

Weight Cycling and Mortality Among Middle-aged or Older Women

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Background: Controversy exists about whether weight cycling increases morbidity and mortality.

Methods: To assess the independent association of weight cycling with mortality, we conducted a prospective study of 44 882 middle-aged or older women in the Nurses' Health Study who provided information on intentional weight losses between 1972 and 1992, survived until at least 1994, had a body mass index (calculated as weight in kilograms divided by height in meters squared) of at least 17, and had no history of cancer (other than nonmelanoma skin cancer) or heart disease. Women who reported they had intentionally lost at least 9.1 kg at least 3 times were classified as severe weight cyclers. Women who had intentionally lost at least 4.5 kg at least 3 times but did not meet the criteria for severe weight cycling were classified as mild weight cyclers. All-cause mortality and cardiovascular mortality were assessed.

Results: Between 1972 and 1992, approximately 18.8% of the women were mild weight cyclers, and 8.0% were severe weight cyclers. During 12 years of follow-up, 2884 women died; of their deaths, 425 were due to cardiovascular events. Weight cyclers gained more weight during follow-up than noncyclers ($P < .001$). After adjusting for BMI at age 18 years, physical activity, smoking, postmenopausal hormone replacement therapy, alcohol intake, net weight change from age 18 years, and change in physical activity, there was no increase in risk of all-cause mortality among mild (relative risk [RR], 0.83; 95% confidence interval [CI], 0.75-0.93) or severe cyclers (RR, 0.89; 95% CI, 0.77-1.04). Similar results were observed for cardiovascular mortality and among women 70 years or younger.

Conclusion: Repeated intentional weight losses were not predictive of greater all-cause or cardiovascular mortality.

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DURING THE PAST 2 DECADES some studies¹⁻⁴ have reported that weight loss, weight variability, and weight cycling are associated with increased health risks. These reports of adverse health outcomes associated with weight cycling or loss have led some to question whether it is prudent to recommend that overweight adults should try to lose weight. Although most of the early studies suggested that weight variability, loss, and cycling^{2,3,5} were associated with an increased risk of mortality or morbidity, findings from the later studies⁶⁻¹² have not been consistent. The discrepancy in results may reflect the fact that a variety of measures of weight cycling or weight variability have been used, and some studies failed to differentiate intentional from unintentional weight loss.^{13,14}

The importance of not accounting for the intentionality of weight losses should not be underestimated. Among a cohort of middle-aged women, French et al¹⁵ observed that the prevalence of intentionally and unintentionally losing 9.1 or more

kg at least once were approximately equal. Moreover, unintentional weight loss has been associated with smoking, poor health status, and age,^{16,17} 3 important confounders of chronic disease morbidity and mortality. Thus, if unintentional weight loss carries risks that are not associated with voluntary weight loss, failure to account for the intentionality of the weight loss could lead to faulty inference.

Relatively few studies have assessed the health consequences of voluntary weight loss or losses, and the results from large cohort studies¹⁸⁻²³ of women have been inconsistent. If 1 or more episodes of intentional weight loss are associated with increased morbidity, the public health implications are enormous. Instead of counseling overweight people to lose weight, all efforts would need to be placed on preventing weight gain if both weight gain and weight loss were associated with increased risk.

To understand better the relationship between weight cycling and mortality, we investigated the independent associations of weight cycling independent of re-

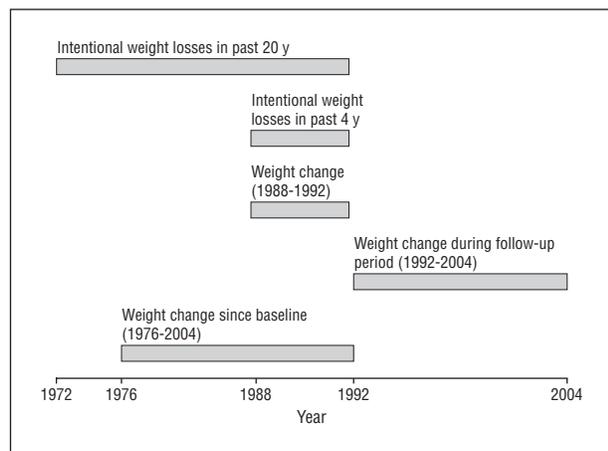


Figure. Periods of intentional weight losses and net weight changes during the study period.

cent and long-term intentional weight losses and net weight change, and mortality among middle-aged or older women in the Nurses' Health Study (NHS).

METHODS

SAMPLE

The NHS cohort was established in 1976, when 121 701 female registered nurses aged 30 to 55 years completed a postal questionnaire about risk factors for, and history of, cancer and cardiovascular disease (CVD). Since 1976, follow-up questionnaires have been sent every 2 years to the entire cohort, updating information on a broad range of risk factors. Women who did not answer the 1988 or 1992 questionnaire ($n=23\,914$), were diagnosed as having cancer (other than nonmelanoma skin cancer) or heart disease ($n=9557$), did not complete all of the intentional weight loss questions ($n=34\,560$), reported no losses in the past 20 years but reported losses in the past 4 years ($n=19$), did not report their weight at age 18 years ($n=5807$), had a body mass index (BMI), calculated as weight in kilograms divided by height in meters squared, of less than 17 ($n=286$), reported bypass surgery (in 1992) ($n=108$), or died in the period of 1988 to 1994 ($n=551$) were excluded from the analysis, thus leaving 44 882 women in the analysis.

The women who did not answer the 1988 or 1992 questionnaires were very slightly younger (42.4 vs 42.9 years) and heavier (BMI, 24.0 vs 23.7) in 1976 than the participants who answered both questionnaires. In contrast, women who completed the intentional weight loss questions were younger (57.8 vs 59.6 years) and slightly heavier (BMI, 26.4 vs 25.9) in 1992 than the women who completed the 1992 questionnaire but did not answer the intentional weight loss questions.

EXPOSURES

Height and weight were ascertained in 1976, and current weight was assessed on each follow-up questionnaire. Body mass index (in 1988) was calculated from self-reported information on weight and height. Current weight was assessed on each follow-up questionnaire. In a validation study within the cohort, the correlation between self-reported and technician-measured body weight was 0.97,²⁴ and the mean self-reported weight was 1.0 kg lower than technician-measured weight. The BMI classification scheme in the US dietary guidelines²⁵ was used to classify women. Women with a BMI of less than 17 were

classified as severely underweight²⁶ and excluded from the analysis. In the statistical analysis, the remaining women were classified as underweight or at a healthy weight ($17 < \text{BMI} \leq 24.9$), overweight ($25 \leq \text{BMI} \leq 29.9$), and obese ($\text{BMI} \geq 30.0$).

Net weight change, irrespective of intentionality, was assessed by calculating the difference in weight reported at 2 time points. For example, weight change between age 18 years and 1976 (the closest weight to the beginning of the 1972-1992 weight cycling period) was assessed by subtracting the weight reported at age 18 years from the weight reported in 1976. Recent weight change was defined as weight change from 1992 until the 2-year period closest to when the woman died or was lost to follow-up, or the end of the follow-up period, whichever came first. Field et al²⁷ observed that weight change based on self-reported weights underestimated true weight change (assessed by measured weights) by only 1.0 kg (women) to 1.2 kg (men) among young adults in the Longitudinal Study of Adolescent Health (hereinafter, Add Health).²⁷ Although overweight and obese women underreported their weight more than their leaner peers, they were consistent in their underreporting. Consequently, the discrepancy between weight change based on serial self-reported vs measured weights was significantly smaller among the obese women vs those of a healthy weight (0.2 kg overestimation vs 1.1 kg underestimation; $P < .001$). Because the participants in Add Health are less trained in reporting on health than the participants in the NHS, it is reasonable to assume that the underestimation owing to relying on self-reported weights is similar or less than that observed in Add Health.

The 1992 NHS survey included questions on weight losses that were specifically designed to address the long-term health consequences of intentional weight loss and weight cycling. They were developed after extensive discussion among investigators from the NHS, Centers for Disease Control and Prevention, and the University of Minnesota. The information was used to classify women as noncyclers, mild cyclers, or severe weight cyclers. The questions were, "Within the last 20 years, how many times did you lose each of the following amounts of weight on purpose (excluding illness or pregnancy)?" and "Within the last 4 years, how many times did you lose each of the following amounts of weight on purpose (excluding illness or pregnancy)?" The responses were 0, 1 to 2, 3 to 4, 5 to 6, or 7 or more times for each of the magnitudes of weight loss (2.3-4.1 kg, 4.5-8.6 kg, 9.1-22.2 kg, and ≥ 22.7 kg) (Figure).

To be consistent with the magnitude of the weight loss required by Field et al,⁶ French et al,¹³ and Williamson et al²¹ in their studies of the relation between intentional weight loss and disease, we required that a woman report intentionally losing at least 9.1 kg to be considered a severe weight cyclist. Also, to ensure that the cyclers were women who had repeatedly lost weight, we required that women intentionally lost weight 3 or more times to be classified as severe weight cyclers. Women who had intentionally lost at least 4.5 kg 3 or more times but did not meet the criteria for severe weight cycling were classified as mild weight cyclers. Women who did not meet the criteria described herein for mild or severe weight cycling were classified as noncyclers. The information on body weight, reported on each of the biennial questionnaires, was not used to define weight cyclist status.

Physical activity was assessed with 8 activity-specific questions (walking or hiking, jogging, running, bicycling, calisthenics/aerobics/aerobic dance/rowing machine, tennis/squash/racquetball, lap swimming, or other aerobic recreation), which have been validated in a sample of NHS II participants,²⁸ inquiring about average time per week during the past year that women engaged in specific activities. In addition, the women were asked to report the average number of flights of stairs they climbed each week and their average time spent walking. Total

metabolic equivalent of hours of activity per week were estimated by summing the amount of time spent in each activity multiplied by an estimate of the intensity of the activity.²⁹ Activity was assessed by quintile of activity at baseline and change in quintile of activity. Change in activity was modeled as change in quintiles of activity since 1988.

Dietary intake was calculated using the 136-item food frequency questionnaires (FFQ) completed in 1990, 1994, 1998, and 2002. Alcohol was modeled as average daily intake (grams per day). Using the cigarette smoking information from baseline and each follow-up, participants were classified by current smoking status (current, past, or never) and number of cigarettes currently smoked. Menopausal status, which was based on whether a woman reported that her periods had ceased permanently, was updated at every cycle. Postmenopausal hormone therapy (HT) was defined as never, past, or current use and was updated every cycle.

OUTCOME MEASURES

Deaths were reported by next of kin, the postal service, or ascertained by the National Death Index. We estimate that follow-up for deaths was more than 98% complete.³⁰ We requested death certificates and, when appropriate, requested permission from the next of kin to review medical records. *The International Classification of Diseases, 8th Edition (ICD-8)*, was used to assign the underlying cause of death. The primary end point in this analysis was death from any cause. We also conducted secondary analyses focusing on deaths resulting from CVD (ICD-8 codes 390.0-458.9 and 795.0-795.9).

STATISTICAL ANALYSIS

Cox proportional hazards models were used to assess the association of weight cycling with all-cause and cardiovascular-related mortality. Person-years were calculated from the date of return of the 1992 questionnaire until the date of death or June 1, 2004, whichever came first. Person-years and deaths between 1992 and 1994 were excluded to reduce the effects of preexisting disease on weight.

The relative risk (RR) of death was calculated as the rate of death among women who were severe or mild cyclers compared with that in the reference category of noncyclers. Separate models were run to assess the association with long-term (1972-1992) and recent (1988-1992) weight cycling. Multivariate Cox proportional hazards models, stratified by age in months and calendar time and that controlled for other potential confounders, were used for analysis.

To assess the relative importance of weight change, 3 sets of adjusted analyses were performed. In the first, partially adjusted model, BMI at age 18 years, weight change from 18 years until weight in 1976 (for models assessing cycling during the past 20 years) or 1988 (for models assessing cycling during the past 4 years), smoking status with number of cigarettes currently smoked per day (never; past; current, 1-4; current, 5-24; current, 25-34; current, 35-45; and current, number unknown), postmenopausal HT (premenopausal, never, past, or current), alcohol intake, activity, and change in activity during the follow-up period were added to model 1. In the second, partially adjusted model, net weight change from 1976 (for the models assessing cycling during the past 20 years) or 1988 (for models assessing cycling during the past 4 years) to 1992 (the end of the weight cycling period) were added to model 2. In the final model we included weight change from 1976 (for models assessing cycling during the past 20 years) or 1988 (for models assessing cycling during the past 4 years) until the end of follow-up or 2004, whichever came first, instead of weight change until 1992.

Table 1. Baseline Demographics by Weight Cycling Status Among 44 882 Women in the Nurses' Health Study

Characteristic	Weight Cycling Status Between 1972 and 1992		
	Noncyclers (n=32 836)	Mild Cyclers (n=8452)	Severe Cyclers (n=3594)
Age in 1992, mean (SD), y	57.7 (7.1)	55.6 (6.7)	55.2 (6.5)
BMI in 1992, mean (SD)	25.0 (4.3)	28.7 (4.8)	32.6 (6.2)
BMI categories in 1992			
17.0-20.9	1.0	0.1	0.0
21.0-24.9	53.4	20.1	7.8
25.0-29.9	28.6	42.1	28.0
>30.0	11.4	31.9	58.7
Smoking status			
Never	45.4	44.1	41.6
Past	38.7	45.1	47.4
Current	15.8	10.5	10.7
Alcohol intake, mean (SD), g/day	5.4 (9.8)	4.3 (8.4)	3.1 (7.4)
Postmenopausal HT, %			
Premenopausal	26.9	27.1	27.3
Postmenopausal, never	28.1	27.4	30.0
Postmenopausal, past	14.1	14.3	15.6
Postmenopausal, current	30.4	30.8	26.9
Quintiles of MET hours of activity per week, %			
1 (0.2-3.1 METs)	18.0	18.4	23.6
2 (3.2-8.3 METs)	20.3	20.5	21.7
3 (8.4-11.1 METs)	20.6	19.8	18.3
4 (16.0-21.9 METs)	20.0	21.6	18.2
5 (30.0-53.1 METs)	20.8	19.3	18.0

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HT, hormone therapy; MET, metabolic equivalent.

Several secondary analyses were conducted. Because the relationship between weight and mortality has been shown to be modified by smoking status among women in the NHS³¹ and other cohorts,³² in secondary analyses we restricted the analysis to never smokers. Because weight loss among elderly individuals may be due to loss of lean mass, which has different implications than loss of fat mass, we limited the analysis to women younger than 70 years to assess whether the results varied by age. All analyses were conducted with SAS statistical software (version 9.1; SAS Institute Inc, Cary, North Carolina). All reported *P* values are based on 2-sided tests.

RESULTS

Between 1988 and 1992, approximately 7.0% of the women were mild weight cyclers and 1.5% were severe weight cyclers. Many more women were cyclers between 1972 and 1992. Approximately 18.8% of women had lost 4.5 kg or more 3 or more times between 1972 and 1992, and 8.0% had lost 9.1 kg or more 3 or more times during that time period. Weight cycling was positively associated with BMI at baseline. Approximately 40% of the noncyclers between 1972 and 1992 were overweight or obese compared with 74% of the mild cyclers and 87% of the severe cyclers (**Table 1**). In addition, cycling status was inversely associated with physical activity. During 12 years of follow-up,

Table 2. Prospective Association (HR and 95% CI) Between Weight Cycling and All-Cause Mortality Among 44 882 Middle-aged or Older Women in the Nurses' Health Study

Category	HR (95% CI)					
	Cycling Between 1972 and 1992			Cycling Between 1988 and 1992		
	Noncyclers (n=32 836)	Mild Cyclers (n=8452)	Severe Cyclers (n=3594)	Noncyclers (n=41 045)	Mild Cyclers (n=3142)	Severe Cyclers (n=695)
Deaths, No.	2229	418	237	2647	179	58
Person-years	314 141	81 550	34 472	393 279	30 290	6594
Model						
1 ^a	1 [Reference]	0.91 (0.81-1.01)	1.32 (1.15-1.51)	1 [Reference]	1.13 (0.97-1.31)	1.77 (1.36-2.30)
2 ^b	1 [Reference]	0.81 (0.72-0.90)	0.89 (0.76-1.03)	1 [Reference]	0.99 (0.84-1.15)	1.21 (0.92-1.58)
3 ^c	1 [Reference]	0.82 (0.74-0.92)	0.90 (0.78-1.05)	1 [Reference]	0.99 (0.84-1.15)	1.17 (0.89-1.54)
4 ^d	1 [Reference]	0.83 (0.75-0.93)	0.89 (0.77-1.04)	1 [Reference]	1.00 (0.85-1.17)	1.15 (0.88-1.52)

Abbreviations: CI, confidence interval; HR, hazard ratio.

^aAdjusted for age.

^bAdjusted for age, body mass index at age 18 years, weight change from age 18 years to start of the cycling period (1976 for models assessing cycling during the past 20 years or 1988 for models assessing cycling during the past 4 years), smoking status with number of cigarettes currently smoked per day (never; past; current, 1-4; current, 5-24; current, 25-34; current, 35-45; and current, unknown number), menopausal status, postmenopausal hormone therapy (premenopausal, never, past, or current), alcohol, activity level, and change in activity level.

^cAdjusted for variables in model 2, as well as net weight change from the start of the cycling period (1976 for models assessing cycling during the past 20 years or 1988 for models assessing cycling during the past 4 years) until 1992 (ie, end of the cycling period).

^dAdjusted for variables in model 3, as well as net weight change from the start of the cycling period (1976 for models assessing cycling during the past 20 years or 1988 for models assessing cycling during the past 4 years) until 2004 or the end of the follow-up period, instead of net weight change during the cycling period.

there were 2884 deaths, of which 425 were the result of cardiovascular events. Weight cyclers gained significantly more than noncyclers during the follow-up period (5.2 kg for severe cyclers and 4.1 kg for mild cyclers) compared with 2.6 kg for noncyclers ($P < .001$). In age-adjusted models, severe cyclers in early and middle adulthood had a higher mortality rate (RR, 1.32; 95% confidence interval [CI], 1.15-1.51) than noncyclers, but mild cyclers did not differ significantly from noncyclers (RR, 0.91; 95% CI, 0.81-1.01). However, after adjusting for BMI at age 18 years, weight change from age 18 years until 1976, physical activity, change in activity, smoking, postmenopausal HT, and alcohol intake, the RR was attenuated and there was no longer a suggestion of an increase in risk (**Table 2**). Further adjustment for change in weight from 1976 through the follow-up period did not materially alter the results (Table 2). Similar associations were observed with recent weight cycling.

The crude association of severe cycling and death due to CVD was stronger than the association with all-cause mortality, particularly for recent weight cycling (**Table 3**). In age-adjusted models, women who were severe cyclers from 1988 to 1992 were almost 3 times more likely (RR, 2.89; 95% CI, 1.61-5.18) than noncyclers to die from cardiovascular events during the follow-up period; however, the results were confounded by BMI, activity, and weight change. After adjusting for BMI, weight change, physical activity, change in activity, smoking, postmenopausal HT, and alcohol intake, the RR was attenuated and no longer significant (RR, 1.77; 95% CI, 0.96-3.26). In addition, after adjusting for these factors there was no suggestion of an association with weight cycling between 1972 and 1992 (Table 3).

In secondary analyses, we assessed the associations of weight cycling with mortality among never smokers because the relationship between BMI and mortality is almost linear among never smokers but J-shaped³¹⁻³³ or U-

shaped^{34,35} in the total population. We observed that the associations with weight cycling were attenuated among never smokers. In multivariate models, there was no suggestion of an increased risk among mild cycling between 1972 and 1992 (RR, 0.91; 95% CI, 0.75-1.09); mild cycling between 1988 and 1992 (RR, 1.18; 95% CI, 0.91-1.52), or severe cycling between 1972 and 1992 (RR, 0.97; 95% CI, 0.74-1.26); or severe cycling between 1988 and 1992 (RR, 1.08; 95% CI, 0.63-1.83).

Weight change is complicated to interpret in elderly individuals because older adults may maintain their weight but lose lean mass and shift their body fat distribution to be more centrally located and therefore at higher risk. Thus, we conducted analyses limiting the sample to women 70 years or younger. Among these women, the associations of mild (RR, 0.85; 95% CI, 0.74-0.98) and severe cycling (RR, 0.91; 95% CI, 0.75-1.09) with all-cause mortality were similar to those when all the women were included in the analysis (Table 2).

COMMENT

Among 44 882 middle-aged or older women, we observed that weight cycling was not strongly related to all-cause or cardiovascular mortality. Women who intentionally lost weight multiple times (ie, weight cyclers) gained more weight than their peers, but after controlling for their weight gains and other confounding variables, weight cycling was not predictive of cardiovascular or total mortality. Among never smokers there was no suggestion of an increased risk of total mortality in weight cyclers.

Few studies have collected information on intentional weight losses, repeated weight losses, or weight cycles (gain-loss or loss-gain). In general, intentional weight losses have been found to be protective or unrelated to risk.^{10,12,19} After taking into account preexisting conditions, Wanna-

Table 3. Prospective Association (HRs and 95% CIs) Between Weight Cycling and Cardiovascular Mortality Among 44 882 Middle-aged or Older Women in the Nurses' Health Study

Category	HR (95% CI)					
	Cycling Between 1972 and 1992			Cycling Between 1988 and 1992		
	Noncycler (n=32 836)	Mild Cycler (n=8452)	Severe Cycler (n=3594)	Noncycler (n=41 045)	Mild Cycler (n=3142)	Severe Cycler (n=695)
Deaths, No.	319	65	41	384	29	12
Person-years	315 836	81 874	34 663	395 312	30 421	6641
Model						
1 ^a	1 [Reference]	1.02 (0.77-1.33)	1.73 (1.25-2.41)	1 [Reference]	1.31 (0.90-1.93)	2.89 (1.61-5.18)
2 ^b	1 [Reference]	0.86 (0.65-1.14)	1.08 (0.75-1.55)	1 [Reference]	1.11 (0.75-1.64)	1.77 (0.96-3.26)
3 ^c	1 [Reference]	0.87 (0.66-1.16)	1.14 (0.79-1.64)	1 [Reference]	1.08 (0.73-1.61)	1.78 (0.96-3.29)
4 ^d	1 [Reference]	0.89 (0.67-1.18)	1.08 (0.75-1.56)	1 [Reference]	1.11 (0.75-1.64)	1.65 (0.89-3.05)

Abbreviations: CI, confidence interval; HR, hazard ratio.

^aAdjusted for age.

^bAdjusted for age, body mass index at age 18 years, weight change from age 18 years to start of the cycling period (1976 for models assessing cycling during the past 20 years or 1988 for models assessing cycling during the past 4 years), smoking status with number of cigarettes currently smoked per day (never; past; current, 1-4; current, 5-24; current, 25-34; current, 35-45; current, number unknown), menopausal status, postmenopausal hormone therapy (premenopausal, never, past, or current), alcohol, activity level, and change in activity level.

^cAdjusted for variables in model 2, as well as net weight change from the start of the cycling period (1976 for models assessing cycling during the past 20 years or 1988 for models assessing cycling during the past 4 years) until 1992 (ie, end of the cycling period).

^dAdjusted for variables in model 3, as well as net weight change from the start of the cycling period (1976 for models assessing cycling during the past 20 years or 1988 for models assessing cycling during the past 4 years) until 2004 or the end of the follow-up period, instead of net weight change during the cycling period.

methee et al¹⁶ did not observe evidence of an increase in risk for all-cause or cardiovascular death among men who lost and then gained weight. A similar lack of association was observed by Lissner et al³⁶ among men in the Baltimore Aging Study. However, Folsom et al³⁷ observed that among women in the Iowa Women's Study, large weight cycles (weight losses of $\geq 10\%$ of weight followed by gains of $\geq 10\%$ of weight or vice versa) were associated with increased risk of all-cause mortality. Similarly, Rzehak et al³⁸ observed that there was an 86% increase in risk of all-cause mortality among weight fluctuators in the Erfort Male Cohort Study, and Dyer et al³⁹ observed that weight fluctuations were predictive of cardiovascular mortality among men in the Chicago Western Electric Company Study. Unfortunately, intentionality of the weight losses was not taken into account in these studies.

Weight loss is more complicated to study in elderly persons because it is common for older adults to lose muscle mass. Moreover, because the background death rate is considerably higher among older adults, the RRs tend to be smaller among adults in their 70s, 80s, and 90s.⁴⁰ Nevertheless, a few studies have examined the effect of weight loss among elderly individuals, but none have assessed the association of intentional weight loss with mortality. Although Wedick et al⁴¹ observed that among elderly men and women who reported a history of dieting, which could be viewed as a surrogate marker of intentional weight loss, weight loss was not predictive of all-cause mortality. Newman et al²² observed that among 4714 elderly adults in the United States, weight loss was associated with known mortality risk factors, including having a higher BMI, and higher prevalence of heart disease, stroke, hypertension, and smoking at baseline. Weight loss was a significant predictor of all-cause mortality, but dieting did not have an independent association with all-cause mortality, which implies that intentional weight loss did not have an adverse impact on all-cause mortality. In our study, we did not find evidence

that repeated intentional weight losses of any magnitude were predictive of all-cause or cardiovascular mortality among middle-aged or older women. The results were not materially changed when we limited the sample to women 70 years or younger, which suggests that the main results were not biased downward owing to the age of the sample over the follow-up.

One limitation to our analysis is that we did not collect information on amounts of weight lost unintentionally, so we were unable to estimate the independent associations of both intentional and unintentional weight losses. Moreover, we did not have information on amount regained from each of the intentional weight-loss episodes or from unintentional weight losses, so our net weight change variable may have some measurement error. Despite these limitations, there are many strengths to the current study. First, to our knowledge this is the largest prospective investigation of weight cycling and mortality among a relatively healthy population of adult women. In the Iowa Women's Study,⁴² another cohort from which information on intentional weight losses was collected, women were asked to recall weight changes made many years in the past, thus increasing the chance for misclassification. Moreover, in the current analyses we were able to update information on confounders over the 10 years of follow-up. In addition, unlike the excellent studies by Gregg et al^{10,20} and Williamson et al,^{12,19,21} which studied the association between voluntary weight loss and mortality, ours was the first large study to our knowledge to investigate prospectively the association between weight cycling due to repeated intentional weight losses and all-cause and cardiovascular mortality.

Our results suggest that repeated intentional weight losses are not associated with all-cause or cardiovascular mortality among middle-aged or older women. More research is needed to determine whether weight cycling increases risk among subsets of the population, such as

nonoverweight women, but our results suggest that earlier reports of weight loss being predictive of higher death rate may be due to failing to distinguish intentional from unintentional weight loss, as well as confounding by weight regain. Given that approximately 68% of middle-aged or older American women are overweight or obese, it is encouraging to find that repeated voluntary weight losses are not associated with adverse health consequences because many of these women would be at lower risk if they were able to maintain a lower BMI.

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