

Weight Change, Weight Fluctuation, and Mortality

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Objective: To examine the relation between weight change and weight fluctuation (cycling) and mortality in middle-aged men.

Methods: A prospective study of 5608 men aged 40 to 59 years at screening, drawn from one general practice in each of 24 British towns. Changes in weight observed during a 12- to 14-year period were related to mortality during the subsequent 8 years.

Results: There were 943 deaths from all causes: 458 cardiovascular disease (CVD) and 485 non-CVD deaths. Those with stable weight or weight gain had the lowest total, CVD, and non-CVD mortality. Sustained weight loss or weight fluctuation (loss-gain or gain-loss) showed a significantly higher mortality risk than stable weight even after adjustment for lifestyle variables (relative risk [95% confidence interval], 1.60 [1.32-1.95], 1.50 [1.17-1.91], and 1.63 [1.24-2.14], respectively). Adjustment

or exclusion of men with preexisting disease markedly attenuated the increased risk of CVD and total mortality associated with sustained weight loss and weight gain-weight loss. In long-term nonsmokers, any weight loss since screening was associated with an increased risk of mortality, but this was markedly attenuated by adjustment for preexisting disease. Recent ex-smokers showed the most marked increase in mortality associated with sustained weight loss.

Conclusions: The increased mortality in middle-aged men with sustained weight loss and weight fluctuation (cycling) is determined to a major extent by disadvantageous lifestyle factors and preexisting disease. The evidence suggests that weight loss and weight fluctuation (cycling) in these men does not directly increase the risk of death.

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THE HEALTH consequences of overweight and obesity are well recognized, and it is universally recommended that those who are overweight or obese should lose weight by a combination of dieting and increased physical activity.¹⁻⁴ However, several prospective studies⁵⁻⁸ have reported that those who fluctuate in their body weight, with weight loss followed by weight gain or vice versa (weight cycling), have an increased risk of cardiovascular and all-cause mortality. This has led to questioning as to whether weight cycling or even weight loss alone, intentional or unintentional, increases the risk of mortality.⁹⁻¹¹ It has even been asked whether "weight fluctuations caused by unsuccessful dieting are hazardous to one's health."^{10(p4525)} We have examined the relation between weight change and weight fluctuation (cycling) in middle-aged British men during a 12- to 14-year period of observation and their mortality during the subsequent 8 years.

of one general practice in each of 24 towns in England, Wales, and Scotland. The criteria for selecting the town, the general practice, the subjects, and the methods of data collection have been reported.¹² Five years after the initial examination (January 1983-June 1985), a postal questionnaire (Q5) similar to the one administered at screening was sent to all surviving men, and detailed information was obtained about medical history, changes in smoking and drinking behavior, and other risk factors, including body weight.

In 1992, 12 to 14 years after screening, a similar but more comprehensive questionnaire (Q92) was mailed to participants who were still alive and in Great Britain, now aged 52 to 73 years (average age, 63.0 years). Information was collected on changes in smoking and drinking behavior, leisure time physical activity, and current illness and medication. Of the 6528 surviving and available participants, 5934 (91%) completed Q92. Men with complete information on body weight at all 3 periods constitute the cohort (n=5608) followed up for mortality during an 8-year period.

BODY MASS INDEX

At screening, weight and height were measured and body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Five years later (Q5) and 12 to 14 years later (Q92), the men reported their weight and the BMI was calculated for each man based on reported weight and height at screen-

METHODS

The British Regional Heart Study is a large prospective study of cardiovascular disease (CVD) comprising 7735 men aged 40 to 59 years at screening selected from the age-sex registers

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ing. Obesity is defined as a BMI of 28 or higher, representing the top fifth of the BMI distribution in all men at screening.

WEIGHT CHANGE CATEGORIES

Based on weight change from Q1 (baseline screening) to Q5 and from Q5 to Q92, these men were divided into 5 groups.

1. Stable. Less than 4% change in body weight from Q1 to Q5 to Q92.

2. Sustained gain. Those who gained weight ($\geq 4\%$) since Q1 without weight loss ($\geq 4\%$) during follow-up. This includes weight stability or weight gain from Q1 to Q5 and further weight gain from Q5 to Q92 or weight gain from Q1 to Q5 followed by stable weight.

3. Sustained loss. Those who lost weight ($\geq 4\%$) since Q1 without regaining weight. This includes stability or weight loss from Q1 to Q5 and further weight loss from Q5 to Q92 and weight loss from Q1 to Q5 followed by stable weight.

4. Loss-gain. Weight loss from Q1 to Q5 followed by weight gain from Q5 to Q92.

5. Gain-loss. Weight gain from Q1 to Q5 followed by weight loss from Q5 to Q92.

Groups 4 and 5 are included under the concept of weight fluctuation (cycling), with no assumptions as to whether such weight change was intentional or unintentional.

SMOKING STATUS

At Q1, the men were classified as those who had never smoked, ex-cigarette smokers, and current smokers. At Q5 and at Q92, the men were asked whether they were currently smoking and the number of cigarettes smoked. Those who had only ever smoked pipes or cigars were classified as never smokers. Ex-cigarette smokers who smoked pipes or cigars were regarded as ex-cigarette smokers. Complete information on smoking habits at Q1, Q5, and Q92 was not available for 38 men, and they have been excluded from the analyses, leaving 5570 men. From the combined information on cigarette smoking obtained at screening, at Q5, and at Q92, the 5570 men with complete smoking data were classified into 4 groups.

1. Never smokers (n=1484).

2. Long-term ex-cigarette smokers. These were ex-cigarette smokers at screening who were not smoking cigarettes 12 to 14 years later (Q92) (n=1988).

3. Recent ex-cigarette smokers. These were men who gave up cigarette smoking since screening. This group includes men who gave up at Q5 and at Q92 (n=1035).

4. Current cigarette smokers. This group includes cigarette smokers at baseline who remained cigarette smokers at Q92 and non-cigarette smokers at baseline (predominantly ex-smokers) who were smoking cigarettes at Q92 (n=1063).

In the analysis, long-term nonsmokers include groups 1 and 2.

OTHER CONFOUNDING VARIABLES

Social Class

The longest held occupation of each man was recorded at screening, and the men were grouped into 1 of 6 social classes (1, 2, 3 [nonmanual], 3 [manual], 4, and 5). Those whose longest occupation was in the armed forces formed a separate group.

Physical Activity

At Q92, the men were asked to indicate their usual pattern of physical activity, and a score was derived for each man based on frequency and type of leisure activity.¹³ The men were

grouped into 6 broad physical activity categories based on their total score (inactive, occasional, light, moderate, moderately vigorous, and vigorous).

MEASURES OF PREEXISTING DISEASE

At Q92 (but not at Q1), the men were asked to describe their present health status as excellent, good, fair, or poor. They were asked whether a physician had ever told them that they had angina or myocardial infarction (heart attack or coronary thrombosis), stroke, "other heart trouble," diabetes mellitus, cancer, and several other disorders. The term *preexisting CVD* includes coronary heart disease (CHD), stroke, and diabetes mellitus.

FOLLOW-UP

All men, whether they had evidence of CHD or stroke at the initial examination, were followed up for all-cause mortality for the 8-year period from Q92 to October 1, 2000.¹⁴ Follow-up has been achieved for 99% of the cohort. Information on death was collected through the established procedures provided by the National Health Service registers.

STATISTICAL ANALYSIS

A Cox proportional hazards model was used to assess the relation between weight changes from Q1 to Q92 and 8-year mortality on follow-up¹⁵ and to obtain hazard ratios (relative risks) for the weight change categories, adjusting for potential confounders. Adjustments for confounders and preexisting disease were primarily based on assessment at Q92. In the adjustment, smoking (never, long-term ex-smokers, recent ex-smokers, and current smokers); physical activity (6 levels); social class (7 groups); recall of diabetes mellitus (yes or no), stroke (yes or no), CHD (yes or no), and cancer (yes or no); and self-reported poor health (yes or no) were fitted as categorical variables. The initial BMI was fitted as a continuous variable.

RESULTS

There were 943 deaths from all causes (458 CVD and 485 non-CVD deaths) during the follow-up of 8 years in the 5608 men with complete information on body weight. **Table 1** shows the mean BMI measurements for the 3 time points and the mean weight change from Q1 to Q92 for the 5 weight change groups. The stable group had the lowest mean weight change; the sustained gain and sustained loss groups had the largest mean weight changes. Those who gained and lost weight or lost and gained weight showed little change in mean weight overall.

WEIGHT CHANGE, WEIGHT FLUCTUATION, AND MORTALITY

Table 2 shows the relation between the weight change categories and mortality from all causes, cardiovascular causes, and noncardiovascular causes. Those with stable weight had the lowest risk of total mortality, and men who gained weight since screening showed a similar low risk. When men who gained weight were divided further into those with 4% to 15% weight gain (n=1802) and those with greater than 15% weight gain (substantial weight gain, n=353), those with 15% or less weight gain showed a similar risk to the stable group, but those with substantial weight gain showed an increased (albeit nonsignificant) risk com-

Table 1. Mean BMI at Q1, Q5, and Q92 and Mean Weight Change by Weight Change Category in 5608 Middle-aged Men*

Weight Change Category	No. (%) of Men	Mean BMI, kg/m ²			Mean Weight Change From Q1 to Q92, kg
		Q1	Q5	Q92	
Stable	1663 (30)	25.53	25.59	25.62	0.27
Sustained gain	2155 (38)	24.73	25.82	27.13	7.22
Sustained loss	950 (17)	26.60	26.00	24.49	-6.30
Loss-gain	361 (6)	26.82	24.49	27.32	1.46
Gain-loss	479 (9)	25.42	27.53	25.18	-0.75

*BMI indicates body mass index; Q1, baseline screening; Q5, questionnaire administered 5 years after the initial examination; and Q92, questionnaire administered 12 to 14 years after the initial examination.

Table 2. Age-Adjusted Rates and Adjusted RRs for Mortality in 5608 Middle-aged Men According to Weight Change Category*

Weight Change Category (From Q1 to Q5 to Q92)	Age-Adjusted Rate per 1000 Person-Years†	Adjusted RR (95% CI)‡		
		A	B	C
Total Mortality				
Stable§	16.4 (214/1663)	1.00	1.00	1.00
Sustained gain	21.3 (320/2155)	1.14 (0.87-1.50)	1.07 (0.89-1.29)	1.02
Sustained loss	27.8 (225/950)	1.60 (1.32-1.95)	1.34 (1.09-1.63)	1.30
Loss-gain	27.9 (71/361)	1.50 (1.17-1.91)	1.40 (1.06-1.85)	1.34
Gain-loss	29.6 (113/479)	1.63 (1.24-2.14)	1.31 (1.02-1.68)	0.90
CVD Mortality				
Stable§	8.0 (102/1663)	1.00	1.00	1.00
Sustained gain	9.2 (152/2155)	1.09 (0.85-1.41)	1.08 (0.82-1.42)	1.00
Sustained loss	16.3 (112/950)	1.71 (1.29-2.28)	1.38 (1.03-1.84)	1.23
Loss-gain	14.4 (39/361)	1.65 (1.11-2.44)	1.45 (0.98-2.15)	1.47
Gain-loss	15.1 (53/479)	1.67 (1.18-2.36)	1.44 (1.02-2.04)	1.25
Non-CVD Mortality				
Stable§	8.4 (112/1663)	1.00	1.00	1.00
Sustained gain	12.1 (168/2155)	1.07 (0.89-1.29)	1.04 (0.81-1.34)	1.03
Sustained loss	11.5 (113/950)	1.34 (1.09-1.63)	1.32 (0.99-1.75)	1.34
Loss-gain	13.5 (32/361)	1.40 (1.06-1.85)	1.29 (0.87-1.93)	1.26
Gain-loss	14.5 (60/479)	1.31 (1.02-1.68)	1.18 (0.83-1.67)	0.70

*RR indicates relative risk; Q1, baseline screening; Q5, questionnaire administered 5 years after the initial examination; Q92, questionnaire administered 12 to 14 years after the initial examination; CI, confidence interval; and CVD, cardiovascular disease.

†Data in parentheses are number of cases/number of men.

‡A indicates adjusted for age, social class, smoking status, physical activity, and initial body mass index; B, adjusted for all the variables in A and for preexisting CVD, diabetes mellitus, cancer, and poor health; and C, adjusted for all the variables in A and excluding men with preexisting CVD-related diseases (coronary heart disease, stroke, and diabetes mellitus) and cancer and those reporting poor health (analysis based on 4041 men [n = 477 deaths, total mortality; n = 186 deaths, CVD mortality; and n = 291 deaths, non-CVD mortality]).

§Reference.

||P = .07.

pared with the stable group (relative risk, 1.39). Men with sustained weight loss and those whose weight fluctuated since screening showed a significantly higher risk of total mortality than men whose weight remained stable, even after adjustment for age, social class, smoking status, physical activity, and initial BMI. A similar pattern was seen for cardiovascular and non-cardiovascular causes. When examined by initial BMI (data not shown), these patterns were seen in lean men (BMI, <25) and in heavier men (BMI, ≥25).

ADJUSTMENT AND EXCLUSION

Sustained weight loss and weight fluctuation (involving weight loss at some time) were strongly associated with preexisting cardiovascular conditions, cancer, and self-assessed poor health (Table 3). In a multivariate analysis (Table 2), adjustment for preexisting disease attenu-

ated the increased risk of mortality seen in the sustained weight loss and weight fluctuation groups, but all these groups remained significantly associated with increased risk of total mortality, largely because of an increased risk of cardiovascular mortality. When men with preexisting CVD conditions, cancer, and self-assessed poor health were excluded, these associations were also attenuated. Exclusion markedly attenuated the increased risk of CVD mortality associated with sustained weight loss and with the weight gain-weight loss group, but made little difference to the men who lost and regained weight or to the relative risk of non-CVD mortality.

WEIGHT CHANGE, SMOKING, AND MORTALITY

The relation between weight change and mortality was examined separately by smoking status (Table 4). In

Table 3. Prevalence of Preexisting Disease at Q92 According to Weight Change Category*

Weight Change Category	MI	Angina	Heart Trouble	Stroke	Diabetes Mellitus	Cancer	Poor Health	Any
Stable	7.3	10.4	4.4	3.0	2.4	2.5	2.2	23.3
Sustained gain	8.6	9.9	4.3	3.0	3.3	2.2	4.1	23.8
Sustained loss	14.1	15.3	7.3	5.1	9.3	4.5	7.4	39.4
Loss-gain	11.6	13.3	5.8	4.4	5.3	5.3	5.0	32.1
Gain-loss	12.1	16.3	6.1	4.4	7.5	4.6	7.2	37.2

*Data are given as percentage of men. Q92 indicates questionnaire administered 12 to 14 years after the initial examination; MI, myocardial infarction; and Any, any of the other conditions listed.

Table 4. Smoking Status and Adjusted RRs for Mortality During 8 Years of Follow-up in 5570 Men Aged 52 to 73 Years According to Weight Change Category*

Weight Change Category	Long-term Nonsmokers (n = 3472)			Recent Ex-Smokers (n = 1035)			Current Smokers (Q92) (n = 1063)		
	No. of Men	Adjusted RR†		No. of Men	Adjusted RR†		No. of Men	Adjusted RR†	
		A	B		A	B		A	B
Total Mortality									
	(n = 457 Deaths; 17.0‡)			(n = 211 Deaths; 27.6‡)			(n = 267 Deaths; 34.6‡)		
Stable§	1164	1.00	1.00	201	1.00	1.00	285	1.00	1.00
Sustained gain	1207	1.16	1.06	564	1.26	1.31	376	0.97	0.98
Sustained loss	642	1.47	1.11	106	2.94	2.17	194	1.33	1.30
Loss-gain	207	1.63	1.34	73	1.91	1.66	79	1.18	1.16
Gain-loss	252	1.66	1.26	91	1.80	1.72¶	129	1.17	1.16
CVD Mortality									
	(n = 242 Deaths; 9.0‡)			(n = 110 Deaths; 14.4‡)			(n = 101 Deaths; 13.1‡)		
Stable§		1.00	1.00		1.00	1.00		1.00	1.00
Sustained gain		1.19	1.09		1.70	1.76		0.84	0.79
Sustained loss		1.41¶	1.07		4.83	3.43		1.32	1.27
Loss-gain		1.71	1.30		2.89	2.60		0.98	0.96
Gain-loss		1.74	1.35		2.77	2.72		1.09	0.96
Non-CVD Mortality									
	(n = 215 Deaths; 8.0‡)			(n = 101 Deaths; 13.2‡)			(n = 166 Deaths; 21.5‡)		
Stable§		1.00	1.00		1.00	1.00		1.00	1.00
Sustained gain		1.12	1.00		0.99	1.00		1.05	1.07
Sustained loss		1.54	1.24		1.78	1.44		1.31	1.30
Loss-gain		1.54	1.33		1.28	1.07		1.33	1.30
Gain-loss		1.57	1.16		1.17	1.04		1.21	1.24

*RR indicates relative risk; Q92, questionnaire administered 12 to 14 years after the initial examination; and CVD, cardiovascular disease.

†A indicates adjusted for age, social class, physical activity, and initial body mass index; B, adjusted for all the variables in A and preexisting CVD, cancer, and poor health.

‡Age-adjusted rate per 1000 person-years.

§Reference.

||P < .05.

¶P = .07.

long-term nonsmokers, those who experienced any weight loss since screening showed a significant increase in age-adjusted mortality from all causes, CVD causes, and non-CVD causes, but this increase was markedly attenuated and rendered nonsignificant after adjustment for preexisting disease. However, among men who had given up smoking since screening (recent ex-cigarette smokers), those with sustained weight loss and those who gained and lost weight showed a markedly increased risk of mortality even after adjustment for preexisting disease, largely because of an increased risk of cardiovascular deaths. In current smokers, sustained weight loss and weight fluctuation showed little association with mortality. The mortality pattern in recent ex-smokers reflects the high preva-

lence of preexisting disease in these subjects, seen in particular in those with sustained weight loss and weight fluctuation, who had by far the highest rates of preexisting disease of any smoking groups or weight change groups (data not shown).

COMMENT

Most people who lose weight intentionally eventually regain it.¹⁶ Several prospective studies⁵⁻⁸ have suggested that weight cycling or weight variability per se increases morbidity and the risk of cardiovascular and all-cause mortality. In the present study, men with sustained weight loss or weight fluctuation (cycling) showed a signifi-

cantly increased risk of total and CVD mortality. These men had the highest prevalence of preexisting disease. Adjustment for CVD risk factors and preexisting disease in multivariate analysis attenuated the increased risk, although it still remained significantly increased. This is likely due to residual confounding by preexisting disease because the severity of diseases was not considered. When all men with preexisting CVD, cancer, or poor health were excluded, total and CVD mortality risk in the sustained weight loss and weight fluctuation groups was attenuated to a greater extent than by adjustment. Those who lost and gained weight showed some increase in CVD mortality. The hazardous effect of weight loss and weight fluctuation was most marked in recent ex-smokers. Sustained weight loss and weight fluctuation showed no significant association with mortality in long-term nonsmokers or in current smokers. The increased risk in recent ex-smokers reflects their high prevalence of preexisting disease; more than 50% of these men had one or more diagnoses of CVD, cancer, or poor health. Reporting of poor health among the recent ex-smokers with sustained weight loss was more than 6 times greater than in the recent ex-smokers whose weight remained stable.

WEIGHT FLUCTUATION AND MORTALITY

Several prospective studies⁵⁻⁸ have shown weight fluctuation (gain-loss or loss-gain) or weight variability (defined as the coefficient of variation of weight⁷) to be associated with increased mortality independent of the direction of weight change, but these studies have taken limited account of preexisting disease. In the Western Electric Study,⁵ weight cycling was associated with an increased risk of all-cause mortality and CVD mortality compared with those whose weight remained stable. In the Framingham study,⁷ weight variability was positively associated with total and CHD mortality in men and women in Framingham, Mass, and, in multivariate analysis, this was independent of the direction of weight change. In the Gothenburg (Sweden) study,⁶ weight variability was associated with increased mortality in men and women. The Multiple Risk Factor Intervention Trial⁸ showed weight cycling and weight variability to be associated with increased mortality, but the researchers only excluded men who developed nonfatal cancer and CHD events and the study was based on 4 years of follow-up. The increased risk remaining after the exclusions may well have been due to other diseases associated with weight loss and not taken into account. In the recent study from the Chicago Western Electric Company,¹⁷ weight loss and weight gain were associated with increased mortality, but weight variability was not associated with mortality once weight loss or weight gain was taken into account. Taking preexisting disease into account by examining the association in the first 15 years of follow-up and in the subsequent 10 years of follow-up showed that increased mortality associated with weight loss was only present for cardiovascular mortality and in men aged 55 to 66 years. Exclusion of men with disease during the weight change period was limited to those who developed CHD or cancer. The long-term effects of weight loss on CVD mortality may have been produced by other CVD-related dis-

eases associated with weight loss (eg, diabetes mellitus, stroke, or angina), which were not excluded.

In the Baltimore Longitudinal Study,¹⁸ comprising subjects who were generally healthier than the overall US population, weight variability was not associated with CHD, cancer, or all-cause mortality. The Honolulu Heart Study¹⁹ showed no association between weight variation and weight loss in healthy nonsmoking men. In the Iowa Women's Health Study,²⁰ large cycles of weight change (loss-gain or gain-loss) were associated with increased mortality, but this was attenuated after adjustment for confounding factors and preexisting disease and exclusion of women with poor or fair health.

In the present study (British Regional Heart Study), the finding that weight change and weight fluctuation (cycling) are not associated with mortality in healthy nonsmokers is consistent with the findings of the Honolulu Heart Study. These findings, together with those from the other prospective studies,¹⁷⁻²⁰ suggest that weight variability per se does not increase the risk of mortality.

INTENTIONAL AND UNINTENTIONAL WEIGHT LOSS

The possibility that intentional weight loss may directly increase mortality is of considerable concern, and attention has been drawn to the importance of differentiating between intentional and unintentional weight loss.²¹ A recent cross-sectional report from the British Regional Heart Study on perceived weight change in this cohort indicated that weight loss in older men is likely to be unintentional. However, whether intentional or unintentional, weight loss is often associated with adverse characteristics and disease, and intentional weight loss is likely to be prompted by the presence of obesity-related conditions.²² In this earlier British Regional Heart Study, those who reported weight cycling had the highest rates of preexisting disease, were the heaviest group at baseline, and remained the heaviest group. In the present study, based on reported weight, 50% of the men who lost weight between Q1 and Q5 regained weight. In most studies on weight loss and outcome, weight loss is assessed at only one time point, and this may partly explain why men who lose weight do not experience benefit.

RECENT STUDIES ON INTENTIONALITY

In the Israeli Ischemic Heart Study,²³ voluntary weight loss (for medical reasons or slimming) and involuntary weight loss were associated with increased mortality. Exclusion of early deaths (during the first 5 of 18 years of follow-up) and adjustment for risk factors and ill health markedly reduced the increased relative risks. However, in the Cancer Prevention Study I (United States),²⁴ involving nearly 50 000 overweight (BMI, >27) men, neither intentional nor unintentional weight loss (>9 kg) in healthy men was significantly associated with total, cardiovascular, or cancer mortality after adjustment for lifestyle factors, health history, and symptoms. In the Iowa Women's Health Study,²⁵ intentional weight loss episodes of more than 9 kg during adulthood were not associated with increased total or CVD mortality. Unin-

tentional weight loss was associated with higher total and CVD mortality, but this was confined to women with prevalent disease, hypertension, or diabetes mellitus.

In the present study, although we were not able to differentiate between intentional and unintentional weight loss, exclusion of men with a wide range of preexisting disease attenuated the increased risk associated with sustained weight loss and weight fluctuation. In other studies^{19,26} that have excluded men with preexisting disease and that have stratified by smoking, weight loss is not associated with increased mortality in healthy nonsmokers. These findings suggest that the increased mortality associated with weight loss and weight fluctuation (cycling) is due to the effects of preexisting disease and smoking and is not brought about by the effects of weight loss or weight cycling per se.

CONCLUSIONS

Because many observational studies have reported that weight loss and weight fluctuation (cycling) in older men and women are associated with increased mortality, there is understandable concern that losing weight in older age may be hazardous. Because of the epidemic of overweight and obesity in the industrialized world, this belief could be a barrier to the management of overweight and obesity. The present study and the findings from other recent studies strongly suggest that the increased risk of mortality associated with weight loss, intentional or unintentional, and sometimes involving weight cycling, is determined to a major extent by disadvantageous lifestyle factors and preexisting disease. There is no firm evidence that weight loss or weight fluctuation in otherwise healthy individuals is hazardous, and authorities should continue to encourage and facilitate healthy eating and regular moderate physical activity toward the prevention and management of overweight and obesity.

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