Weight Change, Initial Weight Status, and Mortality among Middle- and Older-Aged Adults

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ABSTRACT

It is not well known how the relationship between weight change and mortality is influenced by initial weight status and the magnitude of weight change. We use a sub-sample of the nationally representative Health and Retirement Study (n = 12,462; follow-up 1992-2004) to examine the relationship between weight change and mortality among 50-70 year old Americans with focus on the influence of initial weight status and the magnitude of weight change. We use Cox proportional hazards regression to estimate the relative mortality risks for two year weight change by initial weight status. We find that large and small losses (2.5-5.0 and 0.5-2.5 body mass index (BMI) units, respectively) were associated with excess mortality unless initial BMI was above 32 (e.g., hazard ratio (HR) for large loss for BMI of 30 = 1.53, 95% confidence interval (CI): 1.26, 1.86; HR for small loss for BMI of 30 = 1.22, 95% CI: 1.05, 1.42). Large or small gains were not associated with excess mortality in any initial BMI group. The inverse association between weight loss and mortality was robust to multiple adjustments for underlying health status and unobserved confounders. The results showing larger excess risk for larger losses and for lower initial weight status suggest that the potential benefits of a lower weight status are offset by the negative effects associated with weight loss.

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INTRODUCTION

Very high and very low levels of body mass index are associated with increased mortality.[1-4] It is not, however, well understood how *changes* in weight affect mortality risk, or how the effect of weight change depends on the magnitude of the change or initial weight status.

Prior studies on weight change and mortality suggest that weight loss is associated with an increase in mortality despite adjustments for baseline health status.[5-12] Results on weight gain are less uniform. While some studies indicate that weight gain has no effect or is associated with decreased mortality [5,9,11,13-17], others have found increased mortality.[8,10,18]

We build on prior work by studying the link between two-year weight change and mortality among adults aged 50-70 years. In contrast to previous work, we simultaneously examine two important modifiers of the weight change – mortality relationship. First, we examine how initial weight status modifies the effect of weight change. Since extreme levels of BMI carry a high mortality risk, we hypothesize that losses from high levels and gains from low levels might be more beneficial (or less harmful) than losses from low levels or gains from high levels. Second, we examine the influence of the magnitude of weight change. We account for potential confounders such as health status, smoking, and physical activity, and we study the sensitivity of our results to unobserved confounders.

While some prior work has addressed the influence of initial weight status or magnitude of weight change, most studies have considered only one of the modifiers at a time. [7-9,12-15,17] Studies which simultaneously examine the influence of both modifiers have considered longer term weight change, measured over decades[11,16] or have been potentially limited in statistical power.[5,6,10] We contribute to the literature on short-term weight change and mortality by simultaneously examining the influence of initial weight status and magnitude of weight change in a large, nationally representative sample of middle- and older-aged adults.

METHODS

Participants

We use the nationally representative Health and Retirement Study (HRS). The HRS has five entry cohorts, and we include persons who were 50-70 years old when entering the study. Our respondents are from the initial HRS cohort, born in 1931-1941 and entering the study in 1992; the Children of Depression cohort (CODA), born in 1924-1930 and entering in 1998; and the War Babies cohort (WB), born in 1942-1947 and entering in 1998.

Two weight measurements are needed to construct change, so we exclude respondents who were in the study for only one wave (7.6% of the sample). Those who were underweight (body mass index (BMI) < 18.5, 1.7%) or morbidly obese (BMI > 40, 2.3%) at the first interview are excluded, as weight change at these extremes may be more likely to reflect underlying illnesses. Finally, those whose BMI changed more than 5 units (3.1%) are excluded since such drastic changes may be caused by illness. This leaves a sample size of 13,513 (10,181 from HRS, 1,442 from CODA and 1,890 from WB). After excluding respondents with missing variables or matching problems with time of death data (9.2%), the remaining sample size is 12,462 with 1,504 deaths over an average follow-up of 8 years.

Variables

Month of death is obtained from the National Death Index (NDI). There were 93 respondents who had died according to HRS but were not found in the NDI register. We include these in our analysis, because censored survival time can still be obtained from HRS.

Initial weight status is measured as BMI (BMI = kg/m^2) and constructed from self-reported weight and height at the first interview. Weight change is measured in BMI units and is based on weight change between the first two interviews, which are approximately two years apart. We categorize weight change as large loss (2.5-5.0 BMI units), small loss (0.5-2.5 units), large gain (2.5-5.0 units) and small gain (0.5-2.5 units). The reference group, stable weight, is BMI change between -0.5 and 0.5 units. For a 5 foot 5 inches (1.65m) tall person stable weight is +/- 3 pounds of change (+/- 1.4kg), small change is 3-15 pounds (1.4-6.8kg), and large change is 15-30 pounds (6.8-13.6kg). Our results were not sensitive to small changes in the cutoff points for BMI change.

We control for both self-reported health conditions and self-rated health. HRS has data on eight conditions (see Table 2) based on responses to two types of questions: "Has a doctor ever told you that you have ..." (first interview) and "Since we last talked to you, that is since [last interview date], has a doctor told you that you have ..." (second interview). We construct eight indicators for the presence of conditions at the first interview, and eight indicators for conditions diagnosed during the weight change period.

We adjust for initial self-rated health and changes in self-rated health during the weight change period. Self-rated health is reported as excellent, very good, good, fair or poor in both the first and second interview. We code these to a 5 point continuous variable with 5 = excellent and 1 = poor. Change in self-rated health (continuous) ranges from -4 (from excellent to poor) to +4 (from poor to excellent). Using categorical rather than continuous variables did not change our results.

Additional control variables are sex, age (years), cohort (HRS/CODA/WB), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other), education (years), physical activity (indicator for 3+ times vigorous activity/week), and smoking (never/former/current).

Statistical models

We use nested proportional hazard models to estimate the hazard ratios for weight change. Model 1 estimates only the main effects of weight change while controlling for initial BMI, BMI squared, sex, age, age squared, race/ethnicity, HRS cohort, education, physical activity, smoking, pre-existing conditions, conditions diagnosed during the weight change period, initial self-rated health and change in self-rated health. We include squared BMI to capture the non-linear effect of initial weight status.[1-4]

Model 2 further considers how initial BMI modifies the effect of weight change by adding an interaction between initial BMI and weight change. Preliminary analyses with initial BMI modeled as a categorical variable suggested that the effect of weight change depends linearly on initial BMI. Therefore we model the interaction with initial BMI as a continuous variable. The results, however, were not sensitive to this choice.

We estimate the models using the Newton-Raphson algorithm and handle ties with the approximate likelihood method.[19] We use time-on-study for time scale and adjust for age and age squared; this approach performed well in a study comparing six different choices of time scale in observational longitudinal studies.[20] Confidence intervals are estimated using bootstrap with 10,000 replicates.[21] We use bootstrap instead of the Wald statistic because i) bootstrapping provides a straightforward approach to estimating confidence intervals for the net effects arising from interactions; and ii) for finite samples, bootstrapping often approximates the true distribution better than asymptotic based statistics.[22]

RESULTS

Descriptive analyses

Tables 1 and 2 show characteristics of the sample for demographic and health variables.

TABLE 1 ABOUT HERE

Table 1 shows that of the 12,462 respondents, 12.1% died during follow-up. The proportion deceased was lowest in the small gain and stable weight categories (10.3% and 10.5%, respectively) and highest in the large loss category (20.9%). Mean follow-up among those who died was shortest in the large loss and large gain categories and longest in the stable weight category. Mean age was 57.5 years at the first interview; 51.4% of the sample were women; and 75.2% were non-Hispanic white.

TABLE 2 ABOUT HERE

Table 2 shows health characteristics of the sample within weight change categories. Only 34.8% in the sample were normal weight, others being overweight or obese. Large weight change was positively associated with high initial BMI: in the large loss category 48.6% and in the large gain category 28.8% were obese, while in the stable weight category only 15.9% were obese. Average self-rated health at first interview was 3.5, which is between good (= 3) and very good (= 4). Self-rated health was lowest in the large loss and highest in the stable weight category. At first interview, 36.6% of respondents were free of pre-existing conditions. During the weight change period 18.1% were diagnosed with a new medical condition. Compared to those with stable weight, pre-existing conditions were more prevalent among those with weight change, particularly those who lost or gained a large amount of weight. The incidence of new conditions during the weight change interval was also highest in these two groups.

The univariate statistics of Table 1 suggest that people who lose or gain weight have a higher mortality risk than those whose weight is stable. Table 2 shows that people experiencing large weight changes are also less healthy and have higher initial weight status than those whose weight changes are small, highlighting the importance of adjusting for both health status and initial BMI.

Regression analyses

Next we consider multivariate analyses where relative mortality hazards for weight change are estimated while controlling for demographic, behavioral and health characteristics. Table 3 shows the estimated relative hazards of death for BMI change by initial BMI for Models 1 and 2**.** For example, the hazard ratio of 3.33 in Model 2 for large loss and initial BMI 18.5 means that given initial BMI 18.5, those who experienced a large weight loss had 3.33 times higher risk of death than those with stable weight.

TABLE 3 ABOUT HERE

FIGURE 1 ABOUT HERE

In Model 1 both large and small losses are associated with increased mortality, but the hazard ratio for large loss is more than 3 times larger (1.72 vs. 1.22). Weight gains, large or small, are not associated with mortality. Model 2 adds interactions between BMI change and initial BMI to Model 1; the interactions were jointly significant ($P = 0.013$). The results, also illustrated in Figure 1, show that the effects of weight loss are significantly modified by initial weight status: large losses are associated with increased mortality, but the higher the initial BMI, the smaller this effect. In fact, the increase in mortality is only significant ($P < 0.05$) up to a BMI of ~32 (see Figure 1). The effect of small losses also loses significance at a BMI ~32, but the gradient with initial weight status is flatter. Large gains are estimated to increase mortality if initial BMI is over ~ 27, but estimates are not statistically significant. Small gains are not associated with mortality for any initial BMI.

In summary, both large and small weight losses are associated with increased mortality, and the larger the loss and the lower the initial weight status, the larger the effect. Among those who were obese at baseline, this negative effect becomes non-significant. Large weight gains may be associated with increased mortality among the obese but the effect is statistically non-significant and substantively small compared to weight loss. Small gains are not associated with increased mortality.

Sensitivity analyses

We study the robustness of our results to unobserved confounders using external adjustment.[23,24] We restrict the analysis to weight loss since the effects of weight gain are small. We consider a confounder whose prevalence among weight losers ranges from 0.0 to 0.8, whose effect on the hazard ratio is 1.5, 2.0 or 2.5 net of other controls, and whose prevalence is 50% higher in the weight loss categories than in the stable weight group. We calculate the confounder-adjusted hazard ratios for large and small weight loss at an initial BMI 25.

The confounder-adjusted hazard ratio for large weight loss stayed statistically significant at all confounder combinations. Even if the confounder prevalence was 0.8 in the weight loss category and the effect of the confounder was 2.5, the adjusted hazard ratio for large weight loss was 1.76 with 95% confidence interval: 1.46, 2.12. The effect of small weight loss lost significance only if both the prevalence in the weight loss category and the effect on mortality were high. For example, for prevalence of 0.4 and effect of 2.0 the adjusted hazard ratio was 1.11 with 95% confidence interval: 1.00, 1.24. The point estimates, however, stayed above 1 at all confounder combinations. In summary, the confounder prevalence and its effect on mortality would need to be very high to account for the estimated effects.

We also studied the sensitivity of our results to smoking and cancer, estimating Models 1 and 2 for never smokers who did not have cancer. The results (not shown) did not change in any meaningful fashion.

DISCUSSION

Short-term weight change is a risk factor for mortality among older Americans. The direction and magnitude of risk, however, depends on the direction and magnitude of the change itself and on initial weight status. In this study, weight loss was associated with increased mortality among normal and *overweight* people. The size of the effect depended on initial BMI and the amount of weight lost, so that the lower the initial weight status and the larger the loss, the larger the effect. The weight loss – mortality association suggests that weight loss itself, or the practices used to lose weight, are harmful, even if one is overweight. In fact, weight loss was associated with a statistically significant increase in mortality up to a BMI of ~32, which includes the lower range of class I obesity (30-34.9).

To minimize confounding from unintentional weight loss due to illness, we controlled for diagnosed conditions and self-rated health before weight change, as well as changes in these factors during the weight change period. We also conducted sensitivity analyses excluding smokers and persons with diagnosed cancer. The observed weight loss – mortality association could still, however, be due to *undiagnosed* conditions. If this were the case, the interaction with initial BMI would support the "obesity paradox" hypothesis[25,26], indicating that when such conditions occur, being obese may be protective.

We also found that weight gain has a much weaker association with mortality than weight loss. We found no statistically significant evidence that large or small gains would change mortality risk in any of the initial BMI groups. However, for large gains there was a weak indication of increased mortality among the obese, decreased mortality among normal weight persons and no effect among the overweight. Though we did not have enough statistical power confirm these findings, the results are substantively interesting and consistent with studies showing that among older people, overweight is not associated with excess mortality.[27-29]

To summarize, the effects of weight changes are asymmetrical: both large and small weight losses are strong indicators of increased mortality among normal and overweight people aged 50-70 years. Weight gain, on the other hand, has a much weaker and non-significant association with mortality.

This study has limitations. First, BMI was constructed from self-reported height and weight. However, self-reported and clinically measured height and weight are known to be highly correlated[30] and among older persons the correlation for weight may be as high as 0.98 because of diminished cultural pressures to be thin.[31,32] Second, the data did not allow us to study causes of death. Recent research has shown that the BMI – mortality association varies by cause of death.[33] The effect of weight change may also vary by cause of death. Prior research has found that weight loss may be associated with increased cardiovascular and coronary heart disease mortality[5,17,34] and non-cancer mortality,[8] but with decreased diabetes-related mortality.[18,35] Further research should study how the weight change – cause-specific mortality relationship is modified by initial BMI. Third, we did not have direct information on whether weight losses were intentional or unintentional. However, our extensive controls for underlying health conditions, as well as changes in these conditions, were designed to adjust for sources of unintentional weight loss. Moreover, prior work has shown increased mortality for both intentional and unintentional weight loss and even higher mortality when weight loss was intentional.[10] We also studied the robustness of our results to an unobserved confounder and found that in order to dissipate the weight loss effects, the confounder would need to have both high prevalence and a very large effect on mortality, *after* controlling for the other variables. Existence of such an unknown confounder seems unlikely.

Despite these limitations, our findings have important implications. We found weight loss to be associated with increased mortality among both overweight and obese persons (up to a BMI ~32). If weight loss from these BMI levels is potentially harmful, public health policy should focus on prevention rather than “treatment” of overweight and obesity. In the U.S., 61.8% of those who considered themselves somewhat overweight and 52.0% of those who considered themselves a little overweight reported that they were trying to lose weight.[36] Even small weight losses were associated with increased mortality, and patients should be educated on the potentially harmful effects of weight loss from unhealthy diets or other weight-loss behaviors. More research is needed on the health effects of various weight loss strategies (dieting, exercise, eating disorder behavior) used by the general population; simply knowing whether the loss is intentional may not be enough.

Our results are not inconsistent with the research showing that weight loss decreases cardiovascular risk factors such as hypertension and hyperlipidemia,[37,38] and may be associated with decreased mortality among overweight diabetics.[9,18] We find, however, no evidence in the *general population* aged 50-70 that weight loss would decrease mortality for overweight persons. In fact, our findings suggest that weight loss may even *increase* mortality for overweight persons, and for obese persons up to a BMI of ~32, despite rigorous adjustments for underlying health status. Among the morbidly obese, large weight loss achieved by bariatric surgery has been shown to decrease mortality.[39,40] This is in line with our estimate of 0.78 for the hazard ratio for large loss from an initial BMI of 40.

In summary, our findings suggest that for older persons, weight loss does not have significant positive health effects and may be harmful among normal and overweight people. Weight gains, large and small, on the other hand, seem to be harmless among the normal and overweight, and potentially harmful only among the obese. Given that only a small proportion of the older population is obese and experiencing large weight gains (7.6 % in this study), and a relatively large proportion is either normal or overweight and losing weight (20.8 % in this study), weight losses might warrant more attention than weight gains.

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Table 1. Baseline Demographic Characteristics (Means and Standard Errors) Within Weight Change Categories. Heart and Retirement Study, 50-70 Year Old Participants, Entry in 1992 and 1998.

	Overall	Stable weight	Large loss	Small loss	Large gain	Small gain
Number of respondents	12,462	3,975	657	3,017	767	4,046
Died, %	12.1	10.5	20.9	14.5	12.4	10.3
Mean follow-up, years						
For those who died	5.0 (2.8)	5.2 (2.7)	4.4 (2.9)	5.0 (2.8)	4.6 (2.6)	5.1 (2.7)
For censored	8.4 (2.5)	8.3 (2.6)	8.4 (2.5)	8.5 (2.5)	8.5 (2.5)	8.4 (2.5)
Years between two first interviews	1.85 (0.2)	1.85 (0.2)	1.86 (0.2)	1.86 (0.2)	1.85 (0.2)	1.85 (0.2)
Age at first interview, years	57.5 (5.4)	57.8 (5.6)	57.7 (5.6)	57.6 (5.4)	56.5 (4.8)	57.1 (5.2)
Women, %	51.4	50.0	56.9	50.6	59.8	50.8
Race/Ethnicity, %						
Non-Hispanic white	75.2	77.7	68.0	74.9	69.5	75.2
Non-Hispanic black	14.6	12.9	19.0	15.0	19.0	14.5
Hispanic	8.1	7.3	11.0	7.6	9.6	8.7
Other	2.0	2.1	2.0	2.5	1.8	1.7
Education, years	12.3 (3.2)	12.5 (3.0)	11.4 (3.7)	12.2 (3.2)	11.6 (3.4)	12.4 (3.1)

Table 2. Baseline Health Characteristics (Means and Standard Errors) Within Weight Change Categories. Heart and Retirement Study, 50-70 Year Old Participants, Entry in 1992 and 1998.

	Overall	Stable weight	Large loss	Small loss	Large gain	Small gain
Initial BMI distribution, %						
18.5-24.9	34.8	42.0	14.5	26.9	28.3	38.2
25.0-29.9	43.3	42.2	36.9	46.6	42.9	43.1
30.0-39.9	21.9	15.9	48.6	26.5	28.8	18.7
Current smoker, %	27.8	27.0	30.9	30.6	31.2	25.5
Previous smoker, %	34.6	34.0	30.3	34.7	30.6	36.5
Phys. activity 3+times/week, %	28.6	31.5	24.7	27.7	21.6	28.4
Self rated health[a]	3.5 (1.2)	3.6 (1.2)	3.1 (1.2)	3.4 (1.2)	3.2 (1.2)	3.5 (1.2)
Change in self rated health[b]	-0.1 (0.9)	-0.1 (0.9)	-0.1 (1.1)	-0.0 (0.9)	-0.2 (0.9)	-0.1 (0.9)
Diagnosed conditions before entering the study, %						
High blood pressure or hypertension	34.6	32.4	41.2	36.8	40.5	33.1
Diabetes or high blood sugar	9.2	7.8	16.4	10.8	10.2	8.2
Cancer or a malignant tumor (not skin cancer)	5.1	4.5	6.7	5.4	6.0	5.0
Chronic lung disease except asthma	4.8	4.3	7.5	5.4	5.6	4.2
Heart attack, cor. heart dis., other heart problems	11.4	9.7	14.9	12.2	11.2	12
Stroke or transient ischemic attack (TIA)	2.8	2.3	5.2	3.2	3.7	2.4
Emotional, nervous, or psychiatric problems	7.1	6.7	10.5	7.3	10.3	6.2
Arthritis or rheumatism	33.4	32.0	38.8	33.9	37.5	32.9
No pre-existing conditions	36.6	40.0	29.7	33.8	32.6	37.2
Conditions diagnosed during the weight change period, %						
High blood pressure or hypertension	3.9	3.7	5.3	3.8	4.6	3.8
Diabetes or high blood sugar	1.8	1.3	3.8	2.3	1.6	1.5
Cancer or a malignant tumor (not skin cancer)	1.4	1.1	3.3	1.4	1.2	1.5
Chronic lung disease except asthma	1.4	1.2	1.2	1.5	2.2	1.5
Heart attack, cor. heart dis., other heart problems	2.5	1.7	4.6	3.3	4.4	2.0
Stroke or transient ischemic attack (TIA)	0.7	0.4	1.8	0.9	0.7	0.8
Emotional, nervous, or psychiatric problems	2.0	1.5	3.5	2.1	2.9	2.1
Arthritis or rheumatism	7.3	7.2	8.8	6.8	9.3	7.3
No new conditions	81.9	84.2	74.1	80.7	77.3	82.6

[a] Measured on a scale from 5 (excellent) to 1 (poor)

[b] Measured on a scale from -4 (from excellent to poor) to +4 (from poor to excellent)

Table 3. Net Effect of Weight Change on Mortality Hazard Ratio[a] and 95% Confidence Interval by Model, Initial Body Mass Index (BMI) and Weight Change Category. Heart and Retirement Study, 50-70 Year Old Participants, 1992-2004.

	Large loss		Small loss		Large gain		Small gain	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Model 1 [b]								
Initial BMI								
d	1.73	1.41, 2.12	1.22	1.07, 1.40	1.02	0.81 ,1.28	1.00	0.88, 1.15
Model 2 [c]								
Initial BMI								
18.5	3.33	2.26, 4.90	1.25	0.98, 1.59	0.88	0.59, 1.32	1.00	0.79, 1.26
20.0	3.01	2.16, 4.20	1.24	1.00, 1.54	0.90	0.63, 1.29	1.00	0.81, 1.23
25.0	2.15	1.76, 2.62	1.23	1.09, 1.40	0.97	0.78, 1.21	1.00	0.88, 1.13
30.0	1.53	1.26, 1.86	1.22	1.05, 1.42	1.05	0.84, 1.31	1.00	0.86, 1.17
35.0	1.10	0.79, 1.53	1.20	0.93, 1.56	1.13	0.79, 1.63	1.00	0.77, 1.31
40.0	0.78	0.47, 1.29	1.19	0.81, 1.75	1.22	0.71, 2.10	1.01	0.68, 1.50

a The net effect is estimated as exp(b1+b2*BMI), where b1 is the main effect for BMI change and b2 is the effect for interaction Initial BMI x BMI change.

b Model 1: Controls for BMI, BMI squared, sex, age, age squared, race/ethnicity, cohort, education, physical activity, smoking, pre-existing conditions, conditions diagnosed during the weight change period, initial self-rated health and changes in self-rated health.

c Model 2: Adds interactions between BMI change and initial BMI to Model 1; likelihood ratio test for interactions was significant with *P* = 0.013.

d For model 1, the net effect is constant since the interaction is omitted.

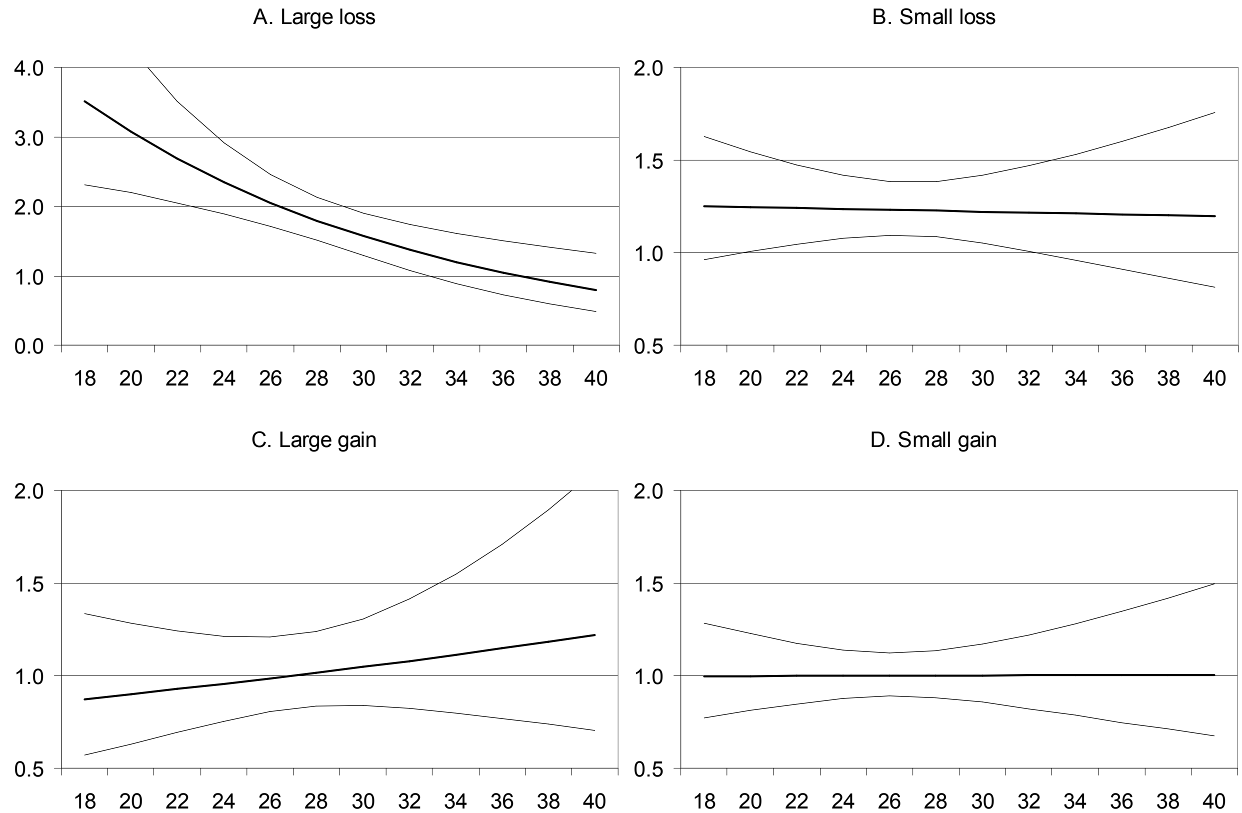

Figure 1. Mortality Hazard Ratio and 95 % Confidence Interval for Weight Change by Initial Body Mass Index (Model 2); Hazard Ratio on Vertical Axis, Initial Body Mass Index on Horizontal Axis. Heart and Retirement Study, 50-70 Year Old Participants, 1992 – 2004.