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**Body Mass Index, Change in Body Mass Index, and Survival in Old and Very Old Persons**

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**Running head:** Change in BMI and Survival in Old Age

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**ABSTRACT**

**Objectives:** To examine how body mass index (BMI) and change in BMI are associated with mortality in old (70–79) and very old ( $\geq 80$ ) individuals.

**Design:** Pooled data from three multidisciplinary prospective population-based studies: OCTO-twin, Gender, and NONA.

**Setting:** Sweden.

**Participants:** Eight hundred eighty-two individuals aged 70 to 95.

**Measurements:** BMI was calculated from measured height and weight as  $\text{kg/m}^2$ . Information about survival status and time of death was obtained from the Swedish Civil Registration System.

**Results:** Mortality hazard was 20% lower for the overweight group than the normal–underweight group (relative risk (RR) = 0.80,  $p = .011$ ), and the mortality hazard for the obese group did not differ significantly from that of the normal–underweight group (RR = 0.93,  $p = .603$ ), independent of age, education, and multimorbidity. Furthermore, mortality hazard was 65% higher for the BMI loss group than for the BMI stable group (RR = 1.65,  $p < .001$ ) and 53% higher for the BMI gain group than for the BMI stable group (RR = 1.53,  $p = .001$ ). Age moderated the BMI change differences. That is, the higher mortality risks associated with BMI loss and gain were less severe in very old age.

**Conclusion:** Old persons who were overweight had a lower mortality risk than old persons who were of normal weight, even after controlling for weight change and multimorbidity. Persons who increased or decreased in BMI had a greater mortality risk than those who had a stable BMI, particularly those aged 70 to 79. This study lends further support to the belief that the World Health Organization guidelines are overly restrictive in old age.

**Key words:** aging, body mass index, mortality, obesity, survival, underweight

Being of normal weight is health ideal for all age groups. Current recommendations from the World Health Organization (WHO) are that individuals should seek to maintain a body mass index (BMI) between 18.5 and 25 kg/m<sup>2</sup>, independent of age.<sup>1</sup> This recommendation is based, in part, on well-established findings that higher BMI in midlife is associated with poorer survival, although there is an ongoing discussion in the literature whether the WHO recommendations apply to old and very old persons.

Gerontologists have studied associations between BMI and mortality outcomes for many years. Comprehensive reviews of the empirical literature tentatively conclude that, in old age, lower rather than higher BMI (overweight and obese) is associated with significantly higher mortality risks.<sup>2,3</sup> These reviews highlight that, before stronger conclusions are warranted, several challenges need to be addressed more thoroughly, including the influence of change in BMI and sex and whether the noted associations hold in the very old segment of the population and with objective (rather than self-report) measures of BMI.<sup>2,3</sup>

During old age, changes in BMI, rather than BMI itself, may drive the association between BMI and survival. For example, low BMI may simply be a symptom of disease-related BMI loss—with the BMI loss itself being the better indicator of mortality risk. A number of studies have found that BMI loss in late life is associated with greater mortality risk,<sup>4-8</sup> although the findings are not consistent.<sup>8</sup> In midlife, BMI gain is associated with poorer survival.

Although some findings suggest that this also holds in late life,<sup>4,9</sup> other studies suggest that gain in BMI in elderly adults is not associated with mortality.<sup>8,10,11</sup>

The mixed findings may result from a variety of methodological challenges, including attempts to generalize across samples that span a wide age range.<sup>5</sup> For example, in young old individuals (e.g., 65), gain in BMI might be a manifestation of health risks (e.g., sedentary behavior), whereas in very old individuals (e.g., 85), gain in BMI might be a sign of health

(e.g., the body is still able to benefit from nutrients). In sum, changes in BMI may be indicative of different processes in young old and very old individuals and thus might have different implications for mortality risk at different ages. Supporting this notion, weight gain was associated with greater mortality risk in the young old participants in the Rotterdam Aging Study but not in the very old participants.<sup>9</sup>

The present study examines how BMI and change in BMI are associated with mortality in old (70–79) and very old ( $\geq 80$ ) individuals.

## **METHOD**

### **Study population**

To examine associations between BMI, change in BMI, and survival, data were pooled from three multidisciplinary population-based studies from Sweden: OCTO-twin,<sup>12</sup> GENDER,<sup>13</sup> and NONA.<sup>14</sup> Overlapping teams of researchers designed and managed these studies, and the across-study consistency of sampling procedures, measures, and protocols has allowed for pooling and integrated analysis of the data. All studies involved prospective data collected by trained research nurses in respondents' homes at approximately 2-year (OCTO-twin, NONA) and 4-year (GENDER) intervals from individuals aged 70 to 95 living in ordinary or institutional housing. Research ethics committees at the Karolinska Institutet (OCTO-twin and GENDER) and Linköping University (NONA) approved the original studies.

### **Participants and Procedure**

Participants in OCTO-twin and GENDER were recruited from the Swedish Twin Registry that lists all instances of multiple births in the country.<sup>15</sup> OCTO-twin is a representative sample of all intact, same-sex twin pairs (mono- and dizygotic) aged 80 and older at baseline. GENDER is a representative sample of opposite-sex twins aged 70 to 79 at baseline. Twin

samples identified from the twin registry were similar to representative samples of same-age singletons in vitality, well-being, physical and cognitive functioning, and healthcare use.<sup>16</sup> In NONA, individuals aged 86, 90, and 94 were selected randomly from the population registry containing the names and birth dates of all residents in the municipality of Jönköping, Sweden. This region includes rural, suburban, and urban settings and is considered representative of the variety of living situations throughout the nation. More than 80% of initially contacted individuals from the three studies agreed to participate, for a pooled sample of 1,581.

Included in the present analyses were 882 participants whose height and weight were assessed on two occasions—the first and the second in-person testing (IPT) of the respective study (see above)—and provided data on all of the correlates of interest (listed below). As one would expect, participants included in the sample were younger than the drop-outs (mean  $80.1 \pm 5.7$ , vs  $82.5 \pm 6.3$ ;  $F(1, 1,355) = 53.2, p < .001$  and lived longer (mean  $8.0 \pm 3.8$  years vs  $3.2 \pm 3.3$ ;  $F(1, 1,118) = 475.5, p < .001$ ). No differences were found between participants and drop-outs in BMI at initial assessment (IPT1), sex proportion, education, and number of medical conditions ( $p > .10$ ).

### ***BMI Status***

Trained research nurses measured height and weight during IPT. Weight was assessed using calibrated mechanical scales in all three studies. One kg was extracted from measured weight to account for the extra weight of clothing. The repeated measures of BMI were calculated as weight (kg) divided by height squared (m). Following the WHO guidelines,<sup>1</sup> initial levels of BMI were categorized into four categories: underweight ( $< 18.5 \text{ kg/m}^2$ ), normal weight ( $18.5\text{--}24.9 \text{ kg/m}^2$ ), overweight ( $25.0\text{--}29.9 \text{ kg/m}^2$ ), and obese ( $\geq 30 \text{ kg/m}^2$ ). With only 35 participants

(4%) having an initial BMI less than 18.5, this group was merged with the normal group (also justified by preliminary analysis indicating that the groups did not differ in mortality risk).

### ***Change in BMI***

The two measures of BMI were used to calculate a proportional change score for each individual:  $\Delta\text{BMI} = 100 \times (\text{BMI}_2 - \text{BMI}_1) / \text{BMI}_1$ . (Scores from GENDER were divided by 2 to account for 4-year v. 2-year follow-up.) Substantial weight change in adults is often defined as a weight change of 3%,<sup>17</sup> but in aging research, definitions of substantial weight change range from 3% to 5%.<sup>7, 10, 11, 18</sup> Taking a conservative approach, in the current study, individuals were categorized into three categories based on their BMI change scores: BMI loss ( $\Delta\text{BMI} \leq -5\%$ ), BMI stable ( $-5\%$  to  $+5\%$ ), and BMI gain ( $\Delta\text{BMI} \geq 5\%$ ). Proportions and characteristics of the resulting three categories of BMI change are given in Table 1.

### ***Mortality***

Information about survival status and time of death for deceased participants was obtained from the Swedish Civil Registration System, which registers date of death of all Swedish persons. Of the 882 participants included in the analyses, 667 participants (75%) died during the 18 years of follow-up. On average, deceased participants were aged  $81.1 \pm 5.1$  (range 70–95) at the initial assessment and died  $8.0 \pm 3.8$  years later (range 1–18 years).

### ***Demographics and Multimorbidity***

Chronological *age* was recorded at the initial assessment as number of years since birth (mean  $80.1 \pm 5.7$ , range 70–95). For the purpose of analyzing age-related differences, the cohort was split on the sample mean, into old (70–79) and very old ( $\geq 80$ ) individuals. Participants reported on the number of years of formal education (mean  $7.3 \pm 2.3$ , range 0–20).

Multimorbidity, as an indicator of overall physical health, was measured as the number of diseases and medical conditions an individual had at the time of the initial interview. Nurse interviewers who reviewed medical information with participants and, when necessary, family informants obtained reports from participants.<sup>13</sup> Such self-reports of medical conditions are often consistent with physicians' diagnoses.<sup>19, 20</sup> Specific diagnoses included arthritis, hip fracture, osteoporosis, stroke, heart attack, chest pain or angina pectoris, diabetes mellitus, asthma, coughing with yellow phlegm, malignant tumor, and Parkinson's disease. On average, this sample had  $1.4 \pm 1.3$  diagnoses (range 0–8).

### Data Analysis

The main objective was to examine whether and how BMI and BMI change were associated with mortality in a sample of old and very old individuals. To do so, proportional hazard regression models were applied to the pooled 18-year follow-up data. The model took the form

$$\begin{aligned} \log h(t_{ij}) = & \log h_0(t_j) + \beta_1(\text{overweight}_i) + \beta_2(\text{obese}_i) + \beta_3(\text{weight loss}_i) + \\ & \beta_4(\text{weight gain}_i) + \beta_5(\text{age}_i) + \beta_6(\text{education}_i) + \beta_7(\text{sex}_i) + \\ & \beta_8(\text{comorbidity}_i) + \beta_{9-12}(\text{age} \times \text{correlate}_i) \quad (1) \end{aligned}$$

$\text{Log}h(t_{ij})$  is the log of individual  $i$ 's risk of dying (or log hazard:  $\log h$ ) at time  $t$ .  $\text{Log}h_0(t_j)$  is the baseline log hazard function, the time-dependent risk of dying, when all other predictors are 0 (for average person of normal, stable BMI). Parameters  $\beta_1$  through  $\beta_8$  indicate the differences in log hazard between BMI and BMI change categories (the association between age, education, sex, and comorbidities and the log hazard), and  $\beta_{9-12}$  indicate the extent to which age moderated those differences and associations. Age was centered at 80, and scores for all measures and groups were effect-coded or -centered so that mortality hazards referred not to a specific group but to the overall sample. All of the age interactions were tested, and

only those that were reliably different from 0 with  $\alpha = .05$  were retained in the final model.

Models were estimated using SAS (PROC PHREG, SAS Institute, Inc., Cary, NC).

## RESULTS

Proportions and characteristics of the three categories of BMI and BMI change are given in Table 1. There were overall differences in age ( $F(2, 879) = 26.08, p < .001$ ), sex ( $\chi^2(2, N=879) = 6.67, p = .04$ ), education ( $F(2, 879) = 4.60, p = .01$ ), and multimorbidity ( $F(2, 879) = 3.89, p = .02$ ) between the BMI groups. Comparisons of those who maintained or changed their BMI showed no overall differences in age ( $F(2, 879) = 1.77, p = .17$ ) or sex ( $\chi^2(2, N=879) = 3.21, p = .20$ ), although there were overall differences in education ( $F(2, 879) = 3.57, p = .03$ ) and multimorbidity ( $F(2, 879) = 3.07, p = .05$ ). Comparisons of three BMI and BMI change groups, based on Bonferroni adjustments, are shown in Table 1.

Results from the final model are presented in Table 2. As expected, older age (relative risk (RR) = 1.11,  $p < .001$ ), male sex (RR = 0.61,  $p < .001$ ), and greater multimorbidity (RR = 1.16,  $p < .001$ ) were all related to greater mortality hazard. Most important for the research question, there were significant differences in mortality hazard associated with BMI and BMI change. Specifically, independent of other effects, mortality hazard was 20% lower for the overweight group than the normal and underweight group (RR = 0.80,  $p = .011$ ), but mortality hazard for the obese group did not differ significantly from that of the normal and underweight group (RR = 0.93,  $p = .603$ ). Mortality hazard was 65% higher for the BMI loss group than the BMI stable group (RR = 1.65,  $p < .001$ ) and 53% higher for the BMI gain group than the BMI stable group (RR = 1.53,  $p = .001$ ). The differences in survival are shown in Figure 1. The left panel illustrates the differences in expected survival time between the BMI categories, with overweight participants dying, on average, almost a full year later than those who were normal or underweight. The right panel illustrates the differences in expected



survival time between the BMI change categories, with the BMI stable group living more than a full year longer than the BMI loss group.

Of additional interest were the age interactions. As seen in Table 2, age moderated the BMI change differences. That is, the higher mortality risks associated with BMI loss and BMI gain were less severe in very old age (age  $\times$  BMI loss, RR = 0.93,  $p < .001$ ; age  $\times$  BMI gain, RR = 0.89,  $p < .001$ ). Differences between the survival curves for typical BMI stable and BMI loss of individuals aged 70 to 79 and those aged 80 and older (the sample mean) are shown in Figure 2. The detrimental effects of BMI change on mortality are discernible in old age (left panel), but not as much in very old age (right panel).

## DISCUSSION

This study examined the effect of BMI and change in BMI on all-cause mortality in older adults and specifically in a sample with a high percentage of very old individuals. To the best of the knowledge of the authors, no previous study has evaluated BMI change in relation to mortality in very old individuals. The results suggest that being overweight is related to lower mortality risk in old and very old age and that change in BMI (gain or loss) increases mortality risk, but the effects differ considerably with age in that, with older age, the detrimental effects of change in BMI become smaller and nonsignificant.

This study further supports that persons being overweight according to the WHO guidelines might not be at greater risk of mortality.<sup>2, 3</sup> Individuals classified as being overweight according to the WHO standards were at lower risk of mortality. The advantage of being overweight could be that fat mass stores energy that can be used during negative energy balance. Although being overweight or obese is a risk factor for several diseases, for example, congestive heart failure, individuals with higher BMI scores have the best survival.<sup>21</sup> The finding that overweight persons had a lower mortality risk remained significant when change

in BMI and multimorbidity were controlled for, which indicates that the reverse association between BMI and mortality in late life cannot be due only to underlying diseases causing weight change, which often is proposed as a potential causal pathway for this seemingly reverse association. The critical reader could argue that persons with the lowest BMI could be causing the association between low BMI and greater mortality risk, but no significant difference was found between the underweight and normal-weight group in mortality risk, hence, it is not likely that those with the lowest BMI determined the association.

BMI gain and BMI loss were associated with greater mortality risk. It has been hypothesized that BMI stability in old age is a sign of health and that the body is able to maintain homeostasis; accordingly, BMI decrease and BMI increase are suggestive of systemic breakdown.<sup>22</sup> Furthermore, BMI loss in old age might be a sign of the body's inability to take up and benefit from nutrients. Declining BMI might also be a manifestation of poorer psychological and emotional well-being, in that reported symptoms include loss of appetite and loss of enjoyment of food. Persons with higher BMI are also at less risk of hip fracture and thereby at less risk of death from surgical and postoperative complications,<sup>23</sup> because adipose tissue reduces impact forces in the case of a fall.<sup>24</sup> In addition, even if an older person regains weight, the lean mass is not often not totally regained, and accordingly, the older person might become sarcopenic.<sup>18</sup> Except for all of the common reasons for increase in BMI, such as high caloric diet and low energy expenditure, gain in BMI in old age might also be a side effect of medication use or physical limitations.

Nevertheless, the negative effects of BMI change were especially pronounced in the younger age segment of this study (<80). A possible explanation is that, in general, there was a difference in follow-up time between the old and very old age individuals in this study, with 4 years of follow-up for those younger than 80 and 2 years for those aged 80 and older. Two years might be too short a follow-up time to capture change in BMI if the changes are small

and insidious; preliminary analyses of multiwave change in BMI in old and very old Swedish adults revealed that within-person change was less than cross-sectional between-person differences (e.g., intraclass correlation  $> 0.80$ ). Another reason why associations may not have been found between change in BMI and mortality in very old individuals is that those with worse health and more weight loss might have dropped out of the study earlier or could not be measured at follow-up. (Research nurses were not always able to assess weight and height for those who had become bedridden or were in wheelchairs.) More studies on weight change in very old individuals are warranted.

The interaction between BMI, BMI change, and multimorbidity was also analyzed, and no significant interaction terms were found. No significant interaction between BMI, BMI change, and sex were found either, supporting a meta-analysis that also did not report any substantial sex differences.<sup>3</sup>

The strength of this study is the large population-based prospective sample with known death dates using BMI based on assessed weight and height in old and very old individuals.

Although BMI is widely used as a measure of body fat, it is criticized as a less-effective assessment of body fat in old age. Although some might suggest that these findings are related to questions of measurement, a recent study using dual-energy X-ray absorptiometry assessing total fat mass in men also showed an association between loss of total fat mass and poorer survival.<sup>7</sup> (Studies using different assessments methods of fat mass receive similar results.)

One potential limitation is that it was unknown whether decline in BMI was intentional.

Although intentional weight loss might have a different origin than unintentional weight loss, the evidence of a positive effect of intentional weight loss on life expectancy in late life is weak.<sup>6</sup> Although information about medical conditions was available, in old age there are many unrecognized health problems that might have affected the association. Finally, as in all studies that include older persons, there is selection bias for those who are healthier and for

overweight or obese individuals, who are less sensitive to the negative effects of being overweight or obese.

In conclusion, older persons who were classified as overweight based on their BMI had a lower mortality risk than those with a BMI less than  $25.0 \text{ kg/m}^2$ , even after controlling for weight change and multimorbidity. Persons who gained or lost weight over a 2- or 4-year period had a higher mortality risk than who had a stable BMI. This study lends further support to the idea that the WHO guidelines considering BMI are overly restrictive in old age. In addition, stable BMI might be an indicator of good health in old age, and clinicians should probably record and pay at least as much attention to changes in BMI as to BMI itself.

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**Author Contributions:** Anna K. Dahl was responsible for drafting the manuscript. Elizabeth B. Fauth designed and pooled the data. Denis Gerstof analyzed the data. Anna K. Dahl, Elizabeth B. Fauth, Marie Ernsth-Bravell, Linda B. Hassing, Nilam Ram, and Denis Gerstof are all responsible for the intellectual content of the manuscript.

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**Table 1. Descriptive Statistics for the Variables under Study (N=882)**

Characteristic	BMI, kg/m <sup>2</sup>			BMI Change		
	<25.0 (Underweight and Normal Weight), n=459	25.0–29.9 (Overweight), n=318	≥30.0 (Obese), n=105	BMI Loss (≥−5%), n=211	Stable BMI, n=533	BMI Gain (≥+5%), n=138
Age, mean±SD	81.4±5.6 <sup>a</sup>	78.8±5.6 <sup>b</sup>	78.4±5.2 <sup>b</sup>	80.4±5.2 <sup>a</sup>	79.8±5.8 <sup>a</sup>	80.7±6.1 <sup>a</sup>
Female, n (%)	288 (63) <sup>a</sup>	172 (54) <sup>b</sup>	67 (64) <sup>a</sup>	137 (65) <sup>a</sup>	308 (58) <sup>a</sup>	82 (59) <sup>a</sup>
Education, mean±SD	7.4±2.4 <sup>a</sup>	7.2±2.3 <sup>a,b</sup>	6.7±1.5 <sup>b</sup>	7.0±2.1 <sup>a</sup>	7.4±2.4 <sup>b</sup>	7.1±2.2 <sup>a,b</sup>
Multimorbidity, mean±SD	1.23±1.28 <sup>a</sup>	1.51±1.43 <sup>b</sup>	1.38±1.34 <sup>a,b</sup>	1.53±1.45 <sup>a</sup>	1.26±1.32 <sup>b</sup>	1.42±1.29 <sup>a,b</sup>

Columns with different superscripts are different from one another at  $p < .05$ , based on Bonferroni adjustments.

BMI=body mass index; SD=standard deviation.

**Table 2. 18-Year Mortality According to Body Mass Index (BMI) and Correlates**

Predictor	Hazard Ratio (95% Confidence Interval)
BMI, kg/m <sup>2</sup> (reference BMI < 25.0 underweight and normal weight)	
25.0–29.9 (overweight)	0.80 (0.67–0.95) <sup>a</sup>
≥ 30.0 (obese)	0.93 (0.71–1.22)
BMI change	
5% loss	1.65 (1.34–2.04) <sup>a</sup>
Stable	
5% gain	1.53 (1.18–1.99) <sup>a</sup>
Age	1.11 (1.09–1.13) <sup>a</sup>
Female	0.61 (0.52–0.72) <sup>a</sup>
Education	1.00 (0.96–1.03)
Multimorbidity	1.16 (1.10–1.23) <sup>a</sup>
Age × 5% BMI loss	0.93 (0.89–0.96) <sup>a</sup>
Age × 5% BMI gain	0.89 (0.85–0.92) <sup>a</sup>

Age was centered at 80, and scores for all measures and groups were effect-coded and - centered so that mortality hazards refer not to a specific group but to the overall sample.

<sup>a</sup>  $p < .05$ .

Figure 1. Survival probabilities over 18 years are shown for groups of older Swedish participants with different levels and rates of change in body mass index (BMI). The left panel illustrates that hazard ratios of mortality were lower for overweight participants than for those who were underweight or normal weight. Average group differences in survival time amount to almost a full year, after residualizing for age, sex, education, and comorbidities. The right panel shows that hazard ratios of mortality were higher for participants with 5% loss in BMI than for those with stable BMI. Average group differences in survival time amount to more than a full year, after residualizing for age, sex, education, and comorbidities.

Figure 2. Illustrating differences between participants with 5% body mass index (BMI) loss (upper panels) or 5% BMI gain (lower panels) and those with stable BMI, separately for people younger than 80 and those aged 80 and older. The detrimental effects of BMI change for mortality are only discernible in people in their 70s (left panels) but not in those aged 80 and older (right panels).

Figure 1.

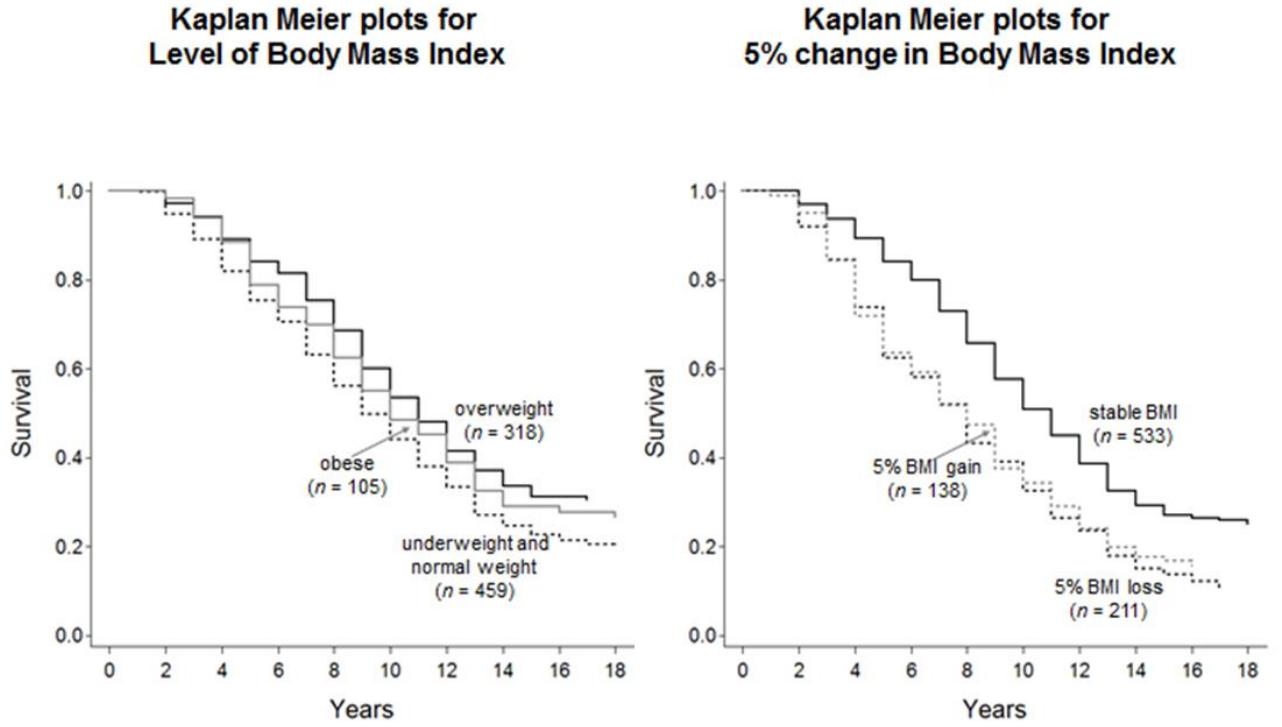


Figure 2.

