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Modification of risk for all-cause and cardiovascular disease-related mortality with changes in the body mass index: a prospective cohort study with 12 years follow up

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Abstract

Background The impact of changes in body mass index (BMI) on the risk of all-cause and cardiovascular disease (CVD)-related mortality has not been extensively studied. We examined whether changes in BMI status over time are associated with risk of all-cause and CVD-related mortality.

Methods This longitudinal study recruited 90,258 adults between 2002 and 2008 from the Taiwan MJ cohort who underwent repeated BMI measurements at an interval of 3.3 years and were followed up for all-cause and CVD-related mortality over 12.1 years. Cox proportional hazard and Fine-Gray sub-distribution hazard models with death from non-CVD causes as the competing risk was used to determine the impact of changes in BMI status on the risk of all-cause or CVD-related mortality, respectively.

Results Over 1,094,606 person-years of follow-up, 2,084 participants died, including 391 (18.8%) CVD-related deaths. After adjusting for other covariates, the risks of all cause (adjusted hazard ratio [aHR], 1.86; 95% confidence interval [CI], 1.43–2.43) and CVD-related (aHR, 2.20; 95% CI, 1.24–3.93) mortalities were significantly higher in those with a BMI decrease of > 10% than in those with stable BMI. Participants with obesity at baseline who had BMI increase of > 10% during the follow-up period had a significantly higher risk of all-cause (aHR = 2.30; 95% CI:1.38–3.85) and CVD-related mortality (aHR = 3.44; 95% CI:1.33–8.89).

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Conclusions A BMI decrease of > 10% was associated with a high risk of all-cause and CVD-related mortalities. Thus, those experiencing significant BMI decreases should undergo a comprehensive evaluation to mitigate mortality risks.

Keywords Body mass index change, Cardiovascular diseases, Mortality, Cohort

Background

Body mass index (BMI) is the most commonly used measure for defining anthropometric height/weight characteristics in adults and for classifying them into weight categories (underweight, healthy weight, overweight, and obesity) [1]. Previous reports have shown that both obesity and being underweight are associated with a higher risk of mortality [2, 3].

Several studies have examined the relationship between baseline BMI and mortality risk, consistently identifying a U-shaped relationship, with increased mortality rates at both extremes of the BMI scale [4–6]. However, since BMI fluctuates over time, changes in BMI—rather than BMI at a fixed time point—may play a more significant role in determining survival [7, 8]. For instance, a low BMI may simply reflect disease-related weight reduction [9], with the BMI loss itself potentially serving as a better predictor of mortality risk. Although changes in BMI over time are of greater public health significance [7, 10], their impact on mortality risk has not been extensively studied and has yielded inconsistent findings. A Korean cohort study including 351,735 participants aged ≥ 40 years reported that > 20% increase in BMI among obese participants at baseline and > 5% decrease in BMI among underweight participants at baseline were significantly associated with a higher risk of all-cause mortality [7]. A Swedish cohort study including 882 individuals aged ≥ 70 years found that the older adults with 5% loss or 5% gain in BMI had a higher risk of all-cause mortality compared to those with stable BMI [10]. Contrarily, a Swiss cohort study of 791 adults aged ≥ 65 years found that BMI gain (defined as a positive slope of BMI change) and BMI loss (defined as a negative slope of BMI change) were not significantly associated with increased all-cause mortality risk [8]. These inconsistencies across studies may be attributed to differences in population characteristics and the definitions of BMI change [7, 8, 10].

Understanding the impact of changes in BMI on all-cause and CVD-related mortality risks would aid in devising future health promotion programs. Therefore, we conducted a population-based longitudinal cohort study to evaluate the association of changes in BMI over time with all-cause and CVD-related mortality in a large sample of adults in Taiwan.

Methods

Data source and study design

This longitudinal cohort study included individuals who participated in a self-funded, comprehensive health surveillance program offered by a private organization, the MJ Health Management Institution in Taiwan, between 2002 and 2008. The institution attracted participants from across Taiwan due to its high-quality services, operational efficiency, and conveniently located key facilities [11–13]. Program membership was mandatory, and regular members who returned for follow-up examinations in subsequent years were offered discounted fees.

The selection process for the study population is illustrated in Fig. 1. A total of 289,315 individuals participated in the MJ Health Surveillance Program between 2002 and 2008. Among them, 115,966 participants who underwent repeated examinations were considered for inclusion. Individuals younger than 18 years ($n = 2,287$) were excluded. To minimize the potential for reverse causality, we excluded participants with a history of CVD prior to their first health screening ($n = 3,036$), as well as those who developed CVD between their first and last screening ($n = 2,583$). Participants with incomplete covariate data ($n = 17,802$) were also excluded. Ultimately, 90,258 individuals were included in the final study cohort. The last screening date on which any changes in BMI could be determined was considered the cohort entry date. At the last screening date, baseline characteristics were collected and follow-up was initiated.

All participants were followed from the cohort entry date until death or December 31, 2018, whichever occurred first. Deaths were confirmed using Taiwan's national death certificate database [14].

Data collection and statement of ethics

All participants in this cohort provided signed consent authorizing the MJ Health Management Institution to process data generated from their medical screenings. As part of the MJ Health Surveillance Program, participants were instructed to complete a self-administered questionnaire covering lifestyle factors and medical history. Each individual underwent a standardized panel of medical assessments, including body measurements, physical examinations, and blood tests. Fasting blood samples were collected and analyzed following an overnight fast.

The study protocol was approved by the Research Ethics Committee of National Changhua University, Taiwan (No. NCUEREC-108-072), which also waived the requirement for additional informed consent. All procedures were conducted in accordance with relevant national and institutional guidelines, as well as the principles outlined in the Declaration of Helsinki.

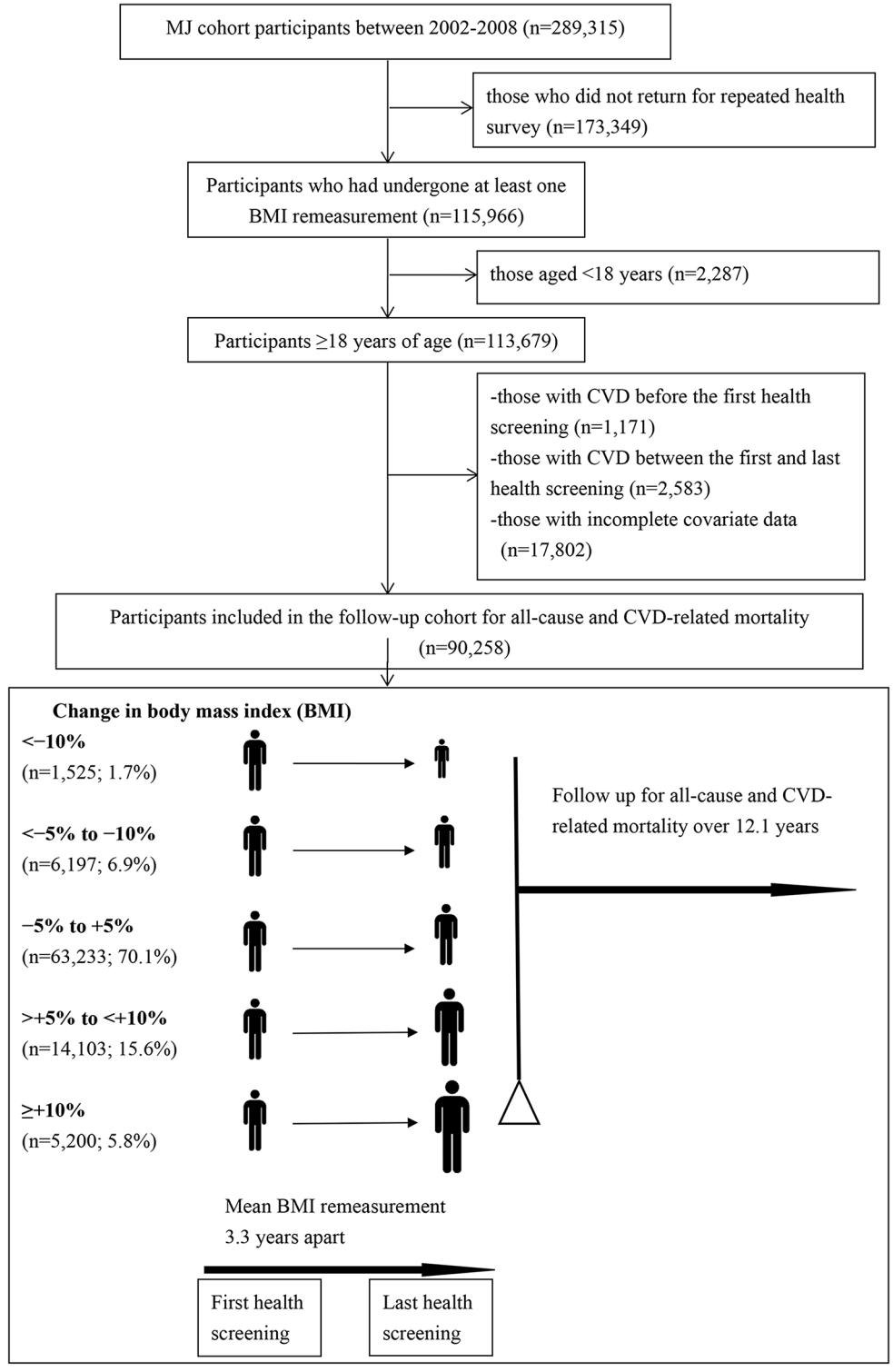

Fig. 1 Flow diagram demonstrating the selection of the study population. Abbreviations: BMI, metabolic syndrome; CVD, cardiovascular disease

Analyzed variables

The outcome variables were all-cause mortality and CVD-related mortality, both confirmed using Taiwan's national death certificate database [14]. In Taiwan, when a patient dies, the law mandates that a physician issues and registers the death certificate in accordance with the International Classification of Diseases (ICD), 9th or 10th revision. Trained medical registrars at the central office

of the National Death Certification Registry review and code all death certificates. As a result, the cause-of-death coding in Taiwan is considered highly accurate [14].

CVD-related mortality among study participants was defined as death due to coronary heart disease (ICD-9 codes 410–414, 420–429; ICD-10 codes I20–I25), stroke (ICD-9 codes 430–438; ICD-10 codes I60–I69), or other circulatory diseases (ICD-9 codes 390–392, 393–398, 401–405, and 440; ICD-10 codes I10–I15, I01–I02.0, I05–I09, I27, I30–I52, I70, and I71), as previously described [11].

Measurement of BMI change

The main exposure variable was the change in BMI. The BMI of study participants was measured by trained nurses during each health screening. It was calculated by dividing their weight in kilograms by the square of their height in meters. The BMI change was expressed as percentage, which was calculated as the change in BMI between the first and last health-screening divided by the first health-screening BMI.

Following previous studies, we defined stable BMI as a change of within 5% during the follow-up period [7, 10]. We further categorized BMI changes into five groups based on the percentage of change: >10% decrease, 5–10% decrease, stable BMI (< 5% change), 5–10% increase, and > 10% increase.

Confounding factors

The control variables in this study included sociodemographic characteristics (age, sex, birth cohort, education level, smoking status, and alcohol consumption), as well as fruit and vegetable intake, leisure-time physical activity (LTPA), occupational physical activity, and the Charlson Comorbidity Index (CCI) score. Birth cohorts were categorized as: <1940, 1940–1949, 1950–1959, 1960–1969, 1970–1979, and ≥ 1980. Education level was grouped into junior high school or lower, senior high school, and university or higher. Alcohol consumption was classified as none/occasional, once per week, or former drinker. Smoking status was categorized as never, current, or former smoker. Fruit and vegetable intake was divided into three categories: <3 servings, 3–4 servings, and ≥ 5 servings per day.

LTPA in the MJ Cohort was calculated using three closed-ended questions regarding the type of activity, intensity (light [2.5 metabolic equivalents of tasks, METs], moderate [4.5 METs], medium-vigorous [6.5 METs], or high-vigorous [8.5 METs]), and the duration spent on each activity [11, 15]. The activity intensity (MET) was multiplied by the duration (hours) to calculate the total volume of LTPA in MET-hours. Participants were then categorized into four groups: inactive (< 1 MET-hour), low (1–7.49 MET-hours), moderate (7.5–14.99 MET-hours), and high (≥ 15 MET-hours) [12] Occupational physical activity was categorized as light (mostly sedentary), moderate (involving repetitive motions while sitting or standing, such as in manufacturing), and heavy (involving heavy lifting, loading, or moving loads). The CCI score was used as an index of the burden of underlying comorbid conditions and was classified as 0, 1, or ≥ 2 [16].

Statistical analyses

Baseline characteristics of BMI change in the groups were compared using the Chi-square test for categorical variables and one-way analysis of variance (ANOVA) for continuous variables, as appropriate.

The unadjusted all-cause and CVD-related mortality per 1000 person-years were calculated among individuals with different BMI changes. The cumulative incidence probabilities of all-cause and CVD-related mortality were plotted using Kaplan-Meier curves and compared between the five BMI groups using the log-rank test.

Multivariable Cox proportional hazards model was used to determine the association between change in BMI (reference group: stable BMI with < 5% change) and the risk of all-cause mortality after adjusting for sociodemographic characteristics, lifestyle behaviors, and CCI score. Fine-Gray sub-distribution hazard model with death from non-CVD causes as the competing risk was used to determine the association between change in BMI and the risk of CVD mortality [17]. Models in the multivariate analysis were adjusted as follows: model 1 was adjusted for age (years), sex, birth cohort, and BMI at the last health screening; and model 2 was adjusted for model 1, and additionally adjusted for level of education, marital status, smoking status, alcohol consumption, fruit and vegetable intake, baseline LTPA, overall level of occupational physical activity, and CCI score.

To examine the robustness of our primary findings, sensitivity analyses were conducted after stratifying the participants based on age and BMI at the first health screening. BMI in study participants at the first health screening was categorized as underweight (< 18.5 kg/m^2), normal (18.5–23.9 kg/m^2), overweight (24–26.9 kg/m^2), and obese (≥ 27 kg/m^2) [18]. All data management and analyses were performed using the SAS software (version 9.4; SAS Institute, Cary, NC, USA).

Results

Baseline characteristics of the study population

Among the 90,258 participants, the overall mean (standard deviation [SD]) age was 42.0 (11.6) years, and 50.8% of the participants were male. The mean (SD) time elapsed before BMI remeasurement was 3.3 (1.7) years, and the duration of follow-up for all-cause and CVD-related mortality was 12.1 (1.6) years.

Table 1 shows the characteristics of the study population according to changes in BMI. Approximately 1.7%, 6.9%, 70.1%, 15.6%, and 5.8% of the study participants were classified into > 10% decrease in BMI, 5–10% decrease in BMI, stable BMI with < 5% change, 5–10% increase in BMI, and > 10% increase in BMI groups, respectively. Compared to participants with a stable BMI with < 5% change, those with a 5% increase in BMI were younger and more likely to be female. Moreover, compared to participants with stable BMI, those with > 10% increase in BMI had the lowest proportion of LTPA ≥ 15 MET-h/week and heavy occupational PA, whereas those with > 10% decrease in BMI had highest proportion of LTPA ≥ 15 MET-h/week and heavy occupational PA.

Cumulative rate of all-cause and CVD-related mortality

Over the 1,094,606 person-years of follow-up, 2,084 participants died, including 391 (18.8%) CVD-related deaths. The crude rates of all-cause mortality per 1,000 person-years differed in the five BMI change groups ($P < 0.001$) as follows: participants with > 10% decrease in BMI, 3.13; those with 5–10% decrease in BMI, 2.76; participants with stable BMI with < 5% change, 1.97; those with 5–10% increase in BMI, 1.30; and participants with > 10% increase in BMI, 1.37. Between-group difference in the incidence rate of CVD-related mortality per 1,000 person-years ($P < 0.001$) was as follows: participants with > 10% decrease in BMI, 0.66; participants with 5–10% decrease in BMI, 0.50; participants with stable BMI with < 5% change, 0.37; participants with 5–10% increase in BMI, 0.26; and participants with > 10% increase in BMI, 0.26. The time to all-cause and CVD-related mortality differed significantly among the five BMI groups (log-rank test, $P < 0.001$; Fig. 2).

Association between BMI changes and the risk of all-cause mortality

The association between changes in BMI and risk of all-cause mortality is shown in Table 2. After adjusting for sociodemographic characteristics, lifestyle behaviors, and the CCI score, compared to participants with stable BMI, a higher risk of all-cause mortality was found in those with > 10% decrease in BMI (adjusted hazard ratio [AHR] = 1.86; 95% CI:1.43–2.43), those with 5–10% decrease in BMI (AHR = 1.33; 95% CI:1.15–1.54), and those with > 10% increase in BMI (AHR = 1.36; 95% CI:1.09–1.70).

Association between BMI changes and the risk of CVD-related mortality

Table 3 shows the association between changes in BMI and the risk of CVD-related mortality. After adjusting for other covariates, participants with > 10% decrease in BMI during the follow-up period had a significantly higher risk of CVD-related mortality (AHR = 2.20; 95% CI:1.24–3.93) than those with stable BMI.

Subgroup analysis for the association of BMI change with all-cause and CVD-related mortality after stratifying study participants by baseline BMI

Figure 3 shows the results of sensitivity analysis for the association of BMI change with all-cause and CVD-related mortality after stratifying the study participants by baseline BMI. Among the participants with normal weight at the first health screening, those with > 10% decrease in BMI during the follow-up period had a significantly higher risk of all-cause (AHR = 2.53; 95% CI:1.71–3.72) and CVD-related mortality (AHR = 4.49; 95% CI:1.96–10.31) compared to individuals with stable BMI. Moreover, among participants with obesity at the first health screening, participants who gained > 10% BMI during the follow-up period had a significantly higher risk of all-cause (AHR = 2.24; 95% CI:1.34–3.75) and CVD-related mortality (AHR = 3.26; 95% CI:1.26–8.44) than individuals with stable BMI.

Subgroup analysis for the association of BMI change with all-cause and CVD-related mortality after stratifying study participants by age and baseline BMI

Supplementary Fig. S1 shows the results of the subgroup analysis of the association of BMI change with all-cause and CVD-related mortality after stratifying the study participants by age and baseline BMI. Among participants aged 18–49 years or ≥ 50 years with normal weight at the first health screening, those with > 10% decrease in BMI during the follow-up period had a significantly higher risk of all-cause mortality than individuals with stable BMI. Moreover, among participants aged 18–49 years or ≥ 50 years with obesity at the first health screening, those with > 10% increase in BMI during the study follow-up period had a significantly higher risk of all-cause mortality than individuals with stable BMI.

Discussion

This prospective cohort study found that a > 10% decrease in BMI over an average follow-up of 12.1 years was associated with a higher risk of all-cause and CVD-related mortality. Considering participants' baseline BMI, individuals who were obese at baseline and experienced a > 10% increase in BMI had a significantly higher risk of all-cause and CVD-related mortality.

We found that individuals who had a BMI loss of > 10% were at high risk of all-cause and CVD-related mortality. An increased mortality risk in individuals with a > 10% decrease in BMI may be driven by underlying diseases, including malignancies and diabetes. A previous study that enrolled 2,677 individuals with unintentional BMI loss found that malignancies and diabetes were

Table 1 Characteristics of the study participants according to changes in BMI

Characteristics	Total ($n=90,258$)	Body mass index change (kg/m2) *n* (%)†					*P* value
		<−10%	<−5% to −10%	−5% to +5%	>+5% to <+10%	≥+10%	
		($n=1,525$)	($n=6,197$)	($n=63,233$)	($n=14,103$)	($n=5,200$)	
Clinical and demographic characteristics							
Age, years							
Mean ± SD	42.0 ± 11.6	41.0 ± 12.4	43.4 ± 12.6	42.8 ± 11.6	39.9 ± 10.5	37.0 ± 9.4	< 0.001
18–49	43,983 (48.7)	832 (54.6)	2785 (44.9)	28,788 (45.5)	7972 (56.5)	3606 (69.4)	< 0.001
≥50	46,275 (51.3)	693 (45.4)	3412 (55.1)	34,445 (54.5)	6131 (43.5)	1594 (30.7)	
Birth cohort							
<1940	3201 (3.6)	70 (4.6)	289 (4.7)	2431 (3.8)	332 (2.4)	79 (1.5)	< 0.001
1940–1949	7276 (8.1)	100 (6.6)	678 (10.9)	5642 (8.9)	706 (5.0)	150 (2.9)	
1950–1959	14,384 (15.9)	221 (14.5)	1160 (18.7)	11,056 (17.5)	1613 (11.4)	334 (6.4)	
1960–1969	29,072 (32.2)	426 (27.9)	1734 (28.0)	20,808 (32.9)	4709 (33.4)	1395 (26.8)	
1970–1979	31,187 (34.6)	559 (36.7)	1886 (30.4)	20,184 (31.9)	5845 (41.5)	2713 (52.2)	
≥ 1980	5138 (5.7)	149 (9.8)	450 (7.3)	3112 (4.9)	898 (6.4)	529 (10.2)	
Sex							
Female	44,394 (49.2)	908 (59.5)	3394 (54.8)	29,843 (47.2)	7310 (51.8)	2939 (56.5)	< 0.001
Male	45,864 (50.8)	617 (40.5)	2803 (45.2)	33,390 (52.8)	6793 (48.2)	2261 (43.5)	
BMI group (kg/m^2) at the first health screening							
Normal (18.5–23.9)	51,457 (57.0)	583 (38.2)	3262 (52.6)	35,572 (56.3)	8670 (61.5)	3370 (64.8)	< 0.001
Underweight (< 18.5)	8020 (8.9)	22 (1.4)	240 (3.9)	5140 (8.1)	1773 (12.6)	845 (16.3)	
Overweight (24–26.9)	20,545 (22.8)	445 (29.2)	1719 (27.7)	15,210 (24.1)	2497 (17.7)	674 (12.9)	
Obese (≥ 27)	10,236 (11.3)	475 (31.2)	976 (15.8)	7311 (11.6)	1163 (8.3)	311 (6.0)	
BMI group (kg/m^2) at the last health screening							
Normal (18.5–23.9)	50,339 (55.8)	943 (61.8)	3960 (63.9)	35,299 (55.8)	7667 (54.4)	2470 (47.5)	< 0.001
Underweight (< 18.5)	6404 (7.1)	216 (14.2)	721 (11.6)	4782 (7.6)	579 (4.1)	106 (2.0)	
Overweight (24–26.9)	21,829 (24.2)	239 (15.7)	1074 (17.3)	15,443 (24.4)	3572 (25.3)	1501 (28.9)	
Obese (≥ 27)	11,686 (13.0)	127 (8.3)	442 (7.1)	7709 (12.2)	2285 (16.2)	1123 (21.6)	
Level of education							
Junior high school or less	10,904 (12.1)	199 (13.1)	974 (15.7)	8204 (13.0)	1237 (8.8)	290 (5.6)	< 0.001
Senior high school	38,920 (43.1)	677 (44.4)	2579 (41.6)	27,007 (42.7)	6255 (44.4)	2402 (46.2)	
University or higher	40,434 (44.8)	649 (42.6)	2644 (42.7)	28,022 (44.3)	6611 (46.9)	2508 (48.2)	
Marital status							
Never married	19,535 (21.6)	425 (27.9)	1350 (21.8)	12,725 (20.1)	3492 (24.8)	1543 (29.7)	< 0.001
Married/cohabiting	65,266 (72.3)	983 (64.5)	4366 (70.5)	46,661 (73.8)	9834 (69.7)	3422 (65.8)	
Other†	5457 (6.1)	117 (7.7)	481 (7.8)	3847 (6.1)	777 (5.5)	235 (4.5)	
Smoking status							
Never	65,234 (72.3)	1133 (74.3)	4652 (75.1)	45,482 (71.9)	10,209 (72.4)	3758 (72.3)	< 0.001
Current	20,411 (22.6)	326 (21.4)	1284 (20.7)	14,546 (23.0)	3139 (22.3)	1116 (21.5)	
Former	4613 (5.1)	66 (4.3)	261 (4.2)	3205 (5.1)	755 (5.4)	326 (6.3)	
Alcohol consumption							
None/Occasional	75,324 (83.5)	1326 (87.0)	5304 (85.6)	52,369 (82.8)	11,867 (84.2)	4458 (85.7)	< 0.001
≥ 1/week	13,184 (14.6)	154 (10.1)	713 (11.5)	9652 (15.3)	2012 (14.3)	653 (12.6)	
Former	1750 (1.9)	45 (3.0)	180 (2.9)	1212 (1.9)	224 (1.6)	89 (1.7)	
Fruit and Vegetable intake							
< 3 serves/day	27,745 (30.7)	442 (29.0)	1812 (29.2)	18,865 (29.8)	4690 (33.3)	1936 (37.2)	< 0.001
3–4 serves/day	49,734 (55.1)	821 (53.8)	3342 (53.9)	35,381 (56.0)	7544 (53.5)	2646 (50.9)	
≥ 5 serves/day	12,779 (14.2)	262 (17.2)	1043 (16.8)	8987 (14.2)	1869 (13.3)	618 (11.9)	
Baseline LTPA (MET-h/week)							
< 1	4758 (5.3)	91 (6.0)	295 (4.8)	3515 (5.6)	661 (4.7)	196 (3.8)	< 0.001
1-7.49	56,069 (62.1)	855 (56.1)	3540 (57.1)	38,101 (60.3)	9651 (68.4)	3922 (75.4)	
7.5-14.99	13,887 (15.4)	233 (15.3)	1043 (16.8)	10,159 (16.1)	1885 (13.4)	567 (10.9)	
≥ 15	15,544 (17.2)	346 (22.7)	1319 (21.3)	11,458 (18.1)	1906 (13.5)	515 (9.9)	

Table 1 (continued)

Characteristics	Total (*n* = 90,258)	Body mass index change (kg/m2) *n* (%)†					*P* value
		<−10%	<−5% to −10%	−5% to +5%	>+5% to <+10%	≥+10%	
		(*n* = 1,525)	(*n* = 6,197)	(*n* = 63,233)	(*n* = 14,103)	(*n* = 5,200)	
Intensity of occupational PA							
Light	60,828 (67.4)	1042 (68.3)	4091 (66.0)	42,354 (67.0)	9716 (68.9)	3625 (69.7)	< 0.001
Moderate	22,094 (24.5)	360 (23.6)	1601 (25.8)	15,552 (24.6)	3350 (23.8)	1231 (23.7)	
Heavy	7336 (8.1)	123 (8.1)	505 (8.2)	5327 (8.4)	1037 (7.4)	344 (6.6)	
Charlson comorbidity index							
0	17,286 (19.2)	284 (18.6)	1075 (17.4)	11,875 (18.8)	2907 (20.6)	1145 (22.0)	< 0.001
1	22,532 (25.0)	382 (25.1)	1484 (24.0)	15,445 (24.4)	3753 (26.6)	1468 (28.2)	
≥2	50,440 (55.9)	859 (56.3)	3638 (58.7)	35,913 (56.8)	7443 (52.8)	2587 (49.8)	
All-cause mortality	2084 (2.3)	57 (3.7)	206 (3.3)	1517 (2.4)	220 (1.6)	84 (1.6)	< 0.001
CVD-related mortality	391 (0.4)	12 (0.8)	37 (0.6)	282 (0.5)	44 (0.3)	16 (0.3)	0.004
Follow-up years, mean (SD)	12.1 ± 1.6	12.0 ± 1.9	12.0 ± 1.7	12.2 ± 1.7	12.0 ± 1.4	12.0 ± 1.3	< 0.001

BMI, body mass index; SD, standard deviation; LTPA, leisure time physical activity; MET, metabolic equivalent of task; PA, physical activity; CVD, cardiovascular disease; †Unless stated otherwise

significant causes of excess loss in BMI [9], which could increase the risk of all-cause and CVD-related mortality. Our findings suggest that individuals experiencing a significant reduction in BMI should undergo a comprehensive evaluation and seek treatment to reduce the risks of all-cause and CVD-related mortality.

This study found that individuals who were obese at baseline and experienced a > 10% increase in BMI during the follow-up period had a higher risk of all-cause and CVD-related mortality compared to those with a stable BMI. Obesity-induced chronic inflammation and insulin resistance may explain the higher risk of all-cause and CVD-related mortality among individuals with obesity with a 10% increase in BMI. Chronic inflammation and insulin resistance are the major contributors to the pathogenesis of obesity-related CVD [19, 20]. A previous meta-analysis reported that obesity-related chronic inflammation could enhance the release of various cytokines, including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) [21]. Roytblat et al. demostrated that obese individuals had significantly higher IL-6 levels than those with normal weight (7.69 vs. 1.28 pg/mL, $p < 0.05$) [22]. High levels of IL-6 can stimulate the expression of vascular cell adhesion molecules and activate the renin-angiotensinogen aldosterone pathway, leading to vascular wall atherosclerosis and subsequent CVD [23]. Furthermore, obesity-related increases in TNF-α [24] can inactivate insulin receptors and impair insulin signaling [25], which results in the development of insulin resistance [26]. Obesity-induced insulin resistance could lead to higher serum viscosity and creation of a prothrombotic state via an increase in circulating cholesterol esters and free fatty acids [19, 27]. which could lead to a higher risk of CVD and all-cause mortality. As obesity is associated with poor health outcomes [28], our study suggests that individuals with obesity should adopt measures to lose body weight to reduce the risk of all-cause and CVD-related mortality.

Our study had several strengths. First, this cohort study had the long follow-up period with repeated BMI measurements to determine the effect of dynamic changes in BMI on the risk of all-cause and CVD-related mortality. Moreover, since our study had comprehensive information regarding mortality due to the linking of the MJ cohort with the death certificate database of Taiwan [14], we used the Fine-Gray sub-distribution method [17] with death as the competing risk, to precisely examine the association between the change in BMI and the risk of CVD-related mortality.

However, some limitations should be considered when interpreting the findings of this large cohort study. First, whether the decrease in BMI among study participants was intentional or unintentional is unknown. Although intentional BMI loss may have a different origin than unintentional BMI loss, a previous meta-analysis showed that the evidence for a positive effect of intentional BMI loss on mortality was weak [29]. Second, although BMI is a widely used measure of obesity [1], Thomas et al. (2013) [30] and Park et al. (2018) [31] proposed the body roundness index (BRI) and the weight-adjusted waist index (WWI) to estimate visceral obesity and fat mass, respectively. Previous studies have shown that, compared to BMI, BRI has a better predictive value for CVD risk [32] but a similar predictive value for all-cause mortality risk [33]. Additionally, higher WWI levels (≥ 11.2 cm/√kg) were associated with an increased risk of all-cause and CVD-related mortality [34]. The effect of changes in BRI and WWI on these mortality risks should be investigated in future studies. Third, information on individuals' income levels and the use of antihypertensive drugs was not available in the Taiwan MJ Health Surveillance dataset. Fourth, participants in the Taiwan MJ Health

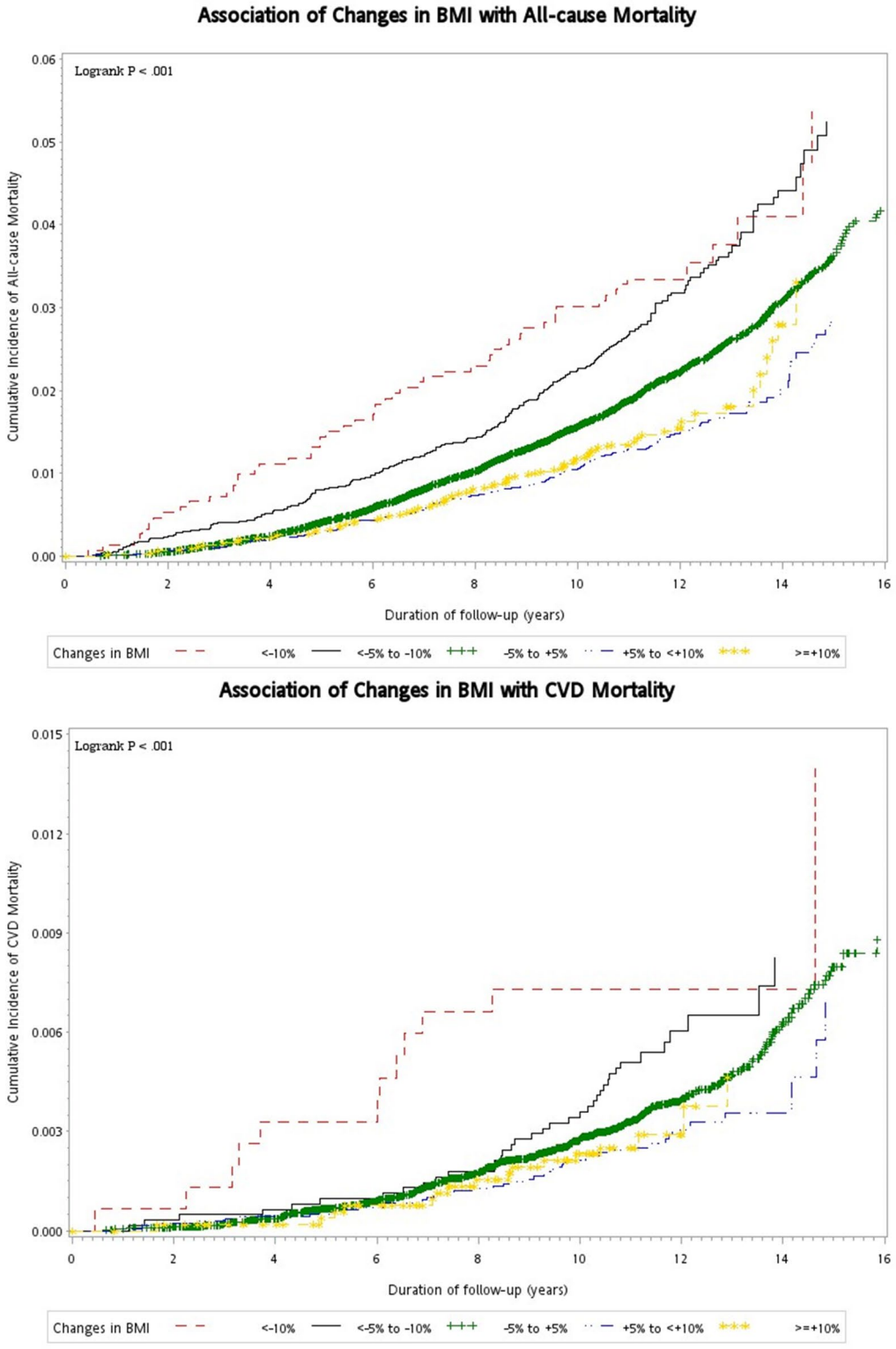

Fig. 2 Kaplan–Meier curves of the time to the events of all-cause and CVD-related mortality. Abbreviations: BMI, metabolic syndrome; CVD, cardiovascular disease

Table 2 Univariate and multivariate analysis for the association between BMI changes and the risk for all-cause mortality

Variables	Number of participants	All-cause mortality	Univariate	Multivariate analysis	
		n (%)	HR (95%CI)	AHR (95%CI)	
				Model 1	Model 2
BMI change					
<−10%	1,525	57 (3.7)	1.62 (1.24–2.10)	1.89 (1.45–2.46)	1.80 (1.38–2.35)
<−5% to − 10%	6,197	206 (3.3)	1.43 (1.23–1.65)	1.36 (1.18–1.58)	1.31 (1.13–1.52)
−5% to + 5%	63,233	1,517 (2.4)	1	1	1
>+5% to < + 10%	14,103	220 (1.6)	0.68 (0.59–0.79)	0.97 (0.84–1.12)	0.94 (0.82–1.09)
≥+10%	5,200	84 (1.6)	0.73 (0.59–0.91)	1.42 (1.13–1.77)	1.35 (1.08–1.69)
BMI group (kg/m^2) at the last health screening					
Normal (18.5–23.9)	51,457	985 (1.9)	1		1
Underweight (< 18.5)	8020	105 (1.3)	0.68 (0.55–0.83)	1.56 (1.28–1.90)	1.57 (1.29–1.91)
Overweight (24–26.9)	20,545	591 (2.9)	1.51 (1.36–1.67)	0.96 (0.87–1.07)	0.91 (0.82–1.02)
Obese (≥ 27)	10,236	403 (3.9)	2.06 (1.83–2.31)	1.37 (1.22–1.54)	1.19 (1.06–1.34)
Clinical and demographic characteristics					
Age, years					
18–49	43,983	263 (12.6)	1		
≥50	46,275	1821 (87.4)	6.95 (6.10–7.91)	1.47 (1.14–1.89)	1.38 (1.07–1.78)
Birth cohort					
<1940	3201	719 (34.5)	1	1	1
1940–1949	7276	486 (23.3)	0.29 (0.26–0.32)	0.29 (0.26–0.33)	0.34 (0.30–0.38)
1950–1959	14,384	354 (17.0)	0.11 (0.09–0.12)	0.11 (0.09–0.12)	0.15 (0.13–0.18)
1960–1969	29,072	340 (16.3)	0.05 (0.04–0.06)	0.05 (0.05–0.06)	0.10 (0.08–0.11)
1970–1979	31,187	169 (8.1)	0.02 (0.02–0.03)	0.03 (0.02–0.04)	0.06 (0.05–0.09)
≥ 1980	5138	16 (0.8)	0.01 (0.01–0.02)	0.02 (0.01–0.03)	0.04 (0.02–0.07)
Sex					
Female	44,394	852 (40.9)	1		
Male	45,864	1232 (59.1)	1.41 (1.29–1.54)	1.61 (1.48–1.77)	1.66 (1.49–1.86)
Level of education					
Junior high school or less	10,904	982 (47.1)	1		
Senior high school	38,920	691 (33.2)	0.20 (0.18–0.22)		0.81 (0.72–0.92)
University or higher	40,434	411 (19.7)	0.11 (0.10–0.13)		0.61 (0.53–0.71)
Marital status					
Never married	19,535	128 (6.1)	1		
Married/cohabiting	65,266	1554 (74.6)	3.76 (3.14–4.50)		0.87 (0.70–1.08)
Other[†]	5457	402 (19.3)	11.80 (9.67–14.39)		1.22 (0.96–1.55)
Smoking status					
Never	65,234	1314 (63.1)	1		
Current	20,411	596 (28.6)	1.42 (1.29–1.57)		1.42 (1.27–1.58)
Former	4613	174 (8.4)	1.91 (1.63–2.23)		1.18 (1.00-1.40)
Alcohol consumption					
None/Occasional	75,324	1574 (75.5)	1		
≥ 1/week	13,184	400 (19.2)	1.46 (1.31–1.63)		1.06 (0.94–1.19)
Former	1750	110 (5.3)	2.99 (2.47–3.63)		1.27 (1.04–1.56)
Fruit and Vegetable intake					
< 3 serves/day	27,745	647 (31.1)	1		
3–4 serves/day	49,734	1122 (53.8)	0.98 (0.89–1.08)		0.91 (0.82-1.00)
≥ 5 serves/day	12,779	315 (15.1)	1.09 (0.95–1.24)		0.95 (0.83–1.09)
Baseline LTPA (MET-h/week)					
< 1	4758	176 (8.5)	1		
1-7.49	56,069	1063 (51.0)	0.68 (0.58–0.80)		1.02 (0.86–1.20)
7.5-14.99	13,887	441 (21.2)	1.14 (0.95–1.35)		0.91 (0.76–1.09)
≥ 15	15,544	404 (19.4)	0.92 (0.77–1.10)		0.81 (0.68–0.97)

Table 2 (continued)

Variables	Number of participants	All-cause mortality	Univariate	Multivariate analysis	
		n (%)	HR (95%CI)	AHR (95%CI)	
				Model 1	Model 2
Intensity of occupational PA					
Light	60,828	1326 (63.6)	1		
Moderate	22,094	492 (23.6)	1.03 (0.93–1.14)		0.88 (0.79–0.98)
Heavy	7336	266 (12.8)	1.68 (1.47–1.92)		0.96 (0.84–1.11)
Charlson comorbidity index					
0	17,286	69 (3.3)	1		
1	22,532	95 (4.6)	1.06 (0.78–1.44)		0.88 (0.65–1.20)
≥2	50,440	1920 (92.1)	9.57 (7.53–12.17)		3.83 (3.00-4.90)

Model 1, adjusted for age (y), sex (male and female), birth cohort, and BMI status at the last health screening

Model 2, additionally adjusted for level of education, marital status, smoking status, alcohol consumption, fruit and vegetable intake, Baseline leisure time physical activity, Intensity of occupational PA, and Charlson comorbidity index

[†]Others: widowed, divorced, separated, or single parent. BMI, body mass index; AHR, adjusted hazard ratio; CI, confident interval; LTPA, leisure time physical activity; MET, metabolic equivalent of task; PA, physical activity

Table 3 Univariate and multivariate analysis for the association between BMI changes and the risk for CVD-related mortality

Variables	Number of participants	CVD-related mortality	Univariate	Multivariate analysis	
		n (%)	HR (95%CI)	AHR (95%CI)	
				Model 1	Model 2
BMI change					
<−10%	1525	12 (0.8)	1.84 (1.03–3.27)	2.29 (1.28–4.11)	2.22 (1.24–3.98)
<−5% to − 10%	6197	37 (0.6)	1.38 (0.98–1.95)	1.40 (0.99–1.98)	1.33 (0.94–1.89)
−5% to + 5%	63,233	282 (0.5)	1		1
>+5% to < + 10%	14,103	44 (0.3)	0.74 (0.54–1.02)	1.09 (0.79–1.50)	1.06 (0.77–1.46)
≥+10%	5200	16 (0.3)	0.77 (0.46–1.27)	1.56 (0.94–2.60)	1.45 (0.87–2.41)
BMI group (kg/m^2) at the last health screening					
Normal (18.5–23.9)	51,457	160 (0.3)	1		
Underweight (< 18.5)	8020	23 (0.3)	0.91 (0.59–1.41)	2.25 (1.44–3.52)	2.21 (1.41–3.45)
Overweight (24–26.9)	20,545	122 (0.6)	1.91 (1.51–2.42)	1.25 (0.98–1.59)	1.22 (0.96–1.55)
Obese (≥ 27)	10,236	86 (0.8)	2.70 (2.08–3.51)	1.98 (1.53–2.56)	1.83 (1.41–2.38)

Model 1, adjusted for age (y), sex (male and female), birth cohort, and BMI status at the last health screening

Model 2, additionally adjusted for level of education, marital status, smoking status, alcohol consumption, fruit and vegetable intake, Baseline leisure time physical activity, Intensity of occupational PA, and Charlson comorbidity inde

BMI, body mass index; CVD, cardiovascular disease; AHR, adjusted hazard ratio; CI, confident interval

Examination Program are not required to undergo annual health examinations repeatedly. Future studies can collect BMI data at annual interval and confirm the finding from our study. Finally, the external validity of our findings may be a concern because almost all the participants in this cohort study were Taiwanese. Therefore, the generalizability of our results to non-Asian ethnic groups requires further investigation.

Conclusion

This prospective cohort study found that a BMI decrease of more than 10% was associated with a higher risk of all-cause and CVD-related mortality. Additionally, individuals who were obese at baseline and experienced a > 10% increase in BMI had a significantly higher risk of all-cause and CVD-related mortality. These findings highlight the need for comprehensive evaluations of individuals experiencing significant BMI reductions to mitigate mortality risks. Furthermore, those with excess adiposity should adopt proactive measures to manage their weight and reduce the risk of premature mortality.

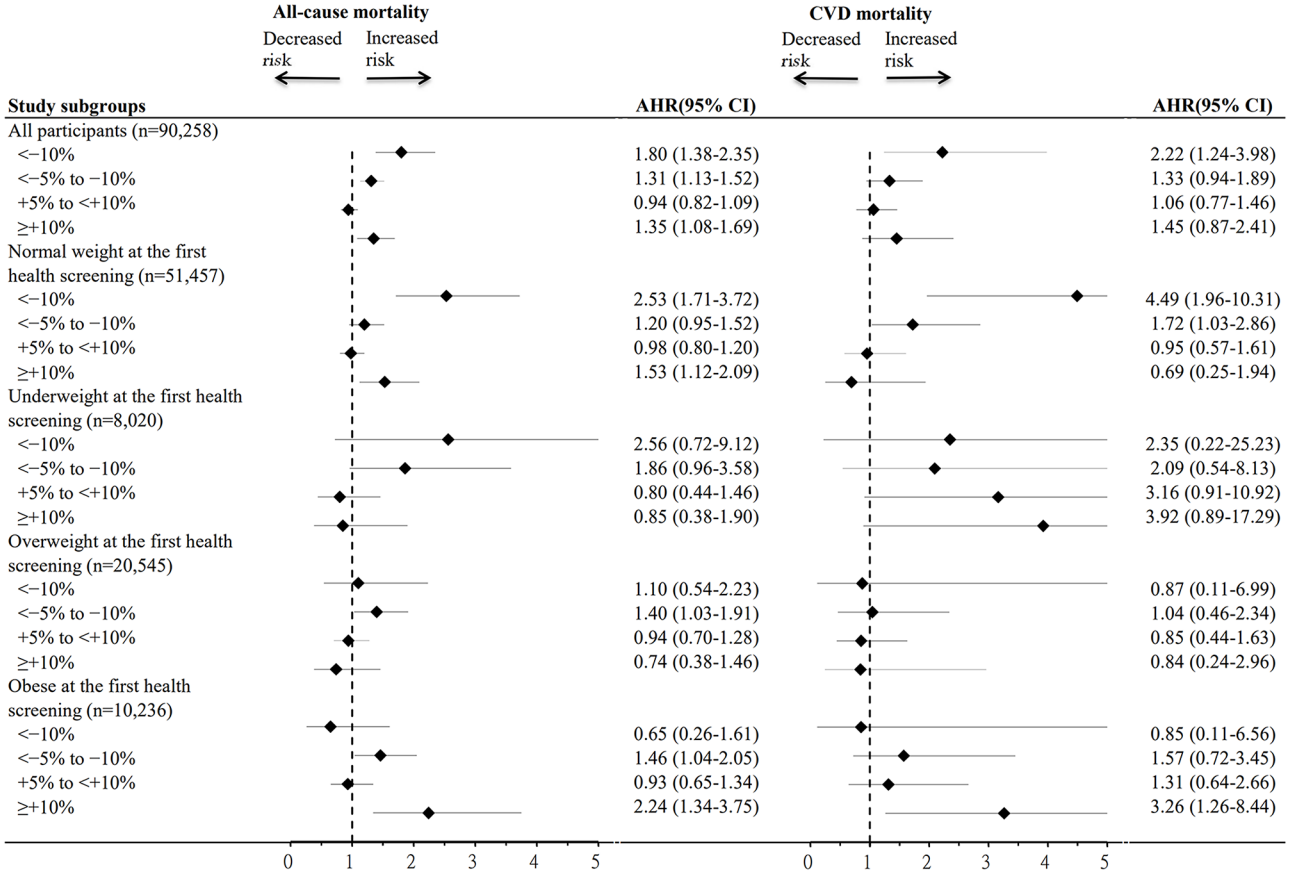

Fig. 3 Subgroup analysis for the association of BMI change with all-cause and CVD-related mortality after stratifying the study participants by baseline BMI. Abbreviations: BMI, metabolic syndrome; CVD, cardiovascular disease; AHR, adjusted hazard ratio; CI, confidence interval

Abbreviations

BMI	Body mass index
CVD	Cardiovascular disease
HR	Hazard ratio
CI	Confidence interval
ICD	International Classification of Diseases
LTPA	Leisure time physical activity
CCI	Charlson Comorbidity Index
MET	Metabolic equivalent of task

Supplementary Information

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Supplementary Material 1

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Author contributions

YJL, YFY, LJC, LFH, PWK, and ES made substantial contributions to the conception and design of the study. LJC, MNA, EIE, RKB, PWK, and ES acquired the data. YJL, YFY, LJC, MNA, EIE, RKB, PWK, and ES contributed to the data interpretation, and the drafting of the manuscript. All authors made critical revisions to the manuscript and approved the final version.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The Research Ethics Committee of National Changhua University, Taiwan (no. NCUEREC-108-072) approved the study protocol and waived the requirement for informed consent. All related procedures were performed in accordance with the relevant national and institutional guidelines, as well as those stipulated in the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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