Original Articles

Rate of Weight Gain, Weight Fluctuation, and Incidence of NIDDM

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The relationships of rate of weight gain and weight fluctuation to incidence of non-insulin-dependent diabetes mellitus (NIDDM) were examined in Pima Indians. The 1,458 subjects were participants in a prospective study with examinations approximately every 2 years. Rate of weight gain was defined as the slope of the regression line of weight with time for two or more consecutive examinations ≥2 years apart and weight fluctuation as the root-mean-square departure from this line for four examinations. Among men, incidence of NIDDM was strongly and significantly related to rate of weight gain (e.g., age-adjusted incidence = 56.7/1,000 person-years in those with weight gain ≥3 kg/year and 16.9/1,000 person-years for those losing weight [$P_{trend} < 0.01$]). In women, weight gain was significantly related to diabetes incidence only in those who were not initially overweight (body mass index <27.3 kg/m^2). In contrast to the relationship with weight gain, weight fluctuation was not associated with incidence of diabetes in either sex. These findings suggest that weight control in overweight individuals may be a more effective strategy for prevention of NIDDM in men than in women, whereas prevention of obesity may prevent diabetes in both sexes. Concern about a diabetogenic effect of weight fluctuation should not deter weight-control efforts. *Diabetes* 43:261–266, 1995

Weight control has been proposed as a means of preventing non-insulin-dependent diabetes mellitus (NIDDM) (1,2). This hypothesis rests largely on the fact that obesity is a powerful risk factor for the development of this disease (3,4), but it does not necessarily follow that weight loss is protective or that weight gain increases the risk of diabetes. There are few data on the association between diabetes and weight changes. A positive association between diabetes and the degree of weight gain has been reported (5,6), but other studies have shown either no association (7) or an inverse relationship (8). Moreover, because the weight that is lost during reduction attempts is often regained (9,10), repeated weight loss efforts may result in weight fluctuation, and some studies have suggested that such fluctuation itself may be diabetogenic (5,11–13). The retrospective design of most studies limits their interpretation, but the implications are cause for concern. If weight gain does not increase the risk of NIDDM, and weight loss is not protective, then efforts to control weight for the purpose of diabetes prevention may be futile. Furthermore, if weight fluctuation is diabetogenic, such efforts may even be counterproductive. This analysis examines the incidence of diabetes in relation to weight fluctuation and rate of weight gain in adult Pima Indians, a Native American population with a high prevalence of both obesity (4) and NIDDM (14,15).

RESEARCH DESIGN AND METHODS

Since 1965, a longitudinal study of diabetes has been conducted in the Gila River Indian Community in central Arizona, where most of the residents are Pima Indians (14). All community residents aged ≥5 years have been invited to participate in research examinations approximately every 2 years. Height and weight were measured at each examination with the subject wearing light clothing and no shoes. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m^2). Beginning in 1990, measurements of waist and hip circumference (to assess waist-to-hip ratio [WHR]) were also made. A 75-g oral glucose tolerance test has been administered at each examination, and each subject's clinical record at the local Indian Health Service hospital has been reviewed. The diagnosis of diabetes was made if a glucose concentration ≥11.1 mmol/l (200 mg/dl) was observed either in the 2-h postload venous plasma or in the course of routine medical care (16). Beginning in 1987, fasting and 2-h postload serum insulin concentrations were measured with a radioassay analyzer (Concept 4, ICN, Harshaw, PA). Individuals were classified as smokers if they had smoked in the preceding year.

For purposes of this analysis, there are three categories of examinations: the first examination conducted when the subject was at least 20 years old is the initial examination; a subsequent examination, before the onset of NIDDM, for which the weight change indexes were calculated is the referent examination; and all examinations subsequent to the referent one are follow-up examinations. Three separate analyses, each of which may have had a different referent examination (Fig. 1), were conducted.

1. Rate-of-weight-gain analysis. The relationship of rate of weight gain to the incidence of NIDDM was examined. The referent examination was the first examination at least 2 years after the initial one. Subjects who were not diabetic at the referent examination and had at least one follow-up visit were included. There were 1,458 such subjects of whom 906 were women and 552 were men.
2. Weight fluctuation analysis. This analysis examined the relationship of weight fluctuation to diabetes incidence. The referent examination was the third examination after the initial one (i.e., the fourth

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NIDDM, non-insulin-dependent diabetes mellitus; BMI, body mass index; WHR, waist-to-hip ratio; RMSE, root-mean-square error; CI, confidence interval; IRR, incidence rate ratios.

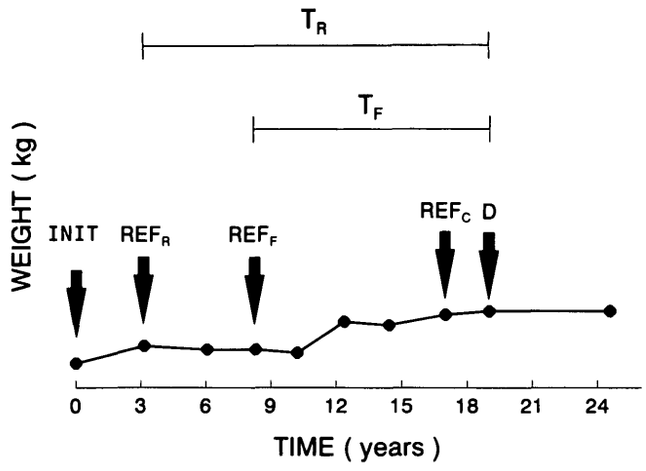

FIG. 1. Diagram of sequential examinations for one study subject indicating the different referent examinations for various analyses. Each point represents an examination. The initial examination is denoted by *INIT* and the time since this point is shown on the *x*-axis. The referent examination for the rate-of-weight-gain study is indicated by REF_R, that for the weight fluctuation study by REF_F, and that for the correlation study by REF_C. *D* represents the date of diagnosis of diabetes, which may occur at an examination or at other times. T_R and T_F represent the duration of follow-up for the rate of weight gain and weight fluctuation studies, respectively. Note that for the prospective analyses, the referent examination is the start of follow-up.

examination). Subjects with at least one follow-up examination who were nondiabetic at the referent examination were included. There were 584 subjects, including 383 women and 201 men.

3. Correlation analysis. This analysis examined correlations between rate of weight gain or weight fluctuation and insulin concentrations, glucose concentrations, and WHR, measured at the referent examination. The referent examination was the last nondiabetic examination. Because a follow-up visit was not required and because insulin and WHR measurements were not made throughout the study, subjects in the correlation study were not necessarily included in prospective analyses.

Weight change indexes. Rate of weight gain (kg/year) was calculated as the slope of the regression line of weight with time for all examinations from the initial to the referent one. The root-mean-square error (RMSE) of this line was used as an index of weight fluctuation. This index, used in other studies (12,13), is a measure of variability in weight, analogous to the SD. The RMSE represents the average fluctuation (in kg) around the regression line; a high value can occur, however, in the absence of cycles of weight gain and loss, if weight changes are nonlinear. Examinations in pregnant women were not considered in determining the initial and referent examinations or in calculating the weight change indexes. However, in prospective analyses, a pregnant woman who met the criteria for diabetes was considered an incident case.

Subjects were grouped into strata of rate of weight gain and RMSE at the referent examination. To evaluate the effect of rate of weight gain in those who might be advised to lose weight, subjects were also categorized by whether they were overweight at the initial examination by the definition used in formulating the National Health Objectives (BMI ≥27.3 kg/m^2 for women or ≥27.8 kg/m^2 for men) (1,17).

Statistical analysis. Comparisons of characteristics among groups were made by the Kruskal-Wallis test for continuous variables and by a χ^2 test for categorical ones. In prospective analyses, subjects were followed from the referent examination to the onset of diabetes or the last examination before March 1, 1992. Age-, sex-, and stratum-specific incidence rates were calculated and expressed in events/1,000 person-years. When an individual moved from one age stratum to the next, person-years were apportioned accordingly. Incidence rates were standardized by the direct method to the age and sex distribution of the 1980 U.S. population. The confidence interval (CI) for the standardized rate was computed from its SE (15). The significance of the difference in incidence rates between rate of weight gain or weight fluctuation categories was calculated from a χ^2 analysis on stratified incidence data (18). The Mantel-Haenszel procedure was used to control for age and sex (19).

TABLE 1
Characteristics of subjects at referent examination by rate-of-weight-gain category

	Weight-gain category (kg/year)					
	<0	0–1	1–2	2–3	≥3	*P* values
Women						
n	196	197	174	155	184	
Age (years)	32	34	30	28	26	<0.01
BMI (kg/m^2)	29.6	31.6	31.2	33.3	34.9	<0.01
Initial-referent time (years)	2.5	3.4	2.9	3.1	2.4	<0.01
Percentage weight gain	−5.8	1.9	6.0	10.1	15.2	<0.01
Smoking (%)	30	28	26	28	24	0.71
Men						
n	133	132	103	76	108	
Age (years)	43	38	34	29	28	<0.01
BMI (kg/m^2)	27.2	28.7	29.4	31.9	34.0	<0.01
Initial-referent time (years)	2.6	3.5	3.8	2.7	2.6	<0.01
Percentage weight gain	−5.3	2.0	6.6	8.9	15.0	<0.01
Smoking (%)	44	47	55	46	47	0.61

P value is for the null hypothesis that the distribution of the variable of interest is the same between weight-gain categories. *P* value was computed by the Kruskal-Wallis test for continuous variables and by a χ^2 test for categorical variables. For age, BMI, initial-referent time, and percentage weight gain, the median value is reported. Initial-referent time is the time between the initial and referent examinations (see METHODS). Percentage weight gain is weight gain between the initial and referent examinations, expressed as a percentage of weight at the initial examination (see METHODS).

The effects of RMSE and rate of weight gain (as continuous variables) on diabetes incidence, adjusted for potentially confounding variables measured at the referent examination, were calculated by proportional hazards regression (20). The validity of the proportionality assumption for each variable was assessed as suggested by Kalbfleisch and Prentice (21). To control for variables that significantly ($P < 0.05$) violated this assumption, models were stratified by categories of these variables. Models for women in the rate-of-weight-gain analysis were stratified by age and BMI and those for men by smoking. Models in the weight fluctuation analysis were also stratified by age. Squared terms for age and BMI were included in models that were not stratified by these variables, as the relationships appeared to be quadratic. Incidence rate ratios (IRR) and 95% CI were calculated from the β-coefficients, their SEs, and, for quadratic variables, their covariances (22). For continuous variables, the IRR must be expressed in terms of some arbitrary difference; the 75th and 25th percentiles were used for this purpose.

In correlation analyses, product-moment correlations of rate of weight gain and RMSE with 2-h plasma glucose level, fasting insulin, insulin response, and WHR were examined. Natural logarithms of insulin and glucose concentrations were used in all analyses to reduce skewness. The insulin response was calculated as the logarithm of the ratio of the 2-h concentration divided by the fasting concentration. Partial correlations were calculated by multiple linear regression to control for potentially confounding variables.

RESULTS

Rate of weight gain. Subsequent rate of weight gain was negatively correlated with age at the initial examination in both women ($r = -0.21$, $P < 0.01$) and men ($r = -0.28$, $P < 0.01$). Controlled for age, initial BMI was negatively correlated with subsequent rate of weight gain; the association was significant in women (partial $r = -0.17$, $P < 0.01$) but not in men (partial $r = -0.05$, $P = 0.29$). Median BMI at the initial examination was significantly different between women (30.1 kg/m^2) and men (28.3 kg/m^2) ($P < 0.01$), but median rate of subsequent weight gain was not (women, 1.4 kg/year; men, 1.1 kg/year; $P = 0.25$). Characteristics at the referent examination by rate-of-weight-gain category are

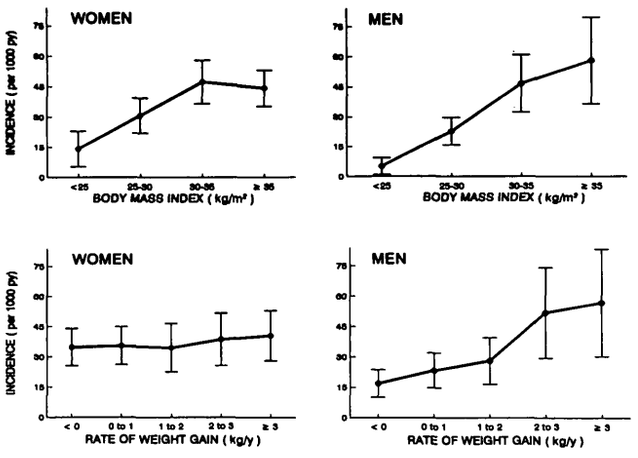

FIG. 2. Age-standardized incidence of diabetes (per 1,000 patient-years [py]) and 95% CI by sex and categories of BMI at the referent examination (*top panels*) and rate of weight gain (*bottom panels*).

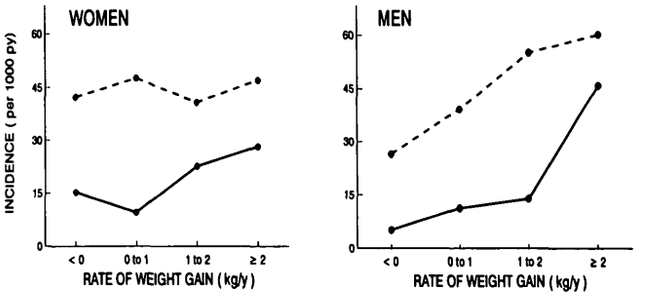

FIG. 3. Age-standardized incidence of diabetes (per 1,000 patient-years [py]) by sex and rate of weight gain, stratified by whether the subject was overweight at the initial examination. Overweight is defined as a BMI ≥27.3 kg/m^2 for women or ≥27.8 kg/m^2 for men (1,17). *Dashed lines* represent overweight individuals and *solid lines* those who are not overweight. The top two rate-of-weight-gain categories in the previous figure are combined to avoid undue influence from small strata.

shown in Table 1. Median age at the referent examination was 30 (range, 22–81) years in women and 34 (22–88) years in men.

Among the women, 306 (34%) developed NIDDM during a median follow-up of 7.4 (range, 0.1–25.0) years. Of the men, 155 (28%) developed diabetes during a median follow-up of 7.2 (0.2–24.6) years. Among men, incidence of diabetes increased with greater rate of weight gain in all age strata, but there was little relationship in women (data not shown). Age-standardized incidence rates by categories of BMI and rate of weight gain are shown in Fig. 2. The age-adjusted incidence of diabetes increased significantly with obesity in both women and men ($P < 0.01$ for each). The incidence also increased significantly with increasing rate of weight gain in men ($P < 0.01$), but the relationship in women was weaker ($P = 0.31$).

The relationship between rate of weight gain and incidence of NIDDM was also examined with proportional hazards models to further control for potentially confounding variables (Table 2). The positive association between rate of weight gain and incidence of diabetes among men persisted with adjustment for age, time between the initial and referent examinations, smoking, and current BMI. After adjustment for these same factors, there was still no significant relationship between rate of weight gain and diabetes incidence in women. The effect of rate of weight gain was significantly different between men and women ($P < 0.01$, controlled for age; $P = 0.01$, controlled for age, smoking, time between the initial and referent examinations, initial BMI, and BMI–rate-of-weight-gain interaction).

TABLE 2
Proportional hazards models of the risk for subsequent diabetes by rate of weight gain

Variable	Comparison	IRR (95% CI)	*P* values
Women			
Initial-referent time (years)	(4.0/2.2)	1.04 (0.93–1.16)	0.50
Smoking	(Yes/no)	1.01 (0.77–1.32)	0.95
Rate of weight gain (kg/year)	(2.7/0.0)	0.98 (0.87–1.11)	0.75
Men			
Age (years)	(47/27)	1.54 (1.06–2.22)	0.02
BMI (kg/m^2)	(34.1/25.9)	3.82 (2.52–5.78)	<0.01
Initial-referent time (years)	(4.4/2.2)	1.11 (0.97–1.27)	0.12
Rate of weight gain (kg/year)	(2.6/0.0)	1.24 (1.04–1.49)	0.02

The IRR is computed comparing the value to the left of the slash with that to the right. These represent the 75th and 25th percentiles for continuous variables. Initial-referent time is the time between the initial and referent examinations. Data for women are controlled for age and BMI by stratification (see METHODS). Data for men are controlled for smoking by stratification (see METHODS). Analysis of BMI includes a quadratic term.

The relationship between diabetes incidence and rate of weight gain, stratified by whether the individual was overweight at the initial examination, is shown in Fig. 3. The association between incidence of NIDDM and rate of weight gain was present both in overweight men and in those who were not overweight ($P_{trend} < 0.01$ for each). Proportional hazards analysis indicated that the association in both groups, controlled for age, smoking, time between the initial and referent examinations, and BMI at the referent examination, was significant. Among women, there was a positive association between rate of weight gain and diabetes incidence in subjects who were not overweight at the initial examination ($P_{trend} = 0.01$) but not in subjects who were overweight ($P_{trend} = 0.38$). To further examine the relationship in overweight women, proportional hazards analysis was carried out separately in moderately and severely (BMI ≥32.3 kg/m^2) overweight subjects (17). Controlled for age, rate of weight gain was not associated with diabetes incidence in either group (comparing 2.7 kg/year with 0.0 kg/year; IRR = 1.00, 95% CI 0.80–1.25 in moderately overweight group; IRR = 1.12, 95% CI 0.96–1.31 in severely overweight group).

Weight fluctuation. Characteristics of subjects at the referent examination by weight fluctuation category are shown in Table 3. During a median follow-up of 6.3 (range 0.1–20.8) years, 162 (28%) of these subjects developed NIDDM. Standardized incidence rates by weight fluctuation category are shown in Fig. 4. There was no significant difference between RMSE categories in the age-standardized incidence rates in men ($P = 0.54$) or women ($P = 0.29$) or in the age-sex standardized rates ($P = 0.52$).

Proportional hazards modeling also showed no association between weight fluctuation and diabetes incidence. Controlled for age, sex, BMI, smoking, rate of weight gain, and the time between the initial and referent examinations, the IRR comparing the 75th percentile of RMSE (4.9 kg) with the 25th percentile (2.0 kg) was 1.03 (95% CI 0.85–1.25). The effect of BMI was significant in this model (IRR comparing 75th and 25th percentiles = 2.04, 95% CI 1.49–2.81). The

TABLE 3
Characteristics at referent examination by weight fluctuation (RMSE) category

	Low-RMSE group	Middle-RMSE group	High-RMSE group	*P* values
n	147	223	214	
Age (years)	44	39	35	<0.01
BMI (kg/m^2)	29.7	30.9	33.8	<0.01
Initial-referent time (years)	7.4	7.6	8.0	0.17
Rate of weight gain (kg/year)	0.71	0.72	1.09	0.09
Men (%)	41	30	34	0.12
Smoking (%)	26	22	33	0.04

RMSE represents the average weight fluctuation accounting for the linear trend in weight over time. Individuals in the low-RMSE group (<2 kg) have less weight fluctuation than those in the middle group (2–4 kg), and those in the high group (≥4 kg) have the greatest degree of weight fluctuation. *P* value is for the null hypothesis that the variable of interest has the same distribution between weight-fluctuation categories. The *P* value was computed from the Mann-Whitney *U* test for continuous variables and from a χ^2 test for categorical variables. For age, BMI, initial-referent time, and rate of weight gain, the median value is reported. Initial-referent time is the time between the initial and referent examinations (see METHODS).

TABLE 4
Correlations of rate of weight gain and weight fluctuation with metabolic variables

		Unadjusted		Partial	
	n	*r*	*P* value	*r*	*P* value
Correlation with rate of weight gain					
Women					
Log 2-h glucose	1183	0.04	0.17	0.06	0.05
Log fasting insulin	415	0.21	<0.01	0.10	0.04
Insulin response	405	−0.06	0.21	−0.01	0.90
WHR	269	−0.06	0.29	−0.10	0.09
Men					
Log 2-h glucose	825	0.10	<0.01	0.07	0.06
Log fasting insulin	242	0.33	<0.01	0.18	0.01
Insulin response	238	−0.10	0.14	0.00	1.00
WHR	183	0.15	0.05	0.15	0.05
Correlation with weight fluctation					
Men + women					
Log 2-h glucose	835	−0.07	0.04	−0.09	0.01
Log fasting insulin	305	0.14	0.02	−0.07	0.20
Insulin response	301	−0.05	0.41	0.04	0.54
WHR	239	0.03	0.61	−0.10	0.14

Correlation between variables measured at the referent examination and previous weight changes. Partial *r* for correlation with rate of weight gain in women and men is adjusted for age, age^2, BMI, (BMI)^2, smoking, and time between the initial and referent examinations. Insulin response is defined as the logarithm of the ratio of the 2-h insulin concentration divided by the fasting insulin concentration. Partial *r* for correlation with weight fluctuation in men + women is adjusted for age, age^2, sex, BMI, (BMI)^2, smoking, time between the initial and referent examination, and rate of weight gain.

effect of RMSE on diabetes incidence did not differ significantly between men and women ($P = 0.17$, controlled for age).

Correlations. Correlations between metabolic variables and weight fluctuation or rate of weight gain are shown in Table 4. Rate of weight gain was positively correlated with 2-h plasma glucose level in both men and women. Rate of weight gain was also significantly and positively correlated with fasting serum insulin concentration in both sexes. The correlations were substantially lower after adjustment for potentially confounding variables; the major confounder was BMI. In general, the associations were modest but were stronger in men than in women. A positive correlation between rate of weight gain and WHR was observed in men but not in women. There was also a stronger correlation between WHR and fasting insulin in men ($n = 88$, $r = 0.39$, $P < 0.01$) than in women ($n = 115$, $r = 0.19$, $P = 0.04$). Weight fluctuation was modestly correlated with fasting serum insulin concentration; the association was no longer present after adjustment for obesity.

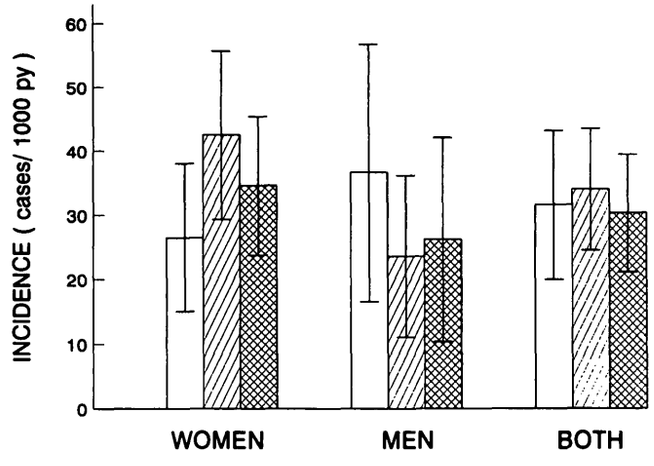

FIG. 4. Age and age-sex standardized incidence of diabetes (cases per 1,000 patient-years [py]) and 95% CI by categories of RMSE. Individuals with a high RMSE have a greater degree of weight fluctuation. Low group (RMSE <2 kg), □; middle group (RMSE 2–4 kg), ▨; and high group (RMSE ≥4 kg), ▩.

DISCUSSION

Obesity is a well-recognized risk factor for the development of NIDDM (3,4), and a high incidence of diabetes in those with a high BMI in this population has been previously described (23). Weight reduction can improve glucose tolerance in both diabetic (24) and nondiabetic (25) individuals, and weight gain is positively correlated with glycemia in diverse populations (26,27). It is thus tempting to speculate that weight loss or prevention of weight gain may be useful for primary prevention of NIDDM, but few studies have examined this issue. A history of weight gain in adult life was associated with a high prevalence of diabetes in elderly subjects (5). A modest positive association between recent weight gain and diabetes incidence in women has also been described (6). Alternatively, other studies of weight gain and diabetes have reported no association (7), an inverse relationship (8), and a U-shaped relationship (28). None of these studies could exclude the possibility that the weight changes occurred after the onset of diabetes, whereas systematic administration of the glucose tolerance test in the Pima Indian population has allowed for more precise characterization of the temporal relationships. This analysis demonstrates that rate of weight gain over a median of 3 years in Pima Indian men is positively associated with the incidence of NIDDM over the next 7 years. The lowest incidence occurred in those who lost weight.

Because obese individuals may have previously experienced rapid weight gain in achieving their current weights, it is difficult to determine whether rate of weight gain and BMI

are independent risk factors for NIDDM. However, weight gain expressed as the percent change between the initial and referent examinations was also associated with a high incidence of diabetes in men (data not shown). Moreover, the effect of rate of weight gain on diabetes incidence persisted when we controlled for BMI in multivariate analysis. Therefore, the effect of weight gain on diabetes incidence appears to be partially independent of obesity, at least in men.

By contrast, women with rapid weight gain were not at significantly increased risk for NIDDM. The reason for the difference between the sexes remains speculative. Differences in the initial BMI do not appear to be the explanation, because the sex differences persisted with control for this variable. The differences between men and women in the relationships between rate of weight gain, fasting insulin concentration, and WHR may provide a partial explanation. Fasting hyperinsulinemia, which in part reflects insulin resistance (29), is associated with a high incidence of NIDDM (30,31). A high WHR is also a risk factor for diabetes (32,33). Therefore, a diabetogenic effect of rapid weight gain may be mediated through increased abdominal obesity or insulin resistance. If so, then the stronger correlations between rate of weight gain, fasting insulin, and WHR in men than in women may explain the stronger effect of rate of weight gain on diabetes incidence. The observation that greater rate of weight gain was associated with higher fasting insulin, even after adjustment for BMI (Table 4), is consistent with the previous finding that the correlation between weight gain and increased insulin resistance could not be explained by the resulting weight (34).

The clinical relevance of these findings must be examined in reference to BMI at the initial examination. The effect of rate of weight gain on subsequent diabetes incidence was seen in overweight men, who might be advised to lose weight. In those who were not overweight, there was an effect in both men and women. The findings support the strategy of inducing weight loss or preventing rapid weight gain for the primary prevention of NIDDM in overweight men. However, efforts to prevent rapid weight gain, targeted to individuals who are not overweight (obesity prevention), may be a more effective strategy, particularly in high-risk populations, because it may benefit both sexes. Weight changes in this study occurred over a relatively short period (median 2.8 years), but incidence of NIDDM in this population also increases with long duration of obesity, particularly after more than 10 years (35). Obesity prevention, therefore, may be a particularly effective strategy for prevention of diabetes in young adults, who would achieve the greatest reduction in duration of obesity and who also were more likely to experience rapid weight gain.

The possibility that weight fluctuation induced by repeated weight loss efforts may have a diabetogenic effect has serious implications for weight control interventions. Animal studies have suggested that weight fluctuation may increase insulin resistance (36), and epidemiological studies have reported a relationship between weight fluctuation and diabetes (5,11,13) or hyperglycemia (12). Most of these studies have been retrospective, and the one prospective study could have included undiagnosed diabetic subjects at baseline (11). Therefore, the effects seen may reflect weight changes occurring after the onset of diabetes. The prospective design of this study, in which weight fluctuation was not associated with the incidence of NIDDM, is not subject to this limitation.

This study, however, cannot exclude a modest effect of weight fluctuation on the development of NIDDM. In fact, the effect reported in the large Taking Off Pounds Sensibly program population (13) is within the CI of IRR in this study. Weight fluctuation in Pima Indians is associated with an increased risk for mortality from traumatic and alcohol-related causes (37). This may reflect a relationship with risk-taking behaviors that may, in turn, be determinants of participation in the research examinations. There was a weak, but significant, inverse correlation between weight fluctuation and the number of follow-up examinations (Spearman's $r = -0.12$, $P < 0.01$). There may, therefore, have been a slight bias against finding a positive association. However, a modest risk for NIDDM induced by weight fluctuation is likely to be offset by reducing obesity and slowing the rate of weight gain.

The results of this epidemiological study in Pima Indians support the use of interventions that induce weight loss or slow the rate of weight gain for the prevention of NIDDM. Whether the results are applicable to populations at lower risk for diabetes is speculative. However, because obesity is a risk factor for NIDDM both in the Pima Indian (23) and in other populations (3), it is reasonable to expect that the effect of weight gain may also be similar across populations. This analysis, however, suggests that weight control interventions delivered to those who are already overweight are likely to be more effective in men than in women. Prevention of obesity, on the other hand, may effectively prevent NIDDM in both sexes. Concern about a possible diabetogenic effect from weight fluctuation that may be induced by such interventions should not deter clinicians from advising weight control efforts for diabetes prevention. The interpretation of these findings, however, is limited by their observational nature and by lack of information about the causes of the observed weight changes. More conclusive evidence about the efficacy of diabetes prevention efforts awaits the results of intervention studies.

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