

DIET, LIFESTYLE, AND THE RISK OF TYPE 2 DIABETES MELLITUS IN WOMEN

FRANK B. HU, M.D., JOANN E. MANSON, M.D., MEIR J. STAMPFER, M.D., GRAHAM COLDITZ, M.D., SIMIN LIU, M.D., CAREN G. SOLOMON, M.D., AND WALTER C. WILLETT, M.D.

ABSTRACT

Background Previous studies have examined individual dietary and lifestyle factors in relation to type 2 diabetes, but the combined effects of these factors are largely unknown.

Methods We followed 84,941 female nurses from 1980 to 1996; these women were free of diagnosed cardiovascular disease, diabetes, and cancer at base line. Information about their diet and lifestyle was updated periodically. A low-risk group was defined according to a combination of five variables: a body-mass index (the weight in kilograms divided by the square of the height in meters) of less than 25; a diet high in cereal fiber and polyunsaturated fat and low in trans fat and glycemic load (which reflects the effect of diet on the blood glucose level); engagement in moderate-to-vigorous physical activity for at least half an hour per day; no current smoking; and the consumption of an average of at least half a drink of an alcoholic beverage per day.

Results During 16 years of follow-up, we documented 3300 new cases of type 2 diabetes. Overweight or obesity was the single most important predictor of diabetes. Lack of exercise, a poor diet, current smoking, and abstinence from alcohol use were all associated with a significantly increased risk of diabetes, even after adjustment for the body-mass index. As compared with the rest of the cohort, women in the low-risk group (3.4 percent of the women) had a relative risk of diabetes of 0.09 (95 percent confidence interval, 0.05 to 0.17). A total of 91 percent of the cases of diabetes in this cohort (95 percent confidence interval, 83 to 95 percent) could be attributed to habits and forms of behavior that did not conform to the low-risk pattern.

Conclusions Our findings support the hypothesis that the majority of cases of type 2 diabetes could be prevented by the adoption of a healthier lifestyle. (N Engl J Med 2001;345:790-7.)

Copyright © 2001 Massachusetts Medical Society.

SEVERAL lifestyle factors affect the incidence of type 2 diabetes. Obesity and weight gain dramatically increase the risk,^{1,2} and physical inactivity further elevates the risk, independently of obesity.³⁻⁶ Cigarette smoking is associated with a small increase^{7,8} and moderate alcohol consumption with a decrease^{9,10} in the risk of diabetes. In addition, a low-fiber diet with a high glycemic index has been associated with an increased risk of diabetes,¹¹⁻¹³ and specific dietary fatty acids may differentially affect insulin resistance and the risk of diabetes.^{14,15}

In most previous studies, dietary and lifestyle factors

have been considered individually, although behavioral factors are typically correlated with one another. We therefore examined simultaneously a set of dietary and lifestyle factors in relation to the risk of type 2 diabetes and estimated the proportion of cases that could theoretically be avoided through the simultaneous adoption of multiple types of low-risk behavior.

METHODS**Study Population**

The Nurses' Health Study began in 1976, when 121,700 female nurses 30 to 55 years of age responded to a questionnaire regarding medical, lifestyle, and other health-related information.¹⁶ Since then, questionnaires have been sent biennially to update this information and identify newly diagnosed cases of various diseases. Diet was first assessed in 1980. For the current analysis, we excluded women with previously diagnosed diabetes, cancer, or cardiovascular diseases at base line and those who left more than 10 items blank on the 1980 dietary questionnaire or had implausibly low or high scores for total intake of food or energy (less than 500 or more than 3500 kcal per day). After these exclusions, the analysis included 84,941 women. The follow-up rate with respect to the incidence of diabetes in the overall cohort was 97 percent of the total potential person-years of follow-up. The study was approved by the institutional review board of Brigham and Women's Hospital in Boston; completion of the self-administered questionnaire was considered to imply informed consent.

Assessment of Diet

In 1980, we assessed diet using a 61-item, semiquantitative food-frequency questionnaire.¹⁷ An expanded dietary questionnaire including approximately 120 items was used to update the information about diet in 1984, 1986, and 1990.¹⁸ We asked how often, on average, a participant had consumed a particular amount of a specific type of food during the previous year. The intake of nutrients was computed by multiplying the frequency of consumption of each unit of food by its nutrient content. Questions about the consumption of beer, wine, and liquor were included in each questionnaire. The reproducibility and validity of the food-frequency questionnaires have been described in detail previously.^{18,19}

Assessment of Nondietary Factors

Every two years, we update participants' smoking status (never smoked, former smoker, or current smoker, including the number of cigarettes smoked per day), menopausal status and use or nonuse of postmenopausal hormone therapy, and body weight. Reported weights have been highly correlated with measured weights ($r=0.96$).²⁰ The presence or absence of a family history of diabetes (in first-degree relatives) was assessed in 1982 and 1988. Information about physical activity was first obtained in 1980 and was updated in 1982, 1986, 1988, and 1992 with the use of a validated ques-

From the Departments of Nutrition (F.B.H., M.J.S., W.C.W.) and Epidemiology (J.E.M., M.J.S., G.C., W.C.W.), Harvard School of Public Health; the Channing Laboratory (J.E.M., M.J.S., G.C., W.C.W.); and the Divisions of Preventive Medicine (J.E.M., S.L.) and General Medicine (C.G.S.), Department of Medicine, Brigham and Women's Hospital and Harvard Medical School — all in Boston. Address reprint requests to Dr. Hu at the Department of Nutrition, Harvard School of Public Health, 665 Huntington Ave., Boston, MA 02115, or at frank.hu@channing.harvard.edu.

tionnaire.⁶ We estimated the amount of time per week spent in moderate-to-vigorous activities (including brisk walking) requiring the expenditure of 3 MET or more per hour.⁶

Definition of the Low-Risk Group

The criteria we used to define a low-risk group according to dietary and lifestyle variables were similar to those used in previous analyses of coronary disease.²¹ In terms of the body-mass index (the weight in kilograms divided by the square of the height in meters), low risk was defined as a value of less than 25.0, the standard cut-off point for the classification of overweight.²² We did not include waist or hip circumferences in the analyses because they were first assessed in 1986 and because a high body-mass index was a much stronger predictor of diabetes in this cohort.²³

In terms of physical activity, low risk was defined as an average of at least one half-hour per day of vigorous or moderate activity, including brisk walking, in keeping with published guidelines.^{24,25} In terms of cigarette smoking, low risk was defined as no current smoking, and in terms of alcohol use, low risk was defined as an average of 5 g or more of alcohol per day (about half a drink or more per day). Because few women in this cohort drank heavily (1.2 percent reported drinking more than 45 g of alcohol per day), we did not define an upper limit for alcohol consumption, although clearly such a limit would be necessary in order to establish public health guidelines.

Previous studies have found that a reduced risk of type 2 diabetes is associated with a higher intake of cereal fiber^{11,12,26} and polyunsaturated fat²⁷ and that an increased risk is associated with a higher intake of trans fat (formed during the partial hydrogenation of vegetable oils)²⁷ and a higher glycemic load (which reflects the effect of diet on the blood glucose level).^{11,12} Therefore, a low-risk diet was defined as a diet low in trans fat and glycemic load and high in cereal fiber, with a high ratio of polyunsaturated to saturated fat. For each dietary factor, we assigned each woman a score between one and five, corresponding to her quintile of intake, with five representing the lowest-risk quintile, and summed her quintile values for the four nutrients. Participants with composite dietary scores in the highest 40 percent among the women in the study were considered to be in the lowest risk category in terms of diet.

Ascertainment of Cases of Diabetes

A supplementary questionnaire regarding symptoms, diagnostic tests, and hypoglycemic therapy was mailed to women who reported having received a diagnosis of diabetes. A case of diabetes was considered to be confirmed if at least one of the following was reported on the supplementary questionnaire: classic symptoms plus a plasma glucose concentration of at least 140 mg per deciliter (7.8 mmol per liter) in the fasting state or a randomly measured plasma glucose concentration of at least 200 mg per deciliter (11.1 mmol per liter); at least two elevated plasma glucose concentrations on different occasions (a concentration of at least 140 mg per deciliter in the fasting state, a randomly measured concentration of at least 200 mg per deciliter, or a concentration of at least 200 mg per deciliter two or more hours after the initiation of oral glucose-tolerance testing) in the absence of symptoms; or treatment with hypoglycemic medication (insulin or an oral hypoglycemic agent). Our criteria for the classification of diabetes are consistent with those proposed by the National Diabetes Data Group.²⁸ The validity of this questionnaire has been verified in a subsample of our study population.⁵ The diagnostic criteria for type 2 diabetes changed in June 1996, and a fasting glucose concentration of 126 mg per deciliter is now considered the threshold for a diagnosis of diabetes.²⁹ We used the earlier criteria because all the cases in our cohort were diagnosed before June 1996.

Statistical Analysis

The duration of follow-up was calculated as the interval between the return of the 1980 questionnaire and the diagnosis of type 2 diabetes, death, or June 1, 1996. Relative risks were calculated by di-

viding the incidence of diabetes among women in the low-risk group by the incidence among the remaining women. To adjust for multiple risk factors, we used pooled logistic regression with two-year intervals,³⁰ which is approximately equivalent to Cox regression for time-dependent covariates. In all models, we simultaneously included terms for age, time (eight periods), presence or absence of a family history of diabetes, menopausal status, and use or nonuse of postmenopausal hormone therapy. In the initial analyses, we calculated the relative risks and 95 percent confidence intervals³¹ for the different categories of each variable that was included in the low-risk profile, adjusting for age, time, presence or absence of a family history of diabetes, menopausal status, and use or nonuse of postmenopausal hormone therapy but not for the other components of the low-risk profile. We then examined the combined low-risk group, defined as women in the low-risk category for each variable, with all other women as the comparison group.

We calculated the population attributable risk,^{31,32} an estimate of the percentage of cases of type 2 diabetes in this population that would theoretically not have occurred if all women had been in the low-risk group, assuming a causal relation between the risk factors and type 2 diabetes. We also conducted analyses stratified according to the presence or absence of a family history of diabetes and according to the body-mass index. Within each stratum, we compared the women in the low-risk category with all the other women.

To obtain the best estimate of long-term dietary intake and physical activity, we used the cumulative-update method,^{33,34} which takes the average of all previous data. For variables unrelated to diet and exercise, we used the most recent information; the body-mass index and smoking status were updated every two years, and the information about alcohol intake was updated in 1984, 1986, and 1990.

RESULTS

During 16 years of follow-up (1,301,055 person-years), we documented 3300 new cases of type 2 diabetes. The most important risk factor for type 2 diabetes was the body-mass index; the relative risk of diabetes was 38.8 for women with a body-mass index of 35.0 or higher and 20.1 for women with a body-mass index of 30.0 to 34.9, as compared with women who had a body-mass index of less than 23.0 (Table 1). Even a body-mass index at the high end of the normal range (23.0 to 24.9) was associated with a substantially higher risk than a body-mass index of less than 23.0 (relative risk, 2.67). In this population, 61 percent of the cases of type 2 diabetes (95 percent confidence interval, 58 to 64 percent) could be attributed to overweight (defined as a body-mass index of 25 or higher).

Lack of exercise, a poor diet, current smoking, and abstinence from alcohol were all associated with a significantly increased risk of diabetes even after adjustment for the body-mass index (Table 1). The inverse association between physical activity and the risk of diabetes was much stronger without body-mass index in the model (the relative risk of diabetes for women who exercised for seven or more hours per week as compared with women who exercised for less than half an hour was 0.48; 95 percent confidence interval, 0.38 to 0.61). Analyses stratified according to the body-mass index showed that the associations between diabetes and diet, physical activity, smoking status, and alcohol use were generally similar among women with a normal body-mass index, those who were overweight, and those who were obese (Table 2). Further

TABLE 1. DISTRIBUTION OF MODIFIABLE RISK FACTORS AND RELATIVE RISK OF TYPE 2 DIABETES AMONG 84,941 WOMEN IN THE NURSES' HEALTH STUDY, 1980 TO 1996.

FACTOR	NO. OF CASES*	PERCENTAGE OF PERSON-YEAR†	RELATIVE RISK (95% CI)‡
Quintile for dietary score§			
1	670	15	1.0
2	1032	27	0.86 (0.78–0.95)
3	561	17	0.77 (0.68–0.86)
4	746	26	0.67 (0.60–0.74)
5	291	15	0.49 (0.42–0.56)
Weekly exercise¶			
<0.5 hr	263	5	1.0
0.5–1.9 hr	1055	29	0.89 (0.77–1.02)
2.0–3.9 hr	734	22	0.87 (0.75–1.00)
4.0–6.9 hr	668	26	0.83 (0.71–0.96)
≥7.0 hr	97	7	0.71 (0.56–0.90)
Body-mass index			
<23.0	121	32	1.0
23.0–24.9	202	18	2.67 (2.13–3.34)
25.0–29.9	884	25	7.59 (6.27–9.19)
30.0–34.9	885	9	20.1 (16.6–24.4)
≥35.0	759	4	38.8 (31.9–47.2)
Smoking status			
Never smoked	1446	43	1.0
Former smoker	1217	35	1.15 (1.07–1.25)
Current smoker			
1–14 cigarettes/day	181	7	1.20 (1.03–1.41)
≥15 cigarettes/day	439	15	1.34 (1.20–1.50)
Daily alcohol consumption			
0 g	1715	34	1.0
0.1–5.0 g	1034	33	0.78 (0.72–0.84)
5.1–10.0 g	189	11	0.56 (0.48–0.65)
>10.0 g	358	21	0.59 (0.52–0.66)

*The total number of cases of type 2 diabetes was 3300, but because of missing values, the numbers for some variables do not add up to 3300.

†The total number of person-years was 1,301,055.

‡Relative risks were adjusted for age (in five-year categories), time (eight periods), presence or absence of a family history of diabetes, menopausal status, and use or nonuse of postmenopausal hormone therapy. All variables were included in the same model. CI denotes confidence interval.

§The intakes of trans fat and cereal fiber, the glycemic load, and the ratio of polyunsaturated-fat intake to saturated-fat intake were categorized in quintiles. Each woman was assigned a score for each nutrient on the basis of her quintile of intake (a higher score represented a lower risk), then the four scores were summed, and the total score was categorized into quintiles.

¶Activities included moderate-to-vigorous sports, jogging, brisk walking, heavy gardening, heavy housework, and other activities "vigorous enough to build up a sweat."

adjustment for the body-mass index as a continuous variable in each stratum did not substantially alter the results. In addition, the individual components of the dietary score were independently and significantly associated with the risk of diabetes when they were entered into the same model (Fig. 1).

Estimates of the reduction in risk among women in the low-risk categories for three, four, or five of the modifiable risk factors are provided in Table 3. Women who were in the low-risk categories for three factors (body-mass index, diet, and exercise) had a relative risk of diabetes of 0.12 (95 percent confidence interval,

0.08 to 0.16) as compared with all other women. The population attributable risk was 87 percent (95 percent confidence interval, 83 to 91 percent), suggesting that 87 percent of the new cases of diabetes in this cohort might have been prevented if all women had been in the low-risk group. The population attributable risk increased to 91 percent (95 percent confidence interval, 83 to 95 percent) when the group included women in the low-risk categories for smoking status and alcohol consumption. Only 3.4 percent of the women were in the low-risk group (as defined in terms of all five risk factors).

To address the possibility of surveillance bias, we conducted a sensitivity analysis restricted to the 2107 women for whom at least one symptom of diabetes was reported at the time diabetes was diagnosed (64 percent of the women with diabetes). In this subgroup, the population attributable risk for the women in the low-risk group was 93 percent (95 percent confidence interval, 83 to 97 percent). To adjust for possible confounding by socioeconomic status, we conducted further analyses in which we controlled for the occupations of the women's parents and the educational level of their husbands. The results did not materially change; the population attributable risk for the women in the low-risk group was 90 percent (95 percent confidence interval, 81 to 95 percent).

The reduction in risk associated with low risk as defined in terms of the five risk factors was similar for women with a family history of diabetes and for those without such a history (Table 4) and for white and nonwhite women (approximately 3 percent of the cohort). Among overweight women (body-mass index, 25.0 to 29.9) and those with normal weight (body-mass index, <25.0), approximately half the cases of diabetes could have been prevented by the combination of a healthy diet, regular exercise, abstinence from smoking, and moderate alcohol consumption (Table 5). Among obese women (body-mass index, ≥30.0), a combination of a healthy diet and regular exercise was associated with a 24 percent reduction in the risk of diabetes. The addition of nonsmoking status and moderate alcohol consumption to the model increased the estimate of risk reduction somewhat but widened the confidence interval because of the small number of women with these characteristics.

Because a body-mass index at the high end of the normal range was associated with an increased risk of diabetes, we repeated the analysis using a body-mass index of 23.0 as the cutoff point. The population attributable risk for the low-risk group (2.3 percent of the cohort) was 96 percent (95 percent confidence interval, 87 to 99 percent). In contrast, when we raised the body-mass-index cutoff point to 27.0 (thereby including 4.1 percent of the cohort in the low-risk group), the population attributable risk for the low-risk group was 88 percent (95 percent confidence interval, 80 to 93 percent).

TABLE 2. MULTIVARIATE RELATIVE RISKS OF TYPE 2 DIABETES ACCORDING TO BODY-MASS INDEX.*

FACTOR	BODY-MASS INDEX		
	<25.0	25.0–29.9	≥30.0
	relative risk (95% confidence interval)		
Quintile for dietary score†			
1	1.0	1.0	1.0
2	0.68 (0.49–0.94)	0.80 (0.66–0.96)	0.89 (0.77–1.03)
3	0.66 (0.46–0.95)	0.69 (0.55–0.86)	0.81 (0.69–0.96)
4	0.51 (0.36–0.72)	0.55 (0.45–0.68)	0.72 (0.62–0.84)
5	0.38 (0.25–0.58)	0.42 (0.32–0.55)	0.49 (0.40–0.61)
Weekly exercise‡			
<0.5 hr	1.0	1.0	1.0
0.5–1.9 hr	0.74 (0.48–1.16)	0.92 (0.70–1.23)	0.83 (0.69–0.99)
2.0–3.9 hr	0.70 (0.45–1.10)	0.90 (0.67–1.21)	0.82 (0.68–1.00)
4.0–6.9 hr	0.63 (0.40–1.00)	0.91 (0.68–1.21)	0.76 (0.62–0.92)
≥7.0 hr	0.50 (0.25–0.99)	1.06 (0.69–1.63)	0.74 (0.51–1.09)
Smoking status			
Never smoked	1.0	1.0	1.0
Former smoker	0.95 (0.73–1.24)	1.00 (0.86–1.17)	1.24 (1.12–1.39)
Current smoker			
1–14 cigarettes/day	0.72 (0.44–1.18)	1.14 (0.85–1.54)	1.47 (1.17–1.85)
≥15 cigarettes/day	1.39 (1.02–1.88)	1.40 (1.14–1.71)	1.31 (1.10–1.56)
Daily alcohol consumption			
0 g	1.0	1.0	1.0
0.1–5.0 g	0.85 (0.65–1.11)	0.70 (0.60–0.82)	0.81 (0.72–0.90)
5.1–10.0 g	0.64 (0.42–0.98)	0.62 (0.48–0.81)	0.60 (0.48–0.76)
>10.0 g	0.85 (0.63–1.14)	0.57 (0.46–0.71)	0.61 (0.50–0.74)

*Relative risks were adjusted for age (in five-year categories), time (eight periods), presence or absence of a family history of diabetes, menopausal status, and use or nonuse of postmenopausal hormone therapy. All variables were included in the same model.

†The intakes of trans fat and cereal fiber, the glycemic load, and the ratio of polyunsaturated-fat intake to saturated-fat intake were categorized in quintiles. Each woman was assigned a score for each nutrient on the basis of her quintile of intake (a higher score represented a lower risk), then the four scores were summed, and the total score was categorized into quintiles.

‡Activities included vigorous sports, jogging, brisk walking, heavy gardening, heavy housework, and other activities “vigorous enough to build up a sweat.”

DISCUSSION

In this large cohort of middle-aged women, a combination of several lifestyle factors, including maintaining a body-mass index of 25 or lower, eating a diet high in cereal fiber and polyunsaturated fat and low in saturated and trans fats and glycemic load, exercising regularly, abstaining from smoking, and consuming alcohol moderately, was associated with an incidence of type 2 diabetes that was approximately 90 percent lower than that found among women without these factors. These results suggest that in this population the majority of cases of type 2 diabetes could be avoided by behavior modification.

Excess body fat is the single most important determinant of type 2 diabetes. Weight control would be the most effective way to reduce the risk of type 2 diabetes, but current strategies have not been very successful on a population basis,³⁵ and the prevalence of obesity continues to increase.³⁶ The public generally does not recognize the connection between overweight or obesity and diabetes.³⁷ Thus, greater efforts at education are needed.

Our data suggest that the percentage of cases of diabetes that are preventable by diet and exercise independently of body weight is greater among women of normal weight than among obese women. However, even among overweight and obese persons, the combination of an appropriate diet, a moderate amount of exercise, and abstinence from smoking could substantially lower the risk of type 2 diabetes. Although the percentage of cases that could be avoided by means of these lifestyle changes is lower among obese persons, the absolute number of cases avoided among such persons would be greater because of their higher risk. Moreover, diet and exercise are the primary factors in determining weight loss.

Our present results are in agreement with our previous study of coronary disease,²¹ which found that adherence to similar guidelines was associated with an 83 percent reduction in risk. These analyses underscore the common lifestyle-related origins of diabetes and coronary disease and provide further evidence that modifications of diet and lifestyle have large and multiple benefits.

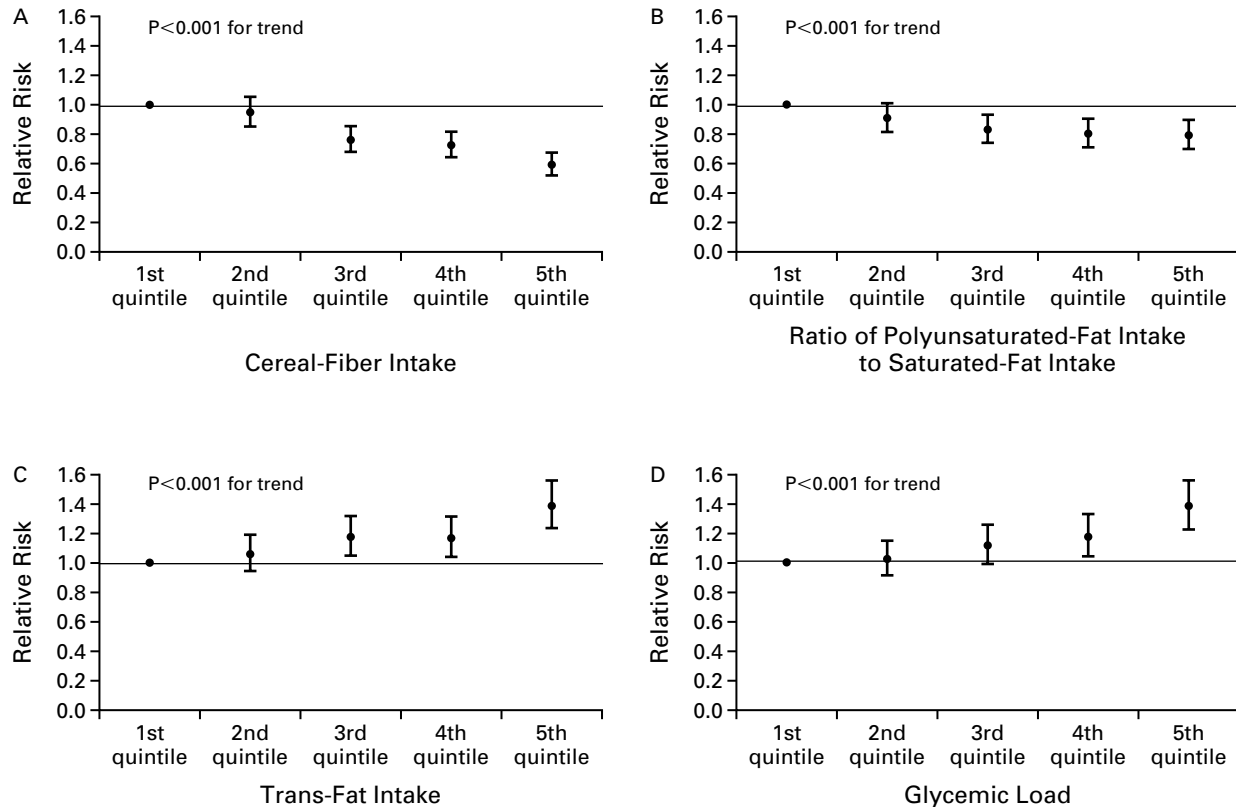


Figure 1. Multivariate Relative Risks (with 95 Percent Confidence Intervals) of Type 2 Diabetes Mellitus According to Ascending Quintiles of Intake of Cereal Fiber (Panel A), the Ratio of Polyunsaturated-Fat Intake to Saturated-Fat Intake (Panel B), Intake of Trans Fat (Panel C), and Glycemic Load (Panel D).

Each of the relative risks was adjusted for the other three dietary variables and for age (in five-year categories), time (eight periods), the presence or absence of a family history of diabetes, menopausal status and the use or nonuse of postmenopausal hormone therapy, smoking status (never smoked; former smoker; current smoker, 1 to 14 cigarettes per day; or current smoker, ≥ 15 cigarettes per day), body-mass index (< 23.0 , 23.0 to 24.9 , 25.0 to 29.9 , 30.0 to 34.9 , or ≥ 35.0), weekly frequency of moderate-to-vigorous exercise (< 0.5 hour, 0.5 to 1.9 hours, 2.0 to 3.9 hours, 4.0 to 6.9 hours, or ≥ 7.0 hours), and daily alcohol consumption (0 g, 0.1 to 5.0 g, 5.1 to 10.0 g, or > 10.0 g).

Clinical trials in China and Finland have demonstrated the feasibility and efficacy of lifestyle-intervention programs in the prevention of diabetes in high-risk populations. Among 577 patients with impaired glucose tolerance in Da Qing, China,³⁸ exercise interventions, dietary interventions, or both resulted in a decrease of 42 to 46 percent in the rate of progression from impaired glucose tolerance to diabetes during six years of follow-up. Recently, the Finnish Diabetes Prevention Program reported that the modification of lifestyle reduced the incidence of type 2 diabetes by 58 percent during 3.2 years of follow-up among 522 middle-aged, overweight participants with impaired glucose tolerance.³⁹ The program included a relatively small reduction in weight (less than 4.5 kg [10 lb]), combined with a diet low in saturated and trans fat and high in fiber and regular moderate exercise. Results from the first three years of the Diabetes Prevention Program in the United States also show that regular exercise and the modification of diet reduced

the incidence of type 2 diabetes by 58 percent among patients with impaired glucose tolerance.⁴⁰ Our results suggest that closer adherence to behavioral guidelines could reduce the risk further in both low-risk and high-risk populations.

Because all the women in our study were health care professionals, our findings may not apply directly to the general population. However, since risk factors for diabetes tend to be more prevalent in the general population, the magnitude of the reduction in risk that would be achievable with adherence to the behavioral guidelines we outline would probably be even greater than the magnitude of the reduction we found. Although some factors we considered — for example, alcohol use and smoking — have not been (and will probably never be) tested in randomized trials with clinical end points, ample observational data support their associations with diabetes. Nevertheless, physicians must exercise caution in recommending alcohol use, since it may lead to overuse. Finally, we did not

TABLE 3. RELATIVE AND POPULATION ATTRIBUTABLE RISKS OF TYPE 2 DIABETES FOR GROUPS DEFINED BY COMBINATIONS OF MODIFIABLE RISK FACTORS.*

SUBGROUP	PERCENTAGE OF WOMEN	NO. OF CASES OF DIABETES	RELATIVE RISK (95% CI)†	POPULATION ATTRIBUTABLE RISK‡
				% (95% CI)
3 Factors in low-risk category (dietary score in upper 2 quintiles, body-mass index <25.0, and moderate-to-vigorous exercise ≥30 min/day)§	9.5	34	0.12 (0.08–0.16)	87 (83–91)
4 Factors in low-risk category (3 above plus nonsmoking)¶	8	27	0.11 (0.07–0.16)	88 (83–92)
5 Factors in low-risk category (4 above plus alcohol use ≥5 g/day)	3.4	10	0.09 (0.05–0.17)	91 (83–95)

*There were 84,941 women in the group, and there were 3300 cases of type 2 diabetes. CI denotes confidence interval.

†Relative risks were adjusted for age (in five-year categories), time (eight periods), presence or absence of a family history of diabetes, menopausal status, and use or nonuse of postmenopausal hormone therapy.

‡The population attributable risk is the percentage of cases of type 2 diabetes in the population that would theoretically not have occurred if all women had been in the low-risk category for these factors. Women with a missing value were considered to be in the high-risk category for that factor.

§The model was adjusted for smoking status and level of alcohol use.

¶The model was adjusted for level of alcohol use.

TABLE 4. RISK OF TYPE 2 DIABETES IN LOW-RISK GROUPS STRATIFIED ACCORDING TO THE PRESENCE OR ABSENCE OF A FAMILY HISTORY OF DIABETES.*

SUBGROUP	PERCENTAGE OF WOMEN	NO. OF CASES OF DIABETES	RELATIVE RISK (95% CI)†	POPULATION ATTRIBUTABLE RISK‡
				% (95% CI)
No family history of diabetes				
3 Factors in low-risk category (dietary score in upper 2 quintiles, body-mass index <25.0, and moderate-to-vigorous exercise ≥30 min/day)§	9.7	25	0.14 (0.10–0.21)	85 (77–89)
4 Factors in low-risk category (3 above plus nonsmoking)¶	8.1	19	0.13 (0.08–0.20)	86 (79–91)
5 Factors in low-risk category (4 above plus alcohol use ≥5 g/day)	3.6	5	0.07 (0.03–0.18)	93 (82–97)
Family history of diabetes				
3 Factors in low-risk category	8.9	9	0.08 (0.04–0.14)	91 (85–96)
4 Factors in low-risk category	7.6	8	0.08 (0.04–0.16)	91 (83–96)
5 Factors in low-risk category	2.9	5	0.12 (0.05–0.30)	88 (70–96)

*There were 84,941 women in the group, and there were 3300 cases of type 2 diabetes. CI denotes confidence interval.

†Relative risks were adjusted for age (in five-year categories), time (eight periods), presence or absence of a family history of diabetes, menopausal status, and use or nonuse of postmenopausal hormone therapy.

‡The population attributable risk is the percentage of cases of type 2 diabetes in the population that would theoretically not have occurred if all women had been in the low-risk category for these factors. Women with a missing value for a given factor were considered to be in the high-risk category for that factor.

§The model was also adjusted for smoking status and level of alcohol use.

¶The model was also adjusted for level of alcohol use.

TABLE 5. RISK OF TYPE 2 DIABETES IN LOW-RISK GROUPS STRATIFIED ACCORDING TO BODY-MASS INDEX.*

SUBGROUP	PERCENTAGE OF WOMEN	NO. OF CASES OF DIABETES	RELATIVE RISK (95% CI)†	POPULATION ATTRIBUTABLE RISK‡
				% (95% CI)
Body-mass index <25.0				
2 Factors in low-risk category (dietary score in upper 2 quintiles, moderate-to-vigorous exercise ≥ 30 min/day)§	18.9	34	0.50 (0.35–0.72)	45 (24 to 60)
3 Factors in low-risk category (2 above plus nonsmoking)¶	15.9	27	0.47 (0.31–0.69)	49 (27 to 65)
4 Factors in low-risk category (3 above plus alcohol use ≥ 5 g/day)	6.8	10	0.44 (0.23–0.83)	54 (16 to 76)
Body-mass index 25.0–29.9				
2 Factors in low-risk category	15.8	102	0.73 (0.59–0.90)	24 (9 to 37)
3 Factors in low-risk category	13.7	84	0.67 (0.54–0.84)	30 (14 to 42)
4 Factors in low-risk category	4.5	18	0.44 (0.28–0.70)	55 (29 to 71)
Body-mass index ≥ 30.0				
2 Factors in low-risk category	11.4	141	0.74 (0.62–0.89)	24 (10 to 35)
3 Factors in low-risk category	10.1	129	0.76 (0.63–0.91)	22 (8 to 34)
4 Factors in low-risk category	2.2	25	0.70 (0.47–1.05)	30 (–5 to 53)

*There were 84,941 women in the group, and there were 3300 cases of type 2 diabetes. CI denotes confidence interval.

†Relative risks were adjusted for age (in five-year categories), time (eight periods), presence or absence of a family history of diabetes, menopausal status, and use or nonuse of postmenopausal hormone therapy.

‡The population attributable risk is the percentage of cases of type 2 diabetes in the population that would theoretically not have occurred if all women had been in the low-risk category for these factors. Women with a missing value were considered to be in the high-risk category for that factor.

§The model was also adjusted for smoking status and level of alcohol use.

¶The model was also adjusted for level of alcohol use.

consider pharmacologic means of preventing diabetes, some of which are being tested in ongoing clinical trials in high-risk populations.

Diagnoses of diabetes in our study were reported by the women but were confirmed by a supplementary questionnaire regarding symptoms, diagnostic tests, and treatment. Our previous study found this confirmation to be highly accurate as compared with a review of the medical records.⁵ Because the women in our cohort who did not have diabetes were not uniformly screened for glucose intolerance, some cases of diabetes may not have been diagnosed. However, when the analyses were restricted to symptomatic cases of diabetes, the findings were not altered substantially, suggesting that surveillance bias is unlikely.

In conclusion, our findings suggest that the majority of cases of type 2 diabetes could be prevented by weight loss, regular exercise, modification of diet, abstinence from smoking, and the consumption of limited amounts of alcohol. Weight control would appear to offer the greatest benefit.

Supported by research grants (DK36798 and CA87969) from the National Institutes of Health and by an American Diabetes Association Research Award (to Dr. Hu).

We are indebted to the participants in the Nurses' Health Study for their cooperation and to Al Wing, Stefanie Bechtel, Gary Chase, Karen Corsano, Lisa Dunn, Barbara Egan, Lori Ward, and Jill Arnold for their unfailing help.

REFERENCES

1. Colditz GA, Willett WC, Stampfer MJ, et al. Weight as a risk factor for clinical diabetes in women. *Am J Epidemiol* 1990;132:501-13.
2. Colditz GA, Willett WC, Rotnitzky A, Manson JE. Weight gain as a risk factor for clinical diabetes mellitus in women. *Ann Intern Med* 1995; 122:481-6.
3. Helmrich SP, Ragland DR, Leung RW, Paffenbarger RS Jr. Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus. *N Engl J Med* 1991;325:147-52.
4. Lynch J, Helmrich SP, Lakka TA, et al. Moderately intense physical activities and high levels of cardiorespiratory fitness reduce risk of non-insulin-dependent diabetes mellitus in middle-aged men. *Arch Intern Med* 1996;156:1307-14.
5. Manson JE, Rimm EB, Stampfer MJ, et al. Physical activity and incidence of non-insulin-dependent diabetes mellitus in women. *Lancet* 1991; 338:774-8.
6. Hu FB, Sigal RJ, Rich-Edwards JW, et al. Walking compared with vigorous physical activity and risk of type 2 diabetes in women: a prospective study. *JAMA* 1999;282:1433-9.
7. Manson JE, Ajani UA, Liu S, Nathan DM, Hennekens CH. A prospective study of cigarette smoking and the incidence of diabetes mellitus among US male physicians. *Am J Med* 2000;109:538-42.
8. Rimm EB, Chan J, Stampfer MJ, Colditz GA, Willett WC. Prospective study of cigarette smoking, alcohol use, and the risk of diabetes in men. *BMJ* 1995;310:555-9.
9. Wei M, Gibbons LW, Mitchell TL, Kampert JB, Blair SN. Alcohol intake and incidence of type 2 diabetes in men. *Diabetes Care* 2000;23:18-22.

10. Ajani UA, Hennekens CH, Spelsberg A, Manson JE. Alcohol consumption and risk of type 2 diabetes mellitus among US male physicians. *Arch Intern Med* 2000;160:1025-30.
11. Salmeron J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. *JAMA* 1997;277:472-7.
12. Salmeron J, Ascherio A, Rimm EB, et al. Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes Care* 1997;20:545-50.
13. Liu S, Manson JE, Stampfer MJ, et al. A prospective study of whole-grain intake and risk of type 2 diabetes mellitus in US women. *Am J Public Health* 2000;90:1409-15.
14. Vessby B. Dietary fat and insulin action in humans. *Br J Nutr* 2000;83:Suppl 1:S91-S96.
15. Hu FB, van Dam RM, Liu S. Diet and risk of type II diabetes: the role of types of fat and carbohydrate. *Diabetologia* 2001;44:805-17.
16. Colditz GA, Manson JE, Hankinson SE. The Nurses' Health Study: 20-year contribution to the understanding of health among women. *J Womens Health* 1997;6:49-62.
17. Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am J Epidemiol* 1985;122:51-65.
18. Willett WC. *Nutritional epidemiology*. 2nd ed. New York: Oxford University Press, 1998.
19. Liu S, Manson JE, Stampfer MJ, et al. Dietary glycemic load assessed by food frequency questionnaire in relation to plasma high-density-lipoprotein cholesterol and fasting plasma triacylglycerols in postmenopausal women. *Am J Clin Nutr* 2001;73:560-6.
20. Willett W, Stampfer MJ, Bain C, et al. Cigarette smoking, relative weight, and menopause. *Am J Epidemiol* 1983;117:651-8.
21. Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC. Primary prevention of coronary heart disease in women through diet and lifestyle. *N Engl J Med* 2000;343:16-22.
22. Obesity: preventing and managing the global epidemic: report of a WHO consultation on obesity. Geneva: World Health Organization, 1998.
23. Carey VJ, Walters EE, Colditz GA, et al. Body fat distribution and risk of non-insulin-dependent diabetes mellitus in women: the Nurses' Health Study. *Am J Epidemiol* 1997;145:614-9.
24. Pate RR, Pratt M, Blair SN, et al. Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA* 1995;273:402-7.
25. NIH Consensus Development Panel on Physical Activity and Cardiovascular Health. Physical activity and cardiovascular health. *JAMA* 1996;276:241-6.
26. Meyer KA, Kushi LH, Jacobs DR Jr, Slavin J, Sellers TA, Folsom AR. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. *Am J Clin Nutr* 2000;71:921-30.
27. Salmeron J, Hu FB, Manson JE, et al. Dietary fat intake and risk of type 2 diabetes in women. *Am J Clin Nutr* 2001;73:1019-26.
28. National Diabetes Data Group. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes* 1979;28:1039-57.
29. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 1997;20:1183-97.
30. D'Agostino RB, Lee M-L, Belanger AJ, Cupples LA, Anderson K, Kannel WB. Relation of pooled logistic regression to time dependent Cox regression analysis: the Framingham Heart Study. *Stat Med* 1990;9:1501-15.
31. Rothman KJ, Greenland S. *Modern epidemiology*. 2nd ed. Philadelphia: Lippincott-Raven, 1998.
32. Wacholder S, Benichou J, Heineman EF, Hartge P, Hoover RN. Attributable risk: advantages of a broad definition of exposure. *Am J Epidemiol* 1994;140:303-9. [Erratum, *Am J Epidemiol* 1994;140:668.]
33. Hu FB, Stampfer MJ, Manson JE, et al. Dietary fat intake and the risk of coronary heart disease in women. *N Engl J Med* 1997;337:1491-9.
34. Hu FB, Stampfer MJ, Rimm E, et al. Dietary fat and coronary heart disease: a comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. *Am J Epidemiol* 1999;149:531-40.
35. Jeffery RW, Drewnowski A, Epstein LH, et al. Long-term maintenance of weight loss: current status. *Health Psychol* 2000;19:Suppl:5-16.
36. Mokdad AH, Serdula MK, Dietz WH, Bowman BA, Marks JS, Koplan JP. The spread of the obesity epidemic in the United States, 1991-1998. *JAMA* 1999;282:1519-22.
37. Manning A. Americans ignore risk of weight and diabetes. *USA Today*. January 8, 2001:D7.
38. Pan X-R, Li G-W, Wang J-X, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. *Diabetes Care* 1997;20:537-44.
39. Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001;344:1343-50.
40. Diet and exercise dramatically delay type 2 diabetes. Press release of the National Institute of Diabetes and Digestive and Kidney Diseases. August 8, 2001. (Accessed August 22, 2001, at http://www.niddk.nih.gov/welcome/releases/8_8_01.htm.)

Copyright © 2001 Massachusetts Medical Society.