Two-Year Weight Loss but Not Body Mass Index Predicts Mortality and Disability in an Older Japanese Community-Dwelling Population(Dissertation_全文)

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（体格指数ではなく2年間の体重減少によって地域在住高齢者の死亡率と介護認定率が予測される）

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Original Study

Two-Year Weight Loss but Not Body Mass Index Predicts Mortality and Disability in an Older Japanese Community-Dwelling Population

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A B S T R A C T

Objective: Previous studies in older populations have shown a cardioprotective effect for obesity, an observation known as the obesity paradox. However, whether a decrease or increase in body weight over a certain period affects disability and mortality in older adults remains unknown. Hence, we examined whether the percent body weight change can predict the risk of mortality and disability in older Japanese adults.

Design: We performed a longitudinal prospective cohort study.

Setting and participants: We investigated 1229 community-dwelling older adults (aged ≥65 years) living in Japan.

Methods: Participants were divided into 3 groups (weight loss, stable weight, and weight gain) based on percentage body weight change (using 1 standard deviation from the mean as cutoff points) between 2011 and 2013. Death and disability incidences were monitored between April 2013 and March 2016. Disability was defined as the need for new long-term care insurance (LTCI).

Results: The rates of death and new LTCI requests over the 3-year follow-up were 2.4% and 4.7%, respectively. The weight loss group (reduction >4.8%) had a 5.0% death rate and an 11.1% new LTCI rate, which were significantly higher than those in the stable weight (1.6% and 3.8%, respectively) and weight gain (ie, gain >3.1%) groups (3.9% and 4.7%, respectively). Cox regression analysis confirmed a higher risk for death [hazard ratio (HR) = 3.10, 95% confidence interval (CI) = 1.31-7.31] and new LTCI requests (HR = 3.03, 95% CI = 1.69-5.43) only in the weight loss group. The body mass index did not significantly influence the risk of death or disability.

Conclusions/Implications: Weight loss over 2 years but not body mass index was associated with a higher death and disability risk during the subsequent 3-year follow-up period among older participants. Weight change surveillance can improve the quality of health care by early identifying frailty and death risk population.

The association between a greater body mass index (BMI) and lower mortality in older persons has been described as the "obesity paradox."[1–3] Individuals categorized as overweight and obese (BMI ≥25), traditionally considered at higher risk for cardiovascular diseases as higher BMI values are associated with higher visceral adiposity and metabolic syndrome, actually have an unexpectedly higher survival rate than normal-weight subjects.[4–7] In contrast, underweight individuals (BMI <18.5) have a significantly higher mortality rate than those in higher BMI categories,[8] as lower BMI values are associated with chronic diseases and wasting disorders in older individuals.[9,10]

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A possible explanation for the obesity paradox is that the BMI calculation does not differentiate fat mass from muscle mass; therefore, higher BMI values in older population studies could reflect individuals with higher proportions of muscle mass, translating into better cardiorespiratory fitness levels and higher survival rates.[11–13]

A recent meta-analysis of 239 prospective studies (encompassing approximately 4 million adults from several countries across 4 continents) investigated all-cause mortality hazard ratios (HRs) according to BMI groups and found that individuals in the overweight and obese BMI categories had a consistently higher risk of death.[14] This finding, which is based on BMI measurements at baseline, challenges the existence of the obesity paradox when applied to a larger sample, especially in younger people (35-70 years old) and non–south Asian cohorts.

Still, the obesity paradox is likely to be present in populations with a wider range of BMI values and a higher proportion of obese individuals, such as in the United States, but not in countries with a low prevalence of obesity such as Japan.[15] A dynamic analysis of body weight as it varies over an individual's life span would be helpful to better understand the influence of body weight in health status.[16–19]

Studies in middle-aged adults with a long-term observation of BMI changes (12 years' follow-up) showed that both BMI increase and decrease are associated with higher all-cause mortality.[20]

Consequently, controversy remains about the recommendations for weight control in older persons. Indeed, some obese individuals with previous cardiovascular disease may not benefit from weight loss; rather, it could increase their mortality risk.[21]

Thus, the aim of this study was to determine the influence of body weight change over 2 years, calculated as the percentage of baseline weight, in the death and disability rates in a community-dwelling population over a subsequent 3-year period of prospective observation. We hypothesized that weight loss would be associated with higher mortality rates and more new certifications for long-term care insurance (LTCI) service needs.

Methods

Study Population

We analyzed data from annual health checkups performed in 2011 (n = 1769) and 2013 (n = 1851) fiscal years—obtained from the local government office in Japan. A longitudinal cohort study involving self-reported surveys commenced in April 2013 (n = 5401) with a follow-up period of 3 years, ending in March 2016, provided additional information. The initially selected patients matched by identification numbers (ID) from both their 2011 and 2013 annual health checkups comprised 1259 community-dwelling older participants (aged 65 years and older as of 2011). After re-matching by their ID number with the longitudinal cohort survey data, 25 additional cases were excluded, and 1234 participants (98%) constituted the study population as of April 2013. We subsequently excluded 5 persons from the analysis owing to the loss of follow-up; hence, the final analyzed study cohort comprised 1229 older adults. During the 3-year monitoring period, 51 participants obtained new LTCI certifications, 7 obtained new LTCI certifications and subsequently died, and 22 died without LTCI certifications by March 2016. We considered a total of 29 incidents of death and 58 incidents of new LTCI requests. The data analyzed in this study were obtained following the guidelines of the Declaration of Helsinki, and approved by the ethics committee of our institution. Details of the collection, inspection, and quality assessment of data were described previously.[22,23]

Measurements (Health Variables)

Annual health checkup data

Twelve variables including age, sex, measured body weight and height, calculated BMI, together with the biochemical analyses of serum hemoglobin levels, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), glucose, and vital signs of measured systolic blood pressure (BP) and diastolic BP were obtained from the health checkup data from fiscal years 2011 and 2013 (ie, an average period of 2 years elapsed between measurements). Medical history of comorbidities including cancer diagnosis, brain ischemic or hemorrhagic stroke, and coronary or noncoronary heart disease was also assessed.

Longitudinal survey data

The 2 endpoint measures of mortality and new certifications for LTCI service outcomes during a 3-year period between April 1, 2013 and March 31, 2016 (survival time) were acquired from the longitudinal cohort survey and confirmed by the local government office. Additionally, the KCL (a self-reported score used in Japan to identify frailty and necessity of LTCI service),[24] the community activities (CA) score (a recently proposed score to predict disability and mortality in older Japanese population),[25] the reported weight loss, and the smoking habits were obtained.

Statistical Analysis

A 2-way mixed analysis of variance (ANOVA) evaluated the effect of the interaction of time repeated measures (from 2011 until 2013) and the comparison between 3 independent subgroups (weight loss, stable weight, or weight gain), with effect size calculations assessed by eta-squared (η^2) values.

The within-subject comparison was performed using a paired *t* test with effect size calculations performed according to Cohen *d* with Hedges correction method, and the between-subject comparison by 1-way analysis of variance (ANOVA).

The participants were divided according to a single standard deviation weight change (ie, ±1 standard deviation from the mean) as a cutoff point, translated as follows: participants with a >4.8% decrease in weight constituted the weight loss group, participants with weight shifts between a 4.8% decrease and a 3.1% increase constituted the stable weight group, and participants with a >3.1% increase constituted the weight gain group. Post hoc analysis was performed by the Tukey method when subgroups had equal variances, or by Games-Howell method in case of unequal variances, and effect size calculations by η^2 method.

Comparisons of categorical groups (sex, age, BMI, comorbidities, smoking habits, KCL score, CA score, reported weight loss, death, and LTCI cases) between 3 weight change groups were performed using the Pearson chi-square (χ^2) test for independence with effect size calculated by Cramer *V*.

Lastly, the HRs for death and new LTCI certifications were calculated by Cox proportional hazards with 95% confidence intervals (CIs) using univariate (crude HRs) and multivariate methodologies for death (model 1a and 1b) and new LTCI case (model 2a and 2b) outcomes, together with the Kaplan-Meier curves analysis, with the omnibus effect assessed by the log-rank (Mantel-Cox) test.

Model 1 assumed the covariates of weight change, age, sex, BMI, comorbidities, and smoking habits, with additional adjustment for anemia based on 2013 hemoglobin values lower than 11.0 g/dL (model 1a)[26] or presence of risk factors for metabolic syndrome based on 2013 values of HDL-C, TG, glucose, and blood pressure (model 1b) adapted from the Japanese criteria, excluding the waist circumference measurement.[27]

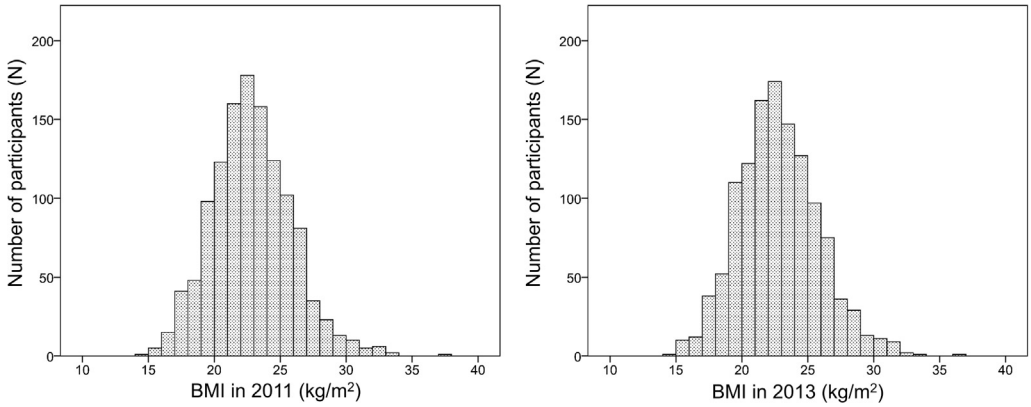

Fig. 1. Histograms of body mass index distribution in 2011 and 2013.

The multivariate model 2 assumed the same covariates as model 1, except that the smoking habits covariate was substituted for CA scores to evaluate physical activity indirectly, as it comprises the following 7 items: volunteer activity, regional activity related to the neighborhood, visiting friends, engaging in hobbies or favorite lessons, earning an income, farm work and growing vegetables, and shopping daily by oneself without others' support. For model 2a, participants were classified as robust, prefrail, or frail based on the total score of KCL.[28] For model 2b, 6 different domains were assessed by the partial score of selected questions divided into instrumental activity of daily life (IADL), physical strength, oral function, socialization, memory, and depressed mood domains.[29]

All data analyses were performed using the SPSS software (statistical medical entry package and missing values, version 22.0; SPSS, Inc, Armonk, NY). The significance threshold value was set at $P < .05$ and the adopted cutoff points for effect size as suggested by Cohen.[30–32]

Results

In 2013, 44.4% of the participants in our study were male, the average age was 74.4 ± 5.1 years with the mean body weight of 54.3 ± 9.4 kg and a BMI of 22.8 ± 3.1, and the average weight lost was 0.5 ± 2.1 kg (0.9% ± 4.0%) in the previous 2 years. The prevalence of comorbidities and frailty was 20.4% and 18.3%, respectively, and all blood tests had normal mean values except the glucose levels (103.8 ± 18.2 mg/dL). Although the mean weight difference between 2011 and 2013 was statistically significant, the mean BMI difference was not. Figure 1 illustrates the distribution of BMI in 2011 and 2013.

Comparisons by 2-way mixed ANOVA analysis (Table 1) showed significant differences ($P < .05$) for all variables except glucose, but only body weight and BMI variables had a large effect size ($\eta^2 > .16$).

The within-subject analysis in the weight loss group confirmed a significant decrease over time in the weight, BMI, TG, and systolic and diastolic BP, with a medium effect size (Cohen $d > .40$).

The between-subject analysis showed that at baseline (2011) weight change groups did not differ for weight, TG, and systolic or diastolic BP, but at follow-up (2013) the weight loss group had the lower values for those variables, with a small effect size ($\eta^2 < .03$). The weight loss group had an average decrease of 4.1 kg (7.5%) in body weight and 1.4 (6.1%) in BMI, a 10-fold difference compared to the stable weight group. This group was of older age (75.5 ± 5.6) and had lower mean values of weight (50.7 ± 9.5), BMI (21.5 ± 3.2), LDL-C (113.9 ± 29.9), TG (85.5 ± 29), systolic BP (130.2 ± 17.6), and diastolic BP (73.3 ± 9.2) than the stable or weight gain group in 2013.

The χ^2 test for independence (Table 2) did not show an interaction of weight change with sex, age, comorbidities, and CA score groups, but showed significant interaction with BMI, smoking habits, KCL score, death, and LTCI group proportions ($P < .05$, Cramer $V = 0.08$-0.20).

Kaplan-Meier analysis of mortality revealed significant differences (log-rank $P = .014$) between the 3 weight change groups; this was evident from the first year of follow-up (Figure 2). Starting with 1229 participants, 29 deaths were registered during the 3-year monitoring period (2.4%), resulting in an overall survival time of 1087.2 ± 2.0 days (mean ± standard deviation). The weight loss, stable weight, and weight gain groups showed 8 deaths out of 160 initial participants (5%) with a mean survival time of 1078.6 ± 7.5, 15 deaths among 915 participants (1.6%) with a mean survival time of 1090 ± 1.9 days, and 6 deaths among 154 participants (3.9%) with a mean survival time of 1079.7 ± 7.9 days, respectively.

Further analysis of mortality outcomes using Cox proportional hazards showed that the weight loss alone influenced survival, with a crude HR of 3.10 (95% CI 1.13-7.31); this remained significant even after adjustments in multivariate model 1a (HR 2.86, 95% CI 1.10-7.46) as well as in multivariate model 1b (HR 2.85, 95% CI 1.12-7.27; Table 3). Likewise, male sex had a higher crude HR of 4.87 (95% CI 1.98-11.96), followed by comorbidities (crude HR 4.27, 95% CI 2.06-8.84) and age range of 75-84 years (crude HR 3.92, 95% CI 1.67-9.23), that later persisted significant in the multivariate analysis. BMI, blood pressure, TG, or HDL-C did not show statistically significant differences in crudes HRs for mortality. The covariates of anemia, being a former smoker, and having high glucose had higher crude HRs, which lost statistical significance in the multivariate analysis.

Kaplan-Meier analysis of new LTCI certifications again indicated significant differences among the 3 frequency plots (log-rank test $P < .001$) starting at 18 months of follow-up (Figure 2). Of 1207 participants, 58 were newly registered for LTCI services (4.7%), resulting in an LTCI-free period of 1072.7 ± 3.4 days. The weight loss group had 17 new LTCI registrations among 153 participants (11.1%), with a mean LTCI-free period of 1050 ± 12.1 days. The stable weight group had 34 LTCI registrations among 904 participants (3.8%), with a mean LTCI-free period of 1076.8 ± 3.6 days. The weight gain group had 7 LTCI registrations among 150 participants (4.7%), with a mean LCTI-free period of 1070.6 ± 10.9 days.

Finally, on the analysis of new LTCI cases, the weight loss group had a crude HR of 3.03 (95% CI 1.69-5.43), which remained significant after model 2a adjustments by the total KCL score (HR 2.27, 95% CI 1.13-4.56) or model 2b adjustment by 6 domains of KCL (HR 2.62, 95% CI 1.26-5.43; Table 4). The highest crude HR was found for age >85 years (crude HR 12.55, 95% CI 5.05-31.21), followed by frail classification by KCL score (crude HR 5.54, 95% CI 2.70-11.37), age range of 75-84 years (crude HR 4.82, 95% CI 2.47-9.42), and IADL domain (crude HR 3.28, 95% CI 1.98-6.37), persisting significance in the multivariate analysis.

Table 1
Participants' Characteristics in 2011 and 2013 With 3-Group Comparisons According to Body Weight Changes During This Time Period

Characteristics	Weight Change Groups (Mean ± SD)				Two-Way* Interaction		Group Effect† Between-Subject		Time Effect‡ Within-Subject	
	Year	Loss (n = 160)	Stable (n = 915)	Gain (n = 154)	*P* Value	η^2	*P* Value	η^2	*P* Value	Effect Size Cohen *d*
Age, y	2013	75.4 ± 5.6	74.3 ± 5.0	73.7 ± 4.8	—	—	.006[a]	<.01	—	—
Height, cm	2011	154.3 ± 8.9	154.5 ± 8.4	155.9 ± 9.2	<.001	.02	.159	—	<.001 (L)	0.09
	2013	153.5 ± 9.0	154.0 ± 8.5	155.5 ± 9.3			.073	—	<.001 (S)	0.06
									<.001 (G)	0.04
Weight, kg	2011	54.8 ± 9.9	55.0 ± 9.1	53.5 ± 9.9	<.001	.69	.164	—	<.001 (L)	0.42
	2013	50.7 ± 9.5	54.6 ± 9.1	56.4 ± 10.2			<.001[a]	.03	<.001 (S)	0.05
									<.001 (G)	0.29
BMI	2011	22.9 ± 3.3	23.0 ± 3.0	21.9 ± 3.0	<.001	.62	<.001[d]	.01	<.001 (L)	0.45
	2013	21.5 ± 3.2	23.0 ± 3.0	23.2 ± 3.0			<.001[a]	.03	.095 (S)	—
									<.001 (G)	0.44
Hb, g/dL	2011	13.5 ± 1.4	13.6 ± 1.3	13.6 ± 1.3	.007	<.01	.640	—	.001(L)	0.21
	2013	13.3 ± 1.3	13.5 ± 1.2	13.6 ± 1.4			.052	—	<.001 (S)	0.12
									.976 (G)	
HDL-C, mg/dL	2011	59.7 ± 14.0	59.6 ± 14.1	61.5 ± 16.2	.006	<.01	.309	—	.372 (L)	—
	2013	60.4 ± 14.9	59.6 ± 14.2	59.5 ± 14.0			.807	—	.888 (S)	—
									.005 (G)	0.13
LDL-C, mg/dL	2011	120.1 ± 31.5	122.1 ± 27.0	116.1 ± 28.1	<.001	.01	.043[e]	<.01	.001(L)	0.20
	2013	114.2 ± 29.9	120.5 ± 26.3	120.4 ± 25.9			.017[b]	<.01	.023 (S)	0.06
									.018 (G)	0.16
TG, mg/dL	2011	106.2 ± 55.2	107.6 ± 54.7	106.7 ± 73.0	<.001	.02	.949	—	<.001 (L)	0.46
	2013	85.6 ± 29.1	102.1 ± 50.5	112.3 ± 75.3			<.001[a]	.02	<.001 (S)	0.10
									.217 (G)	—
Glucose, mg/dL	2011	103.4 ± 16.9	102.2 ± 18.4	100.2 ± 13.1	.146	—	.280	—	.038 (L)	0.13
	2013	105.9 ± 21.4	103.5 ± 17.9	103.8 ± 15.9			.458	—	.007 (S)	0.07
									.001 (G)	0.24
Systolic BP (mmHg)	2011	137.4 ± 17.8	136.8 ± 17.8	134.4 ± 18.2	<.001	.02	.245	—	<.001 (L)	0.42
	2013	130.0 ± 17.6	134.7 ± 17.8	136.5 ± 16.3			.003[a]	<.01	<.001 (S)	0.12
									.064 (G)	—
Diastolic BP (mmHg)	2011	77.9 ± 9.2	77.8 ± 10.0	77.4 ± 9.7	<.001	.02	.867	—	<.001 (L)	0.51
	2013	73.2 ± 9.2	75.7 ± 9.5	77.7 ± 8.9			<.001[c]	.01	<.001 (S)	0.21
									.612 (G)	—

Hb, hemoglobin.

*Two-way mixed ANOVA comparison of time and weight group interaction with effect size calculated using the η^2 method.

†One-way ANOVA with the post hoc test on all pairs comparison by Tukey or Games-Howell method, with statistical significance at $P < .05$ and effect size calculated by η^2 method. (a: significant difference between weight loss and all other groups, b: significant difference between weight loss and stable weight group only, c: significant difference between all combinations of groups, d: significant difference between weight gain and all other groups, e: significant difference between weight gain and stable weight group only).

‡Paired *t* test comparison between 2011 and 2013 for each group (L: weight loss; S: stable weight; G: weight gain) with statistical significance at $P < .05$ and effect size calculated by Cohen *d* method with Hedges correction.

All other 5 KCL domains had significant crude HRs but not in the multivariate model 2b. Sex, BMI, comorbidities, or CA scores did not show significant HRs for new LTCI registrations on both univariate and multivariate methodologies.

Discussion

Our results supported our initial prediction of worse mortality and disability rates in the weight loss group within a short follow-up period of 3 years following a minimal weight change observation period of 2 years. Previous studies[18,33] that included longer periods of survival monitoring (10-15 years) obtained similar results, although the range in weight variation was greater (a reduction of 10%-15% or more), and the period of observation was also longer (5 years). Nevertheless, considering the reported weight loss was predominantly in the last 5 years of life,[19] our total period of observation can be considered adequate for the proposed outcomes of death and new LTCI requests.

There were no significant differences in the HRs for death or disability among the different BMI categories, which is in contrast with results of previous studies.[34,35] This could be explained by the epidemiologic differences in BMI distribution; the Japanese population has a lower average BMI than most other Western countries,[36] as shown in our study (Figure 1), with an overall mean BMI of 22.8 ± 3.1 in 2013.

We adopted the BMI classification proposed by the World Health Organization guidelines for Asian populations[37] (underweight <18.5, normal weight 18.5-22.9, overweight 23.0-27.4, and obese ≥27.5), as the obesity paradox was previously described using these BMI cutoff values in the Japanese population investigated for cardiovascular mortality.[38] Therefore, it might not be appropriate to generalize our results to non-Asian populations, whose older individuals would be heavier and have a higher prevalence of morbid obesity.

Our study results suggest that surveillance of weight change could provide reliable information in the health status of older populations. The weight loss cutoff of 4.8% adopted in our study successfully identified the group with higher HR for death and disability, consistent with previous studies' weight loss cutoff of 5%.[39–41] Criteria such as weight loss of 2 to 3 kg in the preceding 6 months, used for frailty screening,[24,28] could be otherwise misleading because of the under- or overestimation of weight change depending on the initial body weight value.

A major limitation of this study was the lack of body composition analysis to determine fat vs muscle mass. Muscle mass reduction is more plausible in the weight loss group because in the older population it is related to the development of sarcopenia and

Table 2
Participants' Categorical Data From 2013 Survey With 3-Group Comparisons According to Body Weight Changes

Categorical Variables	Weight Loss, n (%)	Stable Weight, n (%)	Weight Gain, n (%)	Total, n (%)	χ^2	*P* Value	Cramer *V*
Sex group							
Male	79 (49.4)	389 (42.5)	78 (50.6)	546 (44.4)	5.4	.069	0.066
Female	81 (50.6)	526 (57.5)	76 (49.4)	683 (55.6)			
Age group, y							
65-74	74 (46.3)	500 (54.6)	94 (61.0)	668 (54.4)	8.0	.092	0.057
75-84	78 (48.8)	384 (42.0)	57 (37.0)	519 (42.2)			
≥85	8 (5.0)	31 (3.4)	3 (1.9)	42 (3.4)			
BMI group							
Underweight	24 (15.0)*	51 (5.6)	6 (3.9)	81 (6.6)	36.6	<.001	0.122
Normal weight	92 (57.5)	438 (47.9)	70 (45.5)	600 (48.8)			
Overweight	36 (22.5)*	367 (40.1)	65 (42.2)	468 (38.1)			
Obese	8 (5.0)	59 (6.4)	13 (8.4)	80 (6.5)			
Comorbidities group							
Presence	37 (23.1)	176 (19.2)	38 (24.7)	251 (20.4)	3.2	.199	0.051
Absence	123 (76.9)	739 (80.8)	116 (75.3)	978 (79.6)			
Smoking habits group							
Current smoker	10 (6.8)	49 (6.0)	7 (5.3)	66 (6.0)	10.9	.027	0.071
Former smoker	43 (29.3)	195 (24.0)	49 (36.8)*	287 (26.2)			
Never smoker	94 (63.9)	570 (70.0)	77 (57.9)*	741 (67.7)			
KCL score group							
Robust	45 (30.0)*	412 (49.0)	62 (44.0)	519 (45.8)	21.8	<.001	0.098
Prefrail	64 (42.7)	293 (34.8)	49 (34.8)	406 (35.9)			
Frail	41 (27.3)*	136 (16.2)	30 (21.3)	207 (18.3)			
CA score group							
Yes (≥2 points)	137 (95.8)	785 (96.8)	131 (94.9)	1053 (96.4)	1.4	.502	0.036
No (0-1 point)	6 (4.2)	26 (3.2)	7 (5.1)	39 (3.6)			
Reported weight loss of 2-3 kg in previous 6 mo							
No	117 (76.0)*	821 (93.5)	132 (91.0)	1070 (90.9)	48.7	<.001	0.204
Yes	37 (24.0)*	57 (6.5)	13 (9.0)	107 (9.1)			
Death until April 2016							
No	152 (95.0)*	900 (98.4)	148 (96.1)	1200 (97.6)	8.5	.014	0.083
Yes	8 (5.0)*	15 (1.6)	6 (3.9)	29 (2.4)			
LTCI until April 2016							
No	136 (88.9)*	870 (96.2)	143 (95.3)	1149 (95.2)	15.5	<.001	0.113
Yes	17 (11.1)*	34 (3.8)	7 (4.7)	58 (4.8)			

Comparison of groups by Pearson chi-square test of independence with effect size calculated using Cramer *V*.
*Groups with differences detected by post hoc analysis of column proportions adjusted by Bonferroni method.

frailty,[42,43] which explains the increased HRs for disability and death. Moreover, the presence of anemia as a significant variable for death's HR (model 1a, Table 2) suggests a higher probability of muscle mass loss, muscle weakening, and a decline in physical performance.[44–46]

Another limitation was not to differentiate intentional weight reduction from unintentional weight loss; only the latter is associated with an increased risk of death and disability and is a clinical sign of the worsening of chronic diseases or a manifestation of wasting disorders such as malnutrition, cachexia, or even aging-related sarcopenia.[41,47–49]

We did not analyze the specific causes of death, but the presence of comorbidities was significantly related only to death (Table 3) and not to new LTCI cases (Table 4), suggesting that death events in our study could be related to cardiovascular and cerebrovascular diseases. However, our results showed the weight loss group reporting the lower average BMI, LDL-C, TG, and systemic BP values in 2013, all of which had values below the cutoff for metabolic

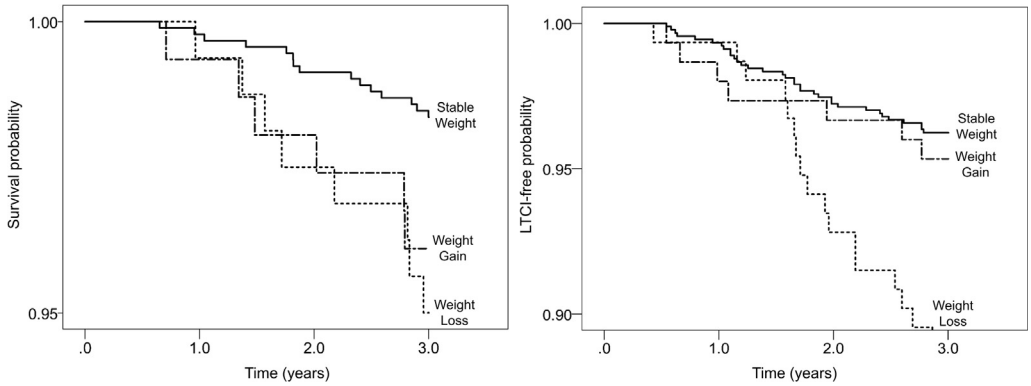

Fig. 2. Kaplan-Meier curves showing the probabilities of participants' survival (left) and freedom from requiring long-term care insurance (LTCI) certification (right) during a 3-year period (April 2013 to March 2016). Participants were stratified into 3 groups based on the body weight change. The log-rank test results for survival outcomes were $\chi^2 = 5.2$, degrees of freedom (df) = 2, *P* value = .014; and for new LTCI certification-free outcomes were $\chi^2 = 15.5$, df = 2, *P* value <.001.

Table 3
Cox Proportional Hazard Models for Mortality

Covariates	Univariate		Model 1a*		Model 1b†		Total	Case (Death)	Survival Time, d	Log Rank‡	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value		n (%)	Mean ± SE	χ^2	*P* Value
Overall							1229	29 (2.4)	1087.2 ± 2.0		
Weight change (from 2011 to 2013)											
Weight loss (<−4.8%)	3.10 (1.31-7.31)	.010	2.86 (1.10-7.46)	.032	2.85 (1.12-7.27)	.028	160	8 (5.0)	1078.6 ± 7.5	8.5	.014
Stable weight (−4.8% to 3.1%) (ref)	1.0	—	1.0	—	1.0	—	915	15 (1.6)	1090.0 ± 1.9		
Weight gain (>3.1%)	2.41 (0.94-6.21)	.069	2.65 (0.92-7.66)	.071	2.71 (0.95-7.76)	.063	154	6 (3.9)	1079.7 ± 7.9		
Sex											
Male (female as ref)	4.87 (1.98-11.96)	<.001	4.85 (1.45-16.18)	.010	4.42 (1.33-14.72)	.015	546	23 (4.2)	1081.1 ± 3.8	14.6	<.001
Age, y (as of April 1, 2013)											
65-74 (ref)	1.0	—	1.0	—	1.0	—	668	7 (1.0)	1092.3 ± 1.9		
75-84	3.92 (1.67-9.23)	.002	3.87 (1.50-9.96)	.005	3.76 (1.46-9.66)	.006	519	21 (4.0)	1080.9 ± 3.9	11.4	.003
≥85	2.30 (0.28-18.69)	.436	2.16 (0.25-18.35)	.482	2.06 (0.24-17.69)	.510	42	1 (2.4)	1082.8 ± 13.1		
BMI category (2013)											
Underweight (BMI <18.5)	1.59 (0.46-5.52)	.468	1.12 (0.25-5.01)	.886	1.55 (0.41-5.85)	.517	81	3 (3.7)	1087.8 ± 6.5		
Normal (BMI 18.5-23) (ref)	1.0	—	1.0	—	1.0	—	600	14 (2.3)	1086.3 ± 3.0	1.1	.789
Overweight (BMI 23-27.5)	1.01 (0.46-2.22)	.987	1.06 (0.45-2.49)	.900	1.00 (0.42-2.39)	.997	468	11 (2.4)	1087.2 ± 3.3		
Obese (BMI >27.5)	0.53 (0.07-4.04)	.542	1.04 (0.13-8.28)	.970	0.96 (0.12-7.67)	.966	80	1 (1.2)	1092.9 ± 3.1		
Comorbidities (2013)											
Yes (absence as ref)	4.27 (2.06-8.84)	<.001	3.34 (1.51-7.40)	.003	3.42 (1.55-7.54)	.002	251	15 (6)	1074.2 ± 6.5	18.1	<.001
Smoking habits											
Current smoker	1.02 (0.13-7.90)	.985	0.43 (0.05-3.63)	.439	0.43 (0.05-3.66)	.443	66	1 (1.5)	1092.7 ± 3.3		
Former smoker	3.34 (1.52-7.36)	.003	0.86 (0.32-2.30)	.764	0.80 (0.30-2.17)	.665	287	14 (4.9)	1080.2 ± 5.2	10.6	.005
Never smoker (ref)	1.0		1.0		1.0		741	11 (1.5)	1090.7 ± 2.0		
Anemia (Hb < 11 g/dL)											
Yes (absence as ref)	4.81 (1.14-20.25)	.032	3.97 (0.73-21.68)	.112			19	2 (10.5)	1073.9 ± 18.4	5.6	.018
High BP (systolic BP ≥ 130 mmHg and/or diastolic BP ≥ 85 mmHg)											
Yes (absence as ref)	1.06 (0.43-2.62)	.905			0.88 (0.34-2.29)	.794	906	21 (2.3)	1088.2 ± 2.2	<0.1	.905
High glucose (≥ 110 mg/dL)											
Yes (absence as ref)	2.94 (1.38-6.26)	.005			2.10 (0.93-4.72)	.073	305	14 (4.6)	1078.2 ± 5.8	8.6	.003
High TG (≥150 mg/dL) and/or low HDL-C (<40 mg/dL)											
Yes (absence as ref)	0.90 (0.34-2.36)	.830			0.93 (0.31-2.73)	.890	195	5 (2.6)	1083.2. ± 5.7	<0.1	.830

df, degrees of freedom; ref, reference value; SE, standard error.

*Model 1a: HR values adjusted for weight change, sex, age, BMI categories, comorbidities (previous diagnosis of cancer, brain ischemic or hemorrhagic stroke, coronary and non-coronary heart disease), smoking habits, and presence of anemia.

†Model 1b: HR values adjusted for weight change, sex, age, BMI categories, comorbidities (previous diagnosis of cancer, brain ischemic or hemorrhagic stroke, coronary and noncoronary heart disease), smoking habits, blood pressure, glucose, triglycerides, and high-density lipoprotein cholesterol values.

‡In the log-rank test, when 3 or more subgroups per covariable were present such as in weight change, age, BMI, and smoking habits, the *P* value is corresponding to the overall comparison.

syndrome, along with higher HRs for death. This apparent paradox is dispelled by the multivariate HR calculations showing that the variables mentioned above are not significantly influencing mortality (model 1b, Table 3).

Regarding the types of disabilities that led to new LTCI service requests, only the IADL domain had persistent statistical significance (model 2b, Table 4), indicating a predominance of physical disabilities rather than cognitive, social, or depressive mood factors to likely predict the necessity of LTCI services.

The possibility of selection bias in the weight loss group cannot be excluded from our results, as we did not have access to more detailed data about smoking habits and alcohol consumption (known factors related to death and weight loss), and this group showed higher proportions of individuals being underweight, frail, and/or reporting weight loss in the previous 6 months, along with lower proportions of overweight participants and robust-classified individuals, when compared to the stable weight and weight gain group.

Nevertheless, weight change did not show interaction with sex, age, and comorbidities (covariates in which the multivariate models 1a and 1b showed significant influence over the death HRs), therefore minimizing the probability of selection bias for mortality.

Finally, although the comparison between weight gain and stable weight groups in 2013 did not reveal any significant differences in average age, height, weight, BMI, hemoglobin, HDL-C, LDL-C, TG, glucose blood levels, and systolic BP values, there was a trend for the weight gain group to have higher death HR but not for new LTCI case HR (Figure 1). A possible explanation is that the cutoff value of 3.1% increase in body weight probably did reflect in increased adiposity, not sufficient to influence metabolic risk factors but enough to show a trend for increased mortality HR, although it also could be translated as preservation of muscle mass that did not affect the new LTCI HR.

Table 4
Cox Proportional Hazard Models for New LTCI Service Certifications

Covariates	Univariate		Model 2a*		Model 2b†		Total	Case (LTCI)	Free- LTCI Time, d	Log-Rank‡	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value		n (%)	Mean ± SE	χ^2	*P* Value
Overall							1207	58 (4.8)	1072.7 ± 3.4		
Weight change (from 2011 to 2013)											
Weight loss (<−4.8%)	3.03 (1.69-5.43)	<.001	2.27 (1.13-4.56)	.021	2.62 (1.26-5.43)	.010	153	17 (11.1)	1050.0 ± 12.1		
Stable weight (−4.8% to 3.1%) (ref)	1.0	—	1.0	—	1.0	—	904	34 (3.8)	1076.8 ± 3.6	15.5	<.001
Weight gain (>3.1%)	1.25 (0.55-2.82)	.592	1.95 (0.83-4.60)	.125	2.09 (0.87-5.02)	.098	150	7 (4.7)	1070.6 ± 10.9		
Sex											
Male (female as ref)	1.30 (0.77-2.17)	.324	1.25 (0.68-2.29)	.467	1.38 (0.72-2.64)	.335	528	29 (5.5)	1068.8 ± 5.5	1.0	.323
Age, y (as of April 1, 2013)											
65-74 (ref)	1.0	—	1.0	—	1.0	—	662	11 (1.7)	1088.8 ± 2.5		
75-84	4.82 (2.47-9.42)	<.001	5.62 (2.45-12.89)	<.001	5.36 (2.23-12.31)	<.001	503	39 (7.8)	1057.2 ± 6.8	43.9	<.001
≥85	12.55 (5.05-31.21)	<.001	16.62 (5.77-47.88)	<.001	14.35 (4.68-43.98)	<.001	42	8 (19.0)	1003.3 ± 32.6		
BMI category (2013)											
Underweight (BMI <18.5)	1.69 (0.70-4.11)	.242	1.72 (0.58-5.11)	.332	1.84 (0.60-5.68)	.287	78	6 (7.7)	1063.7 ± 14.5		
Normal (BMI 18.5-23) (ref)	1.0	—	1.0	—	1.0	—	590	27 (4.6)	1072.5 ± 4.9	1.5	.676
Overweight (BMI 23-27.5)	1.00 (0.56-1.77)	.995	1.27 (0.67-2.41)	.466	1.29 (0.66-2.53)	.455	459	21 (4.6)	1073.7 ± 5.4		
Obese (BMI >27.5)	1.09 (0.38-3.10)	.879	1.08 (0.25-4.71)	.914	0.91 (0.47-4.07)	.904	80	4 (5.0)	1076.7 ± 10.5		
Comorbidities (2013)											
Yes (absence as ref)	1.17 (0.63-2.16)	.627	0.99 (0.50-1.93)	.967	0.94 (0.47-1.90)	.872	241	13 (5.4)	1067.7 ± 8.8	0.2	.627
CA score (cutoff ≥2)											
No (yes as ref)	1.86 (0.58-5.98)	.300	0.77 (0.22-2.68)	.685	0.53 (0.14-2.00)	.346	38	3 (7.9)	1072.3 ± 15.4	1.1	.292
Frailty (Kihon Checklist score)											
Robust (0-3) (ref)	1.0	—	1.0	—			513	11 (2.1)	1085.5 ± 3.5		
Prefrail (4-7)	2.14 (1.01-4.54)	.047	1.30 (0.59-2.86)	.514			396	18 (4.5)	1074.4 ± 5.5	28.2	<.001
Frail (≥8)	5.54 (2.70-11.37)	<.001	3.31 (1.53-7.16)	.002			203	23 (11.3)	1039.9 ± 12.8		
IADL domain (cutoff ≥3)											
Yes (absence as ref)	3.28 (1.68-6.37)	<.001			2.55 (1.16-5.62)	.020	90	11 (12.2)	1047.7 ± 17.1	13.7	<.001
Physical function domain (cutoff ≥3)											
Yes (absence as ref)	3.02 (1.76-5.18)	<.001			1.71 (0.86-3.40)	.124	256	24 (9.4)	1054.3 ± 9.4	17.7	<.001
Oral function domain (cutoff ≥2)											
Yes (absence as ref)	1.90 (1.02-3.55)	.044			1.10 (0.50-2.43)	.808	169	13 (7.7)	1059.1 ± 11.3	4.2	.040
Socialization domain (cutoff ≥2)											
Yes (absence as ref)	2.73 (1.60-4.65)	<.001			1.31 (0.66-2.60)	.444	316	27 (8.5)	1054.7 ± 8.7	14.8	<.001
Cognitive domain (cutoff ≥1)											
Yes (absence as ref)	2.44 (1.43-4.16)	.001			1.38 (0.70-2.73)	.351	363	28 (7.7)	1060.0 ± 7.5	11.4	<.001
Depression domain (cutoff ≥2)											
Yes (absence as ref)	2.48 (1.43-4.30)	.001			1.28 (0.65-2.52)	.471	226	20 (8.8)	1049.7 ± 11.4	11.1	<.001

IADL, instrumental activities of daily living; ref, reference value; SE, standard error.

*Model 2a: HR values adjusted for weight change, sex, age, BMI categories, comorbidities (previous diagnosis of cancer, brain ischemic or hemorrhagic stroke, heart disease, or angina pectoris), CA score, and frailty (assessed using the Kihon Checklist).

†Model 2b: HR values adjusted for weight change, sex, age, BMI categories, comorbidities (previous diagnosis of cancer, brain ischemic or hemorrhagic stroke, heart disease, or angina pectoris), CA score, and for 6 domains of Kihon Checklist (IADL, physical strength, oral function, socialization, cognition, depression).

‡In the log-rank test, when 3 or more subgroups per covariable were present such as in weight change, age, BMI, and frailty, the *P* value is corresponding to the overall comparison.

Conclusions and Implications

Based on our results, weight change classification by the percentage change of body weight proved to be superior to BMI in terms of predicting death and disability in older adults. Weight change is easy to calculate and is most likely related to a decrease in muscle mass and wasting syndrome owing to the worsening of chronic noncardiovascular diseases. Additionally, the weight percentage change cutoff of a 4.8% weight reduction over 2 years in the weight loss group is considerably smaller than what guidelines for frailty consider to be a risk factor (2-3 kg of weight loss over the preceding 6 months) and should be considered an early diagnostic tool for frailty in future studies.

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