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Associations of cumulative exposure and dynamic trajectories of the cholesterol–HDL– glucose index and its obesity-related derivatives with cardiovascular disease: a nationwide prospective cohort study

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Abstract

Background

Integrating metabolic biomarkers with anthropometric indicators has been shown to enhance the predictive capacity for cardiovascular disease (CVD). However, the impact of the cholesterol–HDL–glucose index (CHG) and its derivatives on CVD risk remains unclear. This study aimed to investigate the associations of CHG and its derivatives with CVD and to compare their predictive performance.

Methods

This prospective study included 3,359 CVD-free participants from the China Health and Retirement Longitudinal Study (CHARLS). Repeated measurements obtained in 2011 and 2015 were used to derive cumulative exposure and longitudinal trajectory patterns of CHG and its derivatives. Associations of baseline values, cumulative exposure, and longitudinal trajectories of these indicators with incident CVD and stroke were examined using Cox proportional hazards regression models.

Results

During a median follow-up of 5 years, 466 participants (13.9%) developed CVD. Both CHG and its derivatives were significantly associated with CVD across baseline measurements, cumulative exposure, and longitudinal changes. Cumulative CHG derivatives demonstrated stronger predictive power than isolated cumulative CHG (HR = 1.10), with the highest associations observed for cumulative CHG–waist circumference (CHG-WC; HR = 1.23) and cumulative CHG–Chinese visceral adiposity index (CHG-CVAI; HR = 1.22). Regarding trajectory patterns, participants with stably high CHG-CVAI exhibited the greatest risk compared with those maintaining stable low levels (HR = 1.58), followed by CHG-WC (HR = 1.47). A low-to-high trajectory of CHG-CVAI was also associated with increased risk (HR = 1.57). In contrast, individuals transitioning from high to low levels of CHG and CHG-WC remained at elevated risk (HR = 1.31 and HR = 1.52, respectively).

Conclusions

CHG and its derivatives were strongly associated with incident CVD, with CHG-CVAI, CHG-WC, and their cumulative values exhibiting the most pronounced associations. Moreover, ascending CHG-CVAI and declining CHG-WC trajectories were linked to higher risk, suggesting their potential utility as clinical and public health indicators. Monitoring and maintaining optimal CHG-CVAI and CHG-WC levels may facilitate the identification of individuals at elevated risk for CVD.

Introduction

Cardiovascular disease (CVD) remains the leading cause of mortality worldwide, imposing a substantial burden on global health. Recent estimates indicate that CVD accounts for nearly one-third of all deaths globally, with mortality rising from 12.1 million in 1990 to approximately 20 million in 2022 [1–3]. In China, the prevalence of CVD is particularly concerning, affecting over 300 million individuals, with CVD-related deaths accounting for 44% of total mortality [4]. Extensive epidemiological evidence has identified major risk factors for CVD, with a significant proportion of cases attributable to common modifiable exposures. Among these, metabolic abnormalities represent the largest contributor to cardiovascular burden [5], highlighting the critical role of metabolic disturbances in CVD development and the need for refined assessment strategies to improve risk stratification.

Elevated circulating lipids and glucose levels are well-established risk factors for CVD [6], with insulin resistance (IR) serving as a recognised underlying biological mechanism [7]. In addition, systemic inflammatory responses, which are closely linked to lipid and glucose dysregulation, constitute another important contributor to CVD [8]. The cholesterol–HDL–glucose (CHG) index, calculated from fasting blood glucose (FBG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) [9], integrates glycolipid metabolism and may serve as a surrogate marker of IR and inflammation. Previous studies have demonstrated the predictive utility of CHG for CVD and stroke [10, 11]. Obesity represents another critical metabolic determinant of CVD, promoting atherosclerotic progression through multiple interrelated metabolic pathways [12–14]. To provide a more comprehensive assessment of cardiovascular metabolic risk, composite indices incorporating metabolic markers (e.g., the triglyceride–glucose [TyG] index, the cholesterol–triglyceride index [CTI], and the plasma atherogenic index [AIP]) and obesity-related parameters have been proposed [15–17]. However, evidence systematically evaluating the predictive performance of CHG-derived obesity indices for incident CVD remains limited, and existing studies have predominantly relied on baseline measurements, neglecting the influence of longitudinal changes.

To address these gaps, the present study combined CHG with multiple obesity-related indices, including CHG–body mass index (CHG-BMI), CHG–waist circumference (CHG-WC), CHG–waist-to-height ratio (CHG-WHtR), CHG–body roundness index (CHG-BRI), CHG–Chinese visceral adiposity index (CHG-CVAI), CHG–weight-adjusted waist index (CHG-WWI), and CHG–a body shape index (CHG-ABSI). Leveraging data from a large, nationally representative cohort, this study systematically evaluated the associations of baseline levels, cumulative exposure, and longitudinal trajectories of these indicators with the risks of CVD and stroke.

Methods

Study design and population

Data for this study were obtained from the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative prospective survey of middle-aged and older adults in China [18]. Employing a stratified random sampling design, CHARLS recruited participants from 450 communities across 28 provinces. The initial survey, conducted in 2011, enrolled 17,708 individuals, with subsequent follow-ups in 2013, 2015, 2018, and 2020. This longitudinal framework provides a continuous and reliable source of data for ageing-related research. The study protocol was approved by the Peking University Ethics Review Committee (IRB00001052-11015), and all participants provided written informed consent.

Among participants enrolled at baseline (Wave 1), individuals aged < 45 years (n = 777) and those with pre-existing CVD (n = 2,650) were excluded. Participants lacking sufficient data to calculate CHG or its derivatives at baseline (n = 7,046), as well as those without any follow-up visits (n = 178), were further excluded. Ultimately, Cohort 1 comprised 7,057 participants. For analyses of longitudinal changes in CHG and its derivatives, additional exclusions were applied: participants missing CHG or obesity-related derivative measurements at Wave 3 (n = 2,916), those who developed CVD during Waves 2 or 3 (n = 604), and individuals lost to follow-up (n = 156). This resulted in a final sample of 3,359 participants for Cohort 2 (Fig. 1).

Exposure assessment

Fasting venous blood samples were collected following standardised procedures. Serum concentrations of FBG, HDL-C, TC, and triglycerides (TG) were measured using enzymatic colourimetric methods [19]. During anthropometric measurements, participants wore light, loose-fitting clothing and were barefoot. Height, weight, and WC were recorded accordingly.

$$\mathrm{CHG} = \ln[\frac{\mathrm{TC(mg/dl)*FBG(mg/dl)}}{2*\mathrm{HDL-C(mg/dl)}}]$$

$$\mathrm{BMI} = \frac{\mathrm{Weight\,(kg)}}{\mathrm{Height\,(m)}^2}$$

$$\mathrm{WHtR} = \frac{\mathrm{WC\,(cm)}}{\mathrm{Height\,(cm)}}$$

$$\mathrm{BRI} = 364.2 - 365.5*\sqrt{1 - \frac{[\mathrm{WC(\,m)}/2\pi\,]^2}{[0.5*\mathrm{height(\,m\,)}]^2}}$$

$$\mathrm{CVAI\,[male(\,female)} = -267.93(-187.32) + 0.68(1.71)*\mathrm{age} + 0.03(4.23)*\mathrm{BMI} + 4.00(1.12)*\mathrm{WC} + 22.00(39.76)*\mathrm{log10\,(TG)} - 16.32\,(11$$

$$\mathrm{WWI} = \frac{\mathrm{WC\,(cm)}}{\sqrt{\mathrm{Weight\,(kg)}}}$$

$$\mathrm{ABSI} = \frac{\mathrm{WC\,(m)}}{[\mathrm{BMI}^{\frac{2}{3}}(\mathrm{kg/m^2})*\mathrm{Height}^{\frac{1}{2}}\,(\mathrm{m})]}$$

CHG and its derivatives were calculated as follows: CHG-derived indices were defined as the product of CHG and each obesity index (CHG-BMI, CHG-WC, CHG-WHtR, CHG-BRI, CHG-CVAI, CHG-WWI, and CHG-ABSI). Cumulative CHG and its obesity-related derivatives were computed using the formula: $(\text{indicator}_{2012} + \text{indicator}_{2015})/2 \times \text{time}$ (2015 − 2012).

Dynamic change patterns

To classify longitudinal change patterns for CHG and its derivatives, fixed cutoffs for each indicator were established based on baseline medians (CHG: 5.280; CHG-BMI: 121.976; CHG-WC: 444.671; CHG-WHtR: 2.822; CHG-BRI: 21.208; CHG-CVAI: 483.963; CHG-WWI: 58.717; CHG-ABSI: 0.437). For each indicator, measurements at Waves 1 and 3 were dichotomised as “high” (≥ baseline median) or “low” (< baseline median).

Participants in Cohort 2 were subsequently categorised into four distinct longitudinal patterns for each indicator: (1) stable high (maintaining high at both waves), (2) stable low (maintaining low at both waves), (3) high-to-low (declining from high to low), and (4) low-to-high (ascending from low to high).

Assessment of outcomes

In this study, CVD was defined as the primary outcome, with stroke as a secondary outcome. Heart disease was identified based on self-reported physician-diagnosed conditions, including heart attack, coronary heart disease, angina, congestive heart failure, or other heart-related problems. Stroke was also self-reported. Participants were considered to have CVD if they reported either heart disease or stroke. This definition is consistent with previous studies utilising CHARLS data.

Covariates

Covariates were selected based on prior research and included age, sex, education level (below high school, high school, or college and above), marital status (married or others), residence (urban or rural), drinking and smoking status (ever or never), systolic blood pressure (SBP), diastolic blood pressure (DBP), high-sensitivity C-reactive protein (hs-CRP), kidney disease, diabetes, and hypertension. Hypertension was defined as DBP ≥ 90 mmHg, SBP ≥ 140 mmHg, physician diagnosis, or use of antihypertensive medication. Diabetes was defined as FBG ≥ 126 mg/dL, use of antidiabetic medication, or physician diagnosis. Kidney disease was based on self-reported physician diagnosis.

Handling missing variables

The proportions of missing data are summarised in Tables S1–S2, with overall low missingness. To minimise potential biases and maximise statistical validity, multiple imputation was performed to retain the full analytic sample.

Statistical analysis

Categorical variables are expressed as frequencies and percentages, while continuous variables are presented as medians with interquartile ranges (IQRs). Differences between groups were assessed using the chi-square test for categorical variables and the Kruskal-Wallis test for continuous variables.

Cox proportional hazards regression models were employed to examine the associations of baseline levels and cumulative values of CHG and its derivatives with incident CVD. To facilitate comparability of effect sizes, all continuous exposure variables were standardised using Z-score transformation, with hazard ratios (HRs) and 95% confidence intervals (CIs) reported. Complementary analyses were conducted by categorising baseline measurements into quartiles, with the lowest quartile serving as the reference group. Three models were specified: Model 1 was unadjusted; Model 2 adjusted for age and sex; Model 3 further adjusted for education level, residence, marital status, drinking and smoking status, hypertension, kidney disease, diabetes, and hs-CRP. Longitudinal trajectories of CHG and its derivatives were analysed using the same modelling framework, with the persistent low group as the reference. Potential nonlinear associations between exposure indicators and CVD or stroke risk were evaluated using restricted cubic spline (RCS) regression with four knots. Kaplan-Meier analyses were performed to estimate cumulative incidence of CVD and stroke across categories and trajectory patterns of cumulative CHG and its derivatives. Predictive performance was assessed using receiver operating characteristic (ROC) curves and the corresponding area under the curve (AUC).

Stratified analyses were conducted to examine associations across subpopulations defined by age, sex, drinking and smoking status, diabetes, kidney disease, and hypertension. Sensitivity analyses included: (1) multivariable logistic regression to assess associations of all exposure indicators with incident CVD; (2) k-means clustering to evaluate implications of dynamic change patterns; and (3) restriction of analyses to participants without hypertension, kidney disease, or diabetes at baseline to test robustness of associations [5].

All statistical analyses were performed using R version 4.5.2. Two-sided P-values < 0.05 were considered statistically significant.

Results

Characteristics of study participants

During a median follow-up of 5 years, 3,359 participants were categorised into four CHG change patterns: stable low (n = 1,498), high-to-low (n = 730), low-to-high (n = 182), and stable high (n = 949). Distribution of sex and residence differed across groups, with higher proportions of females and urban residents in the stable high group. Prevalence of hypertension and diabetes was also highest in the stable high group. The stable low group consistently demonstrated the most favourable cardiometabolic profile, characterised by lower levels of SBP, DBP, FBG, TC, and hs-CRP, as well as higher HDL-C. Moreover, the stable high group exhibited the highest incidence of CVD (17.2%) and stroke (7.4%), compared with 11.5% and 4.2%, respectively, in the stable low group (Table 1).

Table 1
Baseline characteristics of 3359 participants according to changes in CHG

Characteristic	Total	Changes in CHG				P-value
		Stable low	High to low	Low to high	Stable high	
N	3359	1498	730	182	949	
Age, years	57.00 (51.00, 63.00)	57.00 (50.00, 63.00)	57.00 (52.00, 63.75)	58.00 (51.25, 66.00)	57.00 (52.00, 63.00)	0.119
Sex, n (%)						0.003
Male	1540 (45.8)	711 (47.5)	360 (49.3)	77 (42.3)	392 (41.3)	
Female	1819 (54.2)	787 (52.5)	370 (50.7)	105 (57.7)	557 (58.7)	
Education level, n (%)						0.627
Below high school	2369 (70.5)	1061 (70.8)	510 (69.9)	127 (69.8)	671 (70.7)	
High school	911 (27.1)	407 (27.2)	202 (27.7)	47 (25.8)	255 (26.9)	
College or above	79 (2.4)	30 (2.0)	18 (2.5)	8 (4.4)	23 (2.4)	
Residence, n (%)						0.004
Urban	445 (13.3)	175 (11.7)	93 (12.7)	20 (11.0)	157 (16.6)	
Rural	2911 (86.7)	1322 (88.3)	637 (87.3)	162 (89.0)	790 (83.4)	
Marital status, n (%)						0.044
Married	3040 (90.5)	1349 (90.1)	668 (91.5)	156 (85.7)	867 (91.4)	
Others	319(9.5)	149(10.0)	62(9.5)	26(14.2)	82(8.6)	
Smoking status, n (%)						0.101
No	2095 (62.4)	917 (61.2)	442 (60.5)	113 (62.1)	623 (65.6)	
Yes	1264 (37.6)	581 (38.8)	288 (39.5)	69 (37.9)	326 (34.4)	
Drinking status, n (%)						0.216
No	2196 (68.9)	956 (67.7)	465 (67.6)	120 (69.8)	655 (71.5)	
Yes	992 (31.1)	456 (32.3)	223 (32.4)	52 (30.2)	261 (28.5)	
Hypertension, n (%)						< 0.001
No	2620 (78.3)	1259 (84.4)	560 (77.2)	138 (75.8)	663 (70.1)	
Yes	725 (21.7)	233 (15.6)	165 (22.8)	44 (24.2)	283 (29.9)	
Kidney disease, n (%)						0.898
No	3211 (95.9)	1434 (95.9)	694 (95.6)	173 (95.6)	910 (96.3)	
Yes	136 (4.1)	61 (4.1)	32 (4.4)	8 (4.4)	35 (3.7)	
Diabetes, n (%)						< 0.001
No	3154 (94.6)	1470 (98.6)	698 (96.7)	172 (94.5)	814 (86.6)	
Yes	181 (5.4)	21 (1.4)	24 (3.3)	10 (5.5)	126 (13.4)	
SBP, mm Hg	124.50 (112.50, 139.00)	120.50 (110.00, 134.00)	125.75 (113.50, 139.38)	126.50 (115.12, 141.38)	129.00 (117.50, 143.00)	< 0.001
DBP, mm Hg	74.00 (66.00, 82.00)	71.50 (64.50, 80.00)	74.50 (67.00, 82.88)	73.50 (65.62, 83.00)	76.50 (69.00, 83.50)	< 0.001
FBG, mmol/L	102.06 (94.50, 111.60)	97.02 (91.08, 103.86)	104.76 (98.10, 115.74)	97.56 (90.27, 104.85)	110.34 (102.24, 129.60)	< 0.001
TC, mg/dL	191.37 (168.56, 216.50)	179.00 (159.67, 201.03)	194.85 (172.23, 219.88)	189.05 (163.24, 208.57)	212.24 (187.50, 238.92)	< 0.001
HDL-C, mg/dL	49.48 (40.98, 59.92)	58.38 (50.26, 67.94)	44.07 (37.89, 50.26)	54.70 (47.55, 63.79)	41.37 (34.79, 48.33)	< 0.001
hs-CRP, mg/L	0.97 (0.54, 1.95)	0.76 (0.46, 1.61)	1.06 (0.59, 2.18)	0.85 (0.55, 1.73)	1.26 (0.71, 2.35)	< 0.001

Values were expressed as medians (quartile interval)

HDL-C, high-density lipoprotein-cholesterol; hs-CRP, high-sensitivity C-reactive protein; TC, total cholesterol; CHG, the cholesterol–HDL–glucose index; CVD, cardiovascular disease; BMI: body mass index; WC: waist circumference; WHtR, waist-to-height ratio; BRI, Body Roundness Index; CVAI, Chinese Visceral Adiposity Index; WWI, Weight-Adjusted Waist Index; ABSI, A Body Shape Index

Characteristic	Total	Changes in CHG				P-value
		Stable low	High to low	Low to high	Stable high	
Cumulative CHG	15.64 (15.04, 16.33)	14.96 (14.56, 15.28)	15.84 (15.63, 16.08)	15.83 (15.64, 16.04)	16.72 (16.36, 17.28)	< 0.001
Cumulative CHG-BMI	366.19 (322.69, 416.56)	329.20 (296.73, 364.83)	376.22 (342.15, 416.71)	374.47 (344.43, 409.58)	423.71 (383.93, 466.49)	< 0.001
Cumulative CHG-WC	1326.33 (1183.94, 1476.73)	1203.06 (1101.39, 1305.25)	1370.16 (1255.54, 1471.12)	1362.77 (1267.82, 1443.81)	1511.69 (1394.80, 1639.59)	< 0.001
Cumulative CHG-WHtR	8.41 (7.48, 9.40)	7.62 (6.95, 8.32)	8.65 (7.95, 9.40)	8.71 (8.03, 9.27)	9.56 (8.79, 10.40)	< 0.001
Cumulative CHG-BRI	63.82 (49.11, 81.19)	53.42 (42.32, 66.34)	67.42 (53.88, 82.48)	69.05 (56.88, 81.13)	80.30 (64.66, 95.97)	< 0.001
Cumulative CHG-CVAI	1505.32 (1076.63, 2010.63)	1154.89 (822.16, 1472.35)	1642.52 (1260.49, 2031.95)	1623.93 (1301.24, 1958.12)	2087.86 (1651.73, 2497.67)	< 0.001
Cumulative CHG-WWI	174.47 (161.13, 187.06)	162.26 (153.27, 171.74)	177.77 (168.28, 185.80)	178.44 (169.69, 186.40)	190.64 (181.46, 202.55)	< 0.001
Cumulative CHG-ABSI	1.29 (1.22, 1.38)	1.22 (1.16, 1.28)	1.32 (1.27, 1.37)	1.32 (1.27, 1.38)	1.41 (1.35, 1.47)	< 0.001
CVD, n (%)						< 0.001
No	2893 (86.1)	1326 (88.5)	619 (84.8)	162 (89.0)	786 (82.8)	
Yes	466 (13.9)	172 (11.5)	111 (15.2)	20 (11.0)	163 (17.2)	
Stroke, n (%)						0.005
No	3174 (94.5)	1435 (95.8)	685 (93.8)	175 (96.2)	879 (92.6)	
Yes	185 (5.5)	63 (4.2)	45 (6.2)	7 (3.8)	70 (7.4)	
Values were expressed as medians (quartile interval)						
HDL-C, high-density lipoprotein-cholesterol; hs-CRP, high-sensitivity C-reactive protein; TC, total cholesterol; CHG, the cholesterol–HDL–glucose index; CVD, cardiovascular disease; BMI: body mass index; WC: waist circumference; WHtR, waist-to-height ratio; BRI, Body Roundness Index; CVAI, Chinese Visceral Adiposity Index; WWI, Weight-Adjusted Waist Index; ABSI, A Body Shape Index						

Baseline characteristics of participants according to CHG quartiles are presented in Table S4. With increasing CHG levels, participants exhibited progressively worse cardiometabolic profiles, accompanied by higher incidence rates of CVD and stroke.

Association of baseline CHG and its derivatives with CVD

As summarised in Table 2, baseline CHG and its derivatives were positively associated with CVD across all models. Specifically, each 1-unit increment in CHG was associated with a 6% higher risk of incident CVD (HR: 1.06, 95% CI: 1.01–1.13). CHG-derived indices demonstrated stronger associations than CHG alone, with CHG-CVAI and CHG-WC showing the most pronounced effects (HR: 1.20, 95% CI: 1.13–1.27; HR: 1.18, 95% CI: 1.12–1.25, respectively), followed by CHG-BMI (HR: 1.17, 95% CI: 1.10–1.23), CHG-BRI (HR: 1.16, 95% CI: 1.10–1.23), and CHG-WHtR (HR: 1.15, 95% CI: 1.09–1.22). CHG-WWI and CHG-ABSI showed comparatively weaker associations. Quartile-based analyses corroborated these findings: although higher CHG quartiles were not independently associated with CVD after full adjustment, all CHG-derived indices remained significantly associated, with the highest quartile of CHG-CVAI exhibiting the largest HR.

Table 2
Associations of baseline CHG and its obesity-related derivatives with incident CVD

	Model I		Model II		Model III	
	HR (95% CI)	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Z-CHG (Per 1 unit)	1.14 (1.09, 1.20)	< 0.001	1.14 (1.08, 1.20)	< 0.001	1.06 (1.01, 1.13)	0.032
Z-CHG-BMI (Per 1 unit)	1.23 (1.17, 1.29)	< 0.001	1.26 (1.20, 1.33)	< 0.001	1.17 (1.10, 1.23)	< 0.001
Z-CHG-WC (Per 1 unit)	1.28 (1.22, 1.35)	< 0.001	1.28 (1.21, 1.34)	< 0.001	1.18 (1.12, 1.25)	< 0.001
Z-CHG-WHtR (Per 1 unit)	1.29 (1.22, 1.35)	< 0.001	1.25 (1.18, 1.31)	< 0.001	1.15 (1.09, 1.22)	< 0.001
Z-CHG-BRI (Per 1 unit)	1.30 (1.23, 1.36)	< 0.001	1.25 (1.19, 1.32)	< 0.001	1.16 (1.10, 1.23)	< 0.001
Z-CHG-CVAI (Per 1 unit)	1.35 (1.29, 1.42)	< 0.001	1.30 (1.23, 1.37)	< 0.001	1.20 (1.13, 1.27)	< 0.001
Z-CHG-WWI (Per 1 unit)	1.24 (1.18, 1.31)	< 0.001	1.16 (1.10, 1.22)	< 0.001	1.09 (1.02, 1.15)	0.006
Z-CHG-ABSI (Per 1 unit)	1.21 (1.15, 1.27)	< 0.001	1.13 (1.07, 1.19)	< 0.001	1.07 (1.01, 1.14)	0.016
Quartiles of Z-CHG						
Q1	1.0		1.0		1.0	
Q2	1.05 (0.90, 1.23)	0.545	1.03 (0.88, 1.21)	0.713	1.00 (0.85, 1.18)	1.000
Q3	1.23 (1.06, 1.44)	0.008	1.21 (1.04, 1.42)	0.014	1.12 (0.95, 1.31)	0.174
Q4	1.39 (1.20, 1.61)	< 0.001	1.36 (1.17, 1.58)	< 0.001	1.15 (0.97, 1.35)	0.099
Quartiles of Z-CHG-BMI						
Q1	1.0		1.0		1.0	
Q2	1.09 (0.93, 1.29)	0.288	1.16 (0.98, 1.37)	0.076	1.10 (0.92, 1.30)	0.293
Q3	1.26 (1.08, 1.48)	0.004	1.36 (1.16, 1.59)	< 0.001	1.21 (1.02, 1.43)	0.029
Q4	1.64 (1.41, 1.91)	< 0.001	1.79 (1.54, 2.09)	< 0.001	1.44 (1.21, 1.70)	< 0.001
Quartiles of Z-CHG-WC						
Q1	1.0		1.0		1.0	
Q2	1.13 (0.96, 1.33)	0.148	1.15 (0.98, 1.36)	0.094	1.08 (0.91, 1.28)	0.384
Q3	1.33 (1.14, 1.56)	< 0.001	1.33 (1.13, 1.56)	< 0.001	1.18 (1.00, 1.40)	0.047
Q4	1.77 (1.52, 2.06)	< 0.001	1.76 (1.52, 2.05)	< 0.001	1.44 (1.22, 1.69)	< 0.001
Quartiles of Z-CHG-WHtR						
Q1	1.0		1.0		1.0	
Q2	1.27 (1.07, 1.49)	0.006	1.25 (1.06, 1.48)	0.008	1.19 (1.00, 1.41)	0.056
Q3	1.43 (1.22, 1.69)	< 0.001	1.38 (1.17, 1.63)	< 0.001	1.23 (1.04, 1.46)	0.018
Q4	1.95 (1.67, 2.28)	< 0.001	1.81 (1.55, 2.13)	< 0.001	1.47 (1.24, 1.75)	< 0.001
Quartiles of Z-CHG-BRI						
Q1	1.0		1.0		1.0	
Q2	1.26 (1.07, 1.49)	0.006	1.26 (1.06, 1.49)	0.007	1.16 (0.98, 1.39)	0.087
Q3	1.39 (1.18, 1.64)	< 0.001	1.36 (1.15, 1.61)	< 0.001	1.18 (0.99, 1.41)	0.061
Q4	2.01 (1.72, 2.34)	< 0.001	1.86 (1.59, 2.19)	< 0.001	1.50 (1.26, 1.79)	< 0.001
Quartiles of Z-CHG-CVAI						
Q1	1.0		1.0		1.0	

HR, hazard ratio; CI, confidence interval; CHG, the cholesterol–HDL–glucose index; CVD, cardiovascular disease; BMI: body mass index; WC: waist circumference; WHtR, waist-to-height ratio; BRI, Body Roundness Index; CVAI, Chinese Visceral Adiposity Index; WWI, Weight-Adjusted Waist Index; ABSI, A Body Shape Index; Z-, variables were standardized as Z-scores (per 1 SD increase).

Model I: unadjusted

Model II: adjusted for age and sex

Model III: further adjusted for education level, residential, marital status, smoking status, drinking status, hypertension, diabetes, kidney disease, and hs-CRP

	Model I		Model II		Model III	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Q2	1.43 (1.20, 1.69)	< 0.001	1.35 (1.13, 1.60)	< 0.001	1.29 (1.08, 1.54)	0.006
Q3	1.68 (1.43, 1.99)	< 0.001	1.52 (1.29, 1.80)	< 0.001	1.39 (1.16, 1.66)	< 0.001
Q4	2.28 (1.94, 2.67)	< 0.001	1.99 (1.69, 2.34)	< 0.001	1.63 (1.36, 1.94)	< 0.001
Quartiles of Z-CHG-WWI						
Q1	1.0		1.0		1.0	
Q2	1.20 (1.02, 1.41)	0.032	1.14 (0.97, 1.34)	0.124	1.10 (0.93, 1.31)	0.277
Q3	1.47 (1.25, 1.72)	< 0.001	1.34 (1.14, 1.57)	< 0.001	1.23 (1.04, 1.45)	0.018
Q4	1.77 (1.51, 2.06)	< 0.001	1.48 (1.26, 1.74)	< 0.001	1.24 (1.04, 1.47)	0.016
Quartiles of Z-CHG-ABSI						
Q1	1.0		1.0		1.0	
Q2	1.21 (1.03, 1.42)	0.021	1.15 (0.98, 1.35)	0.093	1.13 (0.95, 1.33)	0.16
Q3	1.35 (1.16, 1.58)	< 0.001	1.23 (1.05, 1.44)	0.011	1.13 (0.96, 1.34)	0.14
Q4	1.66 (1.43, 1.94)	< 0.001	1.41 (1.21, 1.65)	< 0.001	1.21 (1.02, 1.43)	0.028
HR, hazard ratio; CI, confidence interval; CHG, the cholesterol–HDL–glucose index; CVD, cardiovascular disease; BMI: body mass index; WC: waist circumference; WHtR, waist-to-height ratio; BRI, Body Roundness Index; CVAI, Chinese Visceral Adiposity Index; WWI, Weight-Adjusted Waist Index; ABSI, A Body Shape Index; Z-, variables were standardized as Z-scores (per 1 SD increase).						
Model I: unadjusted						
Model II: adjusted for age and sex						
Model III: further adjusted for education level, residential, marital status, smoking status, drinking status, hypertension, diabetes, kidney disease, and hs-CRP						

Baseline CHG and its derivatives were also positively associated with stroke (Table S5), consistent with the findings for CVD. Notably, CHG-derived indices—particularly CHG-CVAI and CHG-WC—demonstrated stronger associations with stroke than CHG alone.

Association of cumulative CHG and its derivatives with CVD

Associations between cumulative exposure values and incident CVD are shown in Table 3. Cumulative CHG and its derivatives were positively associated with CVD across all models. Each 1-unit increment in cumulative CHG was associated with a 10% higher risk of incident CVD (HR: 1.10, 95% CI: 1.00–1.21). Cumulative CHG-derived indices again exhibited stronger associations than cumulative CHG, with cumulative CHG-WC and cumulative CHG-CVAI showing the strongest effects (HR: 1.23, 95% CI: 1.11–1.36; HR: 1.22, 95% CI: 1.10–1.35, respectively), followed by cumulative CHG-BRI (HR: 1.21, 95% CI: 1.09–1.33), cumulative CHG-WHtR (HR: 1.20, 95% CI: 1.09–1.33), cumulative CHG-WWI (HR: 1.18, 95% CI: 1.06–1.31), and cumulative CHG-ABSI (HR: 1.18, 95% CI: 1.06–1.31).

Table 3
Associations of cumulative levels and changing patterns of CHG and its obesity-related derivatives with incident CVD

	Model I		Model II		Model III	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Z-Cumulative CHG (Per 1 unit)	1.19 (1.09, 1.29)	< 0.001	1.17 (1.08, 1.28)	< 0.001	1.10 (1.00, 1.21)	0.045
Z-Cumulative CHG-BMI (Per 1 unit)	1.22 (1.12, 1.33)	< 0.001	1.25 (1.14, 1.37)	< 0.001	1.16 (1.05, 1.28)	0.003
Z-Cumulative CHG-WC (Per 1 unit)	1.31 (1.19, 1.43)	< 0.001	1.31 (1.19, 1.44)	< 0.001	1.23 (1.11, 1.36)	< 0.001
Z-Cumulative CHG-WHtR (Per 1 unit)	1.32 (1.21, 1.45)	< 0.001	1.29 (1.17, 1.42)	< 0.001	1.20 (1.09, 1.33)	< 0.001
Z-Cumulative CHG-BRI (Per 1 unit)	1.32 (1.21, 1.43)	< 0.001	1.29 (1.18, 1.41)	< 0.001	1.21 (1.09, 1.33)	< 0.001
Z-Cumulative CHG-CVAI (Per 1 unit)	1.34 (1.22, 1.47)	< 0.001	1.30 (1.19, 1.43)	< 0.001	1.22 (1.10, 1.35)	< 0.001
Z-Cumulative CHG-WWI (Per 1 unit)	1.32 (1.20, 1.45)	< 0.001	1.26 (1.14, 1.39)	< 0.001	1.18 (1.06, 1.31)	0.002
Z-Cumulative CHG-ABSI (Per 1 unit)	1.30 (1.18, 1.43)	< 0.001	1.24 (1.13, 1.37)	< 0.001	1.18 (1.06, 1.31)	0.002
Changes in CHG						
Stable low	1.0		1.0		1.0	
High to low	1.36 (1.07, 1.73)	0.011	1.36 (1.07, 1.72)	0.012	1.31 (1.03, 1.67)	0.030
Low to high	0.96 (0.61, 1.53)	0.870	0.90 (0.56, 1.43)	0.646	0.83 (0.51, 1.33)	0.436
Stable high	1.55 (1.25, 1.93)	< 0.001	1.51 (1.22, 1.88)	< 0.001	1.30 (1.04, 1.64)	0.024
Changes in CHG-BMI						
Stable low	1.0		1.0		1.0	
High to low	1.38 (1.00, 1.91)	0.053	1.43 (1.03, 1.98)	0.031	1.30 (0.92, 1.83)	0.134
Low to high	1.23 (0.86, 1.77)	0.254	1.25 (0.87, 1.80)	0.226	1.21 (0.84, 1.76)	0.303
Stable high	1.44 (1.17, 1.76)	< 0.001	1.50 (1.22, 1.84)	< 0.001	1.29 (1.03, 1.61)	0.027
Changes in CHG-WC						
Stable low	1.0		1.0		1.0	
High to low	1.52 (1.12, 2.06)	0.007	1.52 (1.12, 2.07)	0.007	1.52 (1.11, 2.07)	0.009
Low to high	1.45 (1.03, 2.03)	0.031	1.46 (1.04, 2.06)	0.027	1.38 (0.97, 1.96)	0.074
Stable high	1.70 (1.37, 2.10)	< 0.001	1.68 (1.36, 2.08)	< 0.001	1.47 (1.17, 1.85)	< 0.001
Changes in CHG-WHtR						
Stable low	1.0		1.0		1.0	
High to low	1.44 (1.05, 1.97)	0.024	1.38 (1.01, 1.90)	0.044	1.28 (0.92, 1.77)	0.138
Low to high	1.38 (0.98, 1.95)	0.067	1.34 (0.95, 1.91)	0.097	1.28 (0.89, 1.83)	0.180
Stable high	1.62 (1.32, 1.99)	< 0.001	1.53 (1.24, 1.90)	< 0.001	1.32 (1.05, 1.67)	0.017
Changes in CHG-BRI						
Stable low	1.0		1.0		1.0	
High to low	1.38 (0.97, 1.95)	0.070	1.33 (0.94, 1.89)	0.111	1.26 (0.88, 1.81)	0.200
Low to high	1.27 (0.91, 1.77)	0.156	1.25 (0.89, 1.76)	0.190	1.17 (0.83, 1.66)	0.364
Stable high	1.64 (1.33, 2.02)	< 0.001	1.56 (1.25, 1.94)	< 0.001	1.32 (1.04, 1.67)	0.020
Changes in CHG-CVAI						
Stable low	1.0		1.0		1.0	

HR, hazard ratio; CI, confidence interval; CHG, the cholesterol–HDL–glucose index; CVD, cardiovascular disease; BMI: body mass index; WC: waist circumference; WHtR, waist-to-height ratio; BRI, Body Roundness Index; CVAI, Chinese Visceral Adiposity Index; WWI, Weight-Adjusted Waist Index; ABSI, A Body Shape Index; Z-, variables were standardized as Z-scores (per 1 SD increase).

Model I: unadjusted

Model II: adjusted for age and sex

Model III: further adjusted for education level, residential, marital status, smoking status, drinking status, hypertension, diabetes, kidney disease, and hs-CRP

	Model I		Model II		Model III	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
High to low	1.56 (1.03, 2.36)	0.035	1.53 (1.01, 2.31)	0.045	1.43 (0.94, 2.18)	0.094
Low to high	1.78 (1.32, 2.41)	< 0.001	1.74 (1.29, 2.36)	< 0.001	1.57 (1.14, 2.15)	0.005
Stable high	1.96 (1.58, 2.45)	< 0.001	1.83 (1.46, 2.29)	< 0.001	1.58 (1.25, 2.01)	< 0.001
Changes in CHG-WWI						
Stable low	1.0		1.0		1.0	
High to low	1.11 (0.83, 1.49)	0.478	1.05 (0.78, 1.41)	0.731	0.98 (0.73, 1.33)	0.905
Low to high	1.42 (1.03, 1.97)	0.033	1.35 (0.97, 1.87)	0.077	1.24 (0.89, 1.75)	0.208
Stable high	1.67 (1.35, 2.06)	< 0.001	1.50 (1.20, 1.87)	< 0.001	1.26 (0.99, 1.60)	0.058
Changes in CHG-ABSI						
Stable low	1.0		1.0		1.0	
High to low	1.09 (0.83, 1.43)	0.524	1.04 (0.80, 1.37)	0.757	0.97 (0.74, 1.29)	0.853
Low to high	1.25 (0.89, 1.74)	0.195	1.18 (0.84, 1.65)	0.346	1.11 (0.79, 1.57)	0.537
Stable high	1.65 (1.33, 2.04)	< 0.001	1.49 (1.20, 1.86)	< 0.001	1.29 (1.02, 1.62)	0.034
HR, hazard ratio; CI, confidence interval; CHG, the cholesterol–HDL–glucose index; CVD, cardiovascular disease; BMI: body mass index; WC: waist circumference; WHtR, waist-to-height ratio; BRI, Body Roundness Index; CVAI, Chinese Visceral Adiposity Index; WWI, Weight-Adjusted Waist Index; ABSI, A Body Shape Index; Z-, variables were standardized as Z-scores (per 1 SD increase).						
Model I: unadjusted						
Model II: adjusted for age and sex						
Model III: further adjusted for education level, residential, marital status, smoking status, drinking status, hypertension, diabetes, kidney disease, and hs-CRP						

Findings for stroke were comparable (Table S6), with cumulative CHG-derived indices—particularly CHG-CVAI and CHG-WC—exhibiting stronger associations than CHG alone. Associations appeared slightly stronger for stroke than for CVD.

RCS analyses indicated a linear dose–response relationship between cumulative CHG and risk of CVD and stroke (P < 0.001). In contrast, all CHG-derived indices exhibited nonlinear associations (all P for nonlinearity < 0.05), suggesting more complex dose–response patterns (Fig. 3 and Figure S1).

Association of trajectories of CHG and its derivatives with CVD

Regarding the 5-year trajectories of CHG and its derivatives, as presented in Table 3, participants in the stable-high groups demonstrated a greater risk of CVD compared with their corresponding stable-low groups, particularly for CHG-CVAI (HR: 1.58, 95% CI: 1.25–2.01) and CHG-WC (HR: 1.47, 95% CI: 1.17–1.85). Moreover, individuals exhibiting an increasing trajectory of CHG-CVAI showed a 57% higher likelihood of developing CVD relative to the stable-low trajectory (HR: 1.57, 95% CI: 1.14–2.15). Notably, even the decreasing trajectory groups of CHG and CHG-WC remained associated with an elevated risk of incident CVD, with HRs of 1.31 (95% CI: 1.03–1.67) and 1.52 (95% CI: 1.11–2.07), respectively.

Comparable patterns were observed for stroke, as indicated in Table S6, with associations generally exceeding those observed for CVD. In comparison with the stable-low groups, the stable-high groups across all indicators exhibited an increased risk of stroke, particularly for CHG-CVAI and CHG-WC. Similarly, even the decreasing trajectory groups of CHG-WC maintained a higher risk of stroke.

Kaplan–Meier survival analysis and ROC curve analysis

Kaplan–Meier cumulative incidence curves revealed a progressive elevation in risk across ascending categories of cumulative indicators for both CVD and stroke. When stratified into quartiles, a stepwise increase in incidence was evident, with clear separation between curves and statistically significant between-group differences (log-rank P < 0.05). A comparable trend was observed in trajectory analyses, wherein participants with persistently high or increasing levels exhibited the highest incidence rates (log-rank P < 0.01; Fig. 4 and Figure S2).

ROC curve analysis demonstrated modest yet consistent discriminatory performance for CVD, with cumulative CHG-WC (AUC = 0.626) and cumulative CHG-CVAI (AUC = 0.625) exhibiting slightly superior predictive ability compared with cumulative CHG alone (AUC = 0.624). Discriminatory capacity was higher for stroke (Figure S3).

Subgroup analysis and sensitivity analyses

Figure 5 presents results for cumulative indicators, which were broadly consistent across subgroups. A significant interaction was observed for drinking status in the association between cumulative CHG and CVD risk (P for interaction = 0.01), indicating stronger effects among individuals who consumed alcohol. Subgroup analyses of longitudinal changes in CHG and its derivatives are provided in Tables S7–S13. Across most subgroups, “stable high” and

“high-to-low” trajectories were generally associated with an increased risk of CVD. Significant interactions were detected within the kidney disease strata, primarily involving CHG-BMI and CHG-BRI.

Sensitivity analyses further corroborated the robustness of the primary findings. First, results from multivariable logistic regression were consistent with those from Cox proportional hazards models (Tables S14 and S15), with CHG-derived indices—particularly CHG-WC and CHG-CVAI—demonstrating stronger associations than CHG alone. Persistently high trajectories conferred the highest risk, whereas increasing CHG-CVAI and decreasing CHG and CHG-WC trajectories also remained linked to elevated risk. Second, cluster-based analyses revealed higher CVD risk among participants in higher trajectory classes, especially for CHG-WC and CHG-CVAI (Table S16). Third, exclusion of participants with kidney disease, hypertension, or diabetes at baseline did not materially alter these associations, with persistently high trajectories and increasing CHG-CVAI continuing to exhibit elevated risk (Tables S18 and S19).

Discussion

With an 8-year follow-up in this large prospective cohort study, the associations of baseline levels, cumulative exposure, and longitudinal trajectories of CHG and its derivatives with the risks of CVD and stroke were comprehensively evaluated. Elevated CHG levels were consistently associated with higher incidence of both outcomes, and these associations were further reinforced when CHG was integrated with obesity-related indices. Among the derivatives examined, CHG-WC and CHG-CVAI exhibited the strongest associations in both baseline and cumulative analyses. Trajectory analyses further demonstrated that persistently high patterns were associated with the greatest CVD risk, whereas an increasing trajectory of CHG-CVAI and decreasing trajectories of CHG and CHG-WC were also linked to elevated risk. These findings were supported by subgroup and sensitivity analyses.

CHG, as an emerging biomarker integrating TC, HDL-C, and FBG [9], has been preliminarily associated with CVD in a limited number of cohort studies, most of which relied on baseline measurements [10, 11], in accordance with prior evidence. The underlying mechanisms remain incompletely elucidated but are likely related to dysregulation of lipids and glucose, as well as IR [21]. Mechanistically, IR may impair insulin signalling and disrupt glucose homeostasis, thereby inducing endothelial dysfunction, while concomitant dyslipidemia, characterised by atherogenic lipoproteins and reduced HDL-C, further exacerbates vascular inflammation and promotes plaque formation. These interrelated metabolic disturbances act synergistically to accelerate atherosclerotic progression [22, 23], ultimately increasing CVD risk. From a pathophysiological perspective, CHG may offer advantages over established markers. Incorporation of FBG may enhance the predictive value of CHG for hypertension relative to the AIP [24], whereas the inclusion of TC and HDL-C provides complementary atherogenic information beyond the TyG index [11], thereby supporting a more comprehensive characterisation of cardiometabolic risk. Nevertheless, cohort evidence regarding CHG remains limited, particularly with respect to longitudinal assessments [10, 11]. To date, only one Chinese cohort has evaluated the association of cumulative CHG with CVD, demonstrating increased risk with higher cumulative exposure and persistently high-risk trajectories [25]. However, the largely parallel trajectory patterns observed in that study suggest that these associations may have been primarily driven by baseline differences, providing limited insight into the impact of dynamic changes over time. These gaps highlight the necessity of investigating longitudinal changes in CHG to better elucidate its prognostic utility.

Building on these observations, emerging evidence indicates that integrating metabolic indices with obesity-related measures enhances CVD risk stratification, as exemplified by the TyG index [15], the AIP [16], and the CTI [17], suggesting that adiposity contributes additional pathophysiological information beyond conventional metabolic markers. Excess adiposity promotes atherosclerosis through mechanisms including systemic inflammation, ectopic lipid deposition, and IR [20, 26–28]. However, evidence regarding CHG-derived obesity indices remains limited. To date, only one nationwide Chinese cohort has examined associations of CHG and its derivatives—namely CHG–BMI, CHG–WC, CHG–WHtR, CHG–BRI, CHG–CVAI, CHG–WWI, and CHG–ABSI—with stroke [10]. Nevertheless, its reliance on baseline measurements may limit the robustness of the findings [29]. To our knowledge, the present study is the first to investigate the effects of cumulative exposure and dynamic changes in CHG-derived obesity indices. Integration of CHG with obesity-related indicators yielded stronger associations with CVD outcomes than CHG alone, for both baseline and cumulative exposures. These results suggest that combining CHG with adiposity measures provides a more comprehensive assessment of cardiometabolic risk and enhances predictive performance, with potential implications for targeted prevention and management strategies among middle-aged and older adults.

Notably, among the CHG-derived obesity indices, CHG-WC and CHG-CVAI demonstrated the strongest associations. A similar pattern has been observed in a large Chinese cohort that evaluated associations of TyG and its derivatives—including TyG-BMI, TyG-WHtR, TyG-WC, TyG-CVAI, TyG-WWI, TyG-BRI, and TyG-ABSI—with CVD risk, with findings consistent with those of the present study [15]. This may be partly attributable to ethnic-specific differences in fat distribution: Asian populations generally accumulate greater visceral fat at a given BMI compared with Western populations [30], and traditional anthropometric indices such as BMI may be less sensitive for identifying high-risk individuals. The CVAI, developed as a surrogate marker of visceral adiposity in Asian populations [31], has been validated as a practical alternative to CT- or MRI-based assessments in large-scale studies [32, 33], demonstrating superior predictive performance for CVD [34–36] and hypertension [37, 38]. An additional explanation is that CVAI reflects not only visceral fat accumulation but also underlying metabolic dysfunction by incorporating TG and HDL-C in addition to basic anthropometric parameters. When combined with CHG, CHG-CVAI may therefore capture the concurrent deterioration of metabolic status and visceral adiposity [32, 39, 40], thereby amplifying the contribution of combined lipid and glucose abnormalities to risk stratification. Similarly, CHG-WC, as a readily available measure of central obesity, reflects both metabolic dysregulation and abdominal adiposity [41]. This combined index outperformed other anthropometric measures, including WHtR, BRI, and ABSI, consistent with findings from another nationwide Chinese cohort in which TyG-WC exhibited superior predictive performance relative to other TyG-derived obesity indices [42].

Trajectory analyses revealed that persistently elevated levels of CHG and its derivatives were associated with the highest risk of CVD. With the exception of CHG-WWI [15, 43], sustained elevations in CHG and its derivatives consistently conferred the greatest CVD risk, highlighting the deleterious effects of long-term metabolic burden. An ascending trajectory of CHG-CVAI was associated with a significantly higher incidence of CVD compared with a persistently low trajectory, whereas a descending trajectory did not show a significant difference. These findings suggest that increases in CHG-CVAI reflect heightened

cardiovascular risk, whereas reductions may indicate the cumulative benefits of weight loss, lipid regulation, and glycemic control, resulting in risk levels comparable to those of persistently low trajectories. Accordingly, longitudinal changes in CHG-CVAI may serve as a valuable biomarker for monitoring and managing CVD risk. In contrast, declining trajectories of CHG and CHG-WC remained associated with substantially higher cardiovascular risk compared with persistently low levels, whereas other indices—including CHG-WHtR, CHG-BRI, and CHG-ABSI—demonstrated no significant associations, highlighting heterogeneity in predictive utility. The persistently elevated CVD risk observed in the declining CHG and CHG-WC groups likely reflects a high baseline metabolic burden. Early metabolic disturbances may induce lasting vascular injury through a "metabolic memory" effect that is not fully reversible with short-term improvements [44, 45]. These observations are consistent with prior evidence from a Chinese cohort in which participants with high baseline CHG but rapidly declining trajectories remained at greatest risk for incident hypertension [24]. Notably, reductions in WC may not reliably reflect visceral fat loss [46], suggesting that improvements in superficial metabolic parameters alone are insufficient to eliminate residual cardiovascular risk. Collectively, these findings emphasise the need for targeted interventions addressing visceral adiposity and for early, sustained management of key metabolic risk factors.

This study, based on the nationally representative CHARLS cohort, comprehensively evaluated baseline, cumulative, and dynamic changes in CHG and its derivatives in relation to CVD and stroke, providing the first systematic assessment of the combined predictive performance of CHG-centred metabolic and obesity indices. A range of rigorous statistical approaches—including multivariable Cox regression, subgroup analyses, RCS regression, ROC modelling, and k-means clustering—was employed to ensure the reliability and robustness of the findings. Nonetheless, several limitations merit consideration. First, potential misclassification bias may exist because CVD events were ascertained through self-reported information. Nevertheless, evidence from large-scale cohort studies such as the English Longitudinal Study of Ageing (ELSA) indicates good concordance between self-reported and clinically verified CVD events. Second, the exclusion of participants without follow-up or with incomplete data may have slightly underestimated the true associations, particularly for diabetes, CVD, and other chronic conditions. Third, the study included only middle-aged and older adults aged ≥ 45 years, limiting the generalizability of the findings to younger populations. Fourth, the cohort was restricted to a Chinese population, and the results may be influenced by ethnic and geographic variations; additional multicenter studies are needed to validate applicability in diverse populations. Finally, although cumulative exposure and trajectory analyses were conducted, future studies with more frequent longitudinal assessments are warranted to more precisely characterise the dynamic trajectories of CHG and its derivatives in relation to CVD and stroke.

Conclusion

Elevated levels of CHG and its derivatives were significantly associated with increased risk of CVD, with CHG-CVAI and CHG-WC demonstrating the strongest associations. Beyond the impact of persistently high trajectories, ascending trajectories of CHG-CVAI and declining trajectories of CHG-WC were also linked to elevated CVD risk, suggesting that CHG-CVAI functions as a sensitive early predictor, whereas CHG-WC may reflect the enduring consequences of prior metabolic burden. These findings highlight the potential value of combined interventions targeting both metabolic dysfunction and adiposity to achieve enhanced cardiovascular preventive benefits.

Abbreviations

CHG
the cholesterol–HDL–glucose index
BMI
Body mass index
WC
Waist circumference
WHtR
Waist-to-height ratio
BRI
Body Roundness Index
CVAI
Chinese Visceral Adiposity Index
WWI
Weight adjusted waist index
ABSI
A body shape index
CVD
Cardiovascular disease
TC
Total cholesterol
FBG
Fast blood glucose
HDL-C
High-density lipoprotein cholesterol
SBP
Systolic blood pressure
DBP

Diastolic blood pressure
TyG
Triglyceride-glucose
AIP
Atherogenic index of plasma
IR
Insulin resistance
AUC
Area under the curve
CHARLS
China health and retirement longitudinal study
RCS
Restricted cubic spline
HR
Hazard ratios
CI
Confidence interval
ELSA
English Longitudinal Study of Ageing

Declarations

Ethics approval and consent to participate

The CHARLS study received approval from the Institutional Review Board of Peking University (IRB00001052-11015) and was performed in accordance with the principles of the Declaration of Helsinki. All participants provided written informed consent prior to their involvement in the CHARLS study. This research adhered to the STROBE guidelines for reporting observational studies in epidemiology.

Consent for publication

Not applicable.

Availability of data and materials

The dataset supporting the conclusions of this article is available in the CHARLS dataset(http://charls.pku.edu.cn/en).

Competing interests

The authors declare no competing interests.

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Author contributions

XT and HW contributed to the conception and design of the work. DH, YZ and ZS performed data curation, data processing, statistical analysis, and interpretation of the results. HW, GS, GL and CZ engaged in literature review and drafted the original manuscript. XT critically revised the manuscript for important intellectual content. XT and DZ supervised the study. All authors reviewed the manuscript and approved the final version for publication.

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Figures

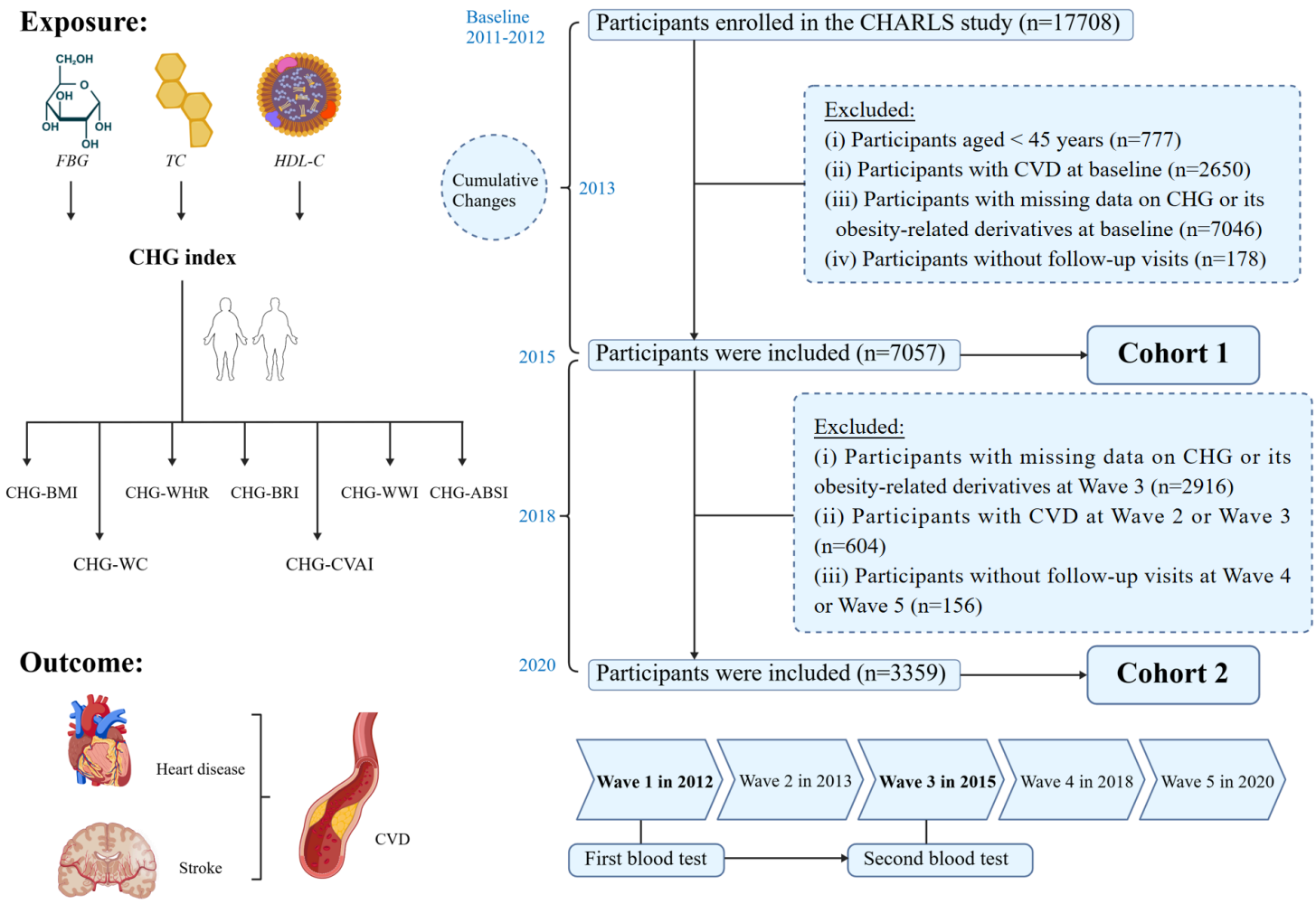

Figure 1

Flowchart of the study population. CHG: cholesterol–HDL–glucose; BMI: body mass index; WC: waist circumference; WHtR: waist-to-height ratio; BRI: body roundness index; CVAI: Chinese visceral adiposity index; WWI: weight-adjusted waist index; ABSI: a body shape index; CVD: cardiovascular disease.

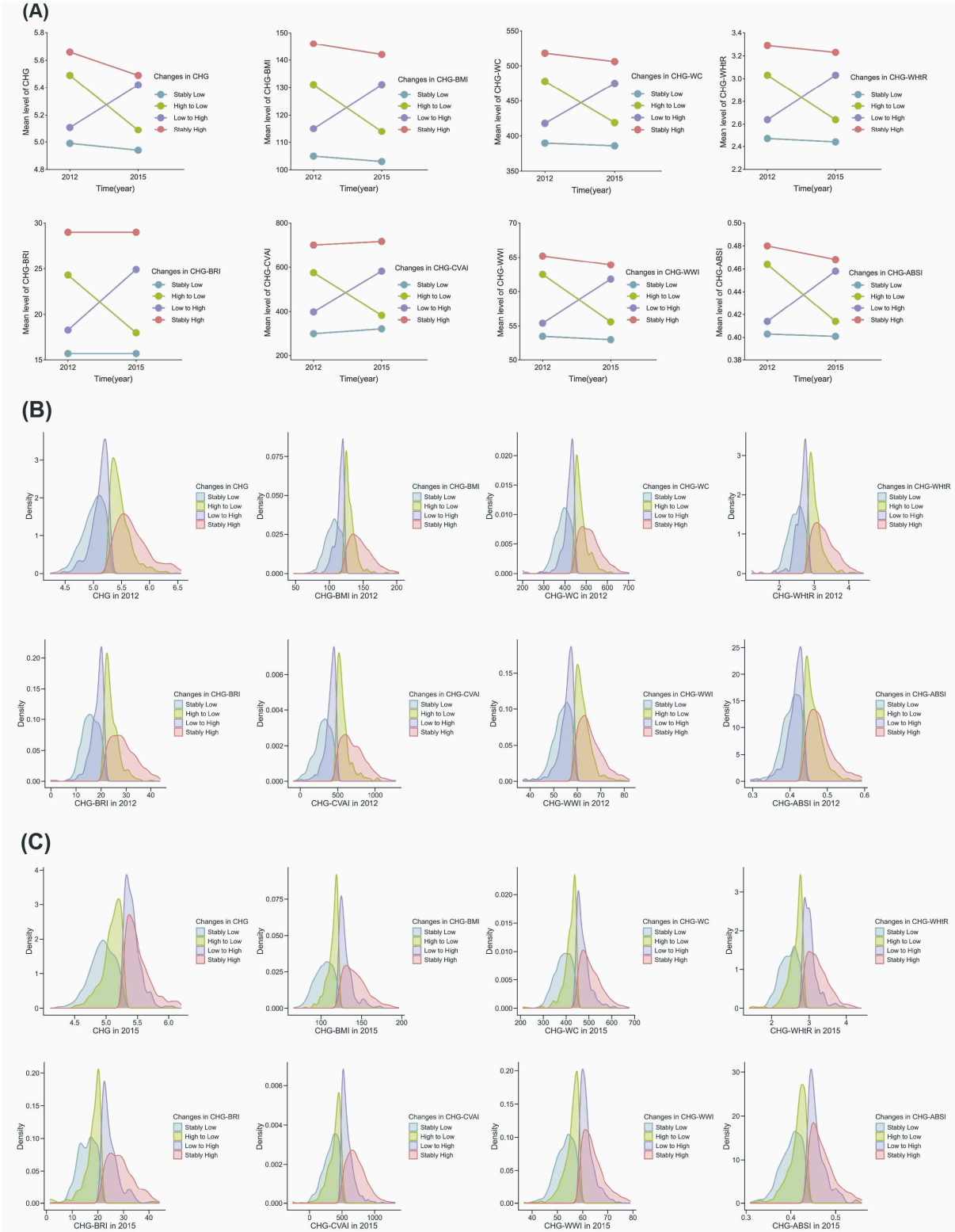

Figure 2

Trajectory patterns of CHG and its derivatives from 2012 to 2015. **(A)** Mean levels in 2012 and 2015 across four trajectory patterns. **(B, C)** Distributions in 2012 and 2015, respectively. CHG: cholesterol–HDL–glucose; BMI: body mass index; WC: waist circumference; WHtR: waist-to-height ratio; BRI: body roundness index; CVAI: Chinese visceral adiposity index; WWI: weight-adjusted waist index; ABSI: a body shape index; CVD: cardiovascular disease.

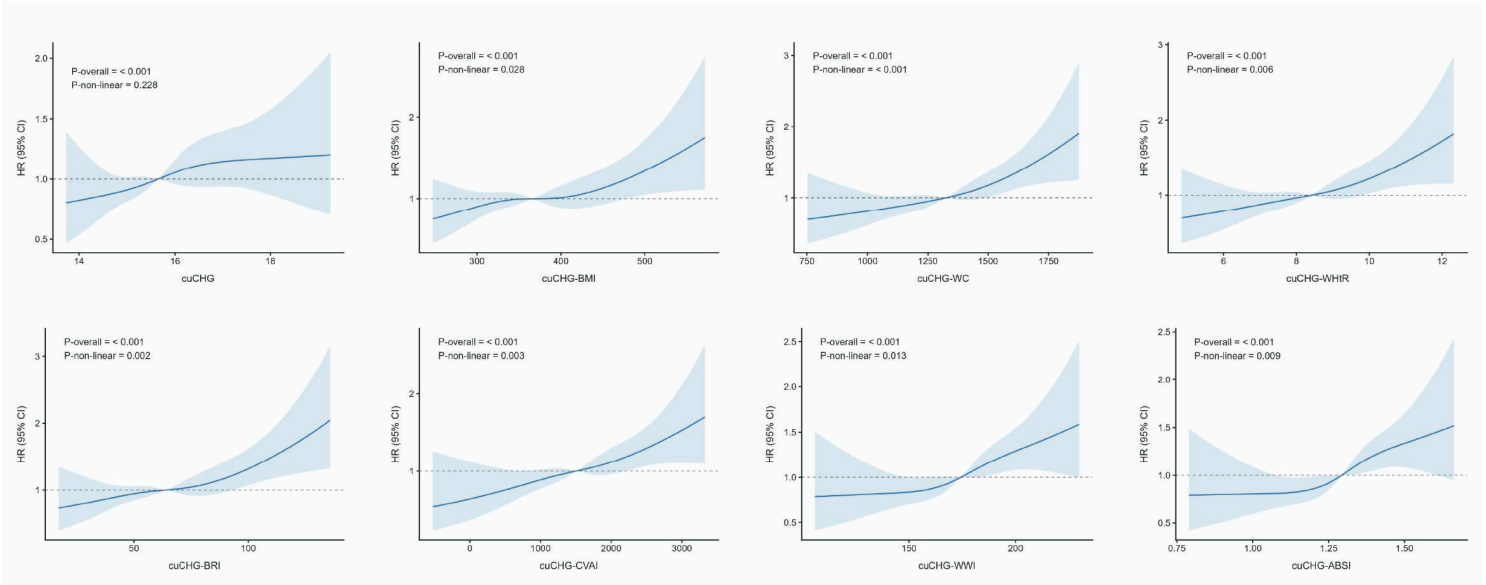

Figure 3

Dose–response relationships of cumulative CHG and its derivatives with CVD incidence, assessed using restricted cubic splines. Models were adjusted for age, sex, education level, residence, marital status, smoking status, drinking status, hypertension, diabetes, kidney disease, and high-sensitivity C-reactive protein (hs-CRP). CHG: cholesterol–HDL–glucose; BMI: body mass index; WC: waist circumference; WHtR: waist-to-height ratio; BRI: body roundness index; CVAI: Chinese visceral adiposity index; WWI: weight-adjusted waist index; ABSI: a body shape index; CVD: cardiovascular disease.

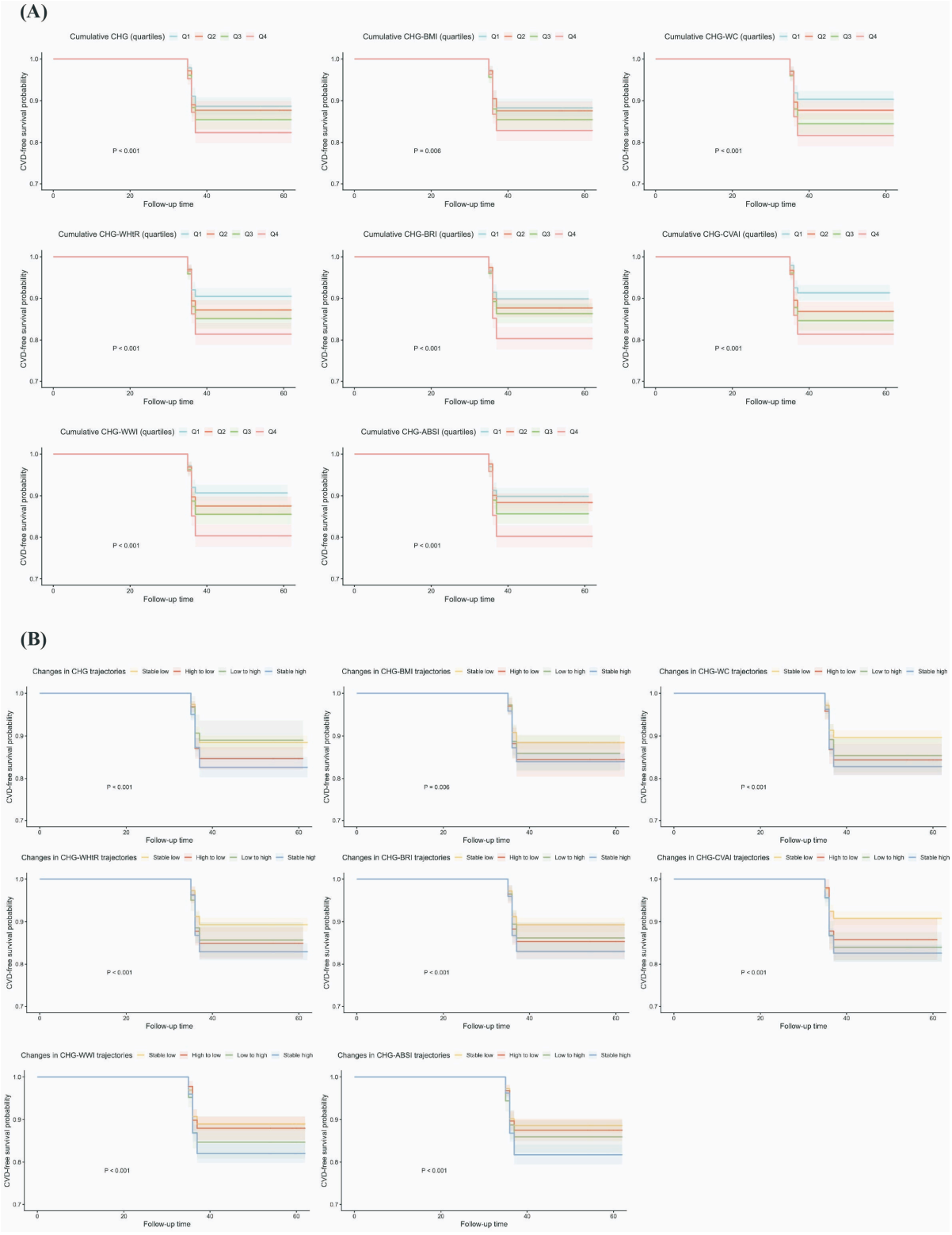

Figure 4

Kaplan–Meier curves for CVD-free survival according to cumulative CHG and its derivatives **(A)** and trajectory groups **(B)**. CHG: cholesterol–HDL–glucose; BMI: body mass index; WC: waist circumference; WHtR: waist-to-height ratio; BRI: body roundness index; CVAI: Chinese visceral adiposity index; WWI: weight-adjusted waist index; ABSI: a body shape index; CVD: cardiovascular disease.

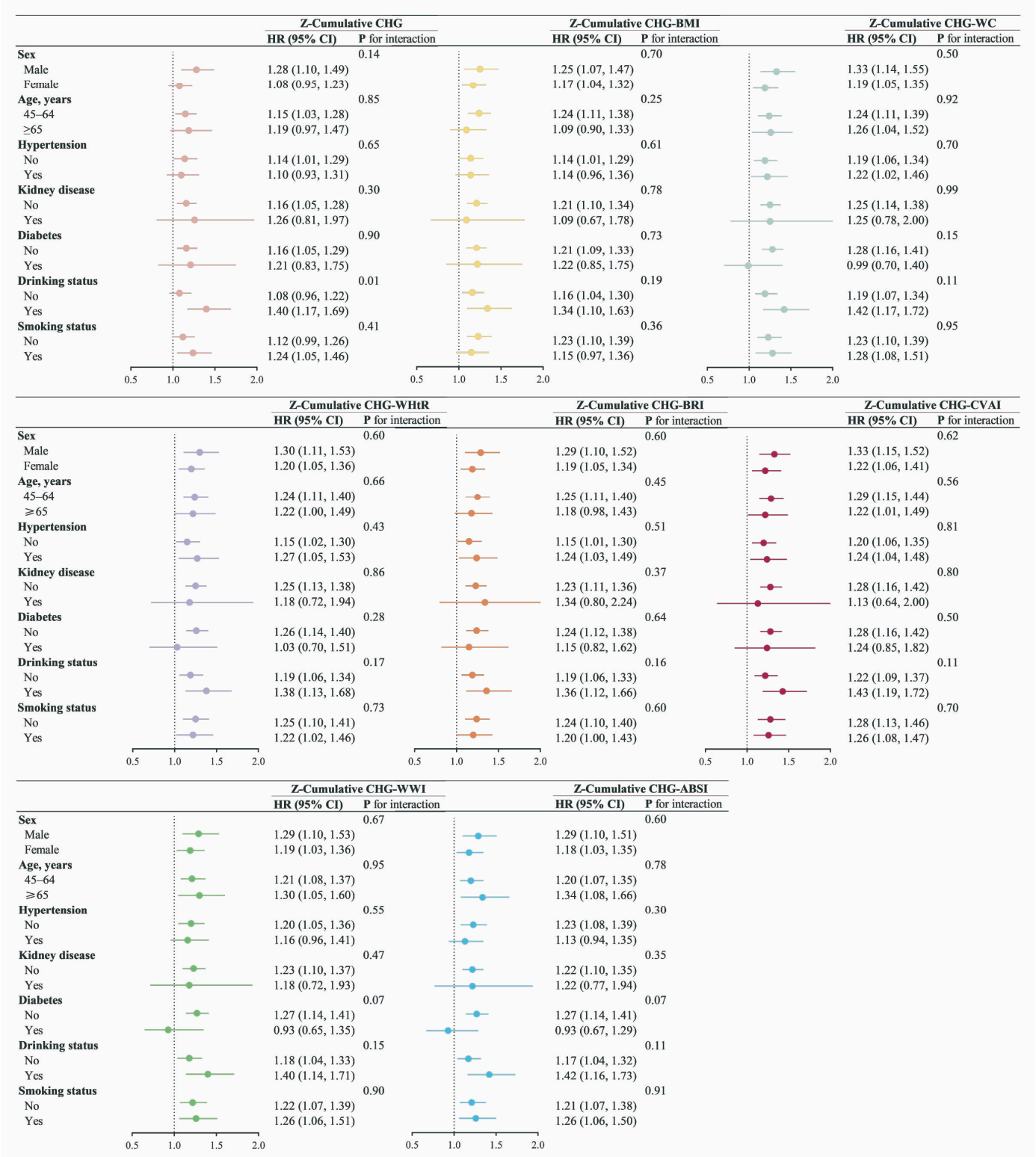

Figure 5

Forest plot illustrating subgroup-specific associations of cumulative CHG and its derivatives with CVD. CHG: cholesterol–HDL–glucose; BMI: body mass index; WC: waist circumference; WHtR: waist-to-height ratio; BRI: body roundness index; CVAI: Chinese visceral adiposity index; WWI: weight-adjusted waist index; ABSI: a body shape index; CVD: cardiovascular disease

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