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THE ASSOCIATION BETWEEN WEIGHT FLUCTUATION AND MORTALITY: RESULTS FROM A POPULATION-BASED COHORT STUDY

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ABSTRACT: Previous studies evaluating the association between weight fluctuation and mortality are limited and have conflicting results. This study will further evaluate the association between weight fluctuation and mortality in a nationally representative cohort by performing survival analysis of NHANES I and NHANES I Epidemiologic Follow-up Study ($n = 8479$; weighted sample = 68,200,905). This cohort was followed from 1971 to 1992 and categorized using weight change over five time points into stable non-obese, stable obese, weight gain, weight loss and weight fluctuation groups. All-cause mortality (ACM) and cardiovascular mortality (CM) were evaluated. Respondents with weight fluctuation had higher ACM (HR: 1.83, 95% CI: 1.25–2.69) and CM hazards ratios (HR: 1.86, 95% CI: 1.10–3.15) than the stable non-obese group, even after controlling for pre-existing disease, initial BMI and excluding those in poor health or incapacitated. Increased mortality was also seen in the weight loss group (ACM HR: 3.36, 95% CI: 2.47–4.55), (CM HR 4.22, 95% CI: 2.60–6.84). The stable obese group did not have increased ACM, but did have increased CM prior to the exclusion of those in poor health or incapacitated. (HR: 2.17, 95% CI: 1.10–4.28). Weight fluctuation is associated with a higher risk of all-cause and cardiovascular disease mortality in the US population, even after adjustment for pre-existing disease, initial BMI and the exclusion of those in poor health or incapacitated. Thus, health care providers should promote a commitment to maintaining weight loss to avoid weight fluctuation and consider patients' weight histories when assessing their risk status.

KEY WORDS: weight fluctuation; weight cycling; mortality; cohort, NHANES.

INTRODUCTION

Weight fluctuation is defined as repeated gains and losses of weight over time. It may occur due to an underlying medical condition, such as

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congestive heart failure or thyroid disease. It can also occur due to unsuccessful dieting, where individuals initially lose weight but then regain it later on. Up to one-third of men and half of women in the United States are trying to lose weight,[1] but only 5–20 percent of those who lose weight will be successful in maintaining the weight loss.[2,3] Thus, unsuccessful maintenance of weight loss can lead to weight fluctuation in a majority of those who diet.

Studies on the metabolic effects of weight fluctuation show conflicting results. Several studies support that weight fluctuation is associated with changes in metabolism. For example, studies have shown an association between weight fluctuations and impaired glucose tolerance,[4–6] elevated blood pressure, [7,8] and a less favorable lipid profile.[9,10] These associations may be due to the presence of ''catch-up fat,'' which occurs when initial weight loss followed by weight gain results in the preferential regain of body fat.[11–13] ''Catch-up fat'' may be associated with insulin resistance and overactive sympathetic activity, risk factors for diabetes, hypertension and cardiovascular disease.[14]

The association between weight fluctuation and mortality has been the focus of a variety of studies. Some studies have found increased risks of mortality while others have not. Studies based on specific population groups with limited generalizability (e.g., nondiabetic Pima Indians) or regional populations (e.g., residents of Framingham, Massachusetts) report higher mortality, even after adjustment for pre-existing illness.[15–20] Other studies, also based on specific population groups with limited generalizability (e.g., British men who never smoked) or regional populations (e.g., residents of Charleston, South Carolina) do not report an increased mortality risk. [5,21–23] Furthermore, these conflicting results are difficult to evaluate due to variable assessments of weight fluctuation, with some studies using only three weight measurements occurring years apart. To help clarify these results, this study will evaluate the association between weight fluctuation and mortality via a nationally representative cohort of adults that includes weight measurements at five different points in time, with two pairs of weight being 6–12 months apart.

METHODS

Survey Description

The National Health and Nutrition Examination Survey I (NHANES I) is a multistage, stratified probability survey of the non-institutionalized civilian United States population. NHANES I Epi-

demiologic Follow-up Study (NHEFS) is a national longitudinal study designed to investigate the relationships between factors assessed in NHANES I and subsequent morbidity and mortality. This cohort follows individuals who were 25–74 years old at the time of the index interview (1971–1974). Follow-up interviews occurred in 1982–1984, 1987 and 1992.

The follow-up information was gathered from surviving subjects. If the subject was incapacitated, a proxy respondent was administered a modified subject questionnaire. If the subject was deceased a separate proxy questionnaire was used and death certificate information was recorded.

Sampling weights were calculated taking into account unequal probabilities of selection due to sample design, non-response and planned oversampling, then matched to known population control totals to be representative of the US population. This strategy allows for the computation of nationally representative estimates. The unweighted number of adults (≥ age 25) with complete data was 8479, which provides a weighted sample size of 66,399,447. There were 979 documented deaths from 1987 to 1992.

Definition of Weight Categories

Weight categories were defined using Body Mass Index (BMI) calculated at five timepoints based on information from the initial exam in 1971–1974, the 1982–1984 and the 1987 follow-ups. Height and weight were measured in the initial exam. In the 1982–1984 interview subjects were asked their current weight, and how it compares to their weight 6 months ago. In 1987, subjects were asked their current weight and how it compares to their weight 12 months ago. Comparisons were characterized as about the same, at least 10 pounds more, or at least 10 pounds less. An average BMI for each individual was obtained based on the five BMI measurements calculated from this information. The absolute value of the difference between each individual BMI measurement and the individual's average BMI was calculated. These absolute values were summed to provide the sum of deviations for each individual.

Respondents with initial and final BMI differing by < 3.0 BMI units were considered to have stable weight if the sum of deviations was less than the average for the entire population (sum of deviations ≤ 5.04). These respondents were also categorized based on their initial BMI as obese (BMI ≥ 30) or non-obese (BMI < 30).[24] Weight gain was defined as an increase of ≥ 3.0 BMI units from initial to final BMI.

Weight loss was defined as a decrease of ≥ 3.0 units from initial to final BMI. Weight fluctuation was defined as a sum of deviations > 5.04 for those with < 3.0 unit difference from the initial to final BMI. These definitions allow us to define weight fluctuation based on an individual's weight variability through time while still accounting for the progressive change in body weight associated with continuous weight loss or gain.

Control Variables

Several control variables were used for these analyses. Race and smoking status were based on self-report. Initial BMI was based on measured weight and height at baseline. The Charlson Comorbidity Index (CCI), which was specifically designed to control for health status in longitudinal studies with mortality as an outcome by accounting for age, cardiovascular risk factors and other comorbid diseases, was calculated according to the method of Charlson et al.[25]

Outcomes

Mortality from 1987 to 1992 was used to calculate the length of time in years until death. This was used as the response variable. Both all-cause and cardiovascular mortality were analyzed. Cardiovascular mortality was defined using the primary cause of death documented on death certificates by ICD-9 codes. Codes consistent with cardiovascular mortality were 401–404, 410–417, 420–429, 440–448.

Analysis

Due to the complex survey design, the appropriate weights were accounted for using SUDAAN (Research Triangle Institute, Research Triangle Park, NC). Survival analyses using Cox proportional hazards models were performed for all-cause and cardiovascular mortality. Hazard ratios were obtained after adjusting for age, gender, race, initial BMI, smoking status and CCI. The non-obese, stable weight group was considered the control group for these analyses. In order to further adjust for underlying health status, hazard ratios were also obtained after the exclusion of individuals with self-reported poor health and/or those who were incapacitated in the 1987 interview, prior to the assessment of mortality for this study. Age, gender, race, initial BMI, smoking status and CCI were again used as control variables, with the stable, non-obese group as the referent category.

RESULTS

Demographic data for each weight change group, based on weighted population estimates, are shown (Table 1). Values are based on the initial examination for each respondent. Mean weight change from the initial examination to the final examination is also shown.

Schoenfeld test of residuals for the proportionality of hazards assumption within the models was computed, and showed proportionality of hazards for this data.[26] Results of survival analysis for all-cause mortality are shown in Table 2. The weight fluctuation and weight loss groups have significantly higher mortality hazards ratios than the stable non-obese group. These results remain significant after the exclusion of those in poor health and/or those who were incapacitated in 1987. The model predicting CVD mortality also showed increased mortality in the stable obese group and the weight loss group. The weight fluctuation group in this model had a hazard ratio of 1.48 (95% CI: 1.00–2.19) (Table 3). When those in poor health or incapacitated in 1987 were excluded, the

TABLE 1

Population Characteristics for US Adults by Weight Change Category

	Stable Weight, Non-obese	*Stable Weight, Obese*	*Weight Gain*	*Weight Loss*	*Weight fluctuation*
Sample size	36,021,912	3,633,457	13,135,170	5,573,637	8,035,271
Gender					
Male (%)	51.2	48.5	41.0	31.0	39.6
Female (%)	48.8	51.5	59.0	69.0	60.4
Race					
Non-Hispanic White (%)	93.9	88.4	89.3	87.0	90.8
African American (%)	5.2	11.0	9.9	13.0	8.5
Other (%)	0.9	0.6	0.8	0.1	0.7
Mean Age (SE)	44.7 (0.24)	47.6 (0.59)	38.9 (0.32)	51.6 (0.56)	43.8 (0.47)
Mean BMI (SE)	24.0 (0.06)	32.8 (0.14)	24.6 (0.16)	30.8 (0.28)	26.8 (0.21)
Mean change in BMI (SE)	0.43 (0.03)	−0.14 (0.11)	5.03 (0.06)	−5.55 (0.10)	0.49 (0.07)

TABLE 2

Hazards Ratios for All-Cause Mortality

	Total Sample		*Excluding Those Incapacitated or in Poor Health in 1987*	
	HR	*95% CI*	*HR*	*95% CI*
Weight Change Category				
Stable Weight, Non-obese	1.00	–	1.00	–
Stable Weight, Obese	1.53	(0.94–2.50)	1.35	(0.64–2.85)
Weight Gain	1.11	(0.78–1.58)	1.10	(0.72–1.67)
Weight Loss	3.88	(2.98–5.04)	3.36	(2.47–4.55)
Weight Fluctuation	1.81	(1.35–2.44)	1.83	(1.25–2.69)
Age Group				
25–34	1.00	–	1.00	–
35–52	3.27	(1.64–6.53)	2.61	(1.20–5.71)
53–69	10.38	(5.20–20.69)	9.29	(4.47–19.30)
>69	23.68	(12.35–45.42)	20.69	(10.35–41.37)
Gender				
Male	1.00	–	1.00	–
Female	0.49	(0.42–0.58)	0.46	(0.38–0.56)
Race				
White	1.00	–	1.00	–
Black	1.39	(0.98–1.97)	1.36	(0.82–2.25)
Other	0.75	(0.28–2.04)	0.29	(0.08–1.10)

Smoking status				
Non-Smoker	1.00	–	1.00	–
Current Smoker	1.60	(1.30–1.97)	1.87	(1.50–2.33)
BMI				
≤30	1.00	–	1.00	–
>30	0.88	(0.66–1.17)	0.97	(0.63–1.49)
CCI Score	1.18	(1.12–1.24)	1.17	(1.10–1.24)

TABLE 3

Hazards Ratios for Cardiovascular Mortality

	Total Sample		*Excluding Those Incapacitated or in Poor Health in 1987*	
	HR	*95% CI*	*HR*	*95% CI*
Weight Change Category				
Stable Weight, Non-obese	1.00	–	1.00	–
Stable Weight, Obese	2.17	(1.10–4.28)	2.37	(0.97–5.75)
Weight Gain	1.15	(0.64–2.04)	1.24	(0.62–2.49)
Weight Loss	3.17	(2.19–4.58)	4.22	(2.60–6.84)
Weight Fluctuation	1.48	(1.00–2.19)	1.86	(1.10–3.15)
Age Group				
25–34	1.00	–	1.00	–
35–52	2.78	(0.91–8.51)	2.23	(0.70–7.08)
53–69	8.70	(3.17–23.86)	6.30	(2.36–16.78)
>69	17.68	(6.15–50.84)	14.38	(4.85–42.64)
Gender				
Male	1.00	–	1.00	–
Female	0.41	(0.31–0.53)	0.33	(0.24–0.46)
Race				
White	1.00	–	1.00	–
Black	1.26	(0.65–2.46)	1.10	(0.36–3.35)
Other	1.08	(0.22–5.22)	0.34	(0.06–1.87)

Smoking status				
Non-Smoker	1.00	–	1.00	–
Current Smoker	1.26	(0.91–1.75)	1.18	(0.80–1.72)
BMI				
≤30	1.00	–	1.00	–
>30	1.34	(0.88–2.06)	1.26	(0.72–2.19)
CCI Score	1.24	(1.15–1.34)	1.29	(1.18–1.40)

hazard ratio for the weight fluctuation group was 1.86 (95% CI: 1.10–3.15).

DISCUSSION

Results from this study indicate weight fluctuation is associated with a significantly increased risk in both all-cause and cardiovascular disease mortality in the adult US population. This finding extends and clarifies conflicting results that have been presented in the more limited studies conducted in the past.[5,15–23]

Previous studies show no association between weight fluctuation and mortality in very healthy individuals.[22,23] This has been attributed to an underlying disease confounding the association between weight fluctuation and mortality, by both causing the weight fluctuation and being associated with increased mortality. Results from this study suggest this may not be an appropriate assumption. First of all, the CCI, used to adjust for health status, was associated with increased risks of both all-cause and cardiovascular mortality, supporting its validity as a control variable. Furthermore, in this study, weight fluctuation was defined in a way that assessed the individual's weight variability over at least 13 years, since when calculating the sum of deviations, the first weight used was assessed in 1971–1974 and the last in 1987. Also, because of the categorization into weight loss and weight gain groups, change in only one direction would not be classified as weight fluctuation, and thus the individual would need to have multiple changes in weight over time to be categorized into the weight fluctuation group. Therefore, for the association between weight fluctuation and mortality to be confounded by an underlying disease, the individual would need to have an underlying disease for a long period of time that was not accounted for by the CCI and that did not lead to poor health or incapacitation when assessed in 1987, but did cause weight fluctuation and mortality within 5 years. This is not a probable scenario.

Considering that weight fluctuation has been associated with deleterious metabolic changes, the lack of association between weight fluctuation and mortality in healthy individuals may instead be due to weight fluctuation taking longer to affect those who are healthy, or a ''healthy population'' effect. We do not know if the association would reappear with longer follow-up of the healthy individuals, and thus cannot conclude from these studies that weight fluctuation is not detrimental to healthy individuals. Therefore, weight fluctuation should be avoided and

patients' weight histories should be considered when defining their risk status.

As higher BMI has already been associated with increased risk of mortality,[24] we controlled for baseline obesity in our analysis. This leads to the finding that groups with stable obesity do not have higher risk of all-cause mortality but did have higher risk of cardiovascular mortality. This points to the impact of weight fluctuation, since its association with increased all-cause mortality is seen whether individuals are obese or not, and unlike the stable obese group, the association with cardiovascular mortality is present even after exclusion of those in poor health or incapacitated in 1987.

Williamson et al. showed intentional weight loss is associated with decreased mortality.[27] Thus, the increased mortality seen in the weight loss group is probably due to unintentional weight loss. These results agree with several previous studies and are generally attributed to older age, which is consistent with our findings since the weight loss group was older than the other weight change groups. In addition, the presence of illnesses such as cancer, depression, and end-stage heart disease, and harmful health behaviors, all of which can lead to unintentional weight loss have been associated with increased mortality.[17,28] In contrast to the weight fluctuation group, the weight loss group does encompass individuals who have one change in weight (weight loss) months prior to the assessment of mortality, and thus could have an underlying disease leading to weight loss and mortality that had not yet been detected in 1987.

There are limitations to this study. Four of five weights used to calculate BMI are self-reported, which may decrease the precision of our estimates. However, previous studies have validated the use of self-reported weight for epidemiologic studies and have found that the overweight usually underreport their weight.[29,30,31] This might lead to the misclassification of those with weight fluctuation or weight gain into stable groups, which would decrease the effect size seen in the weight fluctuation group. Since respondents had their height and weight measured at baseline, initial classifications as obese or non-obese are not affected. This study is not able to assess weight loss intention, and thus we are not able to differentiate between individuals with weight fluctuation due to dieting vs. unintentional weight fluctuation. Generally individuals do no weight cycle intentionally, and as previously stated, due to the definition of weight fluctuation, control variables and exclusions used in this study, it is not likely that an underlying, undetected disease accounted for both the weight fluctuation and increased mortality. Finally, two weights were documented as 10 pounds more or less than

current weight. Since individuals may have lost or gained much more than 10 pounds, it is possible some individuals with weight fluctuation were misclassified into stable weight categories. This would bias our study towards lessening the association between weight fluctuation and mortality, since the stable, non-obese group was used as the reference category.

There are also several strengths to this study. Unlike many other studies, it defines weight fluctuation based on multiple changes that occur over a relatively short period of time, with two pairs of changes evaluated over 6–12 months. This provides a more appropriate definition of weight fluctuation than that based on 3 weights over many years. Finally, since this study uses data from a large national probability sample, it is possible to make population estimates while controlling for a number of other relevant factors in our analysis.

CONCLUSION

Weight fluctuation is associated with a higher risk of all-cause and cardiovascular mortality in the US population, even after adjustment for pre-existing disease, initial BMI and the exclusion of those in poor health and the incapacitated. Thus, health care providers should more aggressively promote a commitment to maintaining weight loss to avoid weight fluctuation and consider patients' weight histories when assessing risk status.

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