First, some potential confounders limited the interpretation of our findings, such as dietary, ethnic, and lifestyle differences. Second, we only included Chinese participants aged 45 years and older, and the applicability among younger age groups and different ethnic groups should be viewed with skepticism. Third, due to the data design of the CHARLS database, subjects in this study may have been affected by selection bias. Finally, this observational study could not determine a causal relationship between NHHR and T2DM risk, only an association between the two.

Methods
Data sources
The data for this study were obtained from CHARLS, a nationwide interdisciplinary survey, which collected comprehensive data on basic information, family structure, physical status, health insurance, work pension, income and expenditure, housing, and laboratory tests by using face-to-face interview methods and structured questionnaires with participants aged 45 years and older in 28 provinces and 450 communities. In addition, CHARLS subjects were fasted for more than 12 h, venous blood samples were collected from the participants, and whole blood specimens were stored at 4℃ and immediately sent for testing to detect the levels of TG, LDL-C, and HDL-C, among others, using enzyme colorimetric assay. Each assay result was merged with the data file by two China CDC staff to ensure accuracy[37].

Study population
This study used data from CHARLS, and the CHARLS study protocol was approved by the Ethics Review Committee of Peking University, China, and written informed consent was obtained from all participants.
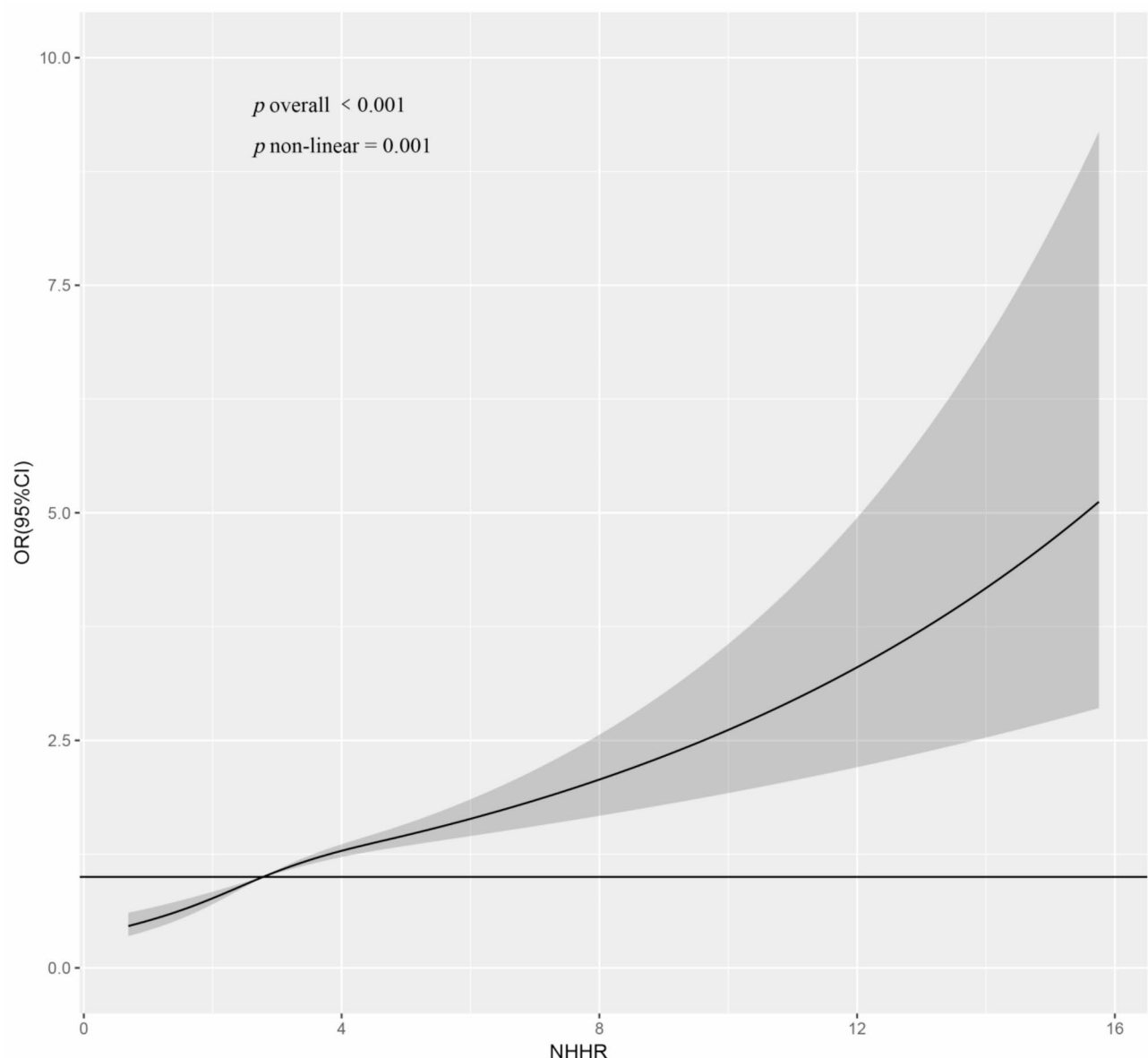
Fig. 1. Restricted cubic spline of the association between NHHR and the risk of T2DM. The model was adjusted for age, gender, education level, location and marital status, smoking status, drinking status, sleep time, SBP, DBP, BMI, stroke, heart disease, and other chronic conditions. The plot shows a non-linear relationship between NHHR and the risk of T2DM. To determine the optimal number of nodes, we initially tested different configurations of 3 to 7 nodes. By comparing the AIC and BIC values of the models and combining them with residual analysis, 4 nodes were finally selected as the optimal configuration.

Our study used two waves of CHARLS data conducted in 2011 and 2015. Baseline participants were selected from the 2011 dataset ($n = 17708$). To determine the final study population, we applied the following exclusion criteria:1. excluding subjects who already had T2DM at baseline, 2. age < 45 years, 3. exclusion of subjects with abnormal BMI (Values more than 3 SDs), 4. excluded participants without complete NHHR data, 5. exclusion of subjects with missing T2DM information at the 2015 follow-up visit. The specific design and participant flow is shown in Fig. 3.

Variables
Non-HDL cholesterol to HDL cholesterol ratio (NHHR).
NHHR indicates the ratio of non-HDL-C to HDL-C, and the difference between serum TC level (mmol/L) minus HDL-C level (mmol/L) is non-HDL-C.
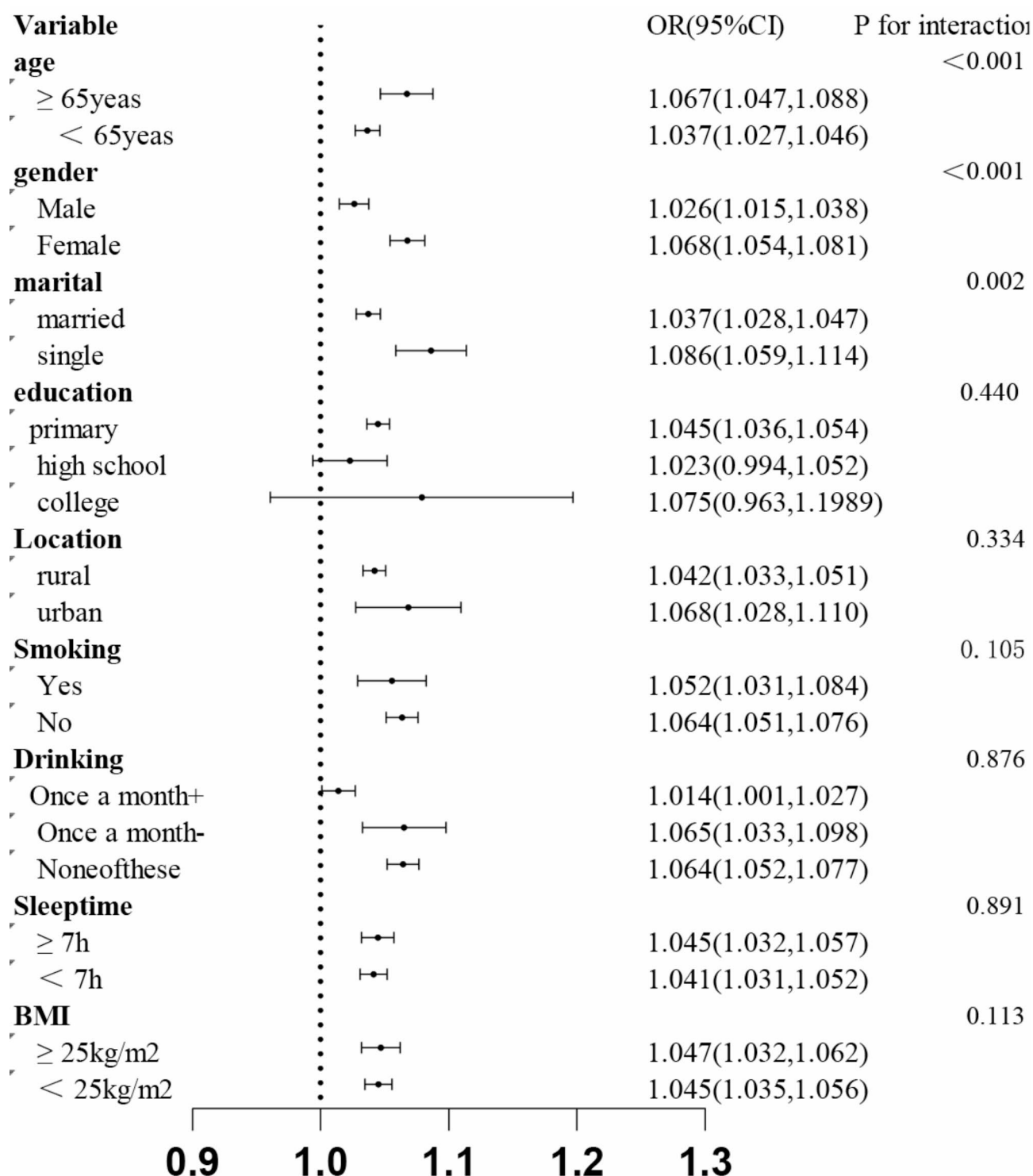
Variable	OR(95%CI)	P for interaction
age		<0.001
≥ 65yeas	1.067(1.047,1.088)	
< 65yeas	1.037(1.027,1.046)	
gender		<0.001
Male	1.026(1.015,1.038)	
Female	1.068(1.054,1.081)	
marital		0.002
married	1.037(1.028,1.047)	
single	1.086(1.059,1.114)	
education		0.440
primary	1.045(1.036,1.054)	
high school	1.023(0.994,1.052)	
college	1.075(0.963,1.1989)	
Location		0.334
rural	1.042(1.033,1.051)	
urban	1.068(1.028,1.110)	
Smoking		0. 105
Yes	1.052(1.031,1.084)	
No	1.064(1.051,1.076)	
Drinking		0.876
Once a month+	1.014(1.001,1.027)	
Once a month-	1.065(1.033,1.098)	
Noneofthese	1.064(1.052,1.077)	
Sleeptime		0.891
≥ 7h	1.045(1.032,1.057)	
< 7h	1.041(1.031,1.052)	
BMI		0.113
≥ 25kg/m2	1.047(1.032,1.062)	
< 25kg/m2	1.045(1.035,1.056)	

Fig. 2. Forest plot of stratified analysis of the association of NHHR with the risk of T2DM.

Diagnosis of type 2 diabetes mellitus

The outcome variable in this study was the occurrence of T2DM events during the follow-up period (2015).The diagnosis of T2DM was determined by one or more of the following criteria: (1) fasting blood glucose ≥ 126 mg/dl (7 mmol/L), (2) random blood glucose ≥ 200 mg/dl (11.1 mmol/L) (3) hemoglobin A1c (HbA1c) ≥ 6.5%, (4) self-reported of "yes" ("Have you ever been diagnosed with diabetes or hyperglycemia?").
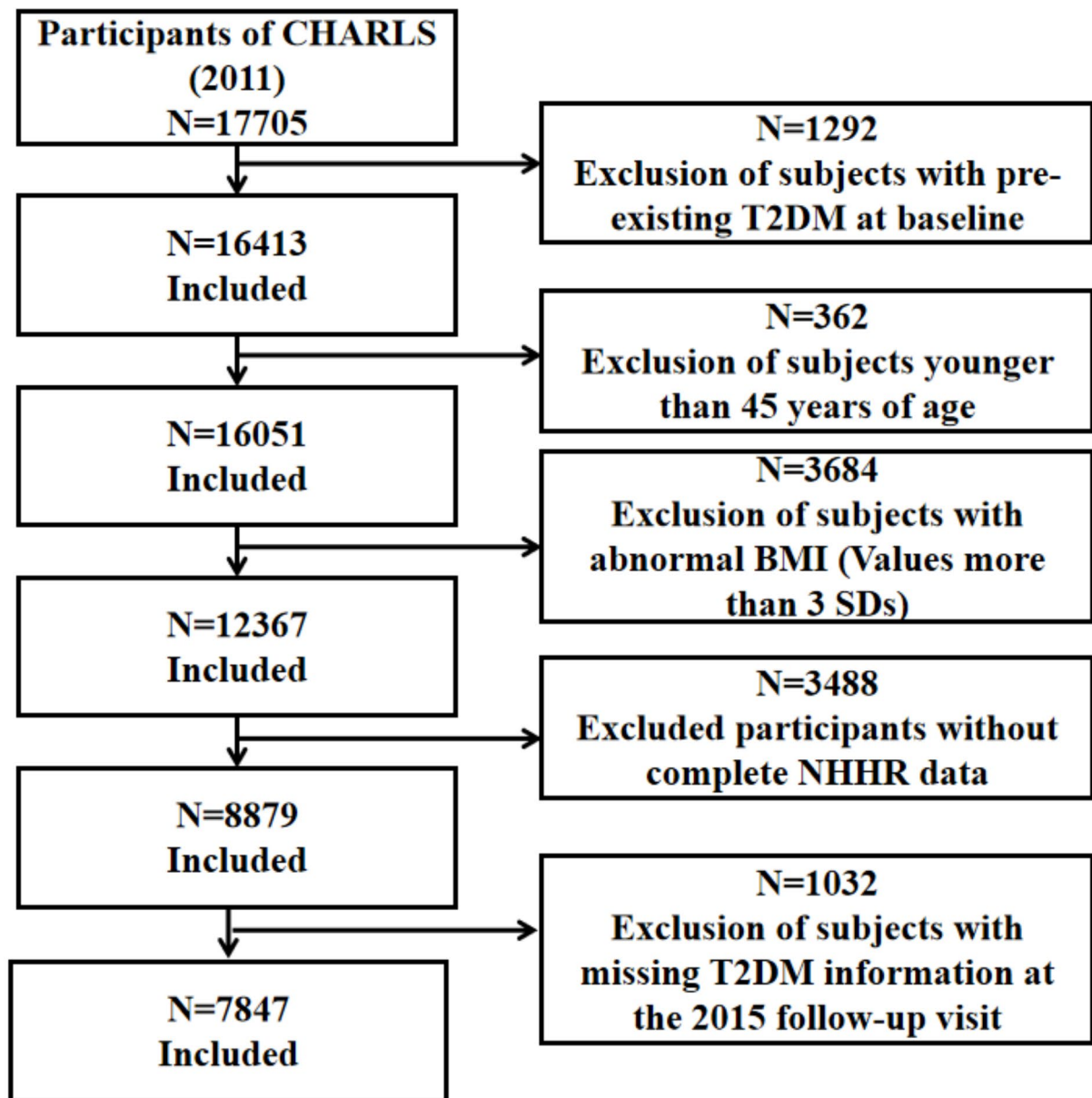
Fig. 3. Flowchart of the study population screening process.

Covariates

Covariate data were selected based on the results of previous studies[6,38], incorporating the following factors as covariates: (1) Categorical variables: gender, education level, marital status, place of residence, smoking status, drinking status, self-reported heart disease, stroke, and other chronic diseases (cancer, chronic lung disease, memory-related disorders, renal disorders, liver disease, arthritis, digestive disorders, asthma, and psychiatric problems). (2) Continuous variables: age, sleep, systolic blood pressure (SBP), diastolic blood pressure (DBP), and BMI. education level was categorized as primary school or below, high school, and college or above. Never smokers were defined as "non-smokers" and smokers, including those who had quit, were defined as "smokers". Alcohol consumption was categorized as "never", "less than once a month" and "more than once a month". Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were the average of three measurements using an Omron HEM-7200 sphygmomanometer.

Statistical analysis

Normally distributed continuous variables are expressed as mean and standard deviation (SD), and abnormally distributed continuous variables are expressed as median (interquartile spacing (IQR)). Categorical variables are expressed as frequencies and percentages. After grouping by NHHR quartiles (Q1, Q2, Q3, and Q4), baseline characteristics and incidence of T2DM were compared using one-way ANOVA, Kruskal-Wallis H test, or chi-square test. Three logistic models were used to estimate the ratio of ratios (OR) for T2DM using NHHR as

a continuous variable (per IQR increment) or a categorical variable (per quartile) with a confidence interval (CI) of 95%. The three different models included (1) Model 1: without any covariates; (2) Model 2: adjusted for sociodemographic factors, including age, gender, education, marital status, and place of residence. (3) Model 3: This model adjusted for all factors, including age, gender, education, marital status, place of residence, smoking status, alcohol consumption status, sleep, systolic blood pressure (SBP), diastolic blood pressure (DBP), BMI, self-reported heart disease, stroke, and other chronic diseases. These results are expressed as OR as well as 95% Cl. Restricted cubic spline was used to test for possible non-linear associations and to visualize the dose-response association between NHHR and T2DM. We performed subgroup analyses based on age (< 65, ≥ 65 years), sex, marital status, education level, place of residence, smoking, alcohol consumption, sleep duration (< 7, ≥ 7 h), and BMI (< 25, ≥ 25 kg/m2). In addition, interaction analyses were performed using the product term [NHHR × (interaction term)] from the main analysis to identify changes in the influence of sociodemographic factors and health-related behaviors in the relationship between NHHR and T2DM. For missing values, we recalculated the data using Multiple Interpolation by Chained Equations (MICE). MICE allows different types of variables to be predicted from each other through a series of regression models to generate plausible filler values. To ensure the quality of the fill, we incorporated a range of auxiliary variables (age, sex, education level, residence, marital status, smoking status, drinking status, sleep duration, SBP, DBP, BMI, heart disease, stroke, and other chronic conditions). To assess the adequacy of the fills, we performed 50 independent fills (i.e., m = 50) and also calculated the proportion of missing information for each variable, as shown in Table 1.

All statistical analyses were performed in R 4.1. Statistical significance was established using a two-tailed test with a threshold of $P < 0.05$.

Conclusion
Higher NHHR levels are strongly associated with the risk of T2DM in Chinese middle-aged and elderly populations. Maintaining an appropriate NHHR range may help reduce the risk of T2DM in middle-aged and older adults, but further studies are needed to verify the causality of this association.

Data availability
The data for this study was obtained from CHARLS, the official website is http://charls.pku.edu.cn/. Researchers who want to use these data can register accounts via the website.

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Jiacong Tan (first author): conceptualization, writing- original draft preparation, methodology, software, Writing- review & editing. Huaxin Zhu: data curation, Writing- review & editing.Yanyang Zeng and Jiawei Li : visualization, Writing- review & editing.Yeyu Zhao : supervision, Writing- review & editing.Xue Xiao : conceptualization, Writing- review & editing.Corresponding author: Meihua Li : Writing- review & editing.All authors contributed to the writing of the final manuscript, Writing- review & editing.

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Declarations

Competing interests

The authors declare no competing interests.

Ethical approval

Ethical principles were strictly followed in this study. This study used data from the China Health and Aged Care Tracking Survey (CHARLS), which was provided by a legally authorized institution, and informed consent was obtained from the participants. No personally identifiable information was involved in the study. The study was reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Nanchang University to ensure that it complied with the ethical standards for medical research.

Additional information

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