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Associations of short-term changes in obesity indices with all-cause mortality and cardiovascular disease

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Abstract

Objective: This study aimed to investigate how short-term changes (1-, 3-, and 5-year) in obesity measures affect mortality and cardiovascular disease (CVD) risk.

Methods: We analyzed longitudinal data from the MJ Health Centre ($n = 43{,}304$ for the 1-year study; 24,295 for the 3-year study; 16,138 for the 5-year study) with median follow-up periods of 15.8, 13.9, and 12.3 years, respectively. Associations of short-term obesity indices changes with mortality and Framingham Risk Score changes were explored using time-dependent coefficient Cox regression models, restricted cubic splines, and multivariable linear regression models.

Results: All-cause mortality was negatively associated with short-term weight and BMI changes, with greater reductions causing poorer outcomes. Compared with stable groups, short-term reduced weight and BMI were associated with greater risks of all-cause mortality and CVD-specific mortality (5-year study only). Also, either 1- and 3-year reduced or 3-year increased waist circumference and waist to height ratio were related to higher all-cause and CVD deaths than stable groups, respectively. Nonlinear relationships indicated lower cutoff values for short-term changes in obesity indices in predicting all-cause mortality. Decreased obesity indices significantly improved CVD profiles.

Conclusions: Short-term changes in obesity indices show complex mortality risks, urging personalized approaches beyond a simple weight loss focus.

INTRODUCTION

Growing evidence has highlighted the importance of changes in general and abdominal obesity indices in clinical outcomes prediction, particularly all-cause and cardiovascular disease (CVD) mortality [1–9]. However, a crucial gap remains in understanding the impacts of their short-term changes, especially among younger populations.

Although two meta-analyses have reported adverse effects of weight loss and gain on all-cause and CVD-specific mortality among middle-aged and older adults, fewer included studies have focused on recommended short-term weight changes (i.e., 1, 3, and 5 years) [10–12]. Furthermore, findings on the associations between short-term changes in weight and body mass index (BMI) and clinical outcomes are inconclusive [1–5]. Some studies have reported increased mortality risks for both 1-year weight gain and loss, whereas another

study only revealed the adverse effects of 2-year weight loss on all-cause mortality [1–3]. Additionally, current research on younger adults has primarily explored weight and BMI changes from early to middle adulthood, overlooking intra-period variability [13, 14]. Furthermore, reliance on self-reported measures and the use of diverse cutoff values for obesity indices changes may contribute to the inconsistent findings. Moreover, limited studies have investigated potential non-linear relationships between changes in weight and BMI and clinical outcomes [15, 16].

Similar disparities exist regarding short-term changes in abdominal obesity indices such as waist circumference (WC), waist to hip ratio (WHR), and waist to height ratio (WHtR). Limited studies on short-term changes in these measures have yielded conflicting results, with some finding no links to mortality and others revealing adverse effects of losses [6–9]. These inconsistencies, coupled with the different cutoff values for changes in abdominal obesity indices, highlight the need for further investigations.

To address these critical gaps, we conducted a comprehensive investigation using intervals of 1, 3, and 5 years, aligning with current guidelines [12, 17]. We aimed to explore both linear and nonlinear relationships between short-term changes in obesity indices and all-cause and CVD-specific mortality. Additionally, given limited evidence on short-term changes in obesity indices impacting estimated CVD risk, we investigated the relationships between short-term changes in obesity indices and concurrent changes in Framingham Risk Score (FRS) [18].

Study Importance

What is already known?

- Weight and BMI reductions and gains are risk factors for both all-cause and cardiovascular disease (CVD) mortality in middle-aged and older adults, and changes in abdominal obesity measurements (e.g., waist circumference) have been linked to various health outcomes.
- Evidence on the impact of recommended short-term changes (i.e., 1, 3, and 5 years) in obesity indices on health outcomes remains limited and inconsistent.

What does this study add?

- Short-term reductions in obesity indices exceeding 5% elevated all-cause mortality, despite lowering estimated CVD risk. Five-year decreased weight and BMI or three-year increased waist circumference and waist to height ratio exceeding 5% escalated CVD-specific mortality.
- The relationships of short-term changes in obesity indices with all-cause and CVD-specific mortality, as well as estimated CVD risk, were found to be influenced by factors such as age, obesity status, and health status.

How might these results change the direction of research or the focus of clinical practice?

- Even for the young general population, rapid weight loss exceeding 5% might present a risk factor for increased mortality. Before developing weight management strategies, researchers should explore the underlying causes of such rapid reductions in obesity indices.
- This study highlights the necessity to find appropriate cutoff values for short-term changes in obesity indices within the context of the young general population.

METHODS

Study population

We used longitudinal data (1996–2017) from an ongoing cohort study conducted in the MJ Health Centre in Taiwan, which provides periodic medical examinations for its members [19]. Since 1996, each participant has completed a self-administered health questionnaire that includes sociodemographic characteristics, medical history, and lifestyle factors. Anthropometric measurements (e.g., weight) and biomedical tests (e.g., lipids) were collected by trained health care professionals following standard procedures. All participants provided informed written consent, and individual identification data were removed to maintain anonymity. We obtained ethical approval for the current study (2022.471) from the Joint Chinese University of Hong Kong (CUHK)-New Territories East Cluster (NTEC) Clinical Research Ethics Committee and the National Cheng Kung University Research Ethics Committee (A-ER-108-081).

We included participants aged 18 years or older. Participants who fit the following criteria were excluded: 1) had invalid anthropometric measures (i.e., weight < 30 kg, BMI < 15 and >60 kg/m^2, WC < 40 and >160 cm, and hip circumference [HC] < 50 and >165 cm); 2) reported CVD and cancers at the baseline; 3) did not complete the baseline questionnaire and medical examination; 4) did not provide information on obesity measures and FRS components (e.g., hypertension, antihypertensive medication use) at follow-up medical examinations; and 5) died within the first 2 years of the follow-up (Figure S1).

Assessment of change in obesity indices

Body weight and height were measured with participants wearing light indoor clothing without shoes and were recorded to the nearest 0.1 kg and 0.1 cm, respectively. WC was measured at the middle between the lower end of the rib cage and the crest of the ilium. HC was measured around the pelvis at the point of maximal protrusion of the buttocks. Both WC and HC were recorded to the nearest 0.1 cm. BMI, WHR, and WHtR were calculated as shown. BMI was classified

as having underweight or normal weight (BMI < 24 kg/m^2), overweight (24 ≤ BMI < 27 kg/m^2), and obesity (BMI ≥ 27.0 kg/m^2) [20]. Abdominal obesity was defined as WC ≥ 80 cm, WHR ≥ 0.85, or WHtR ≥ 0.50 for female individuals and WC ≥ 90 cm, WHR ≥ 0.90, or WHtR ≥ 0.50 for male individuals [20–22]. The 1-, 3- and 5-year changes in obesity indices were expressed as the relative difference between the baseline (t_0) and 1, 3, and 5 years after it (t_1), respectively. As suggested by previous studies, changes in obesity indices were categorized as "loss" (<−5%), "stable" (−5%–5%), and "gain" (>5%) [6, 12].

$$\text{BMI} = \frac{\text{Weight (kilograms)}}{\text{Height (meters)}^2}$$

$$\text{WHR} = \frac{\text{WC (centimeters)}}{\text{HC (centimeters)}}$$

$$\text{WHtR} = \frac{\text{WC (centimeters)}}{\text{Height (centimeters)}}$$

$$\text{Change} = \frac{\text{Measurement}_{t1} - \text{Measurement}_{t0}}{\text{Measurement}_{to}} \times 100\%$$

Assessment of covariates

Participants were required to sit for at least 5 min before measuring their resting blood pressure. Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mm Hg; diastolic blood pressure (DBP) ≥ 90 mm Hg; self-reported, physician-diagnosed hypertension; or the use of antihypertensive medication. Overnight fasting blood samples were collected for biochemical tests. Dyslipidemia was defined as marginally elevated total cholesterol (TC; ≥200 mg/dL), low-density lipoprotein cholesterol (LDL-C; ≥130 mg/dL), non-high-density lipoprotein cholesterol (non-HDL-C [non-HDL-C = TC − HDL-C]; ≥160 mg/dL), or triglycerides (TG; ≥150 mg/dL); decreased HDL-C (<40 mg/dL); or the use of lipid-lowering medication [23]. Diabetes was defined as fasting plasma glucose (GLU) ≥ 126 mg/dL, self-reported physician-diagnosed diabetes, or the use of antidiabetic medication [24].

Participants reported the intensity of occupational physical activity based on the exertion levels: mostly sedentary (e.g., clerk); a combination of sitting, standing, and walking (e.g., nurse); mostly standing or walking (e.g., retail salesperson); and hard labor (e.g., porter). Additionally, participants reported the intensity and duration of weekly leisure-time physical activity in the past month. Four levels of leisure-time physical activity were offered and were assigned a specific metabolic equivalent value (MET; 3.5 mL/kg/min or 1 kcal/kg/h): 2.5 for light (e.g., walking); 4.5 for moderate (e.g., brisk walking); 6.5 for medium-vigorous (e.g., jogging); and 8.5 for high-vigorous (e.g., rope skipping) [25]. The weekly leisure-time physical activity volume was calculated as the product of the MET and duration (minutes) and divided into four groups: 0 MET-min/week; <500 MET-min/week; 500 to 999 MET-min/week; and ≥1000 MET-min/week. Moreover, participants reported their consumption of vegetables and fruit in the past month, including seldom (<1 serving/week), moderate (1–2 servings/day), and frequent (>2 servings/day).

Ascertainment of outcomes

The primary outcomes included all-cause and CVD deaths. Participants' baseline (t_0) was set as the date of their first record in the database. Follow-up started at 1, 3, or 5 years after the baseline (t_1) and ended at whichever came first, i.e., the date of death or May 31, 2019 (Figure S2). Deaths were ascertained by computer linkage to the national death registry using identification numbers. Cardiovascular deaths were identified using the *International Classification of Diseases, Ninth Revision* (ICD-9) codes 390 to 459 and *Tenth Revision* ICD-10 codes 00 to 99. The secondary outcomes were 1-, 3-, and 5-year FRS changes since the baseline. The FRS is calculated based on gender, age, diabetes status, smoking status, hypertension status, SBP, TC, and HDL-C and showed good discrimination in the Asian population [26, 27]. The CVD risk was categorized into three levels: low (<10%); moderate (10%–19%); and high (≥20%), based on percentage FRS, which was transformed from the FRS points.

Statistical analysis

Participants' characteristics were described using mean (SD) or median (interquartile range [IQR]) for continuous variables and frequency (percentage) for categorical variables. To investigate associations of short-term changes in weight, BMI, WC, WHR, and WHtR with mortality and FRS changes, we adjusted baseline covariates in two models. Model 1 included sex, age, marital status, education level, and occupation. Model 2 adjusted for covariates in Model 1 plus hypertension, diabetes, dyslipidemia, chronic obstructive pulmonary disease, thyroid diseases, FRS change, SBP, DBP, LDL-C, HDL-C, TC, TG, GLU, vegetable and fruit intake, sleep duration, occupational and leisure-time physical activity levels, smoking and drinking status, and baseline obesity indices. Covariates with a variance inflation factor exceeding 10 were excluded to prevent multicollinearity. When exploring the relationships between short-term changes in obesity indices and mortality, time-dependent coefficient Cox regression models with a step function were used to address the violation of the proportional hazard assumption. The method applies different coefficient values to different time intervals based on Schoenfeld residuals plots (10 years for 1-year changes; 9 years for 3-year changes; and 9 years for 5-year changes) (Figures S3 and S4). Adjusted restricted cubic splines with three to seven knots were used to detect nonlinear relationships between short-term obesity indices changes and mortality. The model with the lowest Akaike information criterion (AIC) value was selected, and hazard ratios (HRs) were calculated at both sides of the inflection point if nonlinearity was observed. Furthermore, multivariable linear regression models were employed to assess the associations between short-term changes and the concurrent FRS changes.

We conducted subgroup analyses stratified by baseline sex, age, chronic diseases, CVD risk level, BMI, WC, WHR, WHtR, and leisure-time physical activity level. The difference among subgroups was tested using the interaction analysis. To ensure robustness, sensitivity analyses excluded participants with the following: 1) hypertension, diabetes, or dyslipidemia at baseline to minimize potential confounding effects; 2) follow-up duration less than 5 years to reduce the impact of malignant diseases; and 3) underweight status or high-level CVD risk to eliminate confounding effects. Also, to attenuate potential bias arising from missing values, multiple imputation was performed to create 29, 27, and 24 imputed datasets for 1-, 3-, and 5-year studies, respectively, based on the percentage of incomplete cases. Moreover, the Fine-Gray competing risk model was performed for CVD-specific mortality.

The statistical analyses were performed using "survival" (version 3.5.7), "rms" (version 6.7.1), and "stats" (version 4.3.2) in the R software (version 4.2.2) and RStudio (version 2021.09.0). A two-sided $p < 0.05$ was considered statistically significant.

RESULTS

We recruited 43,304 participants for 1-year change analysis; 24,295 participants for 3-year change analysis; and 16,138 participants for 5-year change analysis. Their mean (SD) ages were 39.41 (11.95) years, 38.65 (11.64) years, and 38.15 (11.28) years, respectively. Over median (IQR) follow-up periods of 15.8 (11.3–19.3) years, 13.9 (9.9–17.5) years, and 12.3 (8.8–15.2) years, we recorded 1823/354, 842/155, and 466/78 all-cause/CVD deaths in 1-, 3-, and 5-year change analyses, respectively. The mean (SD) FRS changes were 0.05 (2.22) for 1-year change analysis, 0.48 (2.44) for 3-year change analysis, and 1.12 (2.52) for 5-year change analysis (Table 1). Generally, participants experiencing losses in obesity indices were more likely to be older and to have overweight poorer health and healthier lifestyles (Tables S1–S3).

Linear relationships

In 1-year change analysis, the time point of 10 years was used to split the follow-up period in the time-dependent coefficient Cox regression models due to the violation of the proportional hazard assumption. To the 10-year follow-up, per 1% increment, weight, BMI, and WHR decreased by 3.5% (HR: 0.965 [95% confidence interval (CI): 0.946–0.986]), 3.1% (HR: 0.969 [95% CI: 0.949–0.990]), and 2.6% (HR: 0.984 [95% CI: 0.970–0.999]) risks of all-cause mortality, respectively (Table 2). Compared with stable obesity indices, 1-year losses over 5% in obesity indices were associated with elevated all-cause mortality risks, except for WHR. No significant associations between 1-year changes in obesity indices and CVD deaths were found (Table 2).

Regarding the 3-year changes, to the 9-year follow-up, the HRs of all-cause mortality decreased by 2.5% (HR: 0.975 [95% CI: 0.954–0.997]) per 1% BMI increase, 1.9% (HR: 0.981 [95% CI: 0.964–0.999]) per 1% WC increase, and 1.9% (HR: 0.981 [95% CI: 0.964–0.999]) per 1% WHtR increase (Table 3). Three-year losses over 5% in weight and BMI compared with stable counterparts were associated with greater risks of all-cause mortality. Interestingly, higher all-cause deaths were associated with decreased WC and WHtR before the 9-year follow-up and increased WC and WHtR after the 9-year follow-up when compared with stable groups. Also, increases exceeding 5% in WC and WHtR were associated with 68.6% (HR: 1.686 [95% CI: 1.154–2.461]) and 68.1% (HR: 1.681 [95% CI: 1.152–2.452]) higher risks of CVD-specific mortality, respectively.

In 5-year change analysis, the risks of all-cause mortality were reduced by 2.3% (HR: 0.977 [95% CI: 0.960–0.995]) per 1% weight gain and 2.4% (HR: 0.976 [95% CI: 0.959–0.994]) per 1% BMI gain (Table 4). Also, 5-year weight loss compared with stable groups was associated with higher all-cause deaths (Table 4). However, 5-year changes in abdominal obesity indices did not affect all-cause and CVD deaths (Table 4).

Furthermore, significantly positive associations of 1-, 3-, and 5-year changes in all obesity indices with FRS changes were found (Table 5). Compared with stable obesity indices, reductions in obesity indices were associated with decreased FRS, whereas gains in obesity indices were related to increased FRS (Table 5).

Nonlinear relationships

As presented in Figure 1, L-shaped relationships between all-cause mortality and 1-year changes in weight and BMI were detected. Below the inflection points of −3.7% for 1-year weight changes and −4.2% for 1-year BMI changes, the HRs and 95% CIs of all-cause mortality were 0.886 (95% CI: 0.841–0.934) per 1% weight gain and 0.909 (95% CI: 0.860–0.960) per 1% BMI gain. No significant associations were observed beyond these inflection points. Figure 2 showed U-shaped relationships between all-cause mortality and 3-year changes in obesity indices, except for WHR. For decreases exceeding the inflections points, decreased weight, BMI, WC, and WHtR were associated with elevated risks of all-cause mortality. On the right side of the inflection points, positive associations of 3-year changes in weight and BMI with all-cause mortality were found. However, no nonlinear relationships between short-term changes in obesity indices and CVD deaths were detected.

Subgroup analyses

As shown in Figures S5 through S21, elevated all-cause mortality risks linked to 1-year decreased WC were found in participants with BMI and WHR that indicated obesity or physically inactive participants. Also, among participants who had comorbidities, normal BMI, or WHR that indicated obesity or who were physically inactive, 1-year WHtR loss was related to higher all-cause deaths. Moreover, elevated CVD deaths were associated with 3-year increased WC and WHtR among participants with normal WC. Higher HRs of CVD deaths associated

TABLE 1 Baseline characteristics of participants in the 1-, 3-, and 5-year change study.

Characteristics	1-y change $n = 43,304$	3-y change $n = 24,295$	5-y change $n = 16,138$
Sex (male), *n* (%)	22,761 (52.6)	12,673 (52.2)	8347 (51.7)
Age, mean (SD)	39.41 (11.95)	38.65 (11.64)	38.15 (11.28)
Marital status, *n* (%)			
Unmarried	11,534 (26.6)	6568 (27.0)	4297 (26.6)
Married or cohabitated	29,371 (67.8)	16,531 (68.0)	11,145 (69.1)
Separated, divorced, or widowed	2399 (5.5)	1196 (4.9)	696 (4.3)
Education level, *n* (%)			
Primary school or lower	4979 (11.5)	2506 (10.3)	1558 (9.7)
Middle school	2187 (5.1)	1121 (4.6)	653 (4.0)
High school	8980 (20.7)	5160 (21.2)	3272 (20.3)
Technical school	9653 (22.3)	5714 (23.5)	4130 (25.6)
College or higher	17,505 (40.4)	9794 (40.3)	6525 (40.4)
Occupation, *n* (%)			
Unemployed	5221 (12.1)	3086 (12.7)	2063 (12.8)
Blue-collar worker	6036 (13.9)	3401 (14.0)	2335 (14.5)
Service worker	21,425 (49.5)	11,899 (49.0)	8088 (50.1)
Professional	5873 (13.6)	3299 (13.6)	2048 (12.7)
Manager	4749 (11.0)	2610 (10.7)	1604 (9.9)
Others	5221 (12.1)	3086 (12.7)	765 (4.7)
Hypertension (yes), *n*, %	6539 (15.1)	3231 (13.3)	2019 (12.5)
Diabetes (yes), *n* (%)	1476 (3.4)	695 (2.9)	407 (2.5)
Dyslipidemia (yes), *n* (%)	19,388 (44.8)	10,460 (43.1)	6721 (41.6)
COPD (yes), *n* (%)	956 (2.2)	444 (1.8)	297 (1.8)
Thyroid diseases (yes), *n* (%)	1375 (3.2)	754 (3.1)	474 (2.9)
CVD risk level, *n* (%)			
Low	36,630 (84.6)	21,046 (86.6)	14,156 (87.7)
Middle/high	6674 (15.4)	3249 (13.4)	1982 (12.3)
FRS change, mean (SD)	0.05 (2.22)	0.48 (2.44)	1.12 (2.52)
Vegetable intake, *n* (%)			
Seldom (<1 serving/d)	5998 (13.9)	3298 (13.6)	2164 (13.4)
Moderate (1–2 servings/d)	27,147 (62.7)	15,376 (63.3)	10,264 (63.6)
Frequent (>2 servings/d)	10,159 (23.5)	5621 (23.1)	3710 (23.0)
Fruit intake, *n* (%)			
Seldom (<1 serving/d)	15,752 (36.4)	8865 (36.5)	5632 (34.9)
Moderate (1–2 servings/d)	22,235 (51.3)	12,476 (51.4)	8496 (52.6)
Frequent (>2 servings/d)	5317 (12.3)	2954 (12.2)	2010 (12.5)
Sleep duration, *n* (%)			
<6 h	8522 (19.7)	4569 (18.8)	2916 (18.1)
6 to ≤ 8 h	31,330 (72.3)	17,727 (73.0)	11,914 (73.8)
≥8 h	3452 (8.0)	1999 (8.2)	1308 (8.1)
Occupational physical activity, *n* (%)			
Mostly sedentary	27,184 (62.8)	15,214 (62.6)	10,243 (63.5)
Combination of sitting, standing, and walking	11,465 (26.5)	6558 (27.0)	4300 (26.6)
Mostly standing or walking	3735 (8.6)	2000 (8.2)	1282 (7.9)
Hard labor	920 (2.1)	523 (2.2)	313 (1.9)

TABLE 1 (Continued)

Characteristics	1-y change *n* = 43,304	3-y change *n* = 24,295	5-y change *n* = 16,138
Leisure-time physical activity, *n* (%)			
0 MET-min/wk	20,428 (47.2)	11,845 (48.8)	7900 (49.0)
<500 MET-min/wk	10,236 (23.6)	5640 (23.2)	3778 (23.4)
500 to 999 MET-min/wk	7578 (17.5)	4181 (17.2)	2778 (17.2)
≥1000 MET-min/wk	5062 (11.7)	2629 (10.8)	1682 (10.4)
Smoking status, *n* (%)			
Nonsmoker	31,426 (72.6)	17,905 (73.7)	11,940 (74.0)
Former smoker	2891 (6.7)	1561 (6.4)	1005 (6.2)
Current smoker	8987 (20.8)	4829 (19.9)	3193 (19.8)
Drinking status, *n* (%)			
Never or less than once per week	36,267 (83.7)	20,641 (85.0)	13,694 (84.9)
1 to 3 times/wk	4710 (10.9)	2480 (10.2)	1710 (10.6)
>3 times/wk	2327 (5.4)	1174 (4.8)	734 (4.5)
Weight (kg), mean (SD)	62.43 (12.38)	62.06 (12.19)	61.71 (12.02)
BMI (kg/m), mean (SD)	23.00 (3.48)	22.84 (3.42)	22.72 (3.35)
WC (cm), mean (SD)	77.00 (10.21)	76.53 (10.07)	76.14 (9.96)
WHR, mean (SD)	0.81 (0.08)	0.81 (0.07)	0.81 (0.08)
WHtR, mean (SD)	0.47 (0.06)	0.47 (0.06)	0.46 (0.05)
Weight change, mean (SD)	0.447 (3.980)	1.449 (5.377)	2.339 (6.139)
<−5%, *n* (%)	2987 (6.9)	2214 (9.1)	1500 (9.3)
−5% to 5%, *n* (%)	36,106 (83.4)	16,866 (69.4)	9936 (61.6)
>5%, *n* (%)	4211 (9.7)	5215 (21.5)	4702 (29.1)
BMI change, mean (SD)	0.390 (3.994)	1.413 (5.354)	2.294 (6.070)
<−5%, *n* (%)	3058 (7.1)	2243 (9.2)	1494 (9.3)
−5% to 5%, *n* (%)	36,070 (83.3)	16,886 (69.5)	10,021 (62.1)
>5%, *n* (%)	4176 (9.6)	5166 (21.3)	4623 (28.6)
WC change, mean (SD)	0.221 (5.766)	0.983 (6.479)	1.889 (6.852)
<−5%, *n* (%)	6934 (16.0)	3877 (16.0)	2204 (13.7)
−5% to 5%, *n* (%)	28,675 (66.2)	14,520 (59.8)	9161 (56.8)
>5%, *n* (%)	7695 (17.8)	5898 (24.3)	4773 (29.6)
WHR change, mean (SD)	0.130 (5.095)	0.564 (5.345)	1.156 (5.055)
<−5%, *n* (%)	5858 (13.5)	3171 (13.1)	1872 (11.6)
−5% to 5%, *n* (%)	31,057 (71.7)	16,638 (68.5)	10,633 (65.9)
>5%, *n* (%)	6389 (14.8)	4486 (18.5)	3633 (22.5)
WHtR change, mean (SD)	0.193 (5.775)	0.967 (6.479)	1.868 (6.841)
<−5%, *n* (%)	7118 (16.4)	3922 (16.1)	2241 (13.9)
−5% to 5%, *n* (%)	28,442 (65.7)	14,440 (59.4)	9099 (56.4)
>5%, *n* (%)	7744 (17.9)	5933 (24.4)	4798 (29.7)

Abbreviations: COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; FRS, Framingham Risk Score; MET, metabolic equivalent; WC, waist circumference; WHR, waist to hip ratio; WHtR, waist to height ratio.

with 5-year losses in weight and BMI were observed among participants aged over 45 years, those with middle/high-level CVD risk, or those with normal BMI and WHtR. Additionally, more increments in FRS were observed with per-percentage increases in weight and BMI among participants aged under age 45 years, male individuals, those with comorbidities, and those with higher obesity indices. More increases in FRS were associated with short-term weight gain in participants with higher levels of physical activity and short-term BMI gain in participants with low-level CVD risk. Elevated FRS associated with per-percentage increases in WC, WHR, and WHtR was

TABLE 2 Associations of 1-year change in obesity indices with all-cause and CVD deaths.

Obesity indices	Cases	Person years	Model 1[a] HR (95% CI)	Model 2[b] HR (95% CI)
Outcome: all-cause mortality				
Weight				
Per 1%: strata (t_{group}) = 1[c]	1823	645,203.5	0.968 (0.947–0.988)	0.965 (0.946–0.986)
Per 1%: strata (t_{group}) = 2[c]			1.001 (0.984–1.018)	1.000 (0.983–1.016)
Change category				
−5% to 5%	1544	538,923.7	Ref	Ref
<−5%: strata (t_{group}) = 1	135	43,357.8	1.657 (1.278–2.147)	1.691 (1.303–2.195)
<−5%: strata (t_{group}) = 2			1.114 (0.875–1.418)	1.116 (0.875–1.423)
>5%: strata (t_{group}) = 1	144	62,922.0	1.129 (0.855–1.490)	1.066 (0.806–1.409)
>5%: strata (t_{group}) = 2			1.081 (0.869–1.343)	1.049 (0.842–1.306)
BMI				
Per 1%: strata (t_{group}) = 1	1823	645,203.5	0.971 (0.951–0.992)	0.969 (0.949–0.990)
Per 1%: strata (t_{group}) = 2			0.998 (0.982–1.015)	0.997 (0.980–1.013)
Change category				
−5% to 5%	1548	538,002.1	Ref	Ref
<−5%	131	44,578.9	1.268 (1.060–1.516)	1.294 (1.080–1.550)
>5%	144	62,622.5	1.057 (0.891–1.255)	1.012 (0.851–1.204)
WC				
Per 1%: strata (t_{group}) = 1	1823	645,203.5	0.985 (0.972–0.998)	0.989 (0.975–1.002)
Per 1%: strata (t_{group}) = 2			1.001 (0.992–1.011)	1.005 (0.996–1.015)
Change category				
−5% to 5%	1074	417,082.5	Ref	Ref
<−5%: strata (t_{group}) = 1	421	111,706.5	1.427 (1.185–1.718)	1.368 (1.133–1.652)
<−5%: strata (t_{group}) = 2			1.091 (0.945–1.258)	1.048 (0.906–1.214)
>5%: strata (t_{group}) = 1	328	116,414.5	1.076 (0.873–1.327)	1.081 (0.875–1.336)
>5%: strata (t_{group}) = 2			1.049 (0.900–1.223)	1.067 (0.913–1.248)
WHR				
Per 1%: strata (t_{group}) = 1	1823	645,203.5	0.981 (0.967–0.995)	0.984 (0.970–0.999)
Per 1%: strata (t_{group}) = 2			1.000 (0.990–1.010)	1.002 (0.992–1.013)
Change category				
−5% to 5%	1187	452,334.1	Ref	Ref
<−5%	343	95,393.7	1.141 (1.011–1.287)	1.114 (0.978–1.268)
>5%	293	97,475.7	1.029 (0.905–1.170)	1.029 (0.902–1.173)
WHtR				
Per 1%: strata (t_{group}) = 1	1823	645,203.5	0.985 (0.973–0.998)	0.989 (0.976–1.003)
Per 1%: strata (t_{group}) = 2			1.001 (0.992–1.010)	1.005 (0.995–1.015)
Change category				
−5% to 5%	1075	413,452.0	Ref	Ref
<−5%: strata (t_{group}) = 1	419	114,670.1	1.421 (1.181–1.710)	1.372 (1.137–1.657)
<−5%: strata (t_{group}) = 2			1.057 (0.916–1.220)	1.021 (0.881–1.182)
>5%: strata (t_{group}) = 1	329	117,081.4	1.086 (0.882–1.337)	1.099 (0.890–1.355)
>5%: strata (t_{group}) = 2			1.018 (0.873–1.187)	1.042 (0.891–1.219)
Outcome: CVD mortality				
Weight				
Per 1%	354	645,203.5	0.994 (0.965–1.024)	0.993 (0.964–1.024)

TABLE 2 (Continued)

Obesity indices	Cases	Person years	Model 1[a] HR (95% CI)	Model 2[b] HR (95% CI)
Change category				
−5% to 5%	301	538,923.7	Ref	Ref
<−5%	27	43,357.8	1.357 (0.914–2.015)	1.388 (0.929–2.076)
>5%	26	62,922.0	1.034 (0.692–1.547)	1.022 (0.679–1.537)
BMI				
Per 1%	354	645,203.5	0.994 (0.965–1.025)	0.994 (0.964–1.024)
Change category				
−5% to 5%	302	538,002.1	Ref	Ref
<−5%	24	44,578.9	1.203 (0.793–1.826)	1.254 (0.822–1.913)
>5%	28	62,622.5	1.069 (0.725–1.577)	1.051 (0.709–1.559)
WC				
Per 1%	354	645,203.5	0.997 (0.981–1.014)	1.005 (0.987–1.024)
Change category				
−5% to 5%	200	417,082.5	Ref	Ref
<−5%	82	111,706.5	1.194 (0.922–1.546)	1.079 (0.823–1.415)
>5%	72	116,414.5	1.205 (0.919–1.579)	1.269 (0.962–1.674)
WHR				
Per 1%	354	645,203.5	0.989 (0.971–1.007)	0.997 (0.976–1.018)
Change category				
−5% to 5%	226	452,334.1	Ref	Ref
<−5%	72	95,393.7	1.206 (0.923–1.575)	1.073 (0.802–1.435)
>5%	56	97,475.7	1.008 (0.752–1.352)	1.036 (0.767–1.400)
WHtR				
Per 1%	354	645,203.5	0.997 (0.981–1.014)	1.005 (0.987–1.024)
Change category				
−5% to 5%	205	413,452.0	Ref	Ref
<−5%	79	114,670.1	1.108 (0.854–1.439)	1.006 (0.766–1.322)
>5%	70	117,081.4	1.122 (0.854–1.473)	1.193 (0.902–1.579)

Abbreviations: CVD, cardiovascular disease; HR, hazard ratio; Ref, reference; WC, waist circumference; WHR, waist to hip ratio; WHtR, waist to height ratio.

[a]Model 1 adjusted for sex, age, marital status, education level, and occupation.

[b]Model 2 adjusted for covariates in Model 1 plus hypertension; diabetes; dyslipidemia; chronic obstructive pulmonary disease; thyroid diseases; Framingham Risk Score change; SBP; DBP; LDL-C; HDL-C; triglycerides; fasting plasma glucose; vegetable and fruit intake; sleep duration; occupational and leisure-time physical activity levels; smoking and drinking status; and baseline weight, WHR, and WHtR.

[c]Based on the Schoenfeld residuals, the time point of 10 years was used to separate the data. The split time period was presented as strata (t_{group}) = 1 for the time period from 0 to 10 years and strata (t_{group}) = 2 for the time period from 10 years to the end of the observation.

observed, particularly among male individuals or those with higher baseline obesity indices.

Sensitivity analyses

In the sensitivity analyses, we found that some associations of short-term changes in obesity indices with all-cause and CVD-specific mortality were altered after excluding participants with conventional CVD risk factors and follow-up less than 5 years (Tables S4–S9). All sensitivity analyses supported the adverse effects of short-term increased obesity indices on FRS (Tables S10–S12).

DISCUSSION

In this large cohort study of the general population, our findings demonstrated the adverse effects of short-term weight and BMI reductions on all-cause mortality, with greater reductions causing worse

TABLE 3 Associations of 3-year change in obesity indices with all-cause and CVD deaths.

Obesity indices	Cases	Person years	Model 1[a] HR (95% CI)	Model 2[b] HR (95% CI)
Outcome: all-cause mortality				
Weight				
Per 1%	842	323,431.4	0.986 (0.971–1.000)	0.989 (0.974–1.003)
Change category				
−5% to 5%	593	225,819.6	Ref	Ref
<−5%	121	28,138.1	1.675 (1.375–2.040)	1.558 (1.275–1.903)
>5%	128	69,473.7	1.189 (0.980–1.443)	1.185 (0.973–1.444)
BMI				
Per 1%: strata (t_{group}) = 1[c]	842	323,431.4	0.972 (0.951–0.994)	0.975 (0.954–0.997)
Per 1%: strata (t_{group}) = 2[c]			1.000 (0.981–1.019)	1.003 (0.984–1.022)
Change category				
−5% to 5%	597	225,988.0	Ref	Ref
<−5%	104	28,759.6	1.540 (1.249–1.899)	1.443 (1.168–1.784)
>5%	141	68,683.8	1.203 (0.999–1.448)	1.206 (0.998–1.458)
WC				
Per 1%: strata (t_{group}) = 1	842	323,431.4	0.977 (0.961–0.994)	0.981 (0.964–0.999)
Per 1%: strata (t_{group}) = 2			1.008 (0.994–1.022)	1.012 (0.998–1.027)
Change category				
−5% to 5%	459	190,650.5	Ref	Ref
<−5%: strata (t_{group}) = 1	199	55,743.3	1.415 (1.094–1.831)	1.399 (1.077–1.817)
<−5%: strata (t_{group}) = 2			1.172 (0.941–1.461)	1.142 (0.911–1.431)
>5%: strata (t_{group}) = 1	184	77,037.6	0.906 (0.682–1.203)	0.952 (0.715–1.267)
>5%: strata (t_{group}) = 2			1.288 (1.038–1.599)	1.349 (1.082–1.680)
WHR				
Per 1%	842	32,3431.4	1.001 (0.989–1.013)	1.004 (0.990–1.018)
Change category				
−5% to 5%	529	217,544.8	Ref	Ref
<−5%	141	46,842.3	1.133 (0.940–1.366)	1.098 (0.900–1.340)
>5%	172	59,044.3	1.158 (0.974–1.377)	1.182 (0.989–1.413)
WHtR				
Per 1%: strata (t_{group}) = 1	842	323,431.4	0.977 (0.961–0.994)	0.981 (0.964–0.999)
Per 1%: strata (t_{group}) = 2			1.009 (0.995–1.022)	1.013 (0.999–1.028)
Change category				
−5% to 5%	460	189,567.4	Ref	Ref
<−5%: strata (t_{group}) = 1	192	56,471.1	1.391 (1.073–1.802)	1.371 (1.054–1.784)
<−5%: strata (t_{group}) = 2			1.153 (0.922–1.441)	1.119 (0.890–1.408)
>5%: strata (t_{group}) = 1	190	77,392.9	0.883 (0.665–1.172)	0.931 (0.700–1.239)
>5%: strata (t_{group}) = 2			1.349 (1.091–1.669)	1.416 (1.141–1.758)
Outcome: CVD mortality				
Weight				
Per 1%	155	323,431.4	1.002 (0.968–1.036)	1.002 (0.969–1.037)
Weight				
Change category				
−5 to 5%	115	225,819.6	Ref	Ref
<−5%	17	28,138.1	1.246 (0.746–2.082)	1.168 (0.695–1.965)

TABLE 3 (Continued)

Obesity indices	Cases	Person years	Model 1[a] HR (95% CI)	Model 2[b] HR (95% CI)
>5%	23	69,473.7	1.186 (0.753–1.866)	1.136 (0.713–1.811)
BMI				
Per 1%	155	323,431.4	1.004 (0.970–1.039)	1.005 (0.971–1.039)
Change category				
−5% to 5%	113	225,988.0	Ref	Ref
<−5%	16	28,759.6	1.313 (0.776–2.222)	1.216 (0.713–2.075)
>5%	26	68,683.8	1.252 (0.813–1.927)	1.208 (0.775–1.881)
WC				
Per 1%	155	323,431.4	1.010 (0.985–1.035)	1.014 (0.987–1.042)
Change category				
−5% to 5%	79	190,650.5	Ref	Ref
<−5%	29	55,743.3	1.022 (0.666–1.570)	0.936 (0.600–1.462)
>5%	47	77,037.6	1.607 (1.116–2.312)	1.686 (1.154–2.461)
WHR				
Per 1%	155	323,431.4	0.992 (0.966–1.020)	0.999 (0.968–1.031)
Change category				
−5% to 5%	94	217,544.8	Ref	Ref
<−5%	30	46,842.3	1.344 (0.889–2.033)	1.261 (0.810–1.963)
>5%	31	59,044.3	1.110 (0.736–1.674)	1.189 (0.777–1.819)
WHtR				
Per 1%	155	323,431.4	1.010 (0.986–1.036)	1.014 (0.988–1.042)
Change category				
−5% to 5%	79	189,567.4	Ref	Ref
<−5%	29	56,471.1	1.059 (0.690–1.626)	0.958 (0.613–1.498)
>5%	47	77,392.9	1.604 (1.115–2.309)	1.681 (1.152–2.452)

Abbreviations: CVD, cardiovascular disease; HR, hazard ratio; Ref, reference; WC, waist circumference; WHR, waist to hip ratio; WHtR, waist to height ratio.

[a]Model 1 adjusted for sex, age, marital status, education level, and occupation.

[b]Model 2 adjusted for covariates in Model 1 plus hypertension; diabetes; dyslipidemia; chronic obstructive pulmonary disease; thyroid diseases; Framingham Risk Score change; SBP; DBP; LDL-C; HDL-C; triglycerides; fasting plasma glucose; vegetable and fruit intake; sleep duration; occupational and leisure-time physical activity levels; smoking and drinking status; and baseline weight, WHR, and WHtR.

[c]Based on the Schoenfeld residuals, the time point of 9 years was used to separate the data. The split time period was presented as strata (t_{group}) = 1 for the time period from 0 to 9 years and strata (t_{group}) = 2 for the time period from 9 years to the end of the observation.

outcomes. One- and three-year losses exceeding 5% in WC and WHtR were also linked to higher all-cause deaths compared with stable groups. Nonlinear relationships further revealed the adverse effects of 3-year weight and BMI gains on all-cause mortality and highlighted lower cutoff values for short-term changes in obesity indices. Similarly, 3-year increased WC and WHtR were associated with elevated CVD deaths. Finally, our findings suggested that short-term reduced obesity indices improved CVD profiles.

Our findings somewhat align with previous studies on the negative impacts of short-term reduced weight and BMI on all-cause deaths in middle-aged adults and those with chronic conditions such as diabetes or CVD [4, 7, 28–30]. Inconsistent with previous studies that have involved middle-aged adults, we found no association between 3-year weight and BMI gains exceeding 5% and increased all-cause mortality [4, 30]. However, among participants with gains exceeding 2.1% in weight and 1.4% in BMI, 3-year increased weight and BMI were positively associated with all-cause mortality. This indicates that young adults may be more vulnerable to fat accumulation, and lower cutoff values for changes in weight and BMI should be considered. Our results are also broadly consistent with a study in which 5-year weight loss over 5 kg significantly elevated CVD-specific mortality among middle-aged male individuals [31]. However, contrary to the findings of higher CVD deaths associated with reduced BMI and weight over 1 and 3 years in middle-aged adults and older patients

TABLE 4 Associations of 5-year change in obesity indices with all-cause and CVD deaths.

Obesity indices	Cases	Person years	Model 1[a] HR (95% CI)	Model 2[b] HR (95% CI)
Outcome: all-cause mortality				
Weight				
Per 1%	466	191,175.1	0.981 (0.964–0.998)	0.977 (0.960–0.995)
Change category				
−5% to 5%	304	118,216.8	Ref	Ref
<−5%	78	17,496.2	1.554 (1.209–1.997)	1.537 (1.187–1.991)
>5%	84	55,462.1	1.029 (0.803–1.319)	0.973 (0.756–1.252)
BMI				
Per 1%	466	191,175.1	0.979 (0.962–0.997)	0.976 (0.959–0.994)
Change category				
−5% to 5%	305	119,496.0	Ref	Ref
<−5%	70	17,641.1	1.510 (1.163–1.961)	1.483 (1.133–1.943)
>5%	91	54,038.0	1.034 (0.815–1.312)	0.960 (0.753–1.223)
WC				
Per 1%	466	191,175.1	0.997 (0.984–1.011)	1.003 (0.987–1.018)
Change category				
−5% to 5%	289	107,499.3	Ref	Ref
<−5%	76	28,039.5	0.872 (0.676–1.124)	0.852 (0.652–1.112)
>5%	101	55,636.3	0.846 (0.673–1.062)	0.899 (0.710–1.138)
WHR				
Per 1%	466	191,175.1	0.995 (0.979–1.011)	1.005 (0.986–1.024)
Change category				
−5% to 5%	300	124,750.7	Ref	Ref
<−5%	71	24,376.1	1.156 (0.891–1.500)	1.089 (0.817–1.451)
>5%	95	42,048.3	1.016 (0.805–1.281)	1.110 (0.871–1.414)
WHtR				
Per 1%	466	191,175.1	0.997 (0.983–1.010)	1.002 (0.987–1.018)
Change category				
−5% to 5%	292	106,805.6	Ref	Ref
<−5%	73	28,618.5	0.830 (0.641–1.074)	0.807 (0.616–1.057)
>5%	101	55,751.0	0.794 (0.632–0.996)	0.840 (0.665–1.062)
Outcome: CVD mortality				
Weight				
Per 1%	78	191,175.1	0.934 (0.894–0.977)	0.928 (0.886–0.973)
Change category				
−5% to 5%	52	118,216.8	Ref	Ref
<−5%	17	17,496.2	2.042 (1.172–3.556)	2.018 (1.124–3.623)
>5%	9	55,462.1	0.751 (0.366–1.542)	0.677 (0.326–1.405)
BMI				
Per 1%	78	191,175.1	0.928 (0.888–0.970)	0.923 (0.880–0.968)
BMI				
Change category				
−5% to 5%	53	119,496.0	Ref	Ref
<−5%	14	17,641.1	1.803 (0.994–3.268)	1.772 (0.945–3.323)
>5%	11	54,038.0	0.829 (0.430–1.597)	0.762 (0.390–1.488)

TABLE 4 (Continued)

Obesity indices	Cases	Person years	Model 1[a] HR (95% CI)	Model 2[b] HR (95% CI)
WC				
Per 1%	78	191,175.1	0.967 (0.934–1.001)	0.970 (0.932–1.009)
Change category				
−5% to 5%	50	107,499.3	Ref	Ref
<−5%	14	28,039.5	0.968 (0.533–1.758)	0.951 (0.508–1.778)
>5%	14	55,636.3	0.751 (0.413–1.363)	0.825 (0.442–1.536)
WHR				
Per 1%	78	191,175.1	0.963 (0.926–1.001)	0.979 (0.933–1.026)
Change category				
−5% to 5%	50	124,750.7	Ref	Ref
<−5%	16	24,376.1	1.618 (0.917–2.853)	1.305 (0.690–2.471)
>5%	12	42,048.3	0.813 (0.430–1.535)	0.907 (0.466–1.765)
WHtR				
Per 1%	78	191,175.1	0.966 (0.933–0.999)	0.968 (0.931–1.007)
Change category				
−5% to 5%	53	106,805.6	Ref	Ref
<−5%	13	28,618.5	0.852 (0.463–1.568)	0.834 (0.439–1.582)
>5%	12	55,751.0	0.563 (0.300–1.057)	0.607 (0.317–1.162)

Abbreviations: CVD, cardiovascular disease; HR, hazard ratio; Ref, reference; WC, waist circumference; WHR, waist to hip ratio; WHtR, waist to height ratio.

[a]Model 1 adjusted for sex, age, marital status, education level, and occupation.

[b]Model 2 adjusted for covariates in Model 1 plus hypertension; diabetes; dyslipidemia; chronic obstructive pulmonary disease; thyroid diseases; Framingham Risk Score change; SBP; DBP; LDL-C; HDL-C; triglycerides; fasting plasma glucose; vegetable and fruit intake; sleep duration; occupational and leisure-time physical activity levels; smoking and drinking status; and baseline weight, WHR, and WHtR.

with CVD, we did not find any significant associations [4, 32, 33]. This might be because a lower rate of CVD deaths makes it difficult to detect the difference between the loss and stable groups. Several factors may explain the observed relationships. First, participants reducing weight and BMI were more likely to have overweight. Excessive fat accumulation can result from genetic diseases (e.g., Prader-Willi syndrome) and medication use (e.g., antipsychotics), in that individuals may not benefit significantly from short-term weight loss [34]. Second, decreased weight and BMI could be illness-related loss. Participants with reduced weight and BMI had untreated medical conditions such as hypertension, diabetes, and dyslipidemia, contributing to adverse health outcomes such as CVD and cancers. Third, different weight loss strategies such as aerobic interval training with or without a low-energy diet have various health effects [35]. Moreover, among participants experiencing weight and BMI losses, neither the physical activity level nor the intake of vegetables and fruit met recommended levels, potentially contributing to higher mortality rates [36]. Finally, weight and BMI cannot distinguish between fat and lean mass, making it unclear which mass composition predominantly influences mortality. This study highlights the importance of underlying causes of rapid weight loss, even in individuals with obesity. Tailoring weight management based on age, health status, and obesity severity is crucial.

Inconsistent with a study in patients with myocardial infarction [7], we found the adverse effects of 1-year decreased WC and WHtR on all-cause mortality before the 10-year follow-up. It can be explained by the obesity paradox, in which a lower WC was linked to a worse prognosis [37]. Also, our study found that participants with general and abdominal obesity who experienced 1-year reductions in WC and WHtR had higher all-cause mortality risks. One possible explanation lies in preexisting medical conditions. Participants with obesity reported poorer health in our study. Rapid WC and WHtR reductions in these individuals might be clinical manifestations of worsening underlying diseases. Furthermore, subgroup analyses revealed that physically inactive participants with decreased WC and WHtR had higher mortality risks. This strengthens the notion that unintentional weight loss could drive the observed associations. Moreover, compared with stable groups, either 3-year decreased or increased WC and WHtR were associated with greater risks of all-cause mortality, which is partially consistent with one Chinese study [38]. Our study is also in line with previous studies that have linked 3-year WC increases exceeding 5% to higher CVD mortality [38, 39]. However, our study differs from a study showing significant associations between 6-year WC increases and CVD deaths, especially for 6-year increased WC > 4.7 cm among middle-aged female

TABLE 5 Associations between short-term changes in obesity indices and FRS change.

	1-y		3-y		5-y	
	Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]
Obesity indices	Std. β	Std. β	Std. β	Std. β	Std. β	Std. β
Weight						
Per 1%	0.146*	0.145*	0.172*	0.173*	0.203*	0.197*
Change category						
−5% to 5%	Ref	Ref	Ref	Ref	Ref	Ref
<−5%	−0.086*	−0.081*	−0.101*	−0.093*	−0.107*	−0.099*
>5%	0.065*	0.069*	0.091*	0.095*	0.119*	0.117*
BMI						
Per 1%	0.138*	0.137*	0.166*	0.165*	0.194*	0.188*
Change category						
−5% to 5%	Ref	Ref	Ref	Ref	Ref	Ref
<−5%	−0.081*	−0.078*	−0.096*	−0.087*	−0.110*	−0.099*
>5%	0.063*	0.067*	0.085*	0.089*	0.104*	0.104*
WC						
Per 1%	0.073*	0.092*	0.118*	0.139*	0.142*	0.170*
Change category						
−5% to 5%	Ref	Ref	Ref	Ref	Ref	Ref
<−5%	−0.056*	−0.058*	−0.085*	−0.087*	−0.097*	−0.097*
>5%	0.025*	0.040*	0.051*	0.066*	0.074*	0.091*
WHR						
Per 1%	0.033*	0.055*	0.074*	0.100*	0.107*	0.134*
Change category						
−5% to 5%	Ref	Ref	Ref	Ref	Ref	Ref
<−5%	−0.023*	−0.027*	−0.061*	−0.069*	−0.055*	−0.060*
>5%	0.009	0.020*	0.031*	0.043*	0.067*	0.078*
WHtR						
Per 1%	0.070*	0.089*	0.116*	0.135*	0.138*	0.166*
Change category						
−5% to 5%	Ref	Ref	Ref	Ref	Ref	Ref
<−5%	−0.052*	−0.055*	−0.082*	−0.082*	−0.097*	−0.096*
>5%	0.023*	0.038*	0.051*	0.065*	0.069*	0.085*

Abbreviations: Ref, reference; Std. β, standardized beta coefficient; WC, waist circumference; WHR, waist to hip ratio; WHtR, waist to height ratio.
[a]Model 1 adjusted for sex, age, marital status, education level, and occupation.
[b]Model 2 adjusted for covariates in Model 1 plus hypertension; diabetes; dyslipidemia; chronic obstructive pulmonary disease; thyroid diseases; Framingham Risk score change; SBP; DBP; LDL-C; HDL-C; triglycerides; fasting plama glucose; vegetable and fruit intake; sleep duration; occupational and leisure-time physical activity levels; smoking and drinking status; and baseline weight, WHR, and WHtR.
*$p < 0.001$.

individuals [40]. This discrepancy might be explained by our study population's lower baseline WC, in whom slight increases may not be sufficient to significantly elevate CVD risk [41]. Similarly, 5-year WHR changes did not exhibit significant associations with all-cause or CVD-specific mortality, similar to findings from a study investigating 4-year WHR changes and all-cause mortality [8]. This could be due to WHR reductions reflecting alterations in both WC and HC, as the gluteofemoral fat (measured by -HC) has independent protective effects on cardiovascular profiles [42]. Additionally, abdominal obesity indices cannot differentiate between abdominal subcutaneous and visceral fat mass, introducing uncertainty regarding the ratio of subcutaneous fat to visceral fat area. Future studies should explore the differential effects of changes in these specific fat compartments on mortality outcomes.

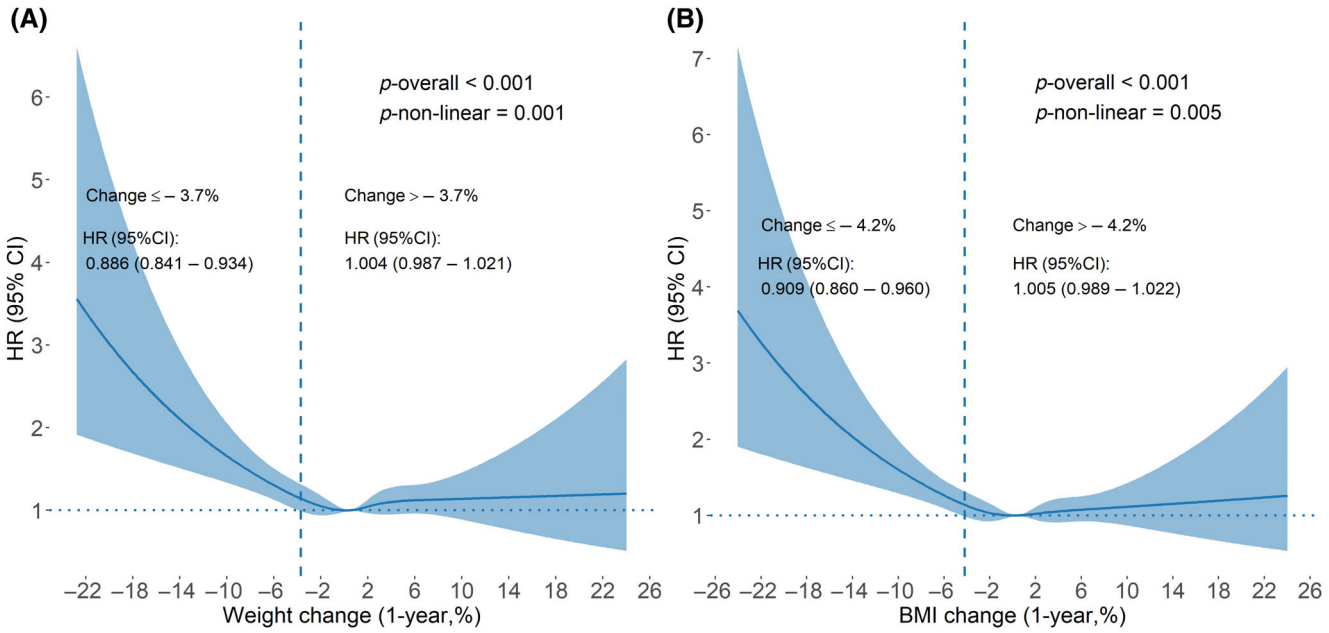

FIGURE 1 Nonlinear relationships of 1-year changes in (A) weight and (B) BMI with all-cause mortality. Blue solid lines represent the calculated hazard ratios (HRs) of all-cause mortality, and shaded areas represent the 95% CIs of the calculated HRs. Vertical dashed lines are inflection points, which are −3.7% for weight change and −4.2% for BMI change. On the left side of the inflection point, the HRs of all-cause mortality increased with 1-year increasing reductions in weight and BMI (per 1% change). [Color figure can be viewed at wileyonlinelibrary.com]

To our knowledge, this is the first study to explore associations of changes in obesity indices, especially abdominal obesity indices, with concurrent changes in estimated CVD risk. Only Chen et al. [18] found that, among smoking quitters, 2-year weight gain elevated 10-year risk of coronary heart disease, which is consistent with our findings. Previous studies have also shown that increases in weight and BMI elevated SBP, DBP, TG, LDL-C, and GLU and reduced HDL-C, regardless of time intervals [43, 44]. Consequently, reduced obesity indices were associated with decreased estimated CVD risk. Surprisingly, this study observed stronger associations between gains in obesity indices and FRS increases in physically active participants than those with lower physical activity levels. This counterintuitive finding might be because our physically active participants were more likely to have higher obesity indices and a higher burden of diseases such as hypertension. Although physical activity could mitigate health risks for these individuals, the presence of diseases could also contribute to a higher FRS. Additionally, our study surprisingly demonstrated that reductions in obesity indices significantly decreased CVD risk while elevating all-cause and cause-specific CVD deaths, even after adjusting for FRS changes. Although challenging to explain, this result might be related to variations in estimated CVD risk over the follow-up, which we did not account for. Serial rather than baseline risk factors may better predict outcomes. Therefore, we suggest that future studies use serial measurements when exploring associations of risk factors with mortality.

Our study, using a large cohort study of general population, advances the current understanding of the associations of short-term changes in obesity indices with all-cause and CVD-specific mortality within a young population. Additionally, we revealed the protective effects of short-term reductions in obesity indices on estimated 10-year CVD risk. Importantly, standardized protocols ensured accurate obesity measurements, minimizing self-reported bias. However, limitations warrant caution. Selection bias due to inclusion criteria (Table S13) might underestimate mortality risks associated with short-term obesity changes because eligible participants were younger and healthier. This limits generalizability. Future studies adjusting for bias or focusing on ineligible participants could offer a more comprehensive picture. Recruitment within the Chinese population and employing a lower obesity threshold also necessitate careful generalization due to racial variations. Self-reported medical history and lifestyle can induce recall bias, miss undiagnosed conditions, and limit the ability to comprehensively understand the associations between short-term changes in obesity indices and cardiovascular outcomes. Accurate objective measurements (e.g., medical records, food diaries) should be considered. Limited information on medications and weight loss strategies hinders mechanistic exploration. Furthermore, CVDs were detected and classified with ICD-9 and ICD-10, which are frequently erroneous in clinical practice [45]. Finally, a lower rate of CVD deaths might reduce the statistical power to detect differences between change categories in obesity indices. Therefore, extended follow-up is crucial for studies involving young, healthy populations.

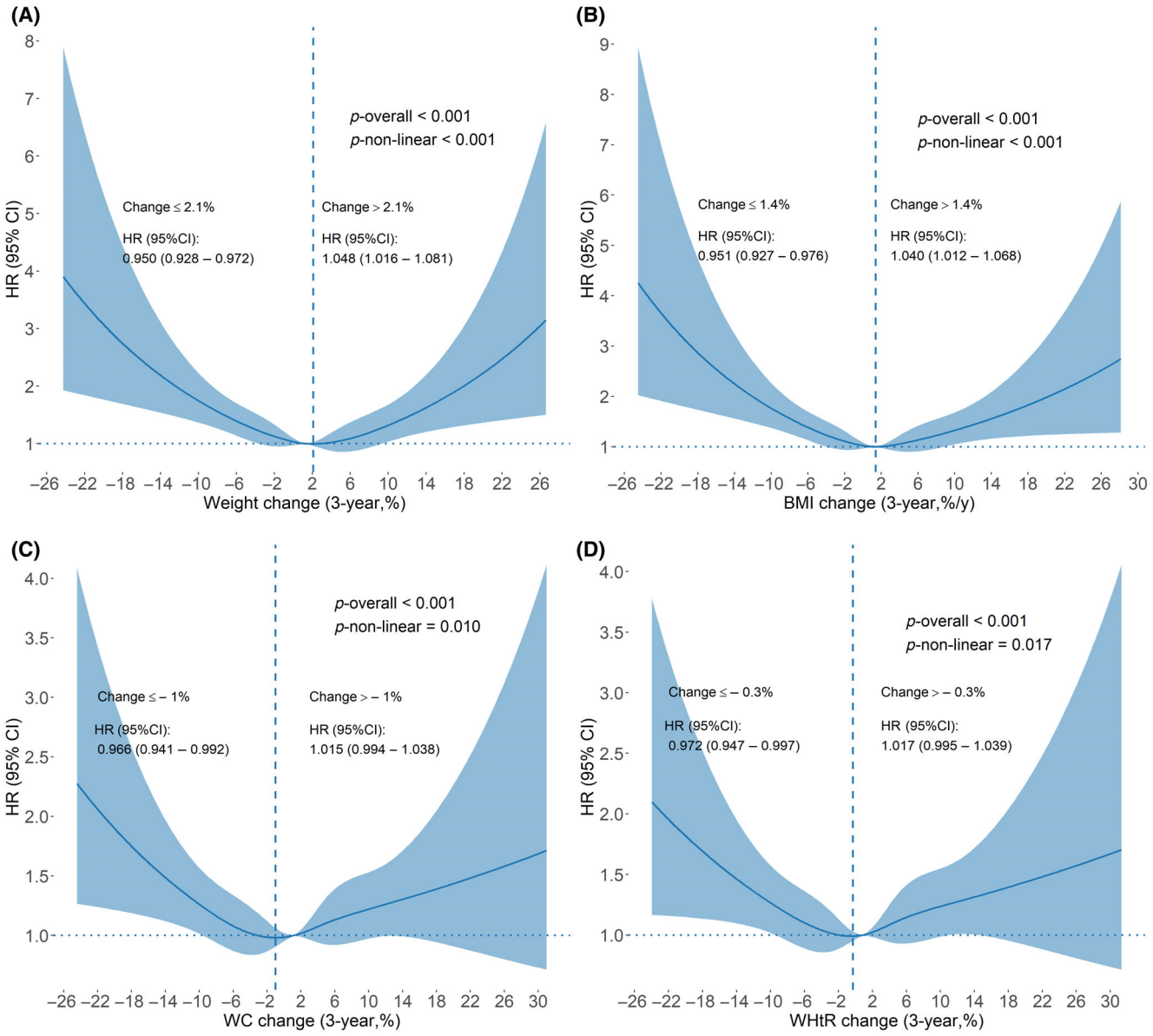

FIGURE 2 Nonlinear relationships of 3-year changes in (A) weight, (B) BMI, (C) waist circumference (WC), and (D) waist to height-ratio (WHtR) with all-cause mortality. Blue solid lines represent the calculated hazard ratios (HRs) of all-cause mortality, and shaded areas represent the 95% CIs of the calculated HRs. Vertical dashed lines are the inflection points, which are 2.1% for weight change, 1.4% for BMI change, −1% for WC change, and −0.3% for WHtR change. On the left side of the inflection point, the HRs of all-cause mortality increased with increasing reductions in weight, BMI, WC, and WHtR. On the right side of the inflection points, the HRs of all-cause mortality increased with increasing gains in weight and BMI. [Color figure can be viewed at wileyonlinelibrary.com]

CONCLUSION

This study revealed the adverse effects of short-term reductions in weight and BMI on deaths from any case and CVD, especially among adults aged over 45 years, those with normal obesity indices, or those in poor health. Faster reductions in weight and BMI worsen outcomes. Similarly, 1- and 3-year reductions in WC and WHtR elevated all-cause mortality, particularly among adults with obesity or poor health. Conversely, 3-year decreased WC and WHtR emerged as protective factors for CVD deaths. Moreover, significant reductions in obesity indices decreased estimated CVD risk. These findings suggest complex reasons behind changes, such as worsening disease or increased activity. Therefore, health care providers should discern the underlying cause of short-term losses in obesity indices. Tailoring weight management based on age, obesity, health, and CVD profiles is crucial for optimal outcomes.O

AUTHOR CONTRIBUTIONS

All authors contributed to the study's conception and design. Tsung Yu performed mortality data collection. Lyu Wang performed data

analysis and wrote the first draft of the manuscript. All authors have commented on the previous versions and approved the final draft of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declared no conflict of interest.

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SUPPORTING INFORMATION

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