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Weight cycling and mortality among middle-aged and older women

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Abstract

Context—Controversy exists around whether weight cycling increases morbidity and mortality.

Objective—To assess the independent association of weight cycling with mortality.

Design, Setting, Participants—A prospective study of 44,876 middle-aged and 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 ≥17 kg/m^2, and had no history of cancer (other than non-melanoma skin cancer) or heart disease. Women who reported they had intentionally lost ≥ 20 lbs at least 3 times were classified as severe weight cyclers. Women who had intentionally lost ≥ lbs at least 3 times, but did not meet the criteria for severe weight cycling, were classified as mild weight cyclers.

Main Outcome Measures—All cause mortality.

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 2,882 women died, of their deaths, 424 were due to cardiovascular events. Weight cyclers gained more weight during follow-up than non-cyclers (p <0.001). After adjusting for BMI at age 18, physical activity, smoking, post-menopausal hormone use, alcohol intake, net weight change from age 18, and change in physical activity, there was no increase in risk among mild (relative risk [RR]=0.84, 95% confidence interval [CI] 0.75–0.93) or severe cyclers (RR=0.90, 95% CI 0.77–1.04). Similar results were observed for cardiovascular mortality and among women 70 years of age or less.

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

Keywords

Females; intentional weight loss; weight cycling; death

During the past two decades some studies have reported that weight loss, weight variability, and weight cycling are associated with increased health risks.[1–4] These reports of adverse

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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, the later studies have not been consistent.[6–12] 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 al.[15] observed that the prevalence of intentionally and unintentionally losing 20 or more pounds at least once were approximately equal. Moreover, unintentional weight loss has been associated with smoking, poor health status, and age,[16, 17] three 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 studies of women have been inconsistent.[18–23] If one or more episodes of intentional weight loss is 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 recent and long-term intentional weight losses and net weight change, and mortality among middle-aged and older women in the Nurses' Health Study.

METHODS

Sample

The Nurse's Health Study (NHS) cohort was established in 1976, when 121,701 female registered nurses between the ages of 30 and 55 years completed a postal questionnaire about risk factors for, and history of, cancer and cardiovascular disease. 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 with cancer (other than non-melanoma skin cancer) or heart disease (n = 9,557) did not complete all of the intentional weight loss questions (n=36,653), 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 (n= 5,807), had a BMI < 17 or >60 (n= 375), reported bypass surgery [in 1992] (n=102), or died between 1988 and 1994 (n= 479), were excluded from the analysis, thus leaving 44,876 women in the analysis.

Exposures

Height and weight were ascertained in 1976 and current weight was assessed on each follow-up questionnaire. Body mass index (BMI, kg/m^2) 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 self-reported weight was, on average, 1.0 kg lower than technician measured weight. The BMI classification scheme in the U.S. Dietary Guidelines was used to classify women. Women with a BMI < 17 were classified as severely underweight (WHO reference) and excluded from the analysis. Women with a BMI > 60 kg/m^2 were also considered outliers and excluded from the analysis. In the statistical analysis the remaining women were classified as underweight or healthy weight ($17 < \text{BMI} \leq 24.9$), overweight ($25 \leq \text{BMI} \leq 29.9$), and obese ($\text{BMI} \geq 30$).

Net weight change, irrespective of intentionality, was assessed by calculating the difference in weight reported at two time points. For example, weight change between age 18 and 1976 (the closest weight to the beginning of the 1972–1992 weight cycling period) was assessed by subtracting the weight reported age 18 from the weight reported in 1976. Recent weight change was defined as weight change from 1992 until the two 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 al.[25] observed that weight change based on self-reported weights underestimated true weight change (assessed by measured weights) by only 2.2 (females) to 2.7 (males) pounds among young adults in the Longitudinal Study of Adolescent Health (Add Health). Among females who gained weight, true weight change was underestimated by 4.1 lbs; whereas, it was overestimated by 5.4 lbs among females who lost weight. Although overweight and obese females under-reported their weight more than their leaner peers, they were consistent in their under-reporting. Consequently, the discrepancy between weight change based on serial self-reports vs. measured weights, was significantly smaller among the obese females versus healthy weight females (0.5 lbs overestimation vs. 2.5 lbs underestimation, $p<0.001$). Since the participants in Add Health are less trained in reporting on health than the participants in the Nurses' Health Study, it is reasonable to assume that the underestimation due to relying on self-reported weights is similar or less to 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 Nurses' Health Study, Centers for Disease Control and Prevention, and University of Minnesota. The information was used to classify women as non-, mild, 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, 1–2, 3–4, 5–6, or 7 or more times for each of the magnitudes of weight loss (5–9 pounds [2.3–4.1 kg], 10–19 pounds [4.5–8.6 kg], 20–49 pounds [9.1–22.2 kg], and 50+ pounds [≥ 22.7 kg].) To be consistent with the magnitude of the weight loss required by Field et al.,[13] French et al.,[13] and Williamson et al.[21] in their studies of the relation between intentional weight loss and disease, we required that a woman report intentionally losing 20 or more pounds (≥ 9.1 kg) to be considered a severe weight cycler. Also, to ensure that the cyclers were women who had repeatedly lost weight, we required that women intentionally lost weight three or more times to be classified as severe weight cyclers. Women who had intentionally lost 10 or more pounds (≥ 4.5 kg) three or more times, but did not meet the criteria for severe weight cycling, were classified as mild weight cyclers. For example, a woman who lost 20 or more pounds (≥ 9.1 kg) twice and 15 pounds (6.8 kg) once would be classified as a mild weight cycler. Women who did not meet the criteria described above for mild or severe weight cycling were classified as non-weight cyclers. The information on body weight, reported on each of the biennial questionnaires, was not used to define weight cycler status.

Physical activity was assessed with eight 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 Nurses Health Study II participants,[26] 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-hours of activity per week (MET hours/wk) was estimated by summing the amount of time spent in each activity multiplied by an estimate of the intensity of the activity.[27] 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 use 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 percent complete. 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 endpoint in this analysis was death from any cause. We also conducted secondary analyses focusing on deaths due to cardiovascular disease (ICD-8 codes 390.0 through 458.9 and 795.0 to 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. Deaths between 1992 and 1994 were excluded to reduce the effects of preexisting disease on weight.

The relative risk 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 non-cyclers. 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, three sets of adjusted analyses were performed. In the first partially-adjusted model, age, body mass index at age 18, weight change from age 18 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, current unknown), and postmenopausal hormone use (premenopausal, never, past, or current) were included in the Cox model. In the second partially-adjusted model, weight change between 1976 and 1992 (for models assessing cycling during the past 20 years, or weight change between 1988 and 1992 for models assessing cycling during the past 4 years) was included in the model. In the final model we included age, smoking status, alcohol use, use or nonuse of hormone-replacement therapy, physical activity (changed from highest to lowest quintile, decreased three quintiles, decreased two quintiles, decreased one quintile, remained in the same quintile, increased one quintile, increased two quintiles, increased three quintiles, increased from the lowest to the highest quintile) and 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.

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 Nurses' Health Study[28] and other cohorts,[29] in secondary analyses we restricted the analysis to never smokers. Because weight loss among the elderly may be due to loss of lean mass, which has different implications than loss of fat mass, we limited the analysis to women less than 70 years of age to assess whether the results varied by age. All analyses were conducted with SAS software (SAS version 9.1, Cary, North Carolina). All reported P values are based on two-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 10 or more lbs three or more times between 1972 and 1992 and 8.0% had lost 20 or more lbs three or more times during that time period. Weight cycling was positively associated with BMI at baseline. Approximately 40% of the non-cyclers between 1972 and 1992 were overweight or obese compared to 74% of the mild cyclers and 87% of the severe cyclers (Table 1). In addition, cycling status was inversely associated with physical activity. During12 years of follow-up, there were 2,882 deaths, of which 424 were due to cardiovascular events. Weight cyclers gained significantly more than non-cyclers during the follow-up period (11.3 lbs for severe cyclers and 9.0 lbs for mild cyclers) compared with 5.8 lbs for non-cyclers (p <0.001). In age-adjusted models severe cyclers in early and middle adulthood had a higher mortality rate (RR=1.32, CI 1.15–1.51) than non-cyclers, but mild cyclers did not differ significantly from non-cyclers (RR=0.91, 95% CI 0.82–1.01). However, after adjusting for BMI at age 18, weight change from age 18 until 1976, physical activity, smoking, post-menopausal hormone use, and alcohol intake, the relative risk was attenuated and there was no longer a suggestion of an increase in risk (Table 2). Further adjustment for change in activity level, smoking status, and weight from 1976 through the follow-up period did not materially alter the results (Table 2). Similar associations were observed with recent weight cycling. However, activity level at baseline and decreases in activity level were strongly predictive of all-cause mortality. Women in the top quintile of physical activity were 63% (RR=0.37, 95% CI 0.32–0.44) less likely to die than women in the lowest quintile. Moreover, women who decreased their activity level by two quintiles were significant more likely (RR=1.28, 95% CI 1.11–1.48) to die than their peers who maintained their activity level.

The crude association of severe cycling and death due to cardiovascular disease 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 between 1988 and 1992 were almost three times more likely (RR=2.94 95% CI, 1.64–5.26) than non-cyclers 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, smoking, post-menopausal hormone use, alcohol intake, the relative risk was attenuated and no longer significant (RR=1.69, 95% CI 0.91–3.13). 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-shaped[28–30] or U-shaped[31, 32] 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 1972–1992: (RR=0.93, 95% CI 0.76–1.12); mild cycling 1988–1992: (RR=1.18, 95% CI 0.91–1.54) or severe cycling 1972–1992: (RR=0.90, 95% CI 0.68–1.18); severe cycling 1988–1992: (RR=1.05, 95% CI 0.61–1.79).

Weight change is complicated to interpret in the elderly because older adults may maintain their weight, but lose lean mass and shift their body fat distribution to be more centrally located and therefore higher risk. Thus, we conducted analyses limiting the sample to women less than or equal to 70 years of age. Among these women, the associations of mild (RR=0.85, 95% CI 0.74–0.98) and severe cycling (RR=0.91, 95% CI 0.75–1.10) with mortality were similar to those when all the women were included in the analysis (Table 2).

COMMENT

Among 44,876 middle-aged and older women, we observed that weight cycling was not strongly related to mortality. Women who intentionally lost weight multiple times (i.e., 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, Wannamethee et al. 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 al. [33] among men in the Baltimore Aging Study. However, Folsom et al. observed that among women in the Iowa Women's Study, weight large cycles (weight losses of ≥ 10% of weight followed by gains of ≥ 10% of weight or vice versa) were associated with increased risk of all-cause mortality. Similarly, Dyer et al. observed that weight fluctuations were predictive of cardiovascular mortality among men in the Chicago Western Electric Company Study[34] and Rzehak et al. observed that there was an 86% increase in risk of death among weight fluctuators in the ERFORT male cohort study. In addition, in the Framingham Heart Study, weight variability was predictive of all-cause mortality among both men and women.[2] Unfortunately, intentionality of the weight losses was not taken into account in these studies.

Weight loss is more complicated to study in the elderly since it is common for older adults to lose muscle mass while maintaining their weight, or to maintain their weight, but have their body fat become more centrally located. Moreover, since the background death rate is considerably higher among older adults, the relative risks tend to be smaller among adults in their 70s, 80s, and 90s.[35] Nevertheless a few studies have examined the effect of weight loss among the elderly, but none have assessed the association of intentional weight loss with mortality. In one of these studies, Wedick et al.[36] followed 1,801 elderly men and women over 12 years. They observed that weight loss, but not weight gain, was predictive of total mortality. Among the 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 mortality among the diabetic women or the non-diabetic men and women. Whereas, Newman et al.[22] observed that among 4,714 elderly adults in the United States, weight loss was associated with having a higher BMI, and higher prevalence of heart disease, stroke, hypertension, and smoking at baseline. Weight loss was a significant predictor of mortality, but dieting did not have an independent association with mortality, which implies that intentional weight loss did not have an adverse impact on mortality. In our study, we did not find evidence that repeated intentional weight losses of any magnitude were predictive of mortality among middle aged or older women. The results were not materially changed when we limited the sample to women no more than 70 years of age, which suggests that the main results were not biased downwards due 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, 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, another cohort where information on intentional weight losses was collected, women were asked to recall weight changes made many years in the past,[37] thus increasing the chance for misclassification. Moreover, in the current analyses we were able to update information on confounders over the ten years of follow-up. In addition, unlike the excellent studies of Gregg et al. [10, 20] and Williamson et al.,[12, 19, 21] which studied the association between voluntary weight loss and mortality, the present study was the first large study to investigate prospectively the association between weight cycling due to repeated intentional weight losses and mortality.

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

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Table 1

Baseline demographics by weight cycling status among 44,876 women in the Nurses' Health Study

	Weight Cycling Status between 1972 and 1992		
	Non-cyclers (n=32,836)	**Mild cyclers (n=8,451)**	**Severe cyclers (n=3,589)**
Mean age in 1992 (SD)	57.7 (7.1)	55.6 (6.7)	55.2 (6.5)
Mean BMI in 1992 (SD)	25.0 (4.3)	28.7 (4.8)	32.6 (6.1)
BMI categories in 1992			
17– 20 kg/m^2	1.0	0.1	0.0
21– 24.9 kg/m^2	53.4	20.1	7.8
25– 29.9 kg/m^2	28.6	42.2	28.1
30+ kg/m^2	11.4	31.9	58.6
Smoking Status			
never smokers	45.4	44.1	41.6
past smokers	38.7	45.1	47.4
current smokers	15.8	10.5	10.7
Mean Alcohol Intake (SD)	5.4 (9.8)	4.3 (8.4)	3.1 (7.4)
Postmenopausal Hormone Use (%)			
pre-menopausal-none	26.9	27.1	27.3
post - never	28.1	27.4	30.0
post - past	14.1	14.3	15.6
post - current	30.4	30.8	26.9
METS per week (quintiles) (%)			
Quintile 1	18.0	18.4	23.5
Quintile 2	20.3	20.4	21.7
Quintile 3	20.6	19.8	18.3
Quintile 4	20.0	21.6	18.2
Quintile 5	20.8	19.3	18.0

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Table 2

Prospective association (hazard ratio and 95% confidence interval) between weight cycling and all-cause mortality among middle-aged and older women in the Nurses' Health Study (n=44,876)

	Cycling between 1972 and 1992			Cycling between 1988 and 1992		
	Non-cycler (n=32,836)	**Mild cycler (n=8,451)**	**Severe Cycler (n=3,589)**	**Non-cycler (n=41,043)**	**Mild cycler (n=3,140)**	**Severe cycler (n=693)**
Cases	2228	418	236	2645	179	58
Person years	314,127	81,536	34,390	393,229	30,269	6,556
Age-adjusted	1.0 (referent)	0.91 (0.82–1.01)	1.32 (1.15–1.51)	1.0 (referent)	1.13 (0.97–1.31)	1.79 (1.37–2.32)
Partially adjusted 1[¶]	1.0 (referent)	0.81 (0.72–0.90)	0.89 (0.76–1.03)	1.0 (referent)	0.99 (0.84–1.15)	1.22 (0.93–1.60)
Partially adjusted 2[†]	1.0 (referent)	0.82 (0.74–0.92)	0.90 (0.78–1.05)	1.0 (referent)	0.99 (0.84–1.15)	1.18 (0.90–1.55)
Fully adjusted[§]	1.0 (referent)	0.84 (0.75–0.93)	0.90 (0.77–1.04)	1.0 (referent)	1.00 (0.85–1.17)	1.17 (0.89–1.53)

[¶]Adjusted for age, BMI at age 18, weight change from age 18 to start of the cycling period (1976 or 1988), smoking status, menopausal status, postmenopausal hormones, alcohol, and activity level

[†]Adjusted for age, BMI at age 18, weight change from age 18 to start of the cycling period (1976 or 1988), 1976, net weight change during the cycling period (1976–1992 or 1988–1992), smoking status, menopausal status, postmenopausal hormones, alcohol, and activity level

[§]Adjusted for age, BMI at age 18, weight change from age 18 to start of the cycling period (1976 or 1988), 1976, net weight change from the beginning of the cycling period (1976 or 1988) until the cycle before the woman died or end of follow-up, smoking status, menopausal status, postmenopausal hormones, alcohol, and activity level

Table 3

Prospective association (hazard ratio and 95% confidence interval) between weight cycling and cardiovascular mortality among middle-aged and older women in the Nurses' Health Study (n=44,876)

	Cycling between 1972 and 1992			Cycling between 1988 and 1992		
	Non-cycler (n=32,836)	**Mild cycler (n=8,451)**	**Severe Cycler (n=3,589)**	**Non-cycler (n=41,043)**	**Mild cycler (n=3,140)**	**Severe cycler (n=693)**
Cases	318	65	41	383	29	12
Person years	314,127	81,536	34,390	393,229	30,269	6,556
Age-adjusted	1.0 (referent)	1.02 (0.78–1.33)	1.74 (1.25–2.42)	1.0 (referent)	1.32 (0.90–1.93)	2.94 (1.64–5.26)
Partially adjusted 1¶	1.0 (referent)	0.87 (0.66–1.15)	1.09 (0.76–1.56)	1.0 (referent)	1.11 (0.75–1.65)	1.80 (0.98–3.31)
Partially adjusted 2†	1.0 (referent)	0.88 (0.66–1.17)	1.15 (0.80–1.66)	1.0 (referent)	1.09 (0.73–1.61)	1.80 (0.97–3.34)
Fully adjusted§	1.0 (referent)	0.90 (0.67–1.19)	1.10 (0.76–1.58)	1.0 (referent)	1.11 (0.75–1.65)	1.69 (0.91–3.13)

¶Adjusted for age, BMI at age 18, weight change from age 18 to start of the cycling period (1976 or 1988), smoking status, menopausal status, postmenopausal hormones, alcohol, and activity level

†Adjusted for age, BMI at age 18, weight change from age 18 to start of the cycling period (1976 or 1988), 1976, net weight change during the cycling period (1976–1992 or 1988–1992), smoking status, menopausal status, postmenopausal hormones, alcohol, and activity level

§Adjusted for age, BMI at age 18, weight change from age 18 to start of the cycling period (1976 or 1988), 1976, net weight change from the beginning of the cycling period (1976 or 1988) until the cycle before the woman died or end of follow-up, smoking status, menopausal status, postmenopausal hormones, alcohol, and activity level.