Intentional Weight Loss and Mortality Among Overweight Individuals With Diabetes

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OBJECTIVE — To estimate the effect of intentional weight loss on mortality in overweight individuals with diabetes.

RESEARCH DESIGN AND METHODS — We performed a prospective analysis with a 12-year mortality follow-up (1959–1972) of 4,970 overweight individuals with diabetes, 40–64 years of age, who were enrolled in the American Cancer Society's Cancer Prevention Study I. Rate ratios (RRs) were calculated, comparing overall death rates, and death from cardiovascular disease (CVD) or diabetes in individuals with and without reported intentional weight loss.

RESULTS — Intentional weight loss was reported by 34% of the cohort. After adjustment for initial BMI, sociodemographic factors, health status, and physical activity, intentional weight loss was associated with a 25% reduction in total mortality (RR = 0.75; 95% CI 0.67–0.84), and a 28% reduction in CVD and diabetes mortality (RR = 0.72; 0.63–0.82). Intentional weight loss of 20–29 lb was associated with the largest reductions in mortality (~33%). Weight loss >70 lb was associated with small increases in mortality.

CONCLUSIONS — Intentional weight loss was associated with substantial reductions in mortality in this observational study of overweight individuals with diabetes.

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Approximately two-thirds of people with type 2 diabetes are overweight (1). In overweight people, weight loss reduces medication costs and improves glycemia, lipoproteinemia, and blood pressure (2). Therefore, weight reduction is an important goal in treating type 2 diabetes (3); in fact, some consider it the cornerstone of diabetes therapy (4).

Despite the physiological benefits of weight loss in individuals with diabetes, the evidence that weight loss increases diabetic patients' longevity is equivocal (5). For instance, in a review of the six published observational studies on this topic (6), one study found no association between weight loss and longevity (7), two found weight loss was associated with decreased mortality (8,9), one reported that weight loss was associated with increased mortality (10), and two found associations with increased and decreased mortality in different subgroups (11,12).

No studies have differentiated between intentional and unintentional weight loss. This fact is important to note because unintentional weight loss may be associated with more severe disease or with unrecognized health problems (2). Alternatively, a positive impact of weight loss may arise from self-selection via the correlation with other beneficial health practices.

This is the first study to use data on weight loss intention in examining the relationship between weight change and mortality in overweight individuals with diabetes.

RESEARCH DESIGN AND METHODS

Between October 1959 and March 1960, 1,051,042 men and women ≥30 years of age were recruited by the American Cancer Society in 25 states for the baseline interview of the Cancer Prevention Study I (CPS-I) (13). Data from personal inquiries made annually from 1960 to 1965 and from 1971 to 1972 were used to determine vital stastistics. Death certificates were obtained from state health departments and coded by a nosologist.

The underlying cause of death and two contributing causes were coded using the *International Classification of Diseases, Seventh Revision* (ICD-7). We examined total mortality and deaths that listed cardiovascular disease (ICD-7: stroke, 330–334; atherosclerotic and degenerative heart disease, 420–422; acute endo-, myo-, or pericarditis, 430–434; hypertensive disease, 440–447; peripheral vascular disease, 453–456; and venous emboli and phlebitis, 460–468) or diabetes (ICD-7: 260) as the underlying cause of death. This combined end point—deaths caused by cardiovascular disease (CVD) and diabetes—accounted for 78% of all deaths, including myocardial infarction (35%), atherosclerotic heart disease (24%), diabetes (21%), cerebral hemorrhage (5%), hypertensive heart disease (5%), and other cardiovascular causes (10%). Of diabetes deaths, 89% listed cardiovascular disease as a contributing cause. Median follow-up was 12.9 years for survivors (n = 3,084) and 7.1 years for decedents (n = 1,886); 91.4% of study subjects had complete mortality follow-up.

Weight change

Current BMI was computed from weight and height in indoor clothing without shoes, as reported by participants at the baseline interview. Questions on weight change were

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Abbreviations: CPS-I, Cancer Prevention Study I; CVD, cardiovascular disease; ICD-7, *International Classification of Diseases, Seventh Revision*; RR, rate ratio.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

asked only at the baseline interview. The first weight change question asked if the respondent had a change in weight (without regard to when the change occurred); respondents checked either a "yes" or a "no" box. If they checked "yes," they were asked if the change was a gain or loss, as well as, "About how many pounds?", "Over what period of time?", and "Did you try to bring about this change? (yes or no)." Before data entry, the amount of weight change (in 10-lb. increments from 1 to ≥90) and the weight-change time interval (in 1-year increments from <1 to ≥9) were precoded into 10 categories. (The original questionnaires are not available.) The weight change categories were "no change," "unintentional loss," "unintentional gain," "intentional gain," "intentional loss," and "unknown" for missing responses. Rate ratios (RRs) for intentional gain are not reported because there were only 19 people and 7 deaths for this category.

Covariates

Covariates were coded as indicator variables. Initial BMI (27 to <29, 29 to <32, 32 to <35, 35 to <38, ≥38) was computed by adding (or subtracting) the amount of weight change to (or from) current body weight using the category mid-range (90 lb was used for the highest category). Underlying illness was assessed by questions regarding history of the following: heart disease, stroke, hypertension, cancer, cirrhosis, current pain in chest, shortness of breath, fatigue, loss of appetite, blood in stool, and blood in urine. The following three questions were also asked to assess underlying illness: "How have you been feeling in the last month or two? (good, fair, or poor)"; "Are you sick at the present time? (yes or no)"; and "If 'yes,' what disease?" (write in response). For pain in chest, shortness of breath, fatigue, loss of appetite, and blood in urine, intensity was reported as "none," "slight," "moderate," or "severe."

One question was asked about physical activity: "How much exercise do you get (work or play)?" with response options, "none," "slight," "moderate," and "heavy." Smoking categories and subcategories were "never smoker," "former cigarette smoker" (for <1, 1–4, or ≥5 years), "current smoker" (of 1–9, 10–19, or ≥20 cigarettes per day), "current smoker of cigars or pipes only," and "former smoker of cigars or pipes only." Education selection options were "primary only," "some high school," "high school graduate," "some college," and "college graduate."

Other covariates included years of age (in 5-year categories), sex, race (white, black, or other), and alcohol intake (none, <1 drink per week, 1–2 drinks per week, >3 drinks per week, or variable amount ≥1 drink per week). Dietary data were not used because only the intake frequency of a limited number of broad food groups was assessed.

Exclusions

We excluded people ≥65 years of age to avoid confounding by aging-related weight loss; we also excluded people ≤40 years of age because this age-group had very few deaths. Of the 1,051,042 participants, 20,849 (2%) reported they had diabetes (10,096 men and 10,753 women); 13,443 of these patients were 40–64 years of age. We excluded 748 (5.7%) because of missing weight data and 310 (2.4%) because of missing height data. We then limited the sample to 5,455 respondents whose initial BMI was ≥27 kg/m^2. Of these 5,455 subjects, we excluded 2 (0.04%) who reported a weight change but were missing data on direction, amount, or intent; we also excluded participants who were missing data on smoking (238 [4.4%]), alcohol (38 [0.7%]), education (47 [0.9%]), physical activity (127 [2.5%]), and race (33 [0.7%]). The final study sample was 4,970 (2,509 men and 2,461 women). For analyses of weight-change time interval, 157 (3.2%) were missing data.

Statistical analysis

Death rates were standardized to the 5-year age distribution of the cohort. Proportional hazards (14) were used to estimate mortality RRs. Respondents with no or unknown weight change were the referent. Compared with the no change category, mortality RRs for the "unknown" category were very close to 1, which suggests that the latter largely represents people with no weight change.

We also analyzed weight change as an ordinal variable, assigning values from 1 (1–9 lb) to 10 (≥90 lb) to its categories. We first fit a model coding each category as an indicator variable, then fit separate models with ordinal linear terms, linear and quadratic terms, linear spline terms, and quadratic spline terms for weight change. Nested models were compared using the χ^2 test of the difference in log-likelihoods, whereas Akaike's Information Criterion (15) compared non-nested models.

We examined evidence that sex, initial BMI, and weight-change time intervals (<1 and ≥1 year) modify the association between weight change and mortality by fitting interaction terms. We also assessed our results' sensitivity to an unmeasured confounder (16).

We examined interactions between the weight change variables and indicator variables for follow-up time (<3, 3 to <6, 6 to <9, and ≥9 years) but found no violation of the proportionality assumption. We then used age, rather than follow-up time, as the time scale and obtained nearly identical results. We examined the fit of the proportional hazards models and found that the models fit the data well.

RESULTS

Study subjects were predominantly white with a mean age of ~55 years (Table 1). Approximately one-third of the study subjects reported intentional weight loss, and death rates were lowest in these individuals. Regarding signs and symptoms of underlying illness, participants who reported intentional weight loss generally had an intermediate amount compared with those with unintentional weight gain (highest amount of underlying illness) and those with unknown weight change (lowest amount of underlying illness).

Study subjects reporting intentional weight loss had the highest initial mean BMI, whereas those reporting unintentional weight gain had the lowest initial BMI. The amount of intentional and unintentional weight loss often exceeded 20 lb; unintentional weight gain was usually <20 lb. The majority of subjects with intentional weight loss reported an interval of <1 year, whereas the majority of those with unintentional weight loss or gain reported an interval of ≥1 year. Correlates of intentional weight loss included having a high school education or higher, higher prevalence of smoking, and low physical activity. Compared with subjects with an initial BMI of 27–29 kg/m^2, the age-, sex-, and smoking-adjusted mortality rates were 5–25% higher with increasing levels of initial BMI (data not shown).

Mortality and weight change

Intentional weight loss was associated with lower total mortality and CVD and diabetes mortality before covariate adjustment (Table 2). After controlling for age, sex, and initial BMI, additional control for physical activity, disease his-

Table 1—*Characteristics of the weight change groups: 4,970 overweight diabetic individuals aged 40–64 years, CPS-I (1959–1972)*

		Weight-change category			
	No change	Unknown	Unintentional gain	Unintentional loss	Intentional loss
n (%)	1,754 (35.3)	739 (14.7)	140 (2.8)	649 (13.1)	1,669 (33.6)
Person-years (*n*)	17,278	7,452	1,331	6,038	16,844
Sex (% women)	54.4	37.3	68.6	44.8	49.6
Age (years)	54.5 ± 6.0	54.7 ± 6.0	53.9 ± 6.2	55.6 ± 5.7	54.5 ± 6.0
Race (% nonwhite)	4.6	6.1	6.4	5.2	2.6
Age-adjusted death rates†					
All causes	40.3 (689)	40.0 (291)	45.6 (58)	44.0 (280)	33.6 (561)
CVD + diabetes	31.8 (543)	30.8 (231)	31.4 (40)	34.1 (218)	26.1 (434)
History of (%)					
Heart disease	13.8	9.2	23.6	16.8	16.1
Stroke	2.6	2.2	5.0	4.6	3.2
Hypertension	31.6	19.9	43.6	25.4	30.7
Cancer	3.9	3.1	7.9	4.4	4.2
Cirrhosis	1.1	0.9	2.9	2.5	1.2
Signs/symptoms (%)*					
Pain in chest	1.1	0.3	0.7	3.4	1.7
Short of breath	1.6	0.3	2.9	3.2	1.4
Fatigue easily	7.2	0.0	12.9	7.9	5.6
Loss of appetite	0.0	0.0	0.0	1.4	0.2
Blood in stool	7.0	2.7	10.7	5.9	6.5
Blood in urine	0.1	0.0	1.4	0.0	0.0
Feel good	26.5	59.5	16.4	26.4	34.4
Feel fair	39.2	16.6	45.7	26.2	23.7
Feel poor	1.8	0.3	1.4	3.1	0.9
Currently “sick”	22.7	9.9	22.1	31.4	28.3
Wrote in a disease	6.8	6.1	12.1	10.5	9.9
Initial BMI	—	—	29.9 ± 2.7	31.8 ± 4.1	33.5 ± 5.0
Current BMI	30.8 ± 3.5	30.3 ± 3.4	34.3 ± 4.3	25.9 ± 3.6	27.7 ± 4.0
Amount of weight change (%)					
1–9 lb	—	—	18.1	4.0	4.1
10–19 lb	—	—	43.3	18.9	20.2
20–29 lb	—	—	22.8	24.8	29.8
30+ lb	—	—	15.7	52.3	46.0
Weight change interval (%)†					
<1 year	—	—	39.4	46.9	56.4
1 to <3 years	—	—	41.7	35.7	33.4
≥3 years	—	—	18.9	17.4	10.3
Education less than high school (%)	57.2	52.3	55.0	58.5	45.2
Current smokers (%)	29.1	33.6	30.7	38.4	37.0
Drink alcohol (%)	25.7	23.4	22.1	21.3	25.6
No physical activity (%)	3.5	2.4	5.7	3.7	3.5
High physical activity (%)	12.3	14.9	12.9	13.9	8.7

Data for BMI are means ± SD. Data for 19 people (7 deaths) who reported intentional weight gain are not shown. *Percent reporting “severe” signs and symptoms; †mortality rates are directly age-standardized to the age distribution of the cohort and expressed per 1,000 person-years; number of deaths is given in parentheses.

tory, and signs and symptoms of illness had little effect on the RR. However, physical activity was inversely associated with mortality. Relative to no physical activity, total mortality RR for the low, moderate, and high physical activity categories were 0.75 (95% CI 0.60–0.95), 0.62 (0.50–0.77), and 0.45 (0.35–0.58), respectively. Results were similar for CVD and diabetes mortality (data not shown).

In fully adjusted models, intentional weight loss was associated with ~25% reduction in mortality. We then included nephrotic kidney disease in CVD and diabetes mortality, and the results were similar. We repeated the analysis for CVD mortality (excluding diabetes mortality), and the intentional weight loss RR was 0.79 (0.69–0.91). We examined mortality due to causes other than CVD and diabetes, and the RR was 0.85 (0.67–1.08).

Neither unintentional weight loss nor gain was associated with mortality. Associations between weight change and mortality did not vary by sex, initial BMI, or weight-loss time interval.

Table 2—*Mortality RRs for weight change categories: prospective data from 4,970 diabetic individuals 40–64 years of age, CPS-I (1959–1972)*

	All causes		CVD + diabetes	
Weight-change category	Deaths	RR (95% CI)	Deaths	RR (95% CI)
No change (referent)*	980	1.00	774	1.00
Unintentional loss	280		218	
Adjusted for				
Crude		1.18 (1.03–1.35)		1.16 (1.00–1.35)
Age, sex, initial BMI		1.06 (0.93–1.22)		1.04 (0.90–1.22)
Full†		0.98 (0.85–1.13)		0.98 (0.83–1.15)
Unintentional gain	58		40	
Adjusted for				
Crude		1.11 (0.85–1.44)		0.97 (0.71–1.33)
Age, sex, initial BMI		1.26 (0.96–1.64)		1.11 (0.80–1.52)
Full†		1.04 (0.79–1.36)		0.90 (0.65–1.25)
Intentional loss	561		434	
Adjusted for				
Crude		0.83 (0.75–0.93)		0.82 (0.73–0.92)
Age, sex, initial BMI		0.78 (0.70–0.87)		0.76 (0.67–0.86)
+ Exercise		0.77 (0.69–0.86)		0.75 (0.66–0.85)
+ Disease history/signs/symptoms		0.75 (0.67–0.84)		0.73 (0.64–0.83)
Full†		0.75 (0.67–0.84)		0.72 (0.63–0.82)

Data for 19 people (7 deaths) who reported intentional weight gain are not shown. *The referent group includes those who did not answer the weight change questions; †adjusted for age, sex, race, smoking, initial BMI, education, drinking, physical activity, disease history, and current signs and symptoms.

Mortality and amount intentionally lost

Amount of unintentional weight loss or gain was unrelated to total mortality or CVD and diabetes mortality (data not shown). We therefore included unintentional weight loss or gain in the referent group. We found that a linear spline with slope changes at 20–29 lb and at 50–59 lb best fit the data. For total mortality (Fig. 1), intentional weight loss was most protective at a loss of 20–29 lb (total mortality RR = 0.67 [0.58–0.77]). Losses >70 lb were associated with slightly increased mortality. CVD and diabetes mortality results were similar (data not shown).

To assess whether the increased mortality associated with large amounts of weight loss occurred because current BMIs were too low, we adjusted for current BMI categories of ≤20, >20 to ≤25, and >25, but the results were unchanged. Model fit was not improved with splines at 10–19 and 30–39 lb.

CONCLUSIONS — We found that overweight people with diabetes who reported intentional weight loss experienced 25% lower total mortality than those not reporting intentional weight loss. The largest mortality reduction (33%) was associated with losses of 20–29 lb (10–15% of initial weight). In contrast, losses of ≥70 lb (≥30% of initial weight) were associated with small increases in mortality. Associations were similar for the combined end point of CVD and diabetes mortality. These mortality reductions parallel the physiological improvements observed after weight reduction (2).

This is an observational study with inherent limitations in the assessment of exposure to intentional weight loss. Therefore, sources of bias and their impact on our findings should be carefully considered. In this study, body weight and weight change were self-reported. Current self-reported and measured body weight are highly correlated, but substantial correlations (ranging from $r = 0.64$ to $r = 0.95$) also exist between recalled weight and weight that was measured up to 60 years in the past (17). This suggests that past weight change can be accurately reported. Furthermore, in a study of weight loss in 4,700 British men, perceived weight change showed good correlation with weight change defined as the difference between body weights reported 4 years apart (18). In that study, 70% of the men who reported that intentional weight loss occurred sometime during the 4-year period had experienced a net weight loss. There is also evidence that reported intentional weight loss is a reliable measure. A study of 29,000 U.S. women found a strong 9-month test-retest correlation of $r = 0.8$ for reported intentional weight loss (19).

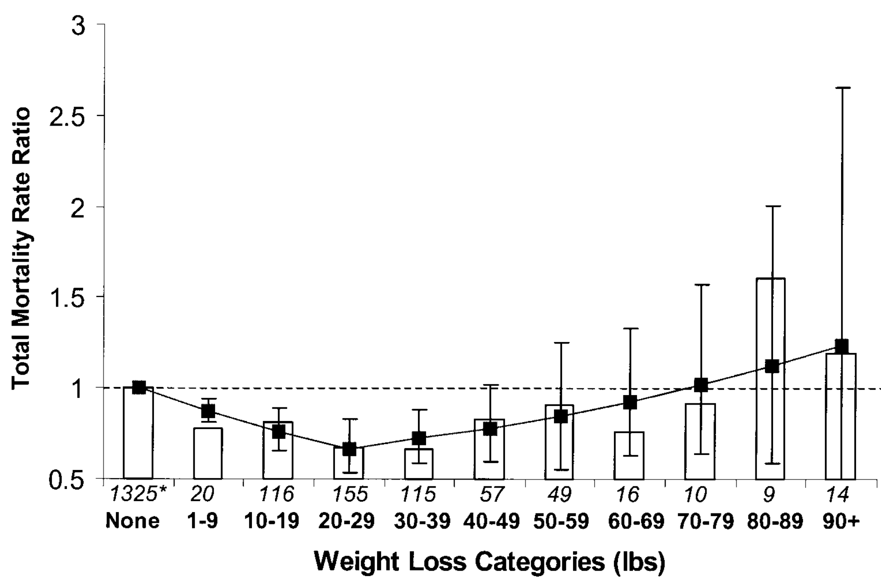

Figure 1—*Amount of intentional weight loss and overall mortality RRs. Bar graph shows RRs for weight loss categories as indicator variables. —, Continuous relationship from a linear spline proportional hazards model with knots at 20–29 and 60–69 lb. RRs are represented by ■, with 95% confidence limits. Prospective data from 4,970 overweight diabetic individuals aged 40–64 years, CPS-I (1959–1972) are shown. *Number of deaths.*

Data from the general population on prevalence and magnitude of intentional weight loss are very limited. We were unable to identify any other prospective studies that reported data on weight loss intention in overweight individuals with diabetes. In our study, one-third of the participants reported intentional weight loss. This finding is very similar to that of a 1989 nationally representative sample of 9,000 U.S. adults ≥45 years of age (20). In that study, participants were classified as having intentional weight loss if they reported trying to lose weight in the past year and if they weighed less than they did a year previously. Among those with BMI ≥30 kg/m^2, ~30% reported intentionally losing weight during the past year. No information, however, was presented for overweight individuals with diabetes.

In our study, the average intentional weight loss was 24 lb or ~11% of initial body weight. The only comparable observational study was a retrospective review of clinic records from 260 British patients with type 2 diabetes (8). In that study, the 1-year weight loss in patients with BMI ≥30 kg/m^2 was 15 lb, or ~8% of initial weight. However, weight loss intention was not assessed.

In the current study, maintained weight losses were not differentiated from transient losses followed by regain. We therefore had no information on whether the reported intentional weight loss was successful. According to conventional wisdom, transitory weight loss has no long-term clinical benefit, but limited evidence suggests that improvements in glycemia can be maintained even after weight regain (22). It is also possible that participants sustained their weight losses because evidence suggests weight fluctuations caused by repeated episodes of dieting were less common in the 1950s and 1960s (23). No information was provided on method of weight loss, but the impact of intentional weight loss may vary with method. The most common method in the 1950s, however, was probably caloric restriction, which remains the most popular method today.

Initial weight was calculated from weight change and current weight. Hence, any errors in weight change are correlated with initial weight. If error in reported weight change is systematically related to both initial weight and mortality, then adjustment for initial BMI could introduce bias. However, we reran the results in Table 2, adjusting only for initial BMI, and found the RRs for intentional weight loss were nearly unchanged.

Using the midpoints of the weight change amount categories may result in biased estimates of weight change, which could, in turn, bias estimates of initial BMI for those reporting weight change. Therefore, we recalculated initial BMI under two extreme assumptions about how participants reported their weight change (i.e., using the upper and lower values of the weight change categories). We reran the results in Table 2 but found that all RRs remained virtually the same, regardless of how initial BMI was calculated.

In our study, the analytic cohort was sampled on initial, rather than current, BMI to simulate a randomized trial. In such a trial, participants would be chosen on the weight at which weight loss was initiated rather than the weight after which weight loss was completed. Although it is uncertain how a respondent with multiple weight changes would answer the questionnaire, it is likely that participants reported their most recent weight change. However, if there was a systematic relationship among errors in reporting the direction of weight change, calculated initial weight, and mortality, then our results may be biased. This bias could be reduced by sampling the participants based on current, rather than initial, weight. We resampled the cohort on current weight (BMI ≥25 kg/m^2) and reran the results in Table 2, and the RRs for intentional weight loss were nearly unchanged.

When covariates are entered in their linear forms, fitting a model with weight loss and current weight is mathematically identical to fitting a model with weight loss and initial weight (21). Fitting the model with initial weight, however, provides a direct estimate of the coefficient for weight loss that would be obtained in a randomized trial (i.e., the change in the mortality rate that is attributable to having lost weight and reached a lower weight), holding initial weight constant.

We found a curve-linear association between the amount of intentionally lost weight and mortality. This finding may be an artifact of misclassifying the amount categories (24), or it may reflect the possibility that very large intentional weight losses include unintentional weight loss related to diabetes severity. Diabetes severity, however, was not assessed in our study. Alternatively, large amounts of intentional weight loss may cause increased mortality because of direct harm to lean tissues, such as the myocardium.

Diabetes status was self-reported in our study. Self-report of diabetes has a high specificity when compared with fasting glucose measurement (25), suggesting that most participants had diabetes. However, because a large proportion of diabetes is undiagnosed (26), the cohort probably included more severe cases of diabetes with clear symptoms. Although type of diabetes was not assessed in this study, it is likely that results are applicable to type 2 diabetes because type 1 diabetes is rare after 45 years of age (27).

It is possible that intentional weight loss was confounded by unmeasured factors. Intentional weight loss may reflect health practices that improve glycemic control. Even before covariate adjustment, mortality in the intentional weight loss group was ~20% lower than that in the referent group. Covariate adjustment increased the protective association by only 10%. Although physical activity was strongly protective, it is not clear whether adjusting for physical activity adequately controlled for confounding by health practices, because physical activity referred to both discretionary (play) and nondiscretionary (work) activity. Conversely, the argument that people reporting intentional weight loss were more health conscious is not supported by their high prevalence of smoking.

However, only an exceptionally protective (mortality RR = 0.5) and highly prevalent confounder (60% prevalence in the intentional weight loss group vs. 10% in the referent group) would have nullified our findings. Control for the confounder would have increased the total mortality RR from 0.75 to 1.02 and the CVD and diabetes mortality RR from 0.72 to 0.98.

It is possible that we have underestimated the protective relationship between intentional weight loss and mortality. In our study, intentional weight loss was assessed at the baseline interview before the study outcome of mortality had occurred. It is therefore likely that misclassification of intentional weight loss is nondifferential (i.e., unrelated to mortality). Also, our sensitivity analyses did not materially alter the RRs for intentional weight loss in the models that were fully adjusted for all covariates, suggesting that misclassification is largely independent of error in the other covariates. When misclassification of a dichotomous exposure is nondifferential and independent of other covariates, bias is toward the null (28).

Although unintentional weight loss is considered a sign of deteriorating health, we found that it was associated with only a slight increase in mortality, perhaps because seriously ill people were unlikely to enroll in the study. Unintentional weight gain was generally unrelated to mortality. Furthermore, weight gain may be less harmful in overweight people than it is in lean individuals, or it may reflect improved glycemic control.

In conclusion, in overweight people with diabetes, intentional weight loss was associated with ~25% reduction in mortality. These results should be replicated in more current observational studies because the benefits of weight loss, compared with current pharmacological treatment of hyperglycemia, lipoprotenemia, and hypertension, may be less prevalent today than during the CPS-I study. Randomized clinical trials can help determine if intentional weight loss decreases morbidity and mortality in overweight individuals with diabetes.

References

1. Cowie CC, Harris MI: Physical and metabolic characteristics of persons with diabetes. In *Diabetes in America*. 2nd ed. Harris MI, Ed. Bethesda, MD, National Institutes of Health, 1995, p. 117–164 (NIH publ. no. 95-1468)
2. Maggio CA, Pi-Sunyer FX: The prevention and treatment of obesity: application to type 2 diabetes. *Diabetes Care* 20:1744–1766, 1997
3. Franz MJ, Horton ES, Bantle JP, Beebe CA, Brunzell JD, Coulston AM, Henry RR, Hoogwerf BJ, Stacpoole PW: Nutrition principles for the management of diabetes and related complications. *Diabetes Care* 17:490–518, 1994
4. The Institute for Medical Studies: Effective weight loss: the cornerstone of treatment for obese NIDDM patients. *Clin Courier* 16: 1–11, 1998
5. Barrett-Connor E: Epidemiology, obesity, and non-insulin-dependent diabetes mellitus. *Am J Epidemiol* 11:172–181, 1989
6. Williamson DF: Weight loss and mortality in persons with type 2 diabetes mellitus: a review of the epidemiological evidence. *Exp Clin Endocrinol Diabetes* 106 (Suppl. 2):14–21, 1998
7. Knatterud GL, Klimt CR, Goldner MG, Hawkins BS, Weisenfeld S, Kreines K, Haddock L: Effects of hypoglycemic agents on vascular complications in patients with adult-onset diabetes. VIII. Evaluation of insulin therapy: final report. *Diabetes* 31 (Suppl. 5):1–81, 1982
8. Lean MEJ, Powrie JK, Anderson AS, Garthwaite PH: Obesity, weight loss and prognosis in type 2 diabetes. *Diabet Med* 7:228–233, 1990
9. Eriksson K-F, Lindgärde F: Prevention of type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise. *Diabetologia* 34:891–898, 1991
10. Bloom E, MacLean CJ, Reed DM, Yano K: Paradoxical impact of weight change on coronary heart disease risk factors and risk of coronary heart disease (Abstract). *South Carolina CVD Epidemiology Newsletter* 41: 117, 1987
11. Chaturvedi N, Fuller JH, WHO Multinational Study Group: Mortality risk by body weight and weight change in people with NIDDM: the WHO Multinational Study of Vascular Disease in Diabetes. *Diabetes Care* 18:766–774, 1995
12. Hanson RL, McCance DR, Jacobsson LTH, Narayan KMV, Nelson RG, Pettitt DJ, Bennett PH, Knowler WC: The U-shaped association between body mass index and mortality: relationship with weight gain in a Native American population. *J Clin Epidemiol* 48:903–916, 1995
13. Williamson DF, Pamuk E, Thun M, Flanders D, Byers T, Heath C: Prospective study of intentional weight loss and mortality in overweight white women aged 40–64 years. *Am J Epidemiol* 149:491–503, 1999
14. SAS Institute: The PHREG procedure. In *SAS/STAT Software: Changes and Enhancements Through Release 6.12*. Cary, NC, SAS Institute, 1997, p. 871–948
15. Akaike H: Information theory and an extension of the maximum likelihood principle. In *Second International Symposium on Information Theory*. Petrov BN, Czáki F, Eds. Budapest, Akademiai Kiadó, 1973, p. 267–281
16. Lin DY, Psaty BM, Kronmal RA: Assessing the sensitivity of regression results to unmeasured confounders in observational studies. *Biometrics* 54:948–963, 1998
17. Perry S, Byers TE, Mokdad AH, Serdula MK, Williamson DF: The validity of self-reports of past body weights by U.S. adults. *Epidemiology* 6:61–66, 1995
18. Wannamethee SG, Shaper AG, Whincup PH, Walker M: Characteristics of older men who lose weight intentionally or unintentionally. *Am J Epidemiol* 151:667–675, 2000
19. French SA, Jeffery RW, Folsom AR, Williamson DF, Byers T: Weight variability in a population-based sample of older women: reliability and intercorrelation of measures. *Int J Obesity* 19:22–29, 1995
20. Meltzer AA, Everhart JE: Unintentional weight loss in the United States. *Am J Epidemiol* 142:1039–1046, 1995
21. Rao RC: *Linear Statistical Inference and Its Applications*. 2nd ed. New York, Wiley, 1973, p. 220–235
22. Wing RR, Marcus MD, Salata R, Epstein LH, Miaskiewicz S, Blair EH: Effects of a very-low-calorie diet on long-term glycemic control in obese type 2 diabetic subjects. *Arch Intern Med* 151:1334–1340, 1991
23. Dwyer JT, Mayer J: Potential dieters: who are they? *J Am Diet Assoc* 56:510–514, 1970
24. Flegal KM, Keyl PM, Nieto FJ: Differential misclassification arising from non-differential errors in exposure measurement. *Am J Epidemiol* 134:1233–1244, 1991
25. Bowlin SJ, Morrill BD, Nafziger AN, Jenkins PL, Lewis C, Pearson TA: Validity of cardiovascular disease risk factors assessed by telephone survey: the Behavioral Risk Factor Survey. *J Clin Epidemiol* 46:561–571, 1993
26. Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, Weidmeyer H-M, Byrd-Hold DD: Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. *Diabetes Care* 21:518–524, 1998
27. Kenny SJ, Aubert RE, Geiss LS: Prevalence and incidence of non-insulin-dependent diabetes. In *Diabetes in America*. 2nd ed. Harris MI, Ed. Bethesda, MD, National Institutes of Health, 1995, p. 47–68 (NIH publ. no. 95-1468)
28. Rothman KJ, Greenland S: *Modern Epidemiology*. 2nd ed. Philadelphia, Lippincott-Raven, 1998, p. 127–129