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PREVENTION OF TYPE 2 DIABETES MELLITUS BY CHANGES IN LIFESTYLE AMONG SUBJECTS WITH IMPAIRED GLUCOSE TOLERANCE

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ABSTRACT

Background Type 2 diabetes mellitus is increasingly common, primarily because of increases in the prevalence of a sedentary lifestyle and obesity. Whether type 2 diabetes can be prevented by interventions that affect the lifestyles of subjects at high risk for the disease is not known.

Methods We randomly assigned 522 middle-aged, overweight subjects (172 men and 350 women; mean age, 55 years; mean body-mass index [weight in kilograms divided by the square of the height in meters], 31) with impaired glucose tolerance to either the intervention group or the control group. Each subject in the intervention group received individualized counseling aimed at reducing weight, total intake of fat, and intake of saturated fat and increasing intake of fiber and physical activity. An oral glucose-tolerance test was performed annually; the diagnosis of diabetes was confirmed by a second test. The mean duration of follow-up was 3.2 years.

Results The mean (\pm SD) amount of weight lost between base line and the end of year 1 was 4.2 ± 5.1 kg in the intervention group and 0.8 ± 3.7 kg in the control group; the net loss by the end of year 2 was 3.5 ± 5.5 kg in the intervention group and 0.8 ± 4.4 kg in the control group ($P < 0.001$ for both comparisons between the groups). The cumulative incidence of diabetes after four years was 11 percent (95 percent confidence interval, 6 to 15 percent) in the intervention group and 23 percent (95 percent confidence interval, 17 to 29 percent) in the control group. During the trial, the risk of diabetes was reduced by 58 percent ($P < 0.001$) in the intervention group. The reduction in the incidence of diabetes was directly associated with changes in lifestyle.

Conclusions Type 2 diabetes can be prevented by changes in the lifestyles of high-risk subjects. (N Engl J Med 2001;344:1343-50.)

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THE incidence of type 2 diabetes mellitus is increasing worldwide. Type 2 diabetes results from the interaction between a genetic predisposition and behavioral and environmental risk factors.¹ Although the genetic basis of type 2 diabetes has yet to be identified, there is strong evidence that such modifiable risk factors as obesity and physical inactivity are the main nongenetic determinants of the disease.²⁻⁹

Impaired glucose tolerance is an intermediate category between normal glucose tolerance and overt diabetes,^{10,11} and it can be identified by an oral glucose-tolerance test. Subjects with impaired glucose tolerance have an increased risk of type 2 diabetes¹² and therefore form an important target group for interventions aimed at preventing diabetes.²⁻⁵ The Finnish Diabetes Prevention Study was conducted to determine the feasibility and effects of a program of chang-

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es in lifestyle designed to prevent or delay the onset of type 2 diabetes in subjects with impaired glucose tolerance.

METHODS

Study Design

The design of the Diabetes Prevention Study has been described in detail elsewhere.¹³ The study was designed on the assumptions of a 35 percent cumulative incidence of diabetes and a 35 percent reduction in incidence in the intervention group, as compared with the control group, during a six-year period. The study protocol was approved by the ethics committee of the National Public Health Institute in Helsinki, Finland, and all the study subjects gave written informed consent.

Study subjects were recruited primarily through the screening of members of high-risk groups, such as first-degree relatives of patients with type 2 diabetes. Overweight persons (defined as those with a body-mass index [the weight in kilograms divided by the square of the height in meters] of 25 or higher) who were 40 to 65 years old and had impaired glucose tolerance were eligible for the study. Impaired glucose tolerance was defined as a plasma glucose concentration of 140 to 200 mg per deciliter (7.8 to 11.0 mmol per liter) two hours after the oral administration of 75 g of glucose in subjects whose plasma glucose concentration after an overnight fast was less than 140 mg per deciliter.¹⁴ The test was repeated in subjects in whom the first result was abnormal, and the mean of the two values was used to determine eligibility. Criteria for exclusion were a diagnosis of diabetes mellitus, the presence of chronic disease rendering survival for six years unlikely, and other characteristics (psychological or physical disabilities) deemed likely to interfere with participation in the study.

Subjects who enrolled in the study were randomly assigned to the intervention group or the control group by the study physician, with the use of a randomization list, with stratification according to center, sex, and the mean plasma glucose concentration two hours after oral glucose challenge (140 to 169 mg per deciliter or 170 to 200 mg per deciliter [7.8 to 9.4 mmol per liter or 9.5 to 11.0 mmol per liter]). The nurses who scheduled the study visits did not have access to the randomization list. However, the staff members involved in the intervention had to be aware of the group assignment; thus, the study was only partly blinded. Laboratory staff did not know the subjects' group assignments, and the subjects were not informed of their plasma glucose concentrations during follow-up unless diabetes was diagnosed.

A total of 523 subjects in five study centers were randomly assigned to one of the two treatment groups. The end-points committee excluded one subject who had diabetes at base line whose diagnosis of diabetes was confirmed at her two-year visit. The subjects in the control group were given general oral and written information about diet (a two-page leaflet) and exercise at base line and at subsequent annual visits, but no specific individualized programs were offered to them. They completed a three-day food diary at base line and at each annual visit, using a booklet illustrating the sizes of portions of food.¹⁵ Nutrient intakes were computed with the use of a program developed at the National Public Health Institute.¹⁶

The subjects in the intervention group were given detailed advice about how to achieve the goals of the intervention, which were a reduction in weight of 5 percent or more, in total intake of fat to less than 30 percent of energy consumed, and in intake of saturated fat to less than 10 percent of energy consumed; an increase in fiber intake to at least 15 g per 1000 kcal; and moderate exercise for at least 30 minutes per day. Frequent ingestion of whole-grain products, vegetables, fruits, low-fat milk and meat products, soft margarine, and vegetable oils rich in monounsaturated fatty acids was recommended. The dietary advice was tailored to each subject on the basis of three-day food records completed four times per year. Each subject in the intervention group had seven sessions with a nutritionist during the first year of the study and one session every

three months thereafter. These subjects also received individual guidance on increasing their level of physical activity. Endurance exercise (such as walking, jogging, swimming, aerobic ball games, or skiing) was recommended as a way to increase aerobic capacity and improve cardiorespiratory fitness. Supervised, progressive, individually tailored, circuit-type resistance-training sessions were also offered with the aim of improving the functional capacity and strength of the large muscle groups; subjects were instructed to perform a moderate to high number of repetitions and to take a break of 15 to 60 seconds between the stations on the circuit. During the first year, the rate of participation in these sessions varied from 50 percent to 85 percent at different centers.

If, at an annual visit, the study physician discovered a clinical condition that required attention, such as a high serum cholesterol concentration or hypertension, the subject was advised to contact his or her own physician for treatment and follow-up.

Clinical Studies

At base line and at each annual visit, all study subjects completed a medical-history questionnaire and underwent a physical examination that included anthropometric and blood-pressure measurements and an oral glucose-tolerance test, as described elsewhere.¹³

Biochemical Assessments

Plasma glucose was measured at each center by means of standard methods. The glucose measurements were standardized by the central laboratory in Helsinki, whose staff analyzed 60 to 80 plasma samples from each center in duplicate. A linear-regression equation was calculated for each center, with the use of the plasma glucose measurement determined at the Helsinki laboratory as the standard. These equations were used to correct the locally measured plasma glucose values. The result of the second oral glucose-tolerance test was considered the base-line value for comparison with values obtained later; in some subjects whose entry into the study was delayed, a third oral glucose-tolerance test was performed whose result was considered the base-line value. The serum insulin concentration was measured by a radioimmunoassay (Pharmacia, Uppsala, Sweden), and serum levels of total cholesterol, high-density lipoprotein cholesterol, and triglycerides were measured by enzymatic assay in the central laboratory in Helsinki.

Assessment of the End Points

Diabetes was defined according to the 1985 criteria of the World Health Organization¹⁴ as either a fasting plasma glucose concentration of 140 mg per deciliter or higher or a plasma glucose concentration of 200 mg per deciliter or higher two hours after an oral glucose challenge. We required confirmation of the diagnosis of diabetes by a second oral glucose-tolerance test; if the diagnosis was not confirmed by the second test, the subject followed the program according to the original random assignment. The diagnosis of diabetes was based on the locally measured plasma glucose values, since these were used for the inclusion of subjects in the study. In the statistical analysis, corrected plasma glucose values were used. The independent end-points committee confirmed all newly diagnosed cases of diabetes. The study centers did not exchange information concerning the number of subjects who reached the end point, and the end-point data were linked to the group assignment at the study center only after a total of 80 subjects had reached the end point, as stated in the study plan.

Statistical Analysis

In March 2000, an independent statistician completed the first analysis of data, which included all cases of diabetes diagnosed before that date. On the basis of the results of this analysis, the end-points committee recommended that the trial be ended.

Two-sided t-tests and chi-square tests were used to analyze the differences between the groups at base line and during follow-up. Survival curves were calculated to estimate the cumulative incidence of diabetes. The difference between the groups in the incidence of

diabetes was tested by means of the two-sided log-rank test. All analyses of end points were based on the intention-to-treat principle. The SAS PHREG procedure was used to derive the basic estimates, such as the survival functions and the 95 percent confidence limits of the estimates (SAS/STAT software, version 6.12, SAS Institute, Cary, N.C.). Subjects who withdrew from the study were considered to be at risk for diabetes until their last oral glucose-tolerance test, at which point data were censored. To estimate the extent of the dependence of the incidence of diabetes on the changes in lifestyle that were achieved, subjects were given a grade for each goal of the intervention at the one-year visit (with 0 indicating that it was not achieved or 1 indicating that it was achieved), and a success score was computed as the sum of these grades. For each subgroup defined according to success score, the proportion of subjects in whom diabetes had developed was calculated. To test for a statistical association between this proportion and the success score, logistic-regression analysis was performed with the use of the SAS GENMOD procedure. The expected proportion was modeled as a linear function of the success score.

RESULTS

The first subject was assigned to a group in November 1993 and the last in June 1998. At that time, 90 percent of the study subjects had been enrolled in the trial for at least 2 years, and the mean duration of follow-up was 3.2 years. The base-line characteristics of the two groups were similar (Table 1). During the first year, the mean (\pm SD) body weight decreased by 4.2 ± 5.1 kg (4.7 ± 5.4 percent) in the intervention group and by 0.8 ± 3.7 kg (0.9 ± 4.2 percent) in the control group ($P < 0.001$) (Table 2). Waist circumference, the fasting plasma glucose concentration, the plasma glucose concentration two hours after oral glucose challenge, and the serum insulin concentration two hours after glucose challenge decreased significantly more among subjects in the intervention group than among those in the control group. At two years, the decrease in weight remained significantly greater in the intervention group (3.5 ± 5.5 kg) than in the control group (0.8 ± 4.4 kg) ($P < 0.001$). At this time, the mean change from base line in the fasting plasma glucose concentration was -2 ± 12 mg per deciliter (-0.1 ± 0.7 mmol per liter) in the intervention group and $+3 \pm 14$ mg per deciliter ($+0.2 \pm 0.8$ mmol per liter) in the control group ($P < 0.001$); the change in the plasma glucose concentrations measured two hours after oral glucose challenge was -14 ± 37 mg per deciliter (-0.8 ± 2.1 mmol per liter) in the intervention group and $+0 \pm 44$ mg per deciliter ($+0 \pm 2.5$ mmol per liter) in the control group ($P < 0.001$). There were also significantly greater decreases in the intervention group than in the control group in the serum insulin concentration two hours after oral glucose challenge, as well as in the triglyceride concentration and blood pressure (data not shown).

The study subjects were asked about their health-related behavior at base line and subsequently at each annual follow-up examination (Table 3). The subjects in the intervention group were more likely to report changes in dietary and exercise habits. Success in achieving the goals of the intervention was estimat-

TABLE 1. BASE-LINE CHARACTERISTICS OF THE SUBJECTS IN THE INTERVENTION AND CONTROL GROUPS.*

CHARACTERISTIC	INTERVENTION GROUP (N=265)	CONTROL GROUP (N=257)
Sex (no.)		
Male	91	81
Female	174	176
Age (yr)	55 ± 7	55 ± 7
Body-mass index	31.3 ± 4.6	31.0 ± 4.5
Waist circumference (cm)	102.0 ± 11.0	100.5 ± 10.9
Hip circumference (cm)	110.4 ± 10.5	109.4 ± 9.7
Plasma glucose (mg/dl)		
Fasting	109 ± 14	110 ± 13
2 Hr after oral glucose challenge	159 ± 27	159 ± 26
Serum insulin (μ U/ml)		
Fasting	15 ± 7	15 ± 8
2 Hr after oral glucose challenge	98 ± 74	93 ± 54
Serum lipids (mg/dl)†		
Total cholesterol	215 ± 37	215 ± 35
High-density lipoprotein cholesterol	46 ± 12	47 ± 11
Triglycerides	154 ± 72	158 ± 69
Blood pressure (mm Hg)‡		
Systolic	140 ± 18	136 ± 17 §
Diastolic	86 ± 9	86 ± 10

*Plus-minus values are means \pm SD. To convert values for glucose to millimoles per liter, multiply by 0.056. To convert values for insulin to picomoles per liter, multiply by 6. To convert values for cholesterol to millimoles per liter, multiply by 0.026. To convert values for triglycerides to millimoles per liter, multiply by 0.011.

†Cholesterol-lowering drugs were being taken by 5 percent of the subjects in the intervention group and 6 percent of the subjects in the control group at base line.

‡Antihypertensive drugs were being taken by 30 percent of the subjects in the intervention group and 31 percent of the subjects in the control group at base line.

§ $P = 0.03$ for the comparison with the intervention group by two-tailed t-test.

ed on the basis of the food records and exercise questionnaires collected at the one-year examination (Table 4). The proportion of subjects in the intervention group who succeeded in achieving a particular goal varied from 25 percent (fiber intake) to 86 percent (exercise).

Diabetes was diagnosed in a total of 86 subjects — 27 in the intervention group and 59 in the control group. The average proportion of subjects in whom impaired glucose tolerance progressed to diabetes was 3 percent per year in the intervention group and 6 percent per year in the control group. The absolute incidence of diabetes was 32 cases per 1000 person-years in the intervention group and 78 per 1000 person-years in the control group.

The cumulative incidence of diabetes was lower in the intervention group than in the control group (Fig. 1). The difference was statistically significant after two years: 6 percent in the intervention group (95 per-

TABLE 2. CHANGES IN SELECTED CLINICAL AND METABOLIC VARIABLES FROM BASE-LINE TO THE END OF YEAR 1 IN THE SUBJECTS IN THE INTERVENTION AND CONTROL GROUPS.*

VARIABLE	INTERVENTION GROUP (N=256)		CONTROL GROUP (N=250)		P VALUE†
	mean ±SD	95% CI	mean ±SD	95% CI	
Change in weight					
In kilograms	-4.2±5.1	-4.8 to -3.6	-0.8±3.7	-1.3 to -0.3	<0.001
Percent change	-4.7±5.4	-5.0 to -4.4	-0.9±4.2	-1.0 to -0.8	<0.001
Change in waist circumference (cm)	-4.4±5.2	-5.1 to -3.9	-1.3±4.8	-1.9 to -0.7	<0.001
Change in plasma glucose (mg/dl)					
Fasting	-4±12	-6 to -2	1±12	0 to 2	<0.001
2 Hr after oral glucose challenge	-15±34	-19 to -11	-5±40	-8 to -2	0.003
Change in serum insulin (μg/ml)					
Fasting	-2±9	-3 to -1	-1±7	-2 to 0	0.14
2 Hr after oral glucose challenge	-29±64	-37 to -21	-11±51	-18 to -4	0.001
Change in serum lipids (mg/dl)‡					
Total cholesterol	-5±28	-8 to -2	-4±28	-7 to -1	0.62
High-density lipoprotein cholesterol	2±7	1 to 3	1±6	0 to 2	0.06
Triglycerides	-18±51	-24 to -12	-1±60	-8 to 6	0.001
Change in blood pressure (mm Hg)§					
Systolic	-5±14	-7 to -3	-1±15	-3 to 1	0.007
Diastolic	-5±9	-6 to -4	-3±9	-4 to -2	0.02

*A total of 15 subjects withdrew from the study within the first year; 1 additional subject did not undergo testing at one year, although she remained in the study. To convert values for glucose to millimoles per liter, multiply by 0.056. To convert values for insulin to picomoles per liter, multiply by 6. To convert values for cholesterol to millimoles per liter, multiply by 0.026. To convert values for triglycerides to millimoles per liter, multiply by 0.011. CI denotes confidence interval.

†P values were determined by a two-tailed t-test for the difference between the groups.

‡Cholesterol-lowering drugs were being taken by 6 percent of the subjects in the intervention group and 8 percent of those in the control group by the end of year 1.

§Antihypertensive drugs were being taken by 30 percent of the subjects in the intervention group and 31 percent of those in the control group by the end of year 1.

TABLE 3. SELF-REPORTED CHANGE IN DIETARY AND EXERCISE HABITS DURING THE FIRST YEAR OF THE INTERVENTION, ACCORDING TO TREATMENT GROUP.*

VARIABLE	INTERVENTION GROUP (N=253)	CONTROL GROUP (N=247)	P VALUE†
	% of subjects		
Decreased consumption of fat	87	70	0.001
Changed the quality of fat	70	39	0.001
Increased consumption of vegetables	72	62	0.01
Decreased consumption of sugar	55	40	0.001
Decreased consumption of salt	59	50	0.03
Decreased consumption of alcohol	26	23	0.43
Increased exercise‡	36	16	0.001

*Seven subjects of 507 who remained in the study at one year had some missing data and are not included in this table.

†P values were determined by the chi-square test for the difference between the groups.

‡Subjects reported the frequency of exercise in terms of a shift to a higher category of the following four categories: (1) "I read, watch television, and work in the household at tasks that don't strain me physically"; (2) "I walk, cycle, or exercise lightly in other ways at least four hours per week"; (3) "I exercise to maintain my physical condition by running, jogging, skiing, doing gymnastics, swimming, playing ball games, etc., for at least 3 hours per week"; or (4) "I exercise competitively several times a week by running, orienteering, skiing, playing ball games, or engaging in other sports involving heavy exertion."

cent confidence interval, 3 to 9 percent) and 14 percent in the control group (95 percent confidence interval, 10 to 19 percent). At four years, the cumulative incidence was 11 percent (95 percent confidence interval, 6 to 15 percent) in the intervention group and 23 percent (95 percent confidence interval, 17 to 29 percent) in the control group. According to the Cox regression analysis of all person-years accumulated, the cumulative incidence of diabetes was 58 percent lower in the intervention group than in the control group (hazard ratio, 0.4; 95 percent confidence interval, 0.3 to 0.7; $P<0.001$). The incidence of diabetes was 63 percent lower among men in the intervention group (95 percent confidence interval, 18 to 79 percent; $P=0.01$) and 54 percent lower among women (95 percent confidence interval, 26 to 81 percent; $P=0.008$).

The study subjects were ranked according to their success in achieving the goals of the intervention (and given a success score between 0 and 5) at the one-year examination, with higher scores indicating more goals met (Fig. 2). There was a strong inverse correlation between the success score and the incidence of diabetes. Thirteen subjects in the intervention group and 48 subjects in the control group did not achieve any of the goals; diabetes developed in 38 percent and 31

TABLE 4. SUCCESS IN ACHIEVING THE GOALS OF THE INTERVENTION BY ONE YEAR, ACCORDING TO TREATMENT GROUP.*

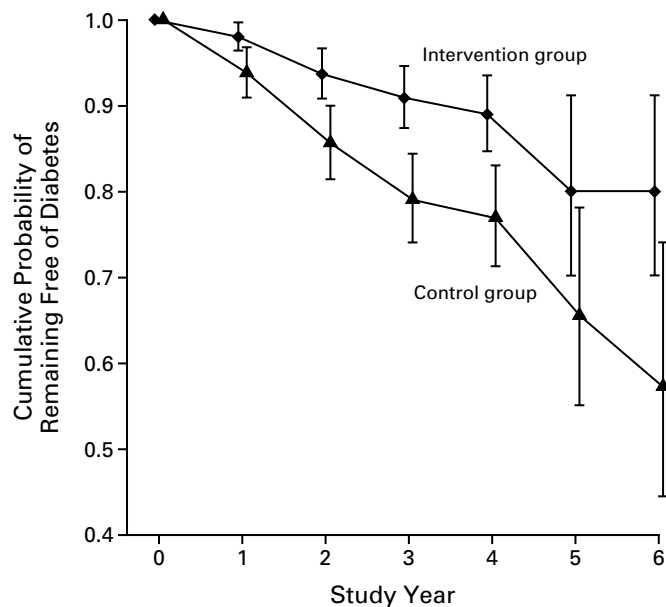
GOAL	INTERVENTION GROUP	CONTROL GROUP	P VALUE†
	% of subjects		
Weight reduction >5%	43	13	0.001
Fat intake <30% of energy intake	47	26	0.001
Saturated-fat intake <10% of energy intake	26	11	0.001
Fiber intake ≥15 g/1000 kcal	25	12	0.001
Exercise >4 hr/wk‡	86	71	0.001

*Nutrient intakes were calculated from three-day food records.

†P values were determined by the chi-square test for the difference between the groups.

‡Exercise frequency was reported by the subjects who chose one of the four categories described in Table 3. The goal identified here was a frequency in category 2 or higher.

percent of these subjects, respectively, during follow-up. Diabetes had not developed in any of the subjects who reached four or five of the goals (49 subjects in the intervention group and 15 in the control group). According to a univariate analysis, the odds ratio for diabetes in subjects in the intervention group who had lost more than 5 percent of their initial weight by the one-year follow-up visit was 0.3 (95 percent confidence interval, 0.1 to 0.7) as compared with those in the intervention group who had lost less weight or none at all; the corresponding odds ratio in the control group was 0.4 (95 percent confidence interval, 0.1 to 1.2). Among the subjects in the intervention group who did not reach the goal of losing 5 percent of their initial weight, the odds ratio for diabetes in those who had achieved the goal with respect to exercise (more than four hours per week) during the first year was 0.2 (95 percent confidence interval, 0.1 to 0.6) as compared with those in the intervention group who maintained a sedentary lifestyle; the corresponding odds ratio in the control group was 0.6 (95 percent confidence interval, 0.3 to 1.1). After adjustment



SUBJECTS AT RISK

Total no.	507	471	374	167	53	27
Cumulative no. with diabetes:						
Intervention group	5	15	22	24	27	27
Control group	16	37	51	53	57	59

Figure 1. Proportion of Subjects without Diabetes during the Trial.

The vertical bars show the 95 percent confidence intervals for the cumulative probability of remaining free of diabetes. The relative risk of diabetes for subjects in the intervention group, as compared with those in the control group, was 0.4 ($P < 0.001$ for the comparison between the groups).

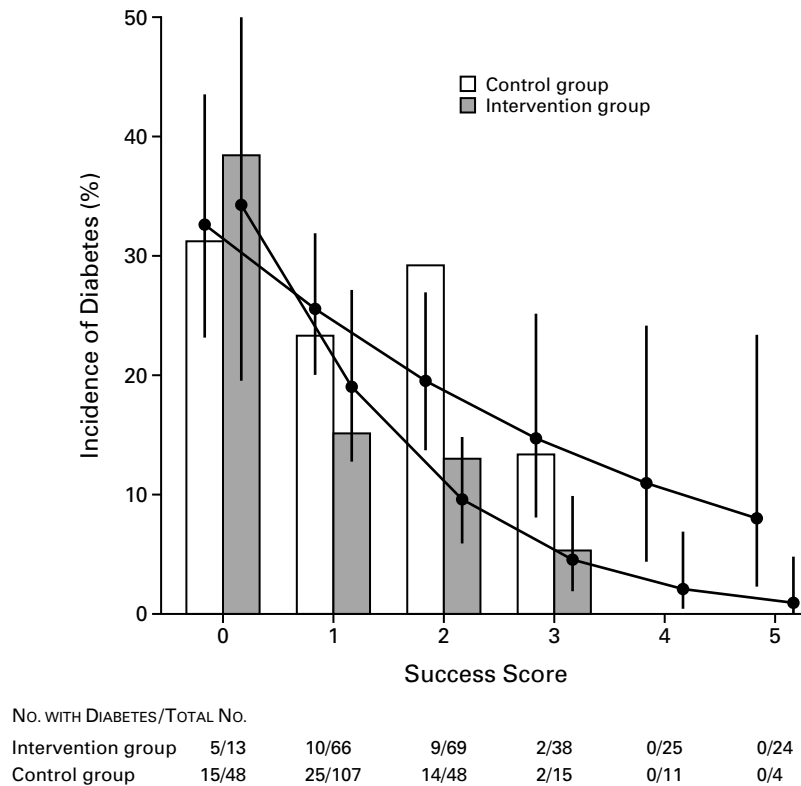


Figure 2. Incidence of Diabetes during Follow-up, According to the Success Score.

At the one-year visit, each subject received a grade of 0 for each intervention goal that had not been achieved and a grade of 1 for each goal that had been achieved; the success score was computed as the sum of the grades. Forty subjects who withdrew from the study when their diabetes status was unknown and 14 subjects with incomplete data were excluded from this analysis. The association between the success score and the risk of diabetes, with 95 percent confidence intervals, was estimated by means of logistic-regression analysis of the observed data. The curves show the model-based incidence of diabetes according to the success score as a continuous variable; the curve whose data points align with the open bars represents the model-based incidence for the control group, and the curve whose data points align with the shaded bars represents the model-based incidence for the intervention group.

for base-line body-mass index, the odds ratio for diabetes in those in the intervention group who had achieved the exercise goal was still statistically significant (odds ratio, 0.3; 95 percent confidence interval, 0.1 to 0.7).

During the study, 40 subjects (8 percent) withdrew — 23 in the intervention group and 17 in the control group. Of these subjects, 9 could not be contacted, 3 withdrew due to severe illness, 1 died, and 27 withdrew for personal reasons.

DISCUSSION

This study provides evidence that type 2 diabetes can be prevented by changes in the lifestyles of both women and men at high risk for the disease. The overall incidence of diabetes was reduced by 58 percent. Our estimate of the effect of the intervention can be considered conservative for two reasons. First, the data

were analyzed according to the intention-to-treat principle, even though some subjects in the intervention group did not follow the recommendations about diet and exercise. Second, for ethical reasons, all subjects assigned to the control group also received general health advice at base line and at annual follow-up visits and may have benefited from this advice.

The results from previous studies in Sweden¹⁷ and China¹⁸ also provide evidence that changes in lifestyle are effective in preventing diabetes, and the magnitude of the benefit in these studies was similar to that in our study. In those two studies, the subjects were not randomly assigned to the intervention and control groups. The randomization in our study was stratified according to clinic, sex, and base-line plasma glucose concentration two hours after oral glucose challenge in order to obtain the best possible comparability between groups. In the Chinese study,¹⁸ an attempt to

determine whether a change in diet or a change in exercise habits was more effective found no difference in outcome between the two interventions. We did not try to separate these changes but, rather, tried to achieve changes in lifestyle that were as extensive as possible for each subject.

The effect of the interventions was assessed after one year because earlier assessment may be biased as a result of changes made only because subjects are conscious of being studied. The effect of the intervention on the incidence of diabetes was most pronounced among subjects who made comprehensive changes in lifestyle; on the other hand, the failure to make any changes resulted in an incidence of diabetes that was close to the estimate of 35 percent for this high-risk population. The average amount of weight lost was not large, yet the difference between the incidence of diabetes in the intervention group and that in the control group was substantial. The low odds ratio for diabetes among those who lost at least 5 percent of their initial weight reveals the importance of even a relatively small reduction in weight in the prevention of diabetes.

Our counseling regarding physical exercise included components designed to improve both cardiorespiratory fitness and muscle strength. Achieving a relatively conservative target of more than four hours of exercise per week was associated with a significant reduction in the risk of diabetes in the subjects who did not lose weight. It is likely that any type of physical activity — whether sports, household work, gardening, or work-related physical activity — is similarly beneficial in preventing diabetes. Many subjects with impaired glucose tolerance are both obese and inactive, and therefore we would expect to find a dose–response relation between the correction of these multiple risk factors and reductions in the risk of diabetes.

The main justification for the type of intervention used in the high-risk subjects in this study is that it may prevent or postpone the onset of type 2 diabetes and the complications related to the disease. Patients with diabetes — with or without symptoms — have an increased prevalence of both macrovascular and microvascular complications at the time when diabetes is diagnosed. Many also have hypertension and an atherogenic serum lipid profile.^{19–22} The changes in lifestyle in our study not only improved glucose tolerance but also reduced the magnitude of several other cardiovascular risk factors.¹³ It is commonly argued that it is difficult to change the lifestyle of obese and sedentary people, but such pessimism may not be justified. The reasonably low dropout rate in our study also indicates that subjects with impaired glucose tolerance are willing and able to participate in a demanding intervention program if it is made available to them.

It is possible to achieve primary prevention of

type 2 diabetes by means of a nonpharmacologic intervention that can be implemented in a primary health care setting. According to our results, 22 subjects with impaired glucose tolerance must be treated in this way for one year — or 5 subjects for five years — to prevent one case of diabetes.

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