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Weight Change over 4 Years and Risk of Cardiovascular Diseases in China: The China Health and Retirement Longitudinal Study

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Keywords
Weight changes · Weight gain · Weight loss · Cardiovascular disease · China Health and Retirement Longitudinal Study · Stroke · Cardiac events

Abstract
Introduction: Previous studies had reported the impact of weight changes in middle age on the incidence of cardiovascular disease (CVD), but the results were inconsistent. In present study, we aimed to investigate the impact of a 4-year weight change on the risk of CVD in middle-aged and elderly Chinese individuals. ***Methods:*** Using nationally representative data from the China Health and Retirement Longitudinal Study, 7,530 participants (age: 58.2 ± 8.9 years) were included. Weight change was calculated by subtracting weight at baseline from that at 4-year follow-up. Weight change over 4 years was divided into 5 categories (loss ≥5 kg; loss 2–5 kg; stable (change ≤2 kg); gain 2–5 kg; and gain ≥5 kg). ***Results:*** During the follow-up period, a total of 758 respondents experienced CVD (including 319 stroke and 477 cardiac events). The multivariable ORs of CVD for gain ≥5 kg compared to stable weight (change ≤2 kg) was 1.50 (95% CI, 1.14–1.97) versus 1.41(1.09–1.83) for losing ≥5 kg. Multivariable-adjusted logistic regression model with restricted cubic splines showed a U-shaped association between weight change and the risk of CVD (*p* for nonlinearity <0.001). The significant associations did not change in subgroup and sensitivity analysis. Weight change was also associated with higher risk of stroke and cardiac events. ***Conclusion:*** Weight changes (weight gain or loss more than 5 kg) during middle age were associated with an increased risk of CVD in middle-aged and elderly Chinese individuals.

Introduction

Cardiovascular diseases (CVD) are the leading cause of global mortality and a major contributor to disability, and the number of CVD deaths reaching 18.6 million in 2019 [1]. Obesity and overweight are well-established risk factor for diabetes mellitus, hypertension, and CVD [2]. Being underweight was also associated with higher risk of several CVD events [3, 4]. Thus, guidelines have recommended weight management for reducing CVD burden attributed to overweight and underweight [5, 6].

Unlike the single measurement of body-weight, in recent years, increasing efforts have been made to assess the relationship between weight change and CVD incidence. Weight change in early to middle age was reportedly as-

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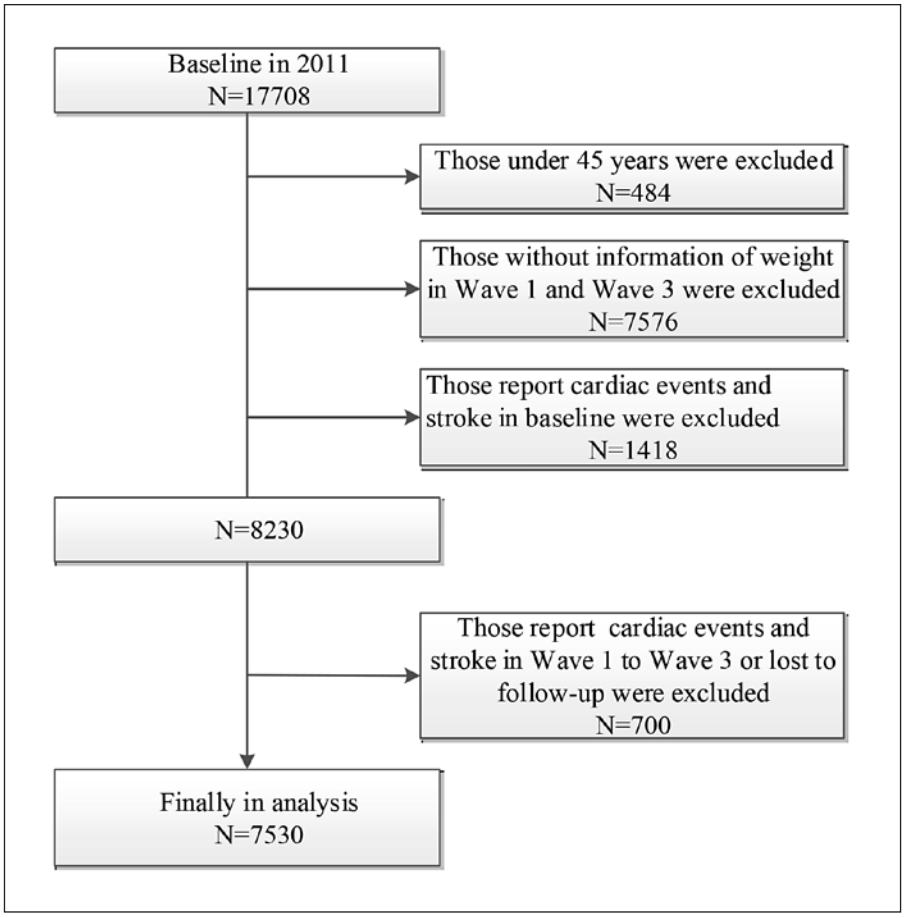

Fig. 1. Flowchart of sample selection and the exclusion criteria.

sociated with an increased risk of CVD [7, 8]. Several studies also examined the associations between short-and long-term weight change during middle age and CVD, but the findings have shown inconclusive and inconsistent associations [9–11]. Diverse findings could be due to differences in overweight/obesity prevalence, lengths of the weight-change intervals, and the time periods between weight changes and events. Furthermore, previous findings from Americans and Japanese may not be simply extrapolated to the Chinese population because the body fat distributions and the case-mix of stroke and coronary heart disease varies according to countries [12, 13]. A recent study analyzed data from 20,737 Chinese patients with hypertension found that higher body mass index (BMI) variability was associated with increased risk of CVD in hypertensive subjects with weight gain but not in those with weight loss [14]. However, the relationship between weight change and incident CVD in the general Chinese population has not been elucidated. Therefore, the aim of present study was to evaluate the impact of weight changes on the incidence of CVD in middle-aged and elderly Chinese, based on the data from the China Health and Retirement Longitudinal Study (CHARLS).

Subjects and Methods

Study Sample

The CHARLS is an ongoing nationally representative longitudinal cohort survey of a middle-aged and elderly population [15]. A total of 17,708 participants aged over 45 randomly selected from 10,257 households in 150 counties, 28 provinces, and autonomous regions of mainland China were included at baseline (2011–2012, Wave 1). The CHARLS respondents were followed up every 2 years, using a face-to-face computer-assisted personal interview. Three subsequent follow-ups were carried out in 2013–2014 (Wave 2), in 2015–2016 (Wave 3), and in 2017–2018 (Wave 4) among survivors, respectively. In the present study of 17,708 participants in baseline, inclusion was limited to the subset of participants [1] aged ≥45 years [2]; reported measurements of weight and BMI in Wave 1 and Wave 3 [3]; and without reported history of stroke and cardiac events in baseline, or incident in Wave 2 and Wave 3 or lost to follow-up. This left 7,530 participants for inclusion (Fig. 1).

Assessment of Weight Changes and Potential Confounding Factors

Weight was measured using the OmronTM HN-286 scale, and height was measured using the SecaTM213 stadiometer. Weight change was calculated by subtracting weight at baseline from that at the 4-year follow-up survey (weight difference between in Wave 3 and Wave 1) and was classified into the following 5 categories: loss ≥5 kg; loss 2–5 kg; stable (change ≤2 kg); gain 2–5 kg; and gain ≥5 kg according to previous study [9].

The covariates were collected at baseline including age, sex, living place (rural vs. urban), smoking status (ever smoking vs. never smoking), educational level (illiteracy; primary school; middle school; high school, or above), drinking status (ever drinking vs. never drinking), body mass index (the weight in kilograms divided by the square of the height in meters), systolic blood pressure, physical activity (vigorous physical activity; moderate physical activity; light physical activity), and the presence or absence of other chronic diseases (dyslipidemia, diabetes, cancer, chronic lung disease, kidney disease, liver disease, arthritis, digestive disease, asthma). "Ever smoking" means that the respondent reports smoking at some point, and "never smoking" means that the respondent reports never having smoked. "Ever drinking" means that the respondent reports having had an alcoholic beverage in the past, and "never drinking" means that the respondent reports not having any alcoholic beverage in the past. Blood pressure was measured with an electronic sphygmomanometer (Omron HEM-7200 Monitor) after 5 min of rest in the sitting position and was defined as the average of 3 separate measurements. Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, current use of antihypertensive medications, or self-reported history of hypertension. Moreover, dyslipidemia was defined as triglycerides ≥150 mg/dL, total cholesterol ≥240 mg/dL, high-density lipoprotein cholesterol <40 mg/dL, low-density lipoproteins cholesterol ≥160 mg/dL, current use of the lipid-lowering medications, or self-reported history of dyslipidemia. Also, diabetes was defined as fasting glucose ≥126 mg/dL, glycosylated hemoglobin (HbA1c) ≥6.5%, treatment for diabetes mellitus, or self-reported history of diabetes. Respondents completed a questionnaire where they reported weekly physical activity in 3 predefined categories (vigorous physical activity; moderate physical activity; light physical activity).

Outcome Assessments

The primary outcome of the present study was incident CVD (stroke or cardiac events), and the secondary outcomes were stroke and cardiac events, separately. Incident of stroke or cardiac events was defined as new events that occurred from Wave 3 to Wave 4, based on self-reported physician's diagnosis ("Has a doctor ever told you that you had any heart disease [myocardial infarction, coronary heart disease, angina, congestive heart failure, or other heart problems] or stroke?"), following previous reported studies in CHARLS [16, 17].

Statistical Analysis

Participants' baseline characteristics are presented as percentages for categorical variables, as the means with standard deviation for normally distributed variables and as medians with interquartile range for non-normally distributed variables. Demographic and clinical characteristics were compared among 5 subgroups by ANOVA or Kruskal-Wallis test for continuous variables and χ^2 test for categorical variables. Odds ratios (ORs) and 95% confidence intervals (CIs) were used to assess the association between weight change and risk of CVD, stroke and cardiac events by using logistic regression model. Potential covariates, such as age, sex, living place, education level, smoking, drinking, systolic blood pressure, physical activity, chronic diseases (dyslipidemia, diabetes mellitus, cancer, chronic lung disease, stroke, liver disease, arthritis, digestive disease, asthma), and medications (antihypertensive, anti-dyslipidemic, and antidiabetic) were included in the multivariable models. We further evaluated the pattern of the association between weight change and risk of CVD, stroke and cardiac events using a logistic regression model with restricted cubic splines for weight change adjusting for aforementioned covariates, with 5 knots placed at the 10th, 30th, 50th, 70th, and 90th percentiles of weight change [18].

In the secondary analyses, we conducted subgroup analyses to assess the robustness of the association between weight change and CVD according to sex, BMI, age, hypertension, smoking, and drinking. Furthermore, we classified participants into 5 subgroups according to BMI as following categories: decrease ≥2; decrease 1–2; stable (decrease 1 to increase 1); increase 1–2; increase ≥2 in sensitivity analysis. In sensitivity analyses, we further excluded those with history of cancer, chronic kidney disease, chronic liver disease, and chronic lung disease. Two tailed $p < 0.05$ was considered to be statistically significant. All statistical analyses were conducted using SAS statistical software (version 9.4, Cary, NC, USA).

Results

Baseline Characteristics

In the present study, 7,530 participants (3,609 men and 3,921 women) were included in the analysis, and the average age was 58.17 ± 8.89 years. The median of weight change was 0.19 (−1.9 to 2.30) kg from Wave 1 to Wave 3. Subjects with weight loss ≥5 kg most live in rural areas were more likely to have high level of education, have high prevalence of dyslipidemia and diabetes, and have high level of BMI. While those with weight gain ≥5 kg were more likely to have high level of education and low prevalence of diabetes (Table 1).

Association between Weight Change and CVD, Stroke and Cardiac Events

From 2015 to 2018 (Wave 3 to Wave 4), a total of 758 respondents experienced a CVD (including 319 stroke and 477 cardiac events). Table 2 shows the ORs for the incident CVD, stroke, and cardiac events according to weight change over the 4 years compared with stable weight (≤2 kg). In the age and sex-adjusted model, a weight loss ≥5 kg was associated with a higher risk of CVD with the corresponding ORs (95% CIs) of 1.58 (1.21–2.07). After further adjusting for living place, education level, smoking, drinking, systolic blood pressure,

Table 1. Baseline characteristics of the study participants according to weight change from Wave 1 to Wave 3

Characteristics	Weight change from Wave 1 to Wave 3					*p* for trend*
	loss of ≥5 kg	loss of 2–5 kg	stable (≤2 kg)	gain 2–5 kg	gain ≥5 kg	
Subjects, *n*	543	1,240	3,678	1,377	692	
Age, years	58.9±9.89	59.14±9.19	58.39±8.8	57.2±8.6	57.2±8.7	0.625
Sex (%)						
Male	231 (42.5)	602 (48.5)	1,760 (47.8)	637 (46.3)	379 (54.8)	0.756
Female	312 (57.5)	638 (51.5)	1,918 (52.2)	740 (53.7)	313 (45.2)	
Living place (%)						
Urban	202 (37.2)	428 (34.6)	1,139 (31.0)	398 (28.9)	202 (29.2)	0.023
Rural	341 (62.8)	812 (65.4)	2,539 (69.0)	979 (71.1)	490 (70.8)	
Education level (%)						
Illiteracy	164 (30.2)	348 (28.1)	1,069 (29.1)	386 (28.0)	204 (29.5)	<0.001
Primary school	203 (36.6)	543 (43.8)	1,568 (42.6)	564 (41.0)	270(39.0)	
Middle school	115 (21.2)	248 (20.0)	719 (19.6)	305 (22.2)	146(21.1)	
High school or above	61 (11.2)	101 (8.1)	322 (8.7)	122 (8.8)	72(10.40)	
Medical history						
Hypertension (%)	104 (19.2)	309 (24.9)	732 (20.0)	266 (19.3)	138 (19.9)	0.302
Dyslipidemia (%)	58 (10.7)	86 (6.9)	234 (6.4)	75 (5.5)	41 (5.9)	0.011
Diabetes (%)	61 (11.2)	77 (6.21)	153 (4.16)	34 (2.47)	21 (3.03)	<0.001
Smoking (%)	185 (34.1)	511 (41.2)	1,457 (39.6)	298 (37.3)	309 (44.7)	0.995
Drinking (%)	182 (33.5)	495 (39.9)	1,462 (39.8)	528 (38.3)	287 (41.5)	0.184
BMI, kg/m^2	25.1 (22.7–28.3)	23.4 (21.0–25.9)	22.7 (20.5–25.1)	22.7 (20.8–24.9)	22.3 (20.3–24.3)	<0.001
SBP, mm Hg	127.3±19.9	127.7±20.7	128.1±19.8	129.8±20.2	130.8±18.5	0.438
DBP, mm Hg	74.2±11.5	74.6±11.6	74.8±11.6	76.2±11.5	77.4±11.7	0.102

Continuous variables are expressed as mean±standard deviation, or as median (interquartile range). Categorical variables are expressed as frequency (percent). BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure. * Linear regression for continuous variables and logistic regression for categorical variables.

Table 2. Multivariable ORs and 95% CIs of CVD according to weight change from Wave 1 to Wave 3

	Weight change from Wave 1 to Wave 3					*p* for linear	*p* for quadratic
	loss of ≥5 kg	loss of 2–5 kg	stable (≤2 kg)	gain 2–5 kg	gain ≥5 kg		
CVD[†]							
Case (%)	76 (14.0)	124 (10.0)	335 (9.1)	141 (10.2)	82 (11.9)		
Unadjusted	1.62 (1.24–2.12)	1.11 (0.93–1.40)	1.00 (Ref)	1.14 (0.93–1.40)	1.34 (1.04–1.73)	0.867	0.011
Age and sex-adjusted	1.58 (1.21–2.07)	1.09 (0.88–1.36)	1.00 (Ref)	1.16 (0.94–1.43)	1.40 (1.08–1.81)	0.654	0.031
Multivariable-adjusted*	1.50 (1.14–1.97)	1.07 (0.86–1.32)	1.00 (Ref)	1.18 (0.85–1.45)	1.41 (1.09–1.83)	0.471	0.001
Stroke							
Case (%)	36 (6.6)	48 (3.9)	140 (3.8)	60 (4.4)	35 (5.1)		
Unadjusted	1.79 (1.23–2.62)	1.02 (0.73–1.42)	1.00 (Ref)	1.15 (0.85–1.57)	1.35 (0.92–1.97)	0.357	0.006
Age and sex-adjusted	1.76 (1.20–2.57)	0.99 (0.71–1.38)	1.00 (Ref)	1.19 (0.88–1.63)	1.39 (0.95–2.03)	0.479	0.017
Multivariable-adjusted*	1.65 (1.12–2.41)	0.97 (0.69–1.36)	1.00 (Ref)	1.22 (0.89–1.66)	1.40 (0.96–2.06)	0.648	0.016
Cardiac events[$]							
Case (%)	46 (8.5)	80 (6.5)	211 (5.7)	89 (6.5)	51 (7.4)		
Unadjusted	1.52 (1.09–2.12)	1.13 (0.87–1.48)	1.00 (Ref)	1.14 (0.88–1.47)	1.31 (0.95–1.80)	0.333	0.028
Age and sex-adjusted	1.47 (1.05–2.05)	1.13 (0.86–1.47)	1.00 (Ref)	1.15 (0.89–1.48)	1.38 (1.00–1.89)	0.233	0.008
Multivariable-adjusted*	1.41 (1.01–1.98)	1.10 (0.84–1.44)	1.00 (Ref)	1.15 (0.89–1.49)	1.38 (1.00–1.91)	0.177	0.015

[†] CVD including stroke and cardiac events. * Multivariable-adjusted for age, sex, living place, education level, smoking, drinking, systolic blood pressure, physical activity, chronic diseases (dyslipidemia, diabetes mellitus, cancer, chronic lung disease, liver disease, arthritis, digestive disease, asthma), and medications (antihypertensive, anti-dyslipidemic, and antidiabetic). [$] Cardiac events included myocardial infarction, coronary heart disease, angina, congestive heart failure, or other heart problems.

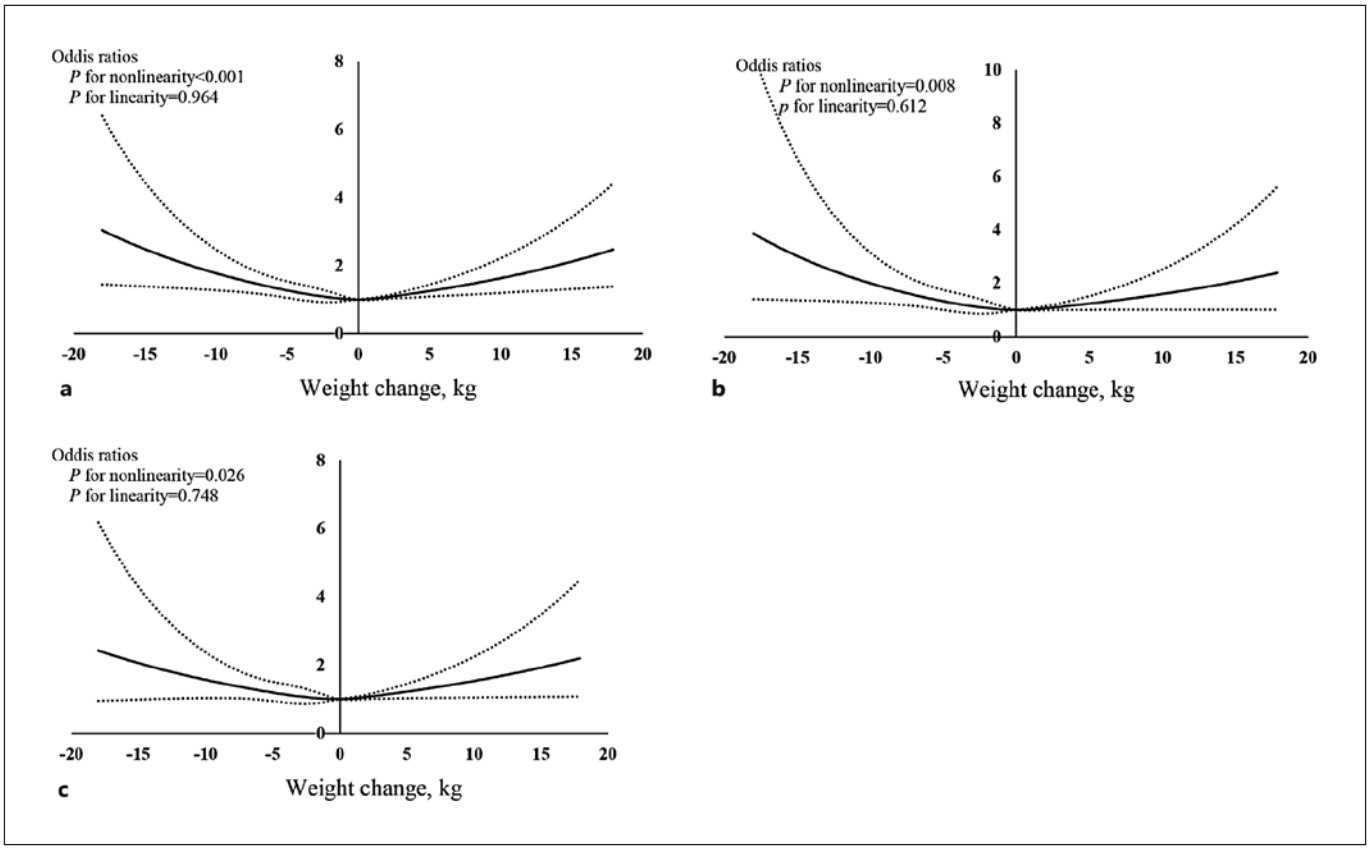

Fig. 2. U-shaped associations between weight change and the risk of study outcome. Odds ratios (ORs) and 95% confidence intervals were derived from a logistic regression model with restricted cubic splines, with knots placed at the 10th, 30th, 50th, 70th, and 90th percentiles of the distribution of weight change. Reference point was the 0 (no change). ORs were adjusted for age, sex, living place, education level, smoking, drinking, systolic blood pressure, physical activity, chronic diseases (dyslipidemia, diabetes mellitus, cancer, chronic lung disease, stroke, liver disease, arthritis, digestive disease, asthma) and medications (antihypertensive, anti-dyslipidemic, and antidiabetic). **a** CVD. **b** Stroke. **c** Cardiac events.

physical activity, chronic diseases (dyslipidemia, diabetes mellitus, cancer, chronic lung disease, stroke, liver disease, arthritis, digestive disease, asthma), and medications (antihypertensive, anti-dyslipidemic, and antidiabetic), individuals with weight loss ≥5 kg were still significantly associated with higher risk of CVD (ORs = 1.50; 95% CIs 1.14–1.97). Subjects with weight gain ≥5 kg also had a significantly higher risk of CVD in age and sex-adjusted model and multivariable model. Similarly, individuals with weight loss ≥5 kg or weight gain ≥5 kg were significantly associated with increased risk of stroke and cardiac events (expect for gain ≥5 kg in stroke risk). As shown in Figure 2, multivariable-adjusted spline regression models showed U-shaped associations of weight change with the risk of CVD, stroke, and cardiac events (all the likelihood ratio test reveals p for nonlinearity <0.005; all the likelihood ratio test reveals p for linearity >0.05) (Table 2; Fig. 2).

We conducted subgroup analyses to examine the potential effect modification by sex, BMI, age, hypertension, smoking, and drinking on the association of weight change with risk of CVD. The modest U-shaped associations between weight change and CVD were observed in almost all subgroups (Table 3).

When we altered the exposure from weight change to BMI change in sensitivity analysis, we observed similar results that both decrease and increase ≥2 of BMI was associated with increased risk of CVD and stroke. But there were no significant association between BMI change and cardiac events (Table 4). When those with history of cancer, chronic kidney disease, chronic liver disease, and chronic lung disease were further excluded, individuals

Table 3. Subgroup analysis of ORs and 95% CIs of CVD according to weight change from Wave 1 to Wave 3

	Weight change from Wave 1 to Wave 3					*p* for linear	*p* for quadratic
	loss of ≥5 kg	loss of 2–5 kg	stable (≤2 kg)	gain 2–5 kg	gain ≥5 kg		
Sex							
Male	1.66 (1.08–2.56)	0.95 (0.67–1.35)	1.00 (Ref)	1.30 (0.94–1.79)	1.66 (1.16–2.39)	0.230	0.007
Female	1.39 (1.04–1.98)	1.11 (0.93–1.40)	1.00 (Ref)	1.10 (0.83–1.45)	1.20 (0.82–1.75)	0.962	0.041
BMI							
<24	1.68 (1.09–2.59)	0.95 (0.69–1.30)	1.00 (Ref)	1.32 (1.01–1.73)	1.38 (0.99–1.93)	0.588	0.024
≥24	1.67 (1.10–2.56)	1.13 (0.82–1.54)	1.00 (Ref)	1.01 (0.71–1.43)	1.18 (0.82–1.68)	0.163	0.089
Age							
<60 years	1.46 (1.01–2.11)	0.86 (0.62–1.19)	1.00 (Ref)	1.02 (0.77–1.36)	1.43 (1.02–1.99)	0.280	0.033
≥65 years	1.58 (1.05–2.37)	1.34 (0.99–1.80)	1.00 (Ref)	1.40 (1.02–1.90)	1.37 (0.91–2.07)	0.914	0.007
Hypertension							
No	1.64 (1.22–2.23)	1.09 (0.85–1.42)	1.00 (Ref)	1.21 (0.95–1.54)	1.59 (1.19–2.12)	0.449	<0.001
Yes	1.04 (0.55–1.96)	0.97 (0.64–1.47)	1.00 (Ref)	1.09 (0.70–1.69)	0.95 (0.52–1.74)	0.789	0.941
Smoking							
No	1.46 (1.06–2.04)	1.17 (0.89–1.53)	1.00 (Ref)	1.05 (0.80–1.38)	1.28 (0.90–1.82)	0.689	0.013
Yes	1.45 (0.90–2.35)	0.87 (0.60–1.27)	1.00 (Ref)	1.41 (1.01–1.96)	1.60 (1.09–2.35)	0.152	0.062
Drinking							
No	1.25 (0.89–1.77)	0.98 (0.73–1.30)	1.00 (Ref)	1.11 (0.85–1.46)	1.36 (0.97–1.92)	0.798	0.110
Yes	2.03 (1.31–3.14)	1.20 (0.85–1.70)	1.00 (Ref)	1.31 (0.94–1.49)	1.53 (1.03–2.29)	0.093	0.001

In the multivariate models, confounding factors such as age, sex, living place, education level, smoking, drinking, systolic blood pressure, physical activity, chronic diseases (dyslipidemia, diabetes mellitus, cancer, chronic lung disease, liver disease, arthritis, digestive disease, asthma), and medications (antihypertensive, anti-dyslipidemic, and antidiabetic) were included unless the variable was used as a subgroup variable.

Table 4. Multivariable ORs and 95% CIs of CVD according to BMI change from Wave 1 to Wave 3

	BMI change from Wave 1 to Wave 3					*p* for linear	*p* for quadratic
	decrease ≥2	decrease 1–2	stable (decrease 1 to increase 1)	increase 1–2	increase ≥2		
CVD[†]							
Case (%)	97 (11.4)	81 (10.3)	373 (9.1)	125 (10.5)	82 (13.4)		
Unadjusted	1.29 (1.02–1.63)	1.15 (0.89–1.48)	1.00 (Ref)	1.17 (0.94–1.45)	1.55 (1.20–2.00)	0.843	0.002
Age and sex-adjusted	1.28 (1.01–1.63)	1.13 (0.88–1.46)	1.00 (Ref)	1.17 (0.94–1.45)	1.45 (1.12–1.88)	0.728	0.004
Multivariable-adjusted*	1.30 (1.02–1.65)	1.12 (0.87–1.44)	1.00 (Ref)	1.18 (0.95–1.46)	1.38 (1.07–1.80)	0.578	0.005
Stroke							
Case (%)	37 (4.5)	32 (4.1)	155 (3.8)	54 (4.5)	41 (6.7)		
Unadjusted	1.16 (0.80–1.67)	1.08 (0.73–1.59)	1.00 (Ref)	1.20 (0.88–1.65)	1.83 (1.28–2.61)	0.341	0.041
Age and sex-adjusted	1.19 (0.82–1.72)	1.07 (0.73–1.58)	1.00 (Ref)	1.23 (0.90–1.70)	1.77 (1.24–2.54)	0.420	0.039
Multivariable-adjusted*	1.21 (0.83–1.74)	1.06 (0.71–1.56)	1.00 (Ref)	1.25 (0.91–1.71)	1.67 (1.16–2.39)	0.558	0.049
Cardiac events[$]							
Case (%)	63 (7.4)	53 (6.7)	235 (5.7)	79 (6.6)	47 (7.7)		
Unadjusted	1.32 (0.99–1.76)	1.19 (0.87–1.62)	1.00 (Ref)	1.16 (0.89–1.51)	1.37 (0.99–1.89)	0.316	0.016
Age and sex-adjusted	1.29 (0.97–1.72)	1.17 (0.86–1.59)	1.00 (Ref)	1.14 (0.88–1.49)	1.26 (0.91–1.75)	0.274	0.038
Multivariable-adjusted*	1.30 (0.97–1.74)	1.16 (0.85–1.58)	1.00 (Ref)	1.15 (0.88–1.51)	1.21 (0.87–1.69)	0.177	0.015

[†] CVD including stroke and cardiac events. * Multivariable-adjusted for age, sex, living place, education level, smoking, drinking, systolic blood pressure, physical activity, chronic diseases (dyslipidemia, diabetes mellitus, cancer, chronic lung disease, liver disease, arthritis, digestive disease, asthma) and medications (antihypertensive, anti-dyslipidemic, and antidiabetic). [$] Cardiac events included myocardial infarction, coronary heart disease, angina, congestive heart failure, or other heart problems.

with weight loss ≥5 kg or weight gain ≥5 kg were significantly associated with increased risk of CVD (online suppl. Table S1; for all online suppl. material, see www.karger.com/doi/10.1159/000526419).

Discussion

The present study addressed the prospective association of weight change with risk of CVD, stroke, and cardiac events in the middle-aged and elderly Chinese population. In this nationally representative prospective cohort study, both weight gain ≥5 kg and weight loss ≥5 kg over 4 years were associated with an increased risk of CVD, stroke, and cardiac events and U-shaped associations were also found. Subgroup and sensitivity subgroup analysis further confirmed these findings. To our knowledge, this is the first study to investigate the association between weight change and CVD, stroke, and cardiac events in the Chinese middle-aged and elderly population.

In recent decades, studies had reported "U-" or "J-shaped" curves in analyses of large cohorts indicate extremes of BMI, underweight, and obesity, associated with increased risk of CVD [19–21]. However, many previous studies have measured weight only once at baseline, and it is not clear whether subsequent weight changes are associated with the risk of diseases and death. Although several studies had evaluated the association between weight change and CVD, there are mixed findings due to differences in study populations, different stages, lengths of the weight-change intervals, and the time periods between weight changes and events. In a large population-based cohort of 121,160 Chinese participants, a moderate weight gains of 2.5 kg between early adulthood and midlife significantly increased the risk of coronary heart disease (CHD) (ORs: 1.18, 95% CIs: 1.05–1.32), stroke (ORs: 1.19, 95% CIs: 1.03–1.38), and total CVD (ORs: 1.15, 95% CIs: 1.04–1.27), and the risk escalated with higher amounts of weight gain [8]. Stevens et al. [11] found that earlier weight gain over a long interval was associated with increased risks of CHD and ischemic stroke, whereas later, weight loss over a shorter interval was associated with increased immediate CHD and stroke risk, when compared with weight maintenance. Katsoulis et al. [22] estimated the effect of 2-year weight change interventions on 7-year risk of CVD, and results found that weight maintenance group had a lower CVD risk compared with the weight gain and the weight-loss group among normal-weight individuals. While, among individuals with overweight, the weight loss and weight gain groups had a slightly higher CVD risk compared with weight maintenance.

When it comes to weight change during middle age, a Japanese study found that weight gain during middle age was associated with an increased risk of stroke in women and an increased risk of CHD in men. Furthermore, weight loss was associated with an increased risk of stroke in both men and women [9]. In another study among 36,338 Singapore Chinese participants aged 45–74 years, both moderate-to-large weight gain and loss conferred excess risk for all-cause and CVD mortality, and the risk was slightly higher for weight loss than weight gain [23]. Furthermore, a systematic review and meta-analysis of 26 prospective studies of healthy middle-aged adults showed that both weight loss and weight gain were associated with an increased risk of all-cause and CVD mortality and there were nonlinear associations between weight change and all-cause mortality risk [24]. Our estimates of the association between weight change and CVD agree with previous studies showing that both weight gain ≥5 kg and weight loss ≥5 kg were associated with an increased risk of CVD, stroke, and cardiac events, and there were U-shaped associations between weight change and CVD, stroke, and cardiac events. Furthermore, the positive association were similar when weight change was calculated according to BMI.

Weight loss unrelated to the underlying disease is considered beneficial because of the known increased risk associated with obesity, and weight gain is considered harmful to health [25]. But previous studies had shown no benefit of weight loss on CVD, while some had even reported significantly increased risk of CVD [26–28]. An increase in fat and a corresponding decrease in muscle mass can lead to muscular dystrophy in the elderly, which leads some authors to suggest that weight loss in old age is dangerous [29]. Unintentional weight loss might reflect an underlying disease, resulting in excess risk of CVD, whereas intentional weight loss is assumed to be beneficial because obesity is associated with increased CVD risk. In addition, unintentional weight loss due to underlying diseases may mask the protective effects of weight loss on cardiovascular disease. We cannot rule out the possibility that those who lose weight may be more willing and able to lose weight in a healthy way than those who do not. Therefore, further research, especially randomized controlled trials, is needed to confirm the impact of weight change on the risk of CVD among the middle-aged and elderly population.

The present study has major strengths, including its large nationally representative cohort study, comprehensive follow-up, and accurately collected information about weight. Several potential confounders were also collected and controlled in the multivariable models. Nevertheless, we acknowledge several limitations in our study. First, data were not available on whether certain weight change was intentional or unintentional, thus we cannot differentiate purposeful from nonpurposeful changes. Second, weight reflects not only fat mass but also lean body mass and muscle mass, and we could not evaluate which body component changes affected the association with CVD risk. Third, our cohort comprises Chinese individuals, thus limiting the generalizability of our findings to other ethnicities. Fourth, this was an observational study and, therefore, the association found between weight changes and end points may not be causal. Finally, the CVD outcomes was based on self-reported doctor's diagnosis of stroke or cardiac events, which may cause information bias. However, self-reported history of disease has been proven to possess relatively good reliability [30].

Conclusion

In this large long-term prospective cohort study, both weight gain and weight loss was associated with an increased risk of CVD in middle-aged and elderly Chinese. Studies are needed to unravel the causal pathways underlying the observed association between weight change and subsequent higher CVD risk.

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Statement of Ethics

The ethics application for collecting data on human subjects in CHARLS was approved by the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015), and all CHARLS participants provided written informed consent and were consent in compliance with the Helsinki Declaration.

Conflict of Interest Statement

No competing interests have been declared.

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Author Contributions

Xiaowei Zheng and Wenyan Wu conceived and designed the research; Wenyan Wu wrote the manuscript; and Wenyan Wu and Xiaowei Zheng performed the data analysis. All the authors reviewed the manuscript.

Data Availability Statement

This analysis uses data or information from the Harmonized CHARLS dataset and Codebook, Version C as of April 2018 developed by the Gateway to Global Aging Data. The development of the Harmonized CHARLS was funded by the National Institute on Aging (R01 AG030153, RC2 AG036619, R03 AG043052). For more information, please refer to www.g2aging.org.

References

1 Global regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet Neurol. 2021;20(10):795–820.

2 Wilson PWF, D'Agostino RB, Sullivan L, Parise H, Kannel WB. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. Arch Intern Med. 2002;162(16):1867–72.

3 Kawate N, Kayaba K, Hara M, Kotani K, Ishikawa S, Jichi Medical School Cohort Study Group. Body mass index and stroke incidence in Japanese community residents: The Jichi Medical School (JMS) Cohort Study. J Epidemiol. 2017;27(7):325–30.

4 Arigo D, Ainsworth MC, Pasko K, Brown MM, Travers L. Predictors of change in BMI over 10 years among midlife and older adults: associations with gender, CVD risk status, depressive symptoms, and social support. Soc Sci Med. 2021;279:113995.

5 Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM, Bischoff JM, et al. 2021 ACC/AHA/SCAI Guideline for coronary artery revascularization: executive summary–a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145(3):e4–17.

6 Kokubo Y. Traditional risk factor management for stroke: a never-ending challenge for health behaviors of diet and physical activity. Curr Opin Neurol. 2012;25(1):11–7.

7 Zheng Y, Manson JE, Yuan C, Liang MH, Grodstein F, Stampfer MJ, et al. Associations of weight gain from early to middle adulthood with major health outcomes later in life. JAMA. 2017;318(3):255–69.
8 Zhu Y, Zheng R, Hu C, Qin G, Wang B, Wang T, et al. Association of early adulthood weight and subsequent weight change with cardiovascular diseases: findings from REACTION study. Int J Cardiol. 2021;332:209–15.
9 Kisanuki K, Muraki I, Yamagishi K, Kokubo Y, Saito I, Yatsuya H, et al. Weight change during middle age and risk of stroke and coronary heart disease: the Japan Public Health Center-based Prospective Study. Atherosclerosis. 2021;322:67–73.
10 Chen C, Ye Y, Zhang Y, Pan XF, Pan A. Weight change across adulthood in relation to all cause and cause specific mortality: prospective cohort study. BMJ. 2019;367:l5584.
11 Stevens J, Erber E, Truesdale KP, Wang CH, Cai J. Long- and short-term weight change and incident coronary heart disease and ischemic stroke: the Atherosclerosis Risk in Communities Study. Am J Epidemiol. 2013;178(2):239–48.
12 Nazare JA, Smith JD, Borel AL, Haffner SM, Balkau B, Ross R, et al. Ethnic influences on the relations between abdominal subcutaneous and visceral adiposity, liver fat, and cardiometabolic risk profile: the International Study of Prediction of Intra-Abdominal Adiposity and Its Relationship With Cardiometabolic Risk/Intra-Abdominal Adiposity. Am J Clin Nutr. 2012;96(4):714–26.
13 Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics-2020 update: a report from the American Heart Association. Circulation. 2020;141(9):e139–596.
14 Cai Z, Wu W, Chen Z, Fang W, Li W, Chen G, et al. Long-term body mass index variability, weight change slope, and risk of cardiovascular outcomes: 7-year prospective study in Chinese hypertensive subjects. Obes facts. 2021;14(5):442–9.
15 Zhao Y, Hu Y, Smith JP, Strauss J, Yang G. Cohort profile: the China Health and Retirement Longitudinal Study (CHARLS). Int J Epidemiol. 2014;43(1):61–8.
16 Li H, He D, Zheng D, Amsalu E, Wang A, Tao L, et al. Metabolically healthy obese phenotype and risk of cardiovascular disease: results from the China Health and Retirement Longitudinal Study. Arch Gerontol Geriatr. 2019;82:1–7.
17 Shi Z, Nicholls SJ, Taylor AW, Magliano DJ, Appleton S, Zimmet P. Early life exposure to Chinese famine modifies the association between hypertension and cardiovascular disease. J Hypertens. 2018;36(1):54–60.
18 Durrleman S, Simon R. Flexible regression models with cubic splines. Stat Med. 1989;8(5):551–61.
19 Li K, Yao C, Yang X, Di X, Li N, Dong L, et al. Body mass index and the risk of cardiovascular and all-cause mortality among patients with hypertension: a population-based prospective cohort study among adults in Beijing, China. J Epidemiol. 2016;26(12):654–60.
20 de Hollander EL, Bemelmans WJ, Boshuizen HC, Friedrich N, Wallaschofski H, Guallar-Castillón P, et al. The association between waist circumference and risk of mortality considering body mass index in 65- to 74-year-olds: a meta-analysis of 29 cohorts involving more than 58,000 elderly persons. Int J Epidemiol. 2012;41(3):805–17.
21 Hong S, Park JH, Han K, Lee CB, Kim DS, Yu SH. Association between obesity and cardiovascular disease in elderly patients with diabetes: a retrospective cohort study. J Clin Endocrinol Metab. 2022;107(2):e515–27.
22 Katsoulis M, Stavola BD, Diaz-Ordaz K, Gomes M, Lai A, Lagiou P, et al. Weight change and the onset of cardiovascular diseases: emulating trials using electronic health records. Epidemiology. 2021;32(5):744–55.
23 Pan XF, Yuan JM, Koh WP, Pan A. Weight change in relation to mortality in middle-aged and elderly Chinese: the Singapore Chinese Health Study. Int J Obes. 2019;43(8):1590–600.
24 Karahalios A, English DR, Simpson JA. Change in body size and mortality: a systematic review and meta-analysis. Int J epidemiol. 2017;46(2):526–46.
25 Willett WC, Dietz WH, Colditz GA. Guidelines for healthy weight. N Engl J Med. 1999;341(6):427–34.
26 Dyer AR, Stamler J, Greenland P. Associations of weight change and weight variability with cardiovascular and all-cause mortality in the Chicago Western Electric Company Study. Am J Epidemiol. 2000;152(4):324–33.
27 Williamson DF, Pamuk E, Thun M, Flanders D, Byers T, Heath C. Prospective study of intentional weight loss and mortality in overweight white men aged 40-64 years. Am J Epidemiol. 1999;149(6):491–503.
28 Strelitz J, Ahern AL, Long GH, Hare MJL, Irving G, Boothby CE, et al. Moderate weight change following diabetes diagnosis and 10 year incidence of cardiovascular disease and mortality. Diabetologia. 2019;62(8):1391–402.
29 Brown RE, Kuk JL. Consequences of obesity and weight loss: a devil's advocate position. Obes Rev. 2015;16(1):77–87.
30 Han L, Shen S, Wu Y, Zhong C, Zheng X. Trajectories of depressive symptoms and risk of cardiovascular disease: evidence from the China Health and Retirement Longitudinal Study. J Psychiatr res. 2021;145:137–43.