Status and transition of normal-weight central obesity and the risk of cardiovascular diseases: A population-based cohort study in China

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Abstract *Background and aims:* Cardiovascular disease (CVD) has become a growing public health concern. Normal weight central obesity (NWCO) has emerged as a potential risk factor for cardiometabolic dysregulation. To date, the association between NWCO and new-onset CVDs remains unclear. We aimed to evaluate the associations of NWCO and its longitudinal transitions with cardiovascular risks in middle-aged and older Chinese.
Methods and results: Data were from the China Health and Retirement Longitudinal Study 2011–2018. NWCO was defined as the combination of a body mass index (BMI) of <24.0 kg/m² and a waist circumference (WC) of >85 cm in males or >80 cm in females. CVDs included heart diseases and stroke. Cause-specific hazard models and subdistribution hazard models with all-cause death as the competing event were applied. In 2011, 9856 participants without prior CVDs were included, of whom 1814 developed CVDs during a 7-year follow-up. Compared to normal weight and non-central obesity (NWNCO), NWCO was significantly associated with new-onset CVDs, with cause-specific hazard ratios (cHRs) and 95% confidence intervals (CIs) of 1.21 (1.04–1.41) for heart diseases and 1.40 (1.11–1.76) for stroke. From 2011 to 2013, 571 NWNCO participants developed NWCO who subsequently demonstrated a 45% higher risk of CVDs than those with maintained NWNCO.
Conclusion: NWCO and transition from NWNCO to NWCO are associated with higher risks of CVDs. Identification and prevention of NWCO may be useful in the management of CVDs.
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1. Introduction

Cardiovascular diseases (CVDs) have become a serious public health problem worldwide, with a rise in the number of deaths from 12.1 million to 18.6 million during the past three decades [1]. According to the latest data reported by the China Death Surveillance Point System [2], CVDs, principally including coronary heart disease and stroke, are the leading causes of death in China, with a mortality rate of 364.5 per 100 000 population in 2019. The average monthly treatment expenditures for CVDs ranged between US$ 300 and US$ 1000, resulting in enormous socioeconomic and medical burdens [3,4].

Prior research has shown that obesity is significantly related to diabetes, hypertension, and other metabolic abnormalities [5−7], all of which have been proven to be risk factors for CVDs. Traditionally, body mass index (BMI) has been used as the primary indicator of adiposity. However, it cannot reflect regional body fat distribution and ectopic fat accumulation [8]. Waist circumference (WC) has been widely used as a cost-effective and reliable indicator to further identify central obesity, which is characterized by abdominal fat distribution [9]. Previous studies indicated that subgroups of elevated WC in a given BMI category were also significantly associated with cardiovascular mortality risk [10,11]. Considering the limitations of BMI or WC as a single indicator in defining adiposity, simultaneous interpretation of those two anthropometric measurements is suggested to comprehensively capture the heterogeneity and phenotypes of obesity [12,13].

Recently, a distinct obesity phenotype named normal weight with central obesity (NWCO), characterized by normal BMI and abdominal obesity [14−16], has become prevalent and received growing research attention [17]. Previous studies have demonstrated that NWCO is related to multiple cardiovascular risk factors (i.e., hypertension, diabetes, and dyslipidemia) [18−20] and an elevated risk of cardiovascular mortality [11,21]. People with NWCO, however, are frequently overlooked in clinical guidelines and risk-reduction strategies [22]. For example, in the latest Chinese expert consensus on the procedure of bodyweight management among patients with overweight or obesity [23], preventive interventions were only recommended for people with BMI-defined overweight/ obesity. Identification of suboptimal health status at the early stage of CVD is essential for the promotion of ideal cardiovascular health [24,25].

To date, limited longitudinal studies have specifically explored the associations between NWCO and CVDs. To add evidence to this research area, we conducted this prospective longitudinal study among Chinese adults aged 45 years and older to investigate the risk of CVDs in people with NWCO and whether the transition from normal weight with non-central obesity (NWNCO) to NWCO may lead to an increased risk of new-onset CVDs.

2. Methods

2.1. Study population

This study used data from the 2011−2018 waves of the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative survey of residents aged 45 years and older in Mainland China. The detailed procedures of CHARLS have been reported elsewhere [26]. In brief, a stratified multistage probability sampling strategy was adopted to recruit participants from 450 villages/urban communities in 28 provinces across China. Subsequently, random sampling was applied to select households from communities, and individuals aged 45 and above were chosen as the main respondents within each household. The baseline survey was conducted from 2011 to 2012. Participants were followed up every two years, with a small share of new respondents recruited simultaneously. In total, three follow-up surveys were conducted, one each in 2013, 2015, and 2018. Ethical approval for this study was granted by the Institutional Review Board at Peking University. Each respondent who agreed to participate in the survey has signed the written informed consent.

2.2. Assessment and definition of obesity phenotypes

In 2011 and 2013, physical measurements, including height, weight, and WC were collected by trained healthcare workers. BMI was calculated as weight (kg)/height squared (m^2). Waist-to-height ratio (WHtR) was calculated as WC (cm)/height (cm). Abnormal weight was defined as a BMI of ≥ 24 kg/m^2, and participants with a BMI of <24 kg/m^2 were classified as normal weight [27]. Central obesity was defined as a WC of >85 cm in males or >80 cm in females [27].

Four obesity phenotypes were classified according to the combination of abnormal weight and central obesity: NWCO, NWNCO, abnormal weight with central obesity (AWCO), and abnormal weight with non-central obesity (AWNCO). From 2011 to 2013, seven obesity transition patterns related to NWCO were defined to investigate the association between transition of NWCO and incident CVDs: NWNCO to NWCO (vs. maintained NWNCO); NWCO to NWNCO and NWCO to AWCO (vs. maintained NWCO); and AWCO to NWCO (vs. maintained AWCO).

2.3. Assessment of outcomes

CVDs were self-reported by respondents. At the baseline survey in 2011 and the subsequent follow-up surveys (2013, 2015, and 2018), participants were asked through a questionnaire whether and when they had been diagnosed to have heart diseases (including heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems) or stroke. Those who answered as having either heart diseases or stroke were considered to have CVDs. Furthermore, the time-to-CVDs was defined as 1−7 years (diagnosed between 2012 and 2018) after 2011.

CHARLS only recorded the exact year of death for participants who died between 2011 and 2013. The specific year of death for participants who died after 2013 was not accurately recorded but was uniformly reported at the 2015 and 2018 follow-ups. For example, those who died in 2016 were recorded as dead in 2018. Hence, the time-to-death was defined as 1 (died in 2012), 2 (died in 2013), 4 (died between 2013 and 2015), and 7 (died between 2015 and 2018) years after 2011.

2.4. Measurement of covariates

Information on age, sex, residence, education, marital status, economic status, smoking history, and drinking history was collected through face-to-face interviews. Residence was classified as rural or urban. Education was categorized as illiterate, literate, primary school, or middle school or higher. Marital status was classified as single or married/cohabited. Economic status was evaluated by the natural logarithm of per capita expenditures (ln [PCE]) [28] and was divided into bottom, middle, and top tertiles, respectively, representing poor, middle, and rich groups. Smoking history was classified as never smoker or ever and current smoker. Drinking history was similarly classified as never drinker or ever and current drinker.

Physicians' diagnoses of hypertension, diabetes, and dyslipidemia were self-reported at baseline. Blood pressure was measured three times at 45 s intervals using a sphygmomanometer (Omron™ HEM-7200, Dalian, China) and was recorded to the nearest mmHg. Venous blood samples of each participant were collected using standard blood-taking materials to measure plasma glucose concentration and glycated hemoglobin (HbA1c). Hypertension was identified if any of the following criteria occurred: (1) having physician-diagnosed hypertension; (2) mean systolic blood pressure (SBP) $\geq$ 140 mmHg; (3) mean diastolic blood pressure (DBP) $\geq$ 90 mmHg; and (4) on antihypertensive drugs [29]. Diabetes was defined as meeting any of the following criteria: (1) reported physician-diagnosed diabetes; (2) fasting plasma glucose $\geq$ 7.0 mmol/L; (3) random plasma glucose $\geq$ 11.1 mmol/L; (4) HbA1c $\geq$ 6.5%; and (5) on antidiabetic medication [30].

2.5. Statistical analysis

The characteristics of included participants by obesity phenotypes were described as medians with interquartile ranges (IQRs) for continuous variables and number and percent (%) for categorical variables. Wilcoxon rank sum tests for continuous variables and Chi-square tests for categorical variables were utilized to calculate P values.

Competing-risks regression models were utilized in the current longitudinal analyses given the all-cause death serving as a competing event for CVDs. The cumulative incidence of CVDs (including heart diseases and stroke) and death was estimated using the cumulative incidence function (CIF). First, the cause-specific hazard regression models were conducted to investigate the associations

(cause-specific hazard ratio [cHR] with 95% CI) of obesity phenotypes in 2011 with new-onset CVDs, including heart diseases and stroke between 2011 and 2018. The subdistribution hazard regression models were simultaneously performed to estimate the effects of NWCO on the relative incidence of CVDs with a subdistribution hazard ratio (sHR) and 95%CI. Models were adjusted for age, sex (except for sex-specific analysis), residence, education, economic status, marital status, smoking history, drinking history, hypertension, diabetes, and dyslipidemia.

Second, the associations of NWCO transitions from 2011 to 2013 (including NWNCO to NWCO, NWCO to NWNCO, NWCO to AWCO, and AWCO to NWCO) with new-onset CVDs, heart diseases, and stroke between 2013 and 2018 were investigated utilizing the cause-specific hazard regression models (cHR with 95% CI) and subdistribution hazard regression models (sHR with 95% CI), with the maintained status as reference (including maintained NWNCO, maintained NWCO, and maintained AWCO).

Third, sensitivity analyses were performed using a WHtR of >0.5 to define central obesity for the robustness of the associations of NWCO and its related transition patterns with incident CVD events [31,32].

Reporting of this study was done in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. All analyses were conducted using SAS statistical software (version 9.4; SAS Institute Inc., Cary, NC, USA). All analyses were two-sided, and a P value of <0.05 or a 95% CI that did not cross 1.00 was considered statistically significant.

3. Results

The study flow chart is presented in Fig. 1. A total of 17 708 adults were recruited at baseline in 2011. For the current investigation, those who were under the age of 45 years or with incomplete data on sex, education, or economic status (n = 3089), who had incomplete data on smoking history, drinking history, BMI, WC, marital status, hypertension, diabetes, or dyslipidemia (n = 3233), and who had prior CVDs (n = 1530) were excluded, leaving 9856 participants included for analysis, of whom 1914 (19.4%) had NWCO. From 2011 to 2018, 1814 participants developed new-onset CVDs, 1388 developed new-onset heart diseases, and 594 developed new-onset strokes. Table 1 shows the baseline characteristics of included participants. The cumulative incidence of CVDs (including heart diseases and stroke) and all-cause death is separately presented in Fig. 2.

The associations between obesity phenotypes and CVDs are shown in Table 2. Those with NWCO had higher risks of developing incident CVDs, heart diseases, and stroke than those with NWNCO, with adjusted cHRs (95% CI) of 1.22 (1.06−1.39), 1.21 (1.04−1.41), and 1.40 (1.11−1.76), respectively (Table 2 and Table S1). Sex-stratified analyses demonstrated similar patterns only in males but not in females. Additionally, AWCO status was remarkably associated with an increased hazard of CVDs. No significant associations were found between AWNCO and CVDs in
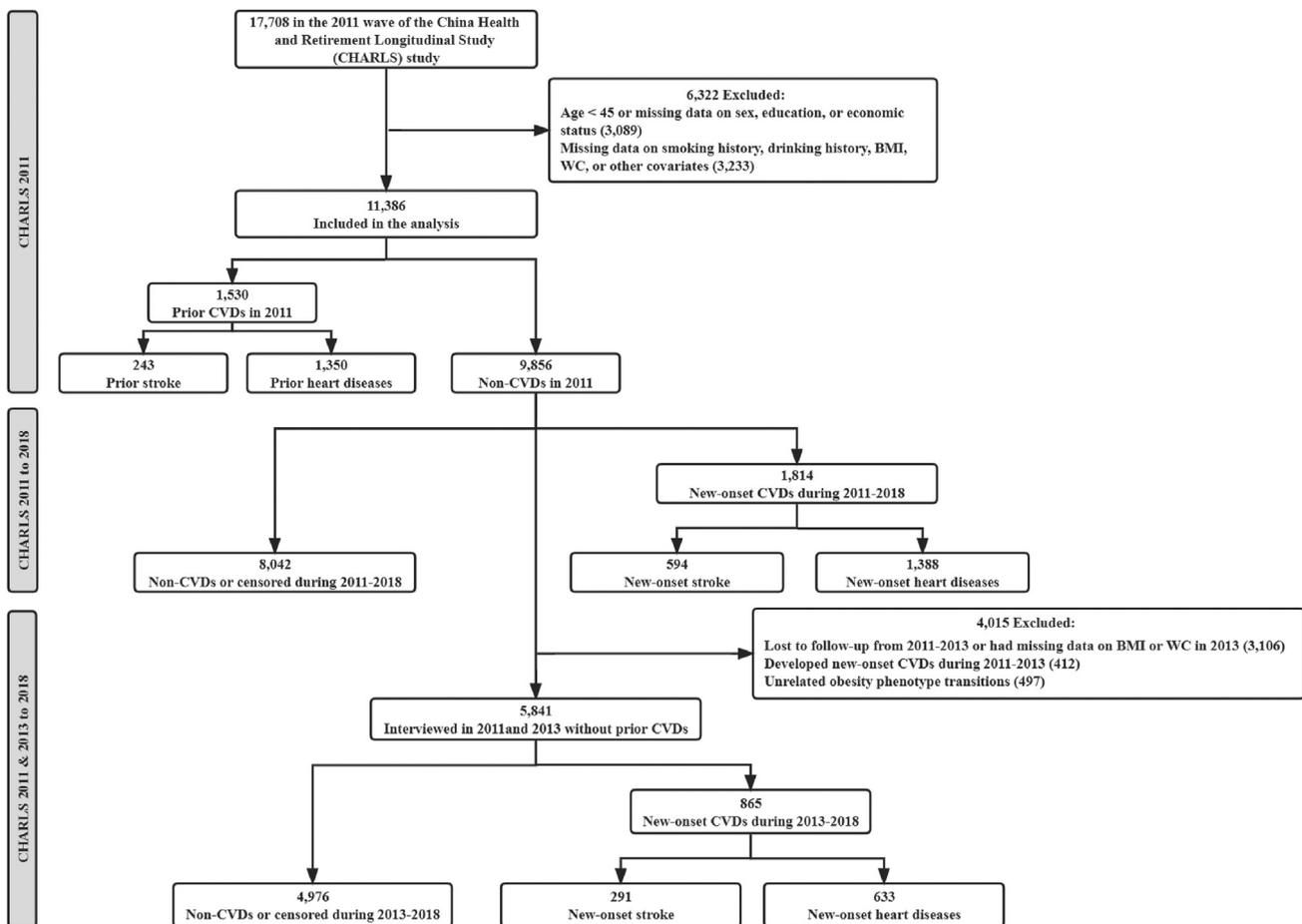
Figure 1 Study flowchart of participant selection.
Note: BMI, body mass index. CVDs are cardiovascular diseases and include heart diseases and stroke.

either sex. These results were in line with those depicted by sHRs (95%CI) (Table 2 and Table S1). In sensitivity analyses using a WHtR of >0.5 to define central obesity, significant associations between NWCO and new-onset CVD events were also found (Table S2).

Between 2011 and 2013, 3106 participants who were lost to follow-up or had incomplete data on BMI or WC in 2013, 412 who developed new-onset CVDs, and 497 who had obesity phenotype transitions unrelated to NWCO were excluded. Ultimately, 5841 eligible participants were included to explore the association between transitions of NWCO from 2011 to 2013 and incident CVDs during 2013 and 2018. The transition patterns of obesity phenotypes of the 5841 participants interviewed in both 2011 and 2013 are shown in a sex-stratified Sankey diagram (Fig. S1). Among these participants, 1928 (33.0%) maintained NWNCO, 571 (9.8%) transformed from NWNCO to NWCO, 626 (10.7%) maintained NWCO, 272 (4.7%) turned from NWCO to NWNCO, 286 (4.9%) transformed from NWCO to AWCO, 1977 (33.9%) maintained AWCO, and 181 (3.1%) transformed from AWCO to NWCO during 2011−2013. The characteristics of participants by transition patterns are described in Table S3.

As shown in Fig. 3 and Table S4, the transition from NWNCO to NWCO was significantly associated with new-onset CVDs (cHR 1.45, 95% CI 1.13−1.87) and heart diseases (cHR 1.49, 95% CI 1.12−2.00) when compared to maintained NWNCO. The associations remained significant for CVDs in sex-stratified analyses. Furthermore, we found that the transition pattern of NWCO to NWNCO was significantly associated with decreased risks of CVDs in the total population (cHR 0.64, 95% CI 0.42−0.97) and stroke in females (cHR 0.22, 95% CI 0.05−0.92) when compared to maintained NWNCO, as shown in Fig. 3. Associations estimated by sHRs were consistent with those described by cHRs (Fig. S2 and Table S4). We further conducted sensitivity analyses using a WHtR of >0.5 to define central obesity and derive similar results, as shown in Table S5.

4. Discussion

This study found that NWCO was significantly associated with a higher risk of CVDs, heart diseases, and stroke in comparison to NWNCO. Transition from NWNCO to NWCO was also identified to be associated with a higher risk of CVDs than maintained NWNCO in both sexes. Furthermore, participants with transition from NWCO to NWNCO had lower cause-specific risks and a relative incidence of CVDs, especially stroke, when compared with those who maintained NWCO.

Table 1 Baseline characteristics of participants in longitudinal analysis from 2011 to 2018 (N = 9856).

Baseline characteristics	NWNCO	NWCO	AWNCO	AWCO	P value
Participants	4110 (41.7)	1914 (19.4)	268 (2.7)	3564 (36.2)	
Age, year	58.0 (52.0–66.0)	59.0 (54.0–67.0)	56.0 (49.0–62.0)	56.0 (49.0–63.0)	<0.001
Sex					<0.001
Male	2537 (61.7)	710 (37.1)	158 (59.0)	1423 (39.9)	
Female	1573 (38.3)	1204 (62.9)	110 (41.0)	2141 (60.1)	
Residence					<0.001
Rural	3031 (73.8)	1233 (64.4)	161 (60.1)	2061 (57.8)	
Urban	1079 (26.3)	681 (35.6)	107 (39.9)	1503 (42.2)	
Education					<0.001
Illiterate	2010 (48.9)	989 (51.7)	93 (34.7)	1510 (42.4)	
Literate	946 (23.0)	403 (21.1)	66 (24.6)	767 (21.5)	
Primary education	781 (19.0)	344 (18.0)	73 (27.2)	821 (23.0)	
Middle school or higher	373 (9.1)	178 (9.3)	36 (13.4)	466 (13.1)	
Marital status					<0.001
Single	553 (13.5)	306 (16.0)	23 (8.6)	302 (8.5)	
Married or cohabited	3557 (86.6)	1608 (84.0)	245 (91.4)	3262 (91.5)	
Economic status					<0.001
Bottom tertile	1533 (37.3)	665 (34.7)	93 (34.7)	1030 (28.9)	
Middle tertile	1414 (34.4)	631 (33.0)	80 (29.9)	1165 (32.7)	
Top tertile	1163 (28.3)	618 (32.3)	95 (35.5)	1369 (38.4)	
Smoking history					<0.001
Ever or current smoker	2132 (51.9)	628 (32.8)	110 (41.0)	1119 (31.4)	
Never smoker	1978 (48.1)	1286 (67.2)	158 (59.0)	2445 (68.6)	
Drinking history					<0.001
Ever or current drinker	1306 (31.8)	426 (22.3)	74 (27.6)	796 (22.3)	
Never drinker	2804 (68.2)	1488 (77.7)	194 (72.4)	2768 (77.7)	
Hypertension					<0.001
Yes	1129 (27.5)	757 (39.6)	104 (38.8)	1741 (48.9)	
No	2981 (72.5)	1157 (60.5)	164 (61.2)	1823 (51.2)	
Diabetes					<0.001
Yes	290 (7.1)	243 (12.7)	28 (10.5)	561 (15.7)	
No	3820 (92.9)	1671 (87.3)	240 (89.6)	3003 (84.3)	
Dyslipidemia					<0.001
Yes	571 (13.9)	443 (23.2)	61 (22.8)	1127 (31.6)	
No	3539 (86.1)	1471 (76.9)	207 (77.2)	2437 (68.4)	
BMI, kg/m^2	20.6 (19.2–21.9)	22.7 (21.6–23.4)	24.8 (24.3–26.0)	26.5 (25.2–28.3)	<0.001
WC, cm	76.6 (73.0–79.9)	86.9 (84.0–89.8)	80.0 (76.7–83.0)	93.1 (89.0–98.2)	<0.001
New-onset CVDs					<0.001
Yes	581 (14.1)	374 (19.5)	45 (16.8)	814 (22.8)	
No	3529 (85.9)	1540 (80.5)	223 (83.2)	2750 (77.2)	
New-onset heart diseases					<0.001
Yes	435 (10.6)	287 (15.0)	38 (14.2)	628 (17.6)	
No	3675 (89.4)	1627 (85.0)	230 (85.8)	2936 (82.4)	
New-onset stroke					<0.001
Yes	182 (4.4)	129 (6.7)	12 (4.5)	271 (7.6)	
No	3928 (95.6)	1785 (93.3)	256 (95.5)	3293 (92.4)	

Notes: Values are presented as number (N) with percent (%) or medians with interquartile ranges (IQRs). NWCO, normal weight with central obesity. NWNCO, normal weight with non-central obesity. AWNCO, abnormal weight with non-central obesity. AWCO, abnormal weight with central obesity. BMI, body mass index. WC, waist circumference. CVDs, cardiovascular diseases.

Our findings are in accordance with previous studies. Several cross-sectional studies have demonstrated significant associations between NWCO and CVDs [20,33]. In a Korean cohort study, Choi D et al. indicated that NWCO individuals aged 40 years or older had an elevated risk of developing major adverse cardiovascular events and stroke [34]. However, their study utilized multivariable Cox proportional hazard regression models to examine the effects of NWCO. Our study, comparatively, adopted competing-risks regression including cause-specific hazard models and subdistribution hazard models, which took competing outcomes into account and prevented biased results estimated by the traditional Cox regression function. Moreover, this study explored the transition of NWCO on the risk of CVDs, which greatly extends beyond the scope of previous research. A prior study of 9447 participants in Jilin, China demonstrated that 27.0% of NWCO individuals self-assessed themselves as abnormal status and only 12.7% took methods to reduce weight [35], showing a severe lack of public awareness of NWCO and its adverse impacts on health management. The results depicted in our study imply the significant health risk of
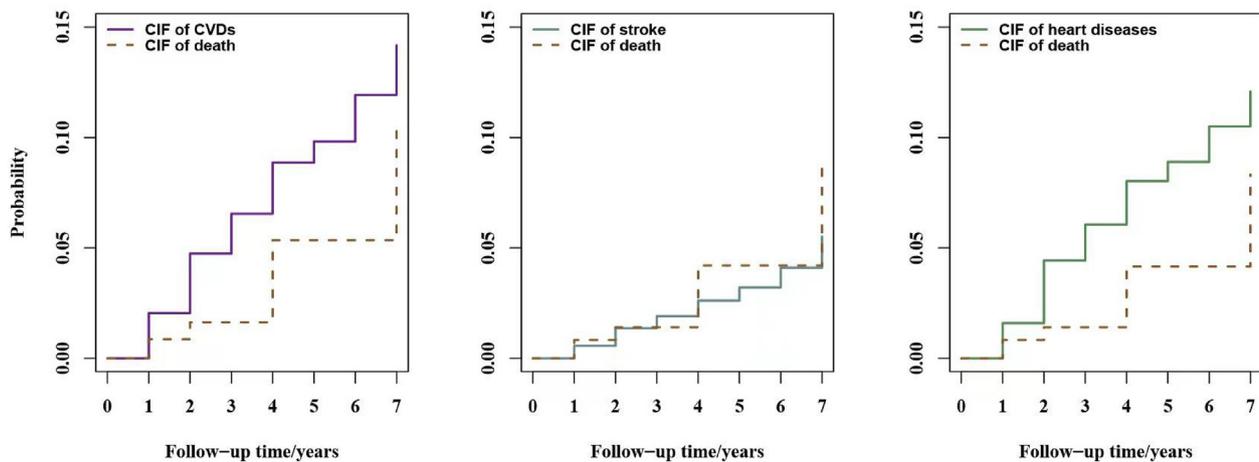
Figure 2 Cumulative incidence function of CVDs, stroke and heart diseases with all-cause death as a competing risk event Notes: CIF, cumulative incidence function. CVD, cardiovascular disease.

NWCO status and highlight the need for public health attention and relevant clinical guidelines.

Generally, people with NWCO possess more visceral adipose tissue than those with NWNCO [36–38], which has been proven to be positively associated with an increased risks of multiple cardiovascular events and metabolic disorders [39–41]. The visceral adipose tissue can express multiple inflammatory cytokines including interleukin-6 (IL-6) and C-reactive protein (CRP) to cause low-grade inflammation and oxidative stress, contributing to the prothrombotic state of the cardio-cerebrovascular smooth muscle and endothelium. Higher levels of central fat are also positively related to increases in pro-inflammatory immunoglobulin G (IgG) N-glycans [42,43], which appear to play an important role in the inflammatory cascade and acceleration of the aging process [16,44]. Together with platelet reactivity and impaired fibrinolysis, CVD events will eventually be triggered [45]. Through the activation of the renin-angiotensin-aldosterone system, normal BMI with abdominal obesity status may exert adverse effects on left ventricular systolic function and lead to heart diseases [46]. Additionally, the subcutaneous fat deposits excessively on vital organs such as cardiac and cerebral arteries, contributing to arteriosclerosis and lipotoxicity [38,47,48]. Previous findings have also suggested that NWCO is directly associated with cardiometabolic risk factors including hypertension, diabetes, insulin resistance, dyslipidemia, and circulating triglycerides [17,20,49].

This study found a noticeable association between transition from NWNCO to NWCO and increased risks of CVDs. There is some evidence that fluctuation in body weight and WC serves as an independent risk factor for cardiovascular events [50,51]. Specially, females with transition from NWCO to NWNCO between 2011 and 2013 were found to have a decreased risk of stroke. As previously reported, around 85% of the casualties in stroke patients can be attributed to vascular occlusion [52]. The buildup of arterial thrombus goes through a series of processes, including excess lipid accumulation, immune cell recruitment, and migration and proliferation of smooth muscle cells, which take a relatively long time [53,54]. The finding suggests that reversing NWCO status during the lengthy process of thrombus formation could be effective in preventing stroke. However, eliminating NWCO was not noticeably associated with a reduced stroke risk in males. This might be explained by the sexual disparity in hormonal status and body fat distribution. Under hormonal estrogen influence, premenopausal women store more subcutaneous fat at the gluteofemoral level than men [55], which protects them against metabolic syndrome and various cardiovascular risk factors [5,56]. These cardiometabolic advantages disappear in postmenopausal women due to hormonal homeostatic dysregulation and fat redistribution [57]. Hence, postmenopausal women with central obesity may be more susceptible to CVD events [58]. Eliminating NWCO, on the other hand, appears to have a more significant impact on reducing CVD risks in females. The female participants in our study were of 45 years and older, most of whom were postmenopausal and more likely to benefit from central weight loss. Additionally, the protective effect of transition from NWCO to NWNCO on incident heart diseases was not significant. One possible explanation is that certain heart problems like angina are prone to be detected earlier, prompting people to modify their lifestyles including exercise and diets. Hence, the effect of obesity transitions might be diminished by these potential factors.

To the best of our knowledge, this study is the first to evaluate the longitudinal associations of NWCO and its transitions with CVDs, including heart diseases and stroke, in China. We performed cause-specific hazard models together with subdistribution hazard models considering all-cause death as a competing risk for CVD outcomes. This enables us to obtain a more accurate and comprehensive

Table 2 Associations of obesity phenotypes with incident CVDs.

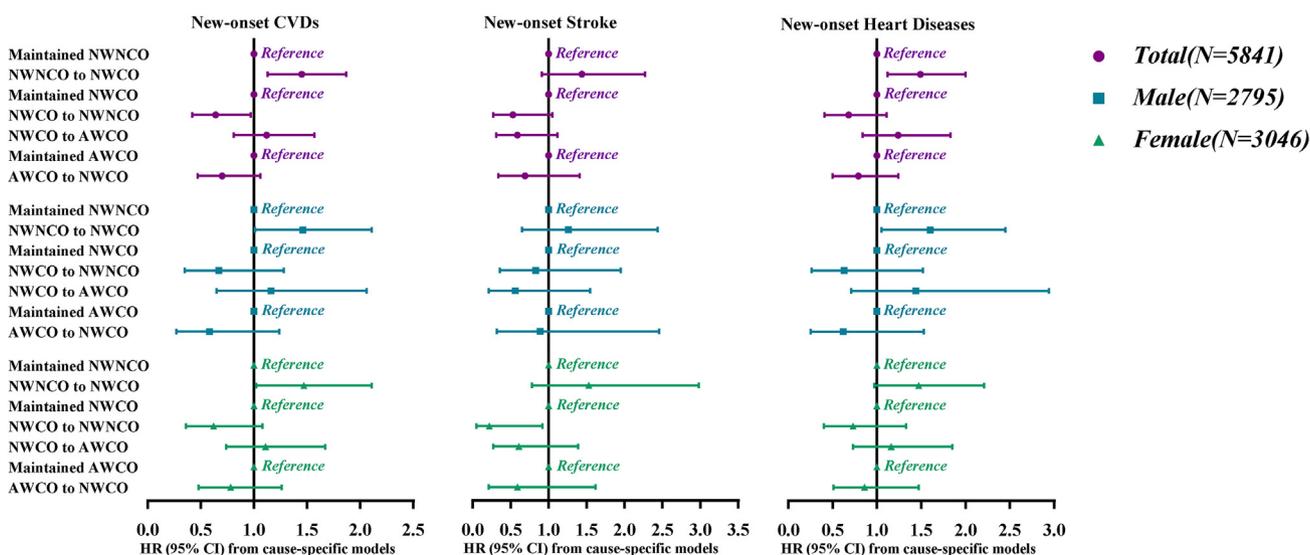|	No. of cases	Cause-Specific Hazard Model	Subdistribution Hazard Model
		cHR (95%CI)	sHR (95%CI)
Total population			
NWNCO	581	Reference	Reference
NWCO	374	1.22 (1.06–1.39)	1.21 (1.06–1.37)
AWNCO	45	1.15 (0.85–1.56)	1.15 (0.85–1.56)
AWCO	814	1.43 (1.27–1.60)	1.41 (1.26–1.57)
Male			
NWNCO	329	Reference	Reference
NWCO	126	1.29 (1.05–1.59)	1.27 (1.04–1.56)
AWNCO	26	1.16 (0.77–1.73)	1.16 (0.78–1.72)
AWCO	297	1.47 (1.24–1.75)	1.45 (1.23–1.71)
Female			
NWNCO	252	Reference	Reference
NWCO	248	1.16 (0.97–1.39)	1.16 (0.98–1.37)
AWNCO	19	1.14 (0.71–1.82)	1.14 (0.72–1.81)
AWCO	517	1.39 (1.18–1.62)	1.37 (1.18–1.59)

Notes: cHR, cause-specific hazard ratio. sHR, subdistribution hazard ratio. CI, confidence interval. CVDs, cardiovascular diseases. NWCO, normal weight with central obesity. NWNCO, normal weight with non-central obesity. AWNCO, abnormal weight with non-central obesity. AWCO, abnormal weight with central obesity. Models were adjusted for age, sex (except for sex-specific analysis), residence, education, economic status, marital status, smoking history, drinking history, hypertension, diabetes, and dyslipidemia.

be more accurate when estimating long-term cardiovascular risks.

Despite the above-mentioned strengths, this study also has some limitations. First, the information on our key outcomes (i.e., CVD events) was collected based on self-reported physician diagnoses, which may be subjected to retrospective biases. Second, CHARLS only covers middle-aged and older adults, thus the associations among the younger population remain unclear. Third, we excluded around 35% of participants at baseline due to missing data, which might influence the representativeness of our findings. Finally, the lack of dietary habits and physical activity as covariates in our analyses might have biased the associations we observed.

In conclusion, our findings demonstrated that NWCO and transition from NWNCO to NWCO were both associated with cardiovascular risks, and this should not be overlooked. The combined use of BMI and measures of central obesity helps to identify targeted obesity phonotypes and serves as crucial identification parameters for preventive strategies of CVDs. Moreover, reducing abdominal adiposity contributes to a lower risk of new-onset CVDs, especially stroke, which might be a modifiable factor in preventive and therapeutic approaches. Individuals with NWCO, especially females, are suggested to be intervened using preventive, predictive, and personalized/precision medicine to reverse this suboptimal state and improve cardiovascular health [24]. To address this burden and attenuate the risk of CVDs, efforts should be made to educate the public, increase access to preventive measures, and develop policy and clinical practice aimed at identifying and reducing NWCO.

understanding of the association between NWCO and CVDs with both cause-specific hazards and cumulative incidence [59,60]. Besides, this study uniquely considered the effect of NWCO transitions on CVD events, rather than using merely obesity phenotypes at baseline, which could

Figure 3 Associations of transition of NWCO between 2011 and 2013 with incident CVDs (cause-specific hazard models).
Notes: HR, hazard ratio. CI, confidence interval. NWCO, normal weight with central obesity. NWNCO, normal weight with non-central obesity. AWCO, abnormal weight with central obesity. CVD, cardiovascular disease. HRs for cause-specific models were adjusted for age, sex (except for sex-specific analysis), residence, education, economic status, marital status, smoking history, drinking history, hypertension, diabetes, and dyslipidemia. Maintained NWNCO is the reference of NWNCO to NWCO; Maintained NWCO is the reference of NWCO to NWNCO and NWCO to AWCO; Maintained AWCO is the reference of AWCO to NWCO.

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Declaration of competing interest

The authors declared no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2022.07.023.

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