Weight Change and Duration of Overweight and Obesity in the Incidence of Type 2 Diabetes

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OBJECTIVE — To examine the relationship between weight change and duration of overweight and obesity and the incidence of type 2 diabetes in a cohort of middle-aged British men.

RESEARCH DESIGN AND METHODS — We carried out a prospective study of cardiovascular disease in men aged 40–59 years at screening (1978–1980), drawn from one general practice in 24 British towns, who completed a postal questionnaire 5 years later (Q5) and for whom data on BMI at year 1 (Q1) and Q5 were available (n = 7,100). Men with diabetes at Q1 or Q5 and men with hyperglycemia at Q1 were excluded from the study (n = 184). The main outcome measure was type 2 diabetes (physician-diagnosed) during a mean follow-up period of 12 years starting at Q5 (1983–1985).

RESULTS — In the 6,916 men with no history or evidence of diabetes, there were 237 incident cases of type 2 diabetes during the mean follow-up period of 12 years, a rate of 3.2/1,000 person-years. Substantial weight gain (>10%) was associated with a significant increase in risk of type 2 diabetes compared with that in men with stable weight (relative risk [RR] 1.61 [95% CI 1.01–2.56]) after adjustment for age, initial BMI, and other risk factors. Excluding men who developed diabetes within 4 years after the period of weight change increased the risk further (1.81 [1.09–3.00]). After adjustment and exclusion of men who developed diabetes early in the follow-up, weight loss (≥4%) was associated with a reduction in the risk of type 2 diabetes, compared with that in the stable group, that reached marginal significance (0.65 [0.42–1.03], P = 0.07). A test for trend that fitted weight change as a continuous covariate showed the risk of diabetes to increase significantly from maximum weight loss to maximum weight gain (P = 0.0009). The lower risk associated with weight loss was seen in obese (≥28 kg/m^2) and nonobese subjects and in men with normal (<6.1 mmol/l) and high (≥6.1 mmol/l) nonfasting blood glucose levels. Although not statistically significant, this is consistent with a benefit from weight loss. Risk of type 2 diabetes increased progressively and significantly with increasing levels of initial BMI and also with the duration of overweight and obesity ($P < 0.0001$).

CONCLUSIONS — This study confirms the critical importance of overweight and obesity, particularly of long duration, in the development of type 2 diabetes. The data support current public health recommendations to reduce the risk of type 2 diabetes by preventing weight gain in middle-aged men who are not overweight and by encouraging weight loss in overweight and obese men.

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Obesity is well recognized as an important risk factor for type 2 diabetes (1–3), and weight control has been proposed as a means of preventing type 2 diabetes (4). Obesity enhances insulin resistance (5), a condition characterized by increased insulin production and impaired glucose intolerance (6), both of which are reversible with weight loss (7,8). It may therefore be expected that weight loss and prevention of weight gain are beneficial for the primary prevention of type 2 diabetes. Weight gain has been associated with an increased risk of type 2 diabetes in both men and women in several U.S. populations (9–13). Although intervention studies in very high-risk subjects (e.g., severely obese subjects, obese subjects with a family history of type 2 diabetes, or subjects with impaired glucose intolerance) have suggested that weight reduction significantly reduces the risk of type 2 diabetes (14–16), the benefits of weight loss have been less consistent in population-based settings. Although weight loss has been shown to be associated with a reduction in the incidence of diabetes in women (12), other studies have found little or no benefit (14). Indeed, some have observed an increased risk of diabetes (17,18), and other studies have suggested that weight fluctuation (weight loss followed by weight gain) may be diabetogenic (19). This article examines the relationship between weight change during a 5-year period and the risk of type 2 diabetes during the subsequent 12 years in a large prospective study of >7,000 men.

RESEARCH DESIGN AND METHODS

— The British Regional Heart Study is a large prospective study of cardiovascular disease consisting of 7,735 men aged 40–59 years selected from the age-sex registers of one group general practice from 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 (20). Research nurses administered a standard questionnaire to each man that included questions on smoking habits,

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Abbreviations: CHD, coronary heart disease; NHANES, National Health and Nutrition Examination Survey; Q1, year 1; Q5, year 5; RR, relative risk.

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

alcohol intake, physical activity, and medical history. Several physical measurements were made, and nonfasting blood samples were taken to measure biochemical and hemotological variables including blood glucose. Glucose concentration was measured in serum with an automated analyzer (Technicon SMA 12/60; Technicon, Tarrytown, NY). Diurnal variation in glucose concentration was modest, with a peak trough difference of 0.4 mmol/l (21). Details of classification methods for smoking status, physical activity, and BMI have been reported (20,22). Five years after the initial examination (Q5) (1983–1985), a postal questionnaire similar to the one administered at screening was sent to all surviving men to obtain information on medical history and changes in smoking, drinking behavior, and weight. The questionnaire was completed by 98% of available survivors (n = 7,262).

BMI

At initial screening, weight and height were measured, and BMI was calculated with weight/height^2 used as an index of relative weight. Five years later (Q5), the men were asked to state their weight in pounds or kilograms, and BMI was calculated for each man based on their reported weight and on measured height at the initial screening. "Lean BMI" was defined as $<$25 kg/m^2, "overweight" was defined as a BMI of 25.0–27.9 kg/m^2, and "obese" was defined as a BMI $\geq$28 kg/m^2, which represents the upper quintile of the BMI distribution in all men at Q1. These cutoffs broadly correspond to the definition of overweight and obesity in the U.K., where $\geq$25 kg/m^2 is considered to be overweight, 28–30 kg/m^2 is considered to be bordering on obesity, and $\geq$30 kg/m^2 is considered to be obese (23). BMI data were available at both Q1 and Q5 in 7,100 men.

Smoking

From the combined information at screening and Q5, the men were classified as having never smoked cigarettes, long-term former smokers (former cigarette smokers at both Q1 and Q5), recent former smokers (former cigarette smokers at Q5 only), and current cigarette smokers at Q5 who were categorized into three groups (1–19, 20, and $\geq$21 cigarettes/day).

Physical activity

At the initial screening, the men were asked to indicate their usual pattern of physical activity, which included regular walking or cycling, recreational activity, and sporting activity. A physical activity score was derived for each man based on frequency and type of activity, and the men were grouped into six broad categories based on their total score: none, occasional, light, moderate, moderately vigorous, and vigorous (22).

Recall of physician diagnosis

At screening and at Q5, the men were asked to recall whether they had ever been told by a physician that they had any of the 12 major specified conditions listed on the questionnaire: ischemic heart disease (angina, heart attack, coronary thrombosis, or myocardial infarction), "other heart trouble," high blood pressure, stroke, gout, diabetes, gall bladder disease, thyroid disease, arthritis, bronchitis, asthma, or peptic ulcer. Subject recall of coronary heart disease (CHD), stroke, and angina has been validated with general practitioners' record reviews, and these have shown to have good agreement (24,25).

Measures of weight change

An index for weight change was determined for each man by calculating the percentage change in body weight since the initial screening (26). For a man of average weight (76 kg), a gain of 3.0 kg (4%) constituted a change in weight. Subjects with weight loss were defined as men who had lost at least 4% of body weight; weight gain was defined as those who had gained $>$4% of body weight. Those who had gained or lost $<$4% of body weight were classified as stable. The men were grouped into four weight-change categories: weight loss, stable, gain of 4–10% of body weight, and gain of $>$10% in body weight.

Follow-up

From initial screening, all men have been followed up for all cause mortality, cardiovascular morbidity, and the development of type 2 diabetes up to December 1995, a mean period of 16.8 years (range 15.5–18.0 years) (27). Information on death was collected through the established "tagging" procedures provided by the National Health Service registers in Southport (for England and Wales) and Edinburgh (for Scotland). New cases of type 2 diabetes were ascertained via a postal questionnaire sent to the men at Q5 for each individual, systematic reviews of primary care records in 1990 and 1992, a further questionnaire to 6,483 surviving members of the cohort residing in Britain in 1992, and a review of all death certificates for any mention of diabetes. The questionnaire at Q5 had a response rate of 98%, and the 1992 questionnaire had a response rate of 91%. A diagnosis of diabetes was not accepted on the basis of questionnaire data unless it was confirmed in the primary care records. All men with a history of diabetes at screening or at the Q5 questionnaires and men with nonfasting blood glucose levels $\geq$11.1 µmol/l at screening were excluded from the analyses (n = 184). This report studied only the 7,100 men who completed the Q5 questionnaire and specifically the 6,916 men who did not have diabetes at screening or on the Q5 questionnaire or hyperglycemia at screening. Data on follow-up since the Q5 questionnaire are presented for an average follow-up of 11.8 years (range 10.5–13.0 years), and follow-up has been achieved for 99% of the cohort.

Statistical methods

The Cox proportional hazards model (28) was used to obtain the relative risks (RRs) for the weight-change groups and BMI groups adjusted for age, smoking, BMI, physical activity, and recall of CHD and high blood pressure. To obtain greater statistical power in assessing the relationship between weight change and risk of type 2 diabetes, weight change was also fitted as a continuous covariate in its original form. In other words, the percentage of weight change in either direction was used, with loss of weight having a negative value and gain in weight having a positive value. The purpose was to determine the significance of the change in risk over the continuum from maximum weight loss to maximum weight gain.

RESULTS — In the 6,916 men with full information on weight change and with no history or evidence of type 2 diabetes, there were 237 incident cases of diabetes during the mean follow-up period of 12 years, a rate of 3.2/1,000 person-years.

Most men (56%) were stable in weight, 31% gained weight, and 13% lost weight (Table 1). One-third of the men who lost weight were obese at Q1, but 5 years later, only 15% remained obese. Of the men who gained a substantial amount of weight ($>$10%), the proportion who were obese increased threefold during the 5 years.

Weight change and risk of type 2 diabetes

Table 2 shows the age-adjusted rate per 1,000 person-years and adjusted RR by the

Table 1—*Weight-change categories with mean weight change and percentage obese at Q1 and Q5*

Weight change	*n* (%)	Mean weight change (kg)	Obese (≥28 kg/m²) (%) Q1	Q5
Loss (≥4%)	937 (13)	−6.3	33	15
Stable	3,844 (56)	+0.2	18	20
Gain				
4–10%	1,673 (24)	+4.7	13	26
>10%	462 (7)	+14.4	12	38

weight-change categories. Risk was increased only in the men who had gained a substantial amount of weight (>10%), although the difference from the stable group was not significant (Table 2, column A). However, initial weight (BMI) was highest in those who had lost weight and lowest in those who had gained >10% weight (26.88 vs. 23.91 kg/m²). Adjustment for initial body weight reduced the risk in the weight-loss group and increased the risk in the weight-gain groups so that the increased risk in the substantial weight-gain group was now significant (Table 2, column B). A test for trend over the continuum of weight change from maximum weight loss to maximum weight gain was significant ($P = 0.0005$).

Weight loss has shown to be associated with smoking status, diagnosis of CHD, high blood pressure, and physical activity (26,29,30), all of which are potential risk factors for type 2 diabetes (1,2,31). Further adjustment for these factors reduced the risk in the weight-loss group, although the difference from the stable group was still not statistically significant, possibly because of small numbers (Table 2, column C). However, a test for trend on the continuum of weight change from maximum weight loss to maximum weight gain was significant ($P = 0.002$). Because weight loss is often associated with ill health and may precede the diagnosis of diabetes, we excluded men who died or developed diabetes within 4 years of follow-up from the Q5 questionnaire (Table 2, column D). Exclusion reduced the risk in the weight-loss group to marginal significance ($P = 0.07$) and increased the risk in the weight-gain groups. Weight gain of >10% remained associated with a significant increase in the risk of diabetes. The trend from maximum weight loss to maximum weight gain became more significant ($P = 0.0009$).

Effect of initial BMI

In all men, the incidence of type 2 diabetes increased progressively with increasing BMI ($P < 0.0001$), and the risk was significantly increased even at BMI levels of 25.0–27.9 kg/m² (Table 3). The age-adjusted RRs and 95% CIs for the three groups (<25, 25.0–27.9, and ≥28 kg/m²) were 1.00, 2.24 (1.54–3.23), and 5.11 (3.60–7.28). We examined the effects of weight loss by initial BMI levels adjusted for age, smoking, physical activity, and recall of high blood pressure and CHD. Within each weight-change category, there was an increasing incidence rate of diabetes with increasing BMI at screening. Weight loss was associated with a modest reduction in RR (27%) compared with the stable group, although this difference was not statistically significant, possibly because of the small numbers involved. Substantial weight gain (>10%) was associated with an increase in risk of diabetes in men who were lean or overweight at baseline. In the latter group, the increase in risk was not significant, presumably because of the small numbers involved. In subjects who were obese (≥28 kg/m²) and already at high risk for developing diabetes, further weight gain made little difference in their RR of type 2 diabetes. Exclusion of men who developed diabetes in the early follow-up made minor differences in the levels of risk. A test for trend on the continuum of weight change from maximum weight loss to maximum weight gain after these exclusions was significant in the lowest BMI category ($P = 0.004$) and was of marginal significance in the heavier BMI groups ($P = 0.06$ and $P = 0.07$ respectively).

Blood glucose, weight loss, and type 2 diabetes

Blood glucose concentration is a major risk factor for type 2 diabetes (1,2,31). We examined the relationship between weight change and risk of diabetes by separating men with screening (nonfasting) glucose levels <6.10 mmol/l (*n* = 5,531, 145 cases) and those with levels ≥6.10 mmol/l, the top fifth of the glucose distribution (*n* = 1,344, 92 cases). Data on blood glucose were not available in 41 men, and these men have been excluded. Men in the top fifth of the glucose distribution showed significantly higher rates than

Table 2—*Age-adjusted rates per 1,000 person-years and adjusted RR for diabetes according to weight-change category*

Weight change	Age-adjusted rate per 1,000 person-years	RR (95% CI) A	B	C	D
Loss (>4%)	3.2 (31/937)	1.07 (0.72–1.58)	0.77 (0.52–1.15)	0.74 (0.49–1.10)	0.66 (0.41–1.04)*
Stable	3.0 (125/3,844)	1.00	1.00	1.00	1.00
Gain					
4–10%	3.3 (60/1,673)	1.11 (0.81–1.52)	1.26 (0.93–1.72)	1.17 (0.85–1.60)	1.21 (0.86–1.70)
>10%	4.4 (21/462)	1.47 (0.93–2.33)	1.89 (1.19–3.01)	1.61 (1.01–2.56)	1.81 (1.09–3.00)
Test for trend-fitting weight change in its original continuous form (*P*)	—	0.24	0.0005	0.002	0.0009

A, age-adjusted; B, age and BMI at screening; C, age, BMI at screening, smoking, physical activity, and recall of CHD and high blood pressure; D, as in C, excluding men who died or developed diabetes (*n* = 342) within 4 years of follow-up from Q5. Analysis was based on 6,574 men and 196 cases of diabetes. *$P = 0.07$.

Table 3—*Age-adjusted diabetes rate per 1,000 person-years and adjusted RR of diabetes by initial BMI and weight-change categories*

Initial BMI (kg/m²)	All men	Weight change			
		Loss (≥4%)	Stable	Gain 4–10%	Gain >10%
<25 (51/3,187)					
Rate per 1,000 person-years	1.4	1.1 (3/262)	1.4 (26/680)	1.2 (12/930)	3.0 (10/315)
Adjusted RR		0.73 (0.22–2.42)	1.00	0.90 (0.45–1.81)	2.49 (1.15–5.41)
Adjusted RR*		0.29 (0.04–2.14)	1.00	0.90 (0.42–1.90)	3.02 (1.36–6.73)
Test for trend*	$P = 0.004$				
25–27.9 (84/2,444)					
Rate per 1,000 person-years	3.1	2.7 (10/363)	2.8 (45/1,467)	4.1 (23/522)	6.4 (6/92)
Adjusted RR		0.91 (0.46–1.82)	1.00	1.32 (0.79–2.22)	1.96 (0.81–4.74)
Adjusted RR*		0.79 (0.45–1.78)	1.00	1.33 (0.74–2.36)	2.02 (0.76–5.32)
Test for trend*	$P = 0.06$				
≥28 (102/1,285)					
Rate per 1,000 person-years	7.0	5.6 (18/312)	7.4 (54/697)	11.0 (25/221)	9.4 (5/55)
Adjusted RR		0.67 (0.39–1.16)	1.00	1.29 (0.80–2.09)	0.95 (0.37–2.42)
Adjusted RR*		0.66 (0.36–1.19)	1.00	1.37 (0.82–2.30)	0.91 (0.32–2.59)
Test for trend*	$P = 0.07$				

Data are cases/*n* of men or RRs (95% CI) and are adjusted for age, smoking status at Q5, physical activity, and recall of CHD and hypertension. *Excluding men who died or developed diabetes within 4 years of follow-up from Q5.

those with levels <6.1 mmol/l (6.6 vs. 2.4/1,000 person-years, $P < 0.0001$). Weight loss was associated with a reduced risk in both blood glucose groups after adjustment for age, initial BMI, physical activity, and recall of hypertension and CHD (RR 0.73 [95% CI 0.42–1.27] and 0.72 [0.40–1.31]), although the difference was not statistically significant, possibly because of the small numbers involved. Modest and substantial weight gains in subjects with glucose levels <6.1 mmol/l were both associated with an increased risk of type 2 diabetes (1.46 [0.99–2.23] and 2.39 [1.38–4.15], respectively). In subjects with high glucose levels, neither moderate nor substantial weight gain indicated an increased risk (0.85 and 0.71, respectively). A test for trend from maximum weight loss to maximum weight gain was significant in those with glucose levels <6.1 mmol/l ($P < 0.0001$) but was not significant in subjects with higher glucose levels.

Duration of obesity and risk of type 2 diabetes

In addition to level of obesity, the duration of obesity has also been considered to be an important risk factor for type 2 diabetes (32). The men were grouped according to their attained BMI at Q5. Those who were overweight (25.0–27.9 kg/m²), obese (28–29.9kg/m²), or markedly obese (≥30 kg/m²) were further divided into those who had already been in these BMI categories at baseline (i.e., for ≥5 years) and those who had become overweight, obese, or markedly obese during the last 5 years. Because of the focus on duration of obesity, all men who lost weight (≥4%) were excluded from this analysis. Table 4 shows the relationship between attained BMI at Q5 and risk of diabetes in men who had not lost weight. The risk of diabetes increased with increasing BMI level and also with the duration of overweight or obesity, even after full adjustment (test for trend across the seven BMI groups, $P < 0.0001$). At each level of BMI ≥25.0 kg/m², men who had been overweight, obese, or markedly obese for ≥5 years consistently had a greater risk of diabetes than men who had been in the BMI category for <5 years. Subjects who had been obese (28–29.9 kg/m²) for <5 years showed a near threefold increase in RR, and this increased to more than fourfold in subjects who had been obese for ≥5 years or those who were markedly obese for <5 years. Men with marked obesity (≥30 kg/m²) for ≥5 years had eight times the risk of developing diabetes compared with men who were not overweight (<25 kg/m²).

Table 4—*Risk of diabetes by BMI at Q5 and duration of overweight and obesity*

BMI at Q5	*n*	Cases of diabetes	Rate per 1,000 person-years	Age-adusted RR	Adjusted RR (95% CI)
<25	2,386	34	1.3	1.00	1.00
25–27.9					
<5 years	623	17	2.5	1.80	1.74 (0.96–3.15)
≥5 years	1,541	50	3.0	2.17	2.25 (1.45–3.47)
28–29.9					
<5 years	408	18	4.0	2.91	2.68 (1.50–4.81)
≥5 years	553	39	6.7	4.87	4.74 (2.99–7.51)
≥30					
<5 years	48	3	6.5	4.92	4.36 (1.33–14.28)
≥5 years	355	42	11.8	8.66	8.04 (5.06–12.74)

*Adjusted for age, smoking status at Q5, physical activity, and recall of CHD and hypertension. Men who have lost weight (≥4%) have been excluded (*n* = 937).

CONCLUSIONS — Obesity is an important and well-established risk factor for diabetes. We have previously reported

on the positive relationship between BMI at baseline and the incidence of type 2 diabetes during 12 years of follow-up (31). The present study, based on 12 years of follow-up starting from Q5, confirms that the risk of diabetes is significantly increased even at levels of BMI (25.0–27.9 kg/m^2) that include the average weight of middle-aged British men. The risk of diabetes increases progressively with increasing BMI. The increase in risk seen at BMI levels of ≥25 kg/m^2 has also been reported in women (33).

Weight gain and type 2 diabetes

Substantial weight gain (>10%) was significantly associated with an increased risk of diabetes. The finding of increased risk of diabetes with weight gain is consistent with several other adult population studies in both men and women (9–13). In the present study, men with below-average BMI who gained a substantial amount of weight showed a significant threefold increase in risk compared with subjects whose weight remained stable, and the risk was twofold (albeit not significant) in subjects who were already overweight (BMI 25.0–27.9 kg/m^2). This is consistent with the findings that weight gain is associated with an increase in insulin resistance (34) and deterioration in glucose tolerance (35), factors that are strongly associated with the development of diabetes. In subjects who were already obese or who had high serum glucose levels and thus already at high absolute risk of developing diabetes, weight gain did not appear to have any further adverse effect. This suggests that the effects of weight gain are mediated through an increase in glucose levels or insulin resistance.

Duration of overweight or obesity was also found to be a risk factor for diabetes as observed in other studies (32). Compared with men with BMI levels <25.0 kg/m^2, the risk of diabetes increased nearly threefold in men who were moderately obese (28.0–29.9 kg/m^2) for <5 years and nearly fivefold in men who were moderately obese for >5 years. In men with marked obesity (≥30 kg/m^2), the RR of diabetes was nearly twice as great in men who had been markedly obese for ≥5 years compared with men whose marked obesity was of shorter duration.

Weight loss and risk of diabetes

The hazards of obesity are well known and include hypertension, dyslipidemia, glucose intolerance, and insulin resistance (36,37). Weight reduction has been shown to be associated with an improvement in blood pressure, blood lipid profile, and glucose intolerance (8,17). With weight loss, insulin sensitivity increases, and even modest amounts of weight loss can produce a significant improvement in glycosylated hemoglobin levels (38,39). It might therefore be expected that weight reduction should diminish the risk of developing diabetes. Evidence for the benefits of weight reduction comes from intervention studies in subjects at very high risk for diabetes. Weight loss in severely obese subjects appears to deter the progression from impaired glucose tolerance to diabetes (15). Weight reduction has been shown to significantly reduce the risk of diabetes in obese subjects with a family history of diabetes (16). In the Malmo study in Sweden, weight loss in persons with impaired glucose tolerance was associated with a reduction in risk of developing diabetes (14). In the few population studies that have examined weight change and the risk of diabetes, the beneficial effects of weight loss on the risk of diabetes have been less consistent. In some population studies, weight loss appeared to have no benefit (13) or was associated with increased risk (17,18), and some studies have even suggested that weight fluctuation (weight gain followed by weight loss) may be diabetogenic (19).

In the present study, weight loss was associated with a reduction in subsequent risk of diabetes during a 12-year period. The apparent benefit of weight loss was seen in both obese and nonobese subjects and in men with low and high glucose levels. Although the reduction in risk in the weight-loss group compared with the stable group was not statistically significant when using grouped data, possibly due to small numbers and lack of statistical power, the trend for increasing risk on the continuum of weight change from maximum weight loss to maximum weight gain was highly significant. This suggests that the more weight one loses, the greater the reduction in risk, and the more weight one gains, the higher the risk. The reduction in risk associated with weight loss is consistent with that reported in the Nurses' Health Study, a large prospective study of >100,000 female nurses in which a significant reduction in risk of diabetes with weight loss was observed (12). Weight loss in women with BMI >27 kg/m^2 was associated with a 30% reduction in the risk of developing diabetes compared with women whose weight did not change. The magnitude of reduction was very similar to our own findings in men with BMI ≥28 kg/m^2. By contrast, the U.S. National Health and Nutrition Examination Survey (NHANES) showed little benefit from weight loss except in the 25–29 kg/m^2 BMI group. Weight loss often precedes the onset of diabetes, and diabetic subjects who were diagnosed early in the study period had not been excluded (13). In the present study, exclusion of men who died or developed diabetes within 4 years of weight loss reduced the risk in the weight-loss group further, and the trend became stronger. The studies that suggest increased risk of diabetes with weight loss were based on prevalence (17,18) or incidence of diabetes during the weight change period, and the increased risk of diabetes in the weight-loss group is likely to be biased by the inclusion of diabetic subjects who have lost weight as a consequence of the disease. Our prospective design avoids the bias of weight change after the diagnosis of diabetes.

Weight fluctuation

Long-term maintenance of a reduced body weight is difficult, and many subjects regain the lost body weight (40). The possibility that weight fluctuation may have a diabetogenic effect has caused concern about weight control interventions. The evidence linking weight fluctuation to increased risk of diabetes has been assessed in a recent study that concludes that earlier findings based mainly on retrospective studies and one prospective study have limitations and biases (11). In this study, weight fluctuation was not associated with increased incidence of diabetes, and it was concluded that concern about the diabetogenic effect of weight fluctuation should not deter weight control efforts (11). Our study provides further support for the concept that weight maintenance in subjects who are not overweight and weight loss in overweight and obese subjects is likely to be effective in the primary prevention of diabetes.

Public health implications

Obesity is an epidemic in the industrialized world and is a major risk factor for the development of diabetes. A recent review of data from NHANES from 1960 to 1991 showed a progressive increase in mean BMI, with 1 in 3 adults aged 20–74 years currently being classified as overweight (i.e., at least 20% heavier than ideal for height) (41). The prevalence of diabetes

(diagnosed and undiagnosed) in U.S. adults aged 40–74 years has increased from 11.4% in 1976–1980 to 14.3% in 1988–1994 (according to World Health Organization criteria), and this reflects the gradual increase in diabetes worldwide (42). It is estimated that, by the year 2025, the world prevalence of diabetes will be 5.4%, involving some 300 million adults, and that the major part of this increase will be in the developing countries and in persons aged 45–64 years rather than persons aged ≥65 years as seen in developed countries (43). Overweight and obesity are the major environmental threads running through this epidemic of diabetes. In Great Britain, nearly half the adult (16–64 years) population is currently overweight (≥25 kg/m^2), and the prevalence of obesity (≥30 kg/m^2) has increased steadily during recent decades such that 16–17% of British men and women are now obese (44). Obesity carries with it a considerably increased risk of diabetes. It is clear that controlling body weight requires a population-oriented approach, and yet the current Health of the Nation target in the U.K. is the reduction of the prevalence of obesity (45) rather than a reduction in the overall distribution of BMI toward lower and more desirable levels (37). In the present study, substantial weight gain (>10%) is associated with a significant increase in the risk of diabetes in middle-aged subjects, and weight reduction in both low- and high-risk subjects is associated with a lower risk of developing diabetes. The study emphasizes that the duration of overweight or obesity is critical in estimating the risk of developing diabetes. The prevention of overweight and obesity and weight reduction in overweight or obese people are both likely to be effective strategies in the primary prevention of diabetes. Given the poor results of maintenance of weight loss, the prevention of overweight and obesity at all ages should be an urgent public health concern.

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