Effects of Diet and Exercise in Preventing NIDDM in People With Impaired Glucose Tolerance

The Da Qing IGT and Diabetes Study

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OBJECTIVE — Individuals with impaired glucose tolerance (IGT) have a high risk of developing NIDDM. The purpose of this study was to determine whether diet and exercise interventions in those with IGT may delay the development of NIDDM, i.e., reduce the incidence of NIDDM, and thereby reduce the overall incidence of diabetic complications, such as cardiovascular, renal, and retinal disease, and the excess mortality attributable to these complications.

RESEARCH DESIGN AND METHODS — In 1986, 110,660 men and women from 33 health care clinics in the city of Da Qing, China, were screened for IGT and NIDDM. Of these individuals, 577 were classified (using World Health Organization criteria) as having IGT. Subjects were randomized by clinic into a clinical trial, either to a control group or to one of three active treatment groups: diet only, exercise only, or diet plus exercise. Follow-up evaluation examinations were conducted at 2-year intervals over a 6-year period to identify subjects who developed NIDDM. Cox's proportional hazard analysis was used to determine if the incidence of NIDDM varied by treatment assignment.

RESULTS — The cumulative incidence of diabetes at 6 years was 67.7% (95% CI, 59.8–75.2) in the control group compared with 43.8% (95% CI, 35.5–52.3) in the diet group, 41.1% (95% CI, 33.4–49.4) in the exercise group, and 46.0% (95% CI, 37.3–54.7) in the diet-plus-exercise group ($P < 0.05$). When analyzed by clinic, each of the active intervention groups differed significantly from the control clinics ($P < 0.05$). The relative decrease in rate of development of diabetes in the active treatment groups was similar when subjects were stratified as lean or overweight (BMI $<$ or $\geq$25 kg/m^2). In a proportional hazards analysis adjusted for differences in baseline BMI and fasting glucose, the diet, exercise, and diet-plus-exercise interventions were associated with 31% ($P < 0.03$), 46% ($P < 0.0005$), and 42% ($P < 0.005$) reductions in risk of developing diabetes, respectively.

CONCLUSIONS — Diet and/or exercise interventions led to a significant decrease in the incidence of diabetes over a 6-year period among those with IGT.

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ANOVA, analysis of variance; IGT, impaired glucose tolerance; WHO, World Health Organization.

Diabetes and its complications are major and increasing health problems in many parts of the world. The most frequent form, NIDDM, leads to vascular complications that give rise to considerable morbidity and premature mortality. Impaired glucose tolerance (IGT), a lesser degree of hyperglycemia, represents an intermediate stage in the development of NIDDM that is associated with a high risk of developing NIDDM (1–3). One- to three-quarters of those with IGT develop diabetes within a decade of discovery of IGT (4), and annual progression rates from IGT to diabetes range from 1 to 10% (5–11). Thus, if progression could be slowed, the incidence of diabetes would be reduced and the onset of its complications prevented or delayed. Risk factors known to influence the rate of progression from IGT to diabetes include age, obesity, hyperinsulinemia, and insulin resistance (4,12).

The effect of interventions on the progression from IGT to diabetes has been examined in a few studies. In two small English studies (5,7), no measurable effect of either diet or oral antidiabetic agents was found on the incidence of subsequent diabetes, whereas in the Malmöhus Study in Sweden (6), subjects with IGT who received oral tolbutamide over a 10-year period had a lower incidence of diabetes. In another Swedish study, the Malmö Study, in which treatment was not randomized, adherence to a diet/exercise program for 5 years reduced the incidence of diabetes (14).

In 1986, 577 people with IGT, identified during a population-based survey of diabetes and IGT in Da Qing, China, agreed to participate in a randomized controlled trial to evaluate the effects of diet and/or exercise interventions on the incidence of diabetes (15). This report presents the results of this trial over a 6-year follow-up period.

RESEARCH DESIGN AND METHODS

— The trial was designed as a controlled clinical trial in which subjects were randomized by clinic to investigate the

Table 1—*Activities required for one unit of exercise*

Intensity	Time (min)	Exercise
Mild	30	Slow walking, traveling by bus, shopping, housecleaning
Moderate	20	Faster walking or walking down stairs, cycling, doing heavy laundry, ballroom dancing (slow)
Strenuous	10	Slow running, climbing stairs, disco dancing for the elderly, playing volleyball or table tennis
Very strenuous	5	Jumping rope, Playing basketball, swimming

effects of dietary and exercise intervention separately, and in combination, on the incidence of diabetes in people with IGT.

Eligibility and exclusion criteria

Da Qing is an industrial city, primarily concerned with oil exploration and production, in the Hei Long Jiang province in the northern part of China. In 1986, the population of Da Qing included 281,589 people over the age of 25, all of whom received health care in designated clinics located throughout the city. Half of these clinics, which served 126,715 people over the age of 25, were selected to participate in a screening study. Between June and December 1986, most (87.3%) of the target population (110,660 total: 55,391 men and 55,269 women) underwent screening at nearby hospitals. The screening consisted of measurement of plasma glucose concentration 2 h (± 5 min) after a standard breakfast, followed by a 75-g oral glucose tolerance test in those who screened positive (15). Details of the study population and validation of the screening procedures have been described previously (15). From the initial screening study, 577 people who met World Health Organization (WHO) criteria for IGT agreed to participate in the intervention study described below. Of these, 530 subjects were followed systematically until endpoints had been reached or for a 6-year period. Most of the 47 lost to follow-up were lost because of migration from the region (see below). Enrollment and treatment of subjects were conducted in accordance with the Helsinki Declaration.

Randomization and baseline measures

Intervention was provided by 33 local health clinics associated with the oil factory communities that are dispersed throughout the city. The number of subjects attending each of these clinics ranged from 5 to 33. Each clinic, rather than each subject, was randomized to carry out the intervention on each of the eligible subjects attending that clinic according to one of the four specified intervention protocols. Study participants in each clinic were categorized according to BMI, with 208 individuals categorized as lean (BMI <25 kg/m^2) and 322 as overweight (BMI ≥ 25 kg/m^2).

A baseline examination was conducted on each participant after a 10- to 12-h overnight fast as described previously (15). Briefly, blood pressure, height, and weight were measured in light clothing without shoes following methods used in the WHO multinational study of vascular disease in diabetes (17). After a fasting blood sample was taken, each subject ingested 75 g of glucose monohydrate dissolved in 300 ml water within a 2-min period. Plasma glucose and lipids were measured in the fasting sample, and glucose was measured in the samples obtained at 60 and 120 min after the glucose load. A urine sample was collected over the 2-h time period of the glucose tolerance test to quantify urinary glucose and albumin excretion. Past medical history and family history of diabetes were assessed by questionnaire. The oral glucose tolerance test was repeated in each subject during systematic evaluation examinations conducted at ~2-year intervals.

Food intake and physical activity were quantified at baseline and at each evaluation examination using standardized forms and interviews. For dietary intake, quantity per day for the past 3 days was ascertained for major food/beverage items, such as pork, beef, shrimp, fowl, eggs, milk, bean curd, bean and pork oils, peanuts, sunflower seeds, fruits, vegetables, wine, and beer. These were converted to major food constituents using a food nutrition database (Database of Nutrition for the Peoples Republic of China version 1.0, 1993). Physical activity was assessed in a standardized way. For occupational activity, the kind of activity and its frequency, as well as the mode and duration of transportation to and from work were assessed. Leisure physical activity was ascertained in minutes per day for major activities, such as walking, running, cycling, ball playing, aerobics, dancing, gardening, and swimming. Activity was ascertained for the previous week and converted to units per day as shown in Table 1.

Interventions

Diet group. In clinics assigned to the diet-only intervention, participants with BMI <25 kg/m^2 were prescribed a diet containing 25–30 kcal/kg body wt (105–126 kJ/kg), 55–65% carbohydrate, 10–15% protein, and 25–30% fat. These participants were encouraged to consume more vegetables, control their intake of alcohol, and reduce their intake of simple sugars. Subjects with BMI ≥ 25 kg/m^2 were encouraged to reduce their calorie intake so as to gradually lose weight at a rate of 0.5–1.0 kg per month until they achieved a BMI of 23 kg/m^2. Individual goals were set for total calorie consumption and for daily quantities of cereals, vegetables, meat, milk, and oils. This was accomplished by providing a list to each individual of the recommended daily intake of commonly used foods and a substitution list to allow exchange within food groups. Patients received individual counseling by physicians concerning daily food intake. In addition, counseling sessions (in small groups) were conducted weekly for 1 month, monthly for 3 months, and then once every 3 months for the remainder of the study.

Exercise group. Participants in clinics assigned to the exercise group were taught and encouraged to increase the amount of their leisure physical exercise by at least 1 U/day (as defined in Table 1) and by 2 U/day if possible for those <50 years of age with no evidence of cardiovascular disease or arthritis. As in the diet group, counseling sessions were conducted weekly for 1 month, monthly for 3 months, and then once every 3 months for the remainder of the study. The rate of increase and type of exercise recommended depended on age, past exercise patterns, and the existence of health problems other than IGT. Appropriate indoor activities were suggested for winter. Exercise units were computed as described in Table 1.

Diet-plus-exercise group. Participants from clinics assigned to this group received instructions and counseling for both diet

and exercise interventions that were similar to those for the diet-only and the exercise-only intervention groups.

Control group. Subjects from clinics assigned to the control group were exposed to general information about diabetes and IGT. Clinic physicians also dispensed informational brochures with general instructions for diet and/or increased leisure physical activities to control group subjects, but no individual instruction or formal group counseling sessions were conducted.

Training. All local physicians, nurses, and technicians involved in the study attended a 2-day training session each year in which they received standardized instruction on the diet and exercise interventions and procedures for the examination. The Da Qing Study Steering Committee provided educational materials on diabetes and IGT via videotapes and brochures. Members of the Steering Committee also talked to the groups to supplement the education classes on diet and/or exercise for the appropriate groups in 1986 and again in 1988.

Follow-up procedures

Systematic evaluation examinations were carried out in 1988, 1990, and 1992. In these examinations, variables, such as blood pressure, weight, skinfold measurements, and diet and physical activity (as used at baseline), were remeasured as described below. All participants were seen at 3-month intervals by local physicians. The general health of each participant was assessed by the physician, and compliance with the intervention regimen was discussed with the nurses and clinic staff. Physicians repeated their counseling and instructions concerning diet and exercise. At each 3-month follow-up visit, weight and blood pressure were measured and urine glucose was assessed using a dipstick. Plasma glucose was measured 2 h after a standard breakfast (100 g steamed bread) if the urinary glucose was positive. If the postmeal plasma glucose concentration was ≥200 mg/dl (11.1 mmol/l), or if the local physician suspected that the subject had developed diabetes, the subject received a 75-g oral glucose tolerance test at the city hospital or, occasionally, at a district hospital. If, at any time during the course of the study, a participant exhibited symptoms of diabetes and repeated fasting plasma glucose measurements were ≥140 mg/dl (7.8 mmol/l) or a casual glucose measurement was ≥200 mg/dl (11.1 mmol/l), a clinical diagnosis of diabetes was made. A standard oral glucose tolerance test was performed on these individuals. If the subject met WHO criteria for diabetes on the basis of these tests, his or her formal participation in the study ended. All decisions concerning whether or not participants had reached endpoints based on the 3-month follow-up examinations were made by the vice chairman of the Study Steering Committee.

Outcome assessment

At 2-year intervals (1988, 1990, and 1992), a systematic evaluation examination of each participant, including those diagnosed at the 3-month follow-up examinations, was performed using methods similar to those of the baseline examination. Physicians from the China-Japan Friendship Hospital in Beijing recorded diet and exercise changes and provided individual advice on intervention adherence. Height, weight, and blood pressure were measured and fasting 2-h plasma glucose was determined after a 75-g oral glucose load. If fasting plasma glucose was ≤140 mg/dl (7.8 mmol/l) and 2-h glucose was ≤200 mg/dl (7.8–11.0 mmol/l), then the assigned treatment regimens were continued. If the results were indicative of diabetes (fasting glucose ≥140 mg/dl [7.8 mmol/l] or 2-h glucose ≥200 mg/dl [11.1 mmol/l]), then the oral glucose tolerance test was repeated after 7–14 days. If the repeat results were normal or in the range of IGT, then the assigned treatment regimen was resumed. If the diagnosis of diabetes was confirmed, the subjects were considered to have reached an endpoint and were referred to receive standard diabetes treatment.

Of the 263 diabetes diagnoses made during the 6 years, 55 (21%) were made initially by the local physicians and confirmed at the city hospital by glucose tolerance test; 208 (79%) were made as a result of the systematic oral glucose tolerance tests performed in 1988, 1990, and 1992. Those who left in 1988 very early in the study and before the first follow-up for reasons unrelated to their randomization group were not included in the analysis. The 11 who died were retained, although none had developed diabetes before death.

Statistical analysis

The cumulative number of subjects who had developed diabetes in each treatment group was determined after conducting the 6-year evaluation examination. Because the randomization was performed at the clinic, rather than at the individual subject level, data were analyzed in each treatment group by comparing the incidence of diabetes in the clinics assigned to each of the treatments. The Ryan-Einot-Gabriel-Welsch multiple F test was used to compare the clinic groups. We also analyzed the data as if individuals had been assigned to specific treatment groups, including clinic as a covariate in the analyses. Multivariate analysis was performed using Cox's proportional hazards analysis taking into account the time to diagnosis. The proportional hazard model was used because a number of individuals (21%) were diagnosed at intermediate points and because the characteristics of the outcome evaluation conform more to the assumptions of the Cox's model than to multiple logistic regression, which might have been more appropriate if there were only a 6-year fixed follow-up. A backwards stepwise procedure was used to identify possible covariates. The level of significance was taken as $P < 0.05$. Interaction terms for glucose * obesity and diet * exercise were included in the model. A subgroup analysis was performed stratifying individuals by BMI. For analysis of data on exercise and diet, groups were compared using analysis of variance (ANOVA).

RESULTS

Incidence of diabetes

Baseline and 6-year follow-up characteristics for the four study groups are summarized in Table 2. Of the 577 subjects with IGT who were randomized, 530 completed the study. Of the remainder, 7 people refused follow-up, 29 left Da Qing in 1988 (mostly because of the establishment of a new oil field elsewhere), and 11 died during the course of the study. No deaths occurred in the exercise-only group. Three deaths occurred in the control group (one pneumonia, two cirrhosis), three in the diet group (two cancer, one septicemia), and five in the diet-plus-exercise group (one stroke, two cancer, one accidental, one Crohn's disease). None of these 11 people were known to have developed diabetes before death. There were no significant differences in baseline values among the four groups.

The mean for 6-year diabetes incidence in each of the clinics was calculated according to the treatment group assigned to that clinic (Table 3, Fig. 1). When the means of diabetes incidence in each clinic by treatment group were compared, there was a

Table 2—*Characteristics of participants at the baseline and 6-year evaluation examinations by intervention group*

	Control	Diet	Exercise	Diet + exercise	Total
n	133	130	141	126	530
Baseline characteristics					
Age (years)	46.5 ± 9.3	44.7 ± 9.4	44.2 ± 8.7	44.4 ± 9.2	45.0 ± 9.1
Sex (M/F)	73/60	59/71	81/60	70/56	283/247
BMI (kg/m²)	26.2 ± 3.9	25.3 ± 3.8	25.4 ± 3.7	26.3 ± 3.9	25.8 ± 3.8
Fasting plasma glucose (mmol/l)	5.52 ± 0.82	5.56 ± 0.81	5.56 ± 0.83	5.67 ± 0.80	5.59 ± 0.81
2-h fasting glucose (mmol/l)	9.03 ± 0.89	9.03 ± 0.94	8.83 ± 0.79	9.11 ± 0.93	9.0 ± 0.89
Results at or before 6-year evaluation					
Diabetes by WHO criteria					
No. with 2-h plasma glucose ≥11.1 mmol/l (%)	90 (67.7)	57 (43.8)	58 (41.1)	58 (46.0)	263 (49.6)
Incidence/100 person-years (95% CI)	15.7 (12.7–18.7)	10.0 (7.5–12.5)	8.3 (6.4–10.3)	9.6 (7.2–12.0)	10.8 (9.6–12.0)
Fasting hyperglycemia					
No. with fasting plasma glucose ≥7.8 mmol/l (%)	55 (41.4)	21 (16.2)	37 (26.2)	33 (26.2)	14.6 (27.5)
Incidence/100 person-years (95% CI)	9.6 (7.2–12.0)	3.7 (2.1–5.3)	5.3 (3.6–7.0)	5.5 (3.7–7.3)	6.0 (5.06–6.94)
Weight change (kg)					
No diabetes	0.27	0.93	0.71	−1.77	−0.31
Diabetes	−1.55	−2.43	−1.93	−3.33	−0.87
Glucose (mmol/l)					
Fasting plasma glucose	7.59 ± 2.59	6.94 ± 4.49	6.83 ± 2.24	7.15 ± 2.72	7.13 ± 3.11
2-h glucose	12.99 ± 4.19	10.51 ± 4.89	10.51 ± 3.93	10.76 ± 4.37	11.05 ± 4.41

Data are means ± SD.

highly significant difference between the groups ($P < 0.0035$), and each group of clinics providing active treatments differed significantly from the clinics in the control group ($P < 0.05$). There were, however, no statistically significant differences in the incidences of diabetes between the groups of clinics providing active treatments.

Among individual subjects in the control group, the incidence of diabetes (defined using WHO criteria) was 15.7/100 person-years (95% CI, 12.7–18.7%). In each of the three intervention groups, the incidence of diabetes was significantly lower than in the control group (10.0 [95% CI, 7.5–12.5], 8.3 [6.4–10.3], and 9.6 [7.2–12.0] per 100 person-years in the diet, exercise, and diet-plus-exercise groups, respectively) ($P < 0.05$ for all) (Table 2). Incidence rates did not differ significantly among the three intervention groups ($P > 0.05$). If an alternative endpoint is defined as fasting glucose ≥140 mg/dl (7.8 mmol/l), incidence rates were 9.6 (95% CI 7.2–12.0) in the control group and 3.7 (2.1–5.3), 5.3 (3.6–7.0), and 5.5 (3.7–7.3) per 100 person-years in the diet, exercise, and diet-plus-exercise groups, respectively ($P < 0.05$ for each).

Comparison of lean and overweight subgroups

Because the dietary advice differed according

Table 3—*6-year cumulative incidence of diabetes by clinic and treatment assignment*

										Clinic mean (%)	SD (%)	95% CI (%)
Control clinics												
No. of subjects	11	15	24	16	15	6	33	13	—			
% developing diabetes	73	60	58	64	53	67	85	62	—	65.9	10.0	57.5–76.3
Diet clinics												
No. of subjects	12	5	17	6	27	8	28	15	12			
% developing diabetes	58	60	67	67	48	38	32	40	50	47.1	10.4	38.7–55.5
Exercise clinics												
No. of subjects	18	16	16	20	20	7	28	8	8			
% developing diabetes	56	38	44	30	55	29	21	75	50	44.2	16.8	31.3–57.1
Diet-plus-exercise clinics												
No. of subjects	16	13	28	15	16	10	28	—	—			
% developing diabetes	38	31	57	53	50	40	43	—	—	44.6	9.2	36.1–53.1

The overall test for a difference among group means is statistically significant ($P = 0.0035$, ANOVA). Pair-wise test indicates statistically significant differences between the control group of clinics and the diet, exercise, and diet-plus-exercise groups ($P < 0.05$, Ryan-Einot-Gabriel-Welsch multiple F test). There were no statistical differences among the diet, exercise, and diet-plus-exercise groups.

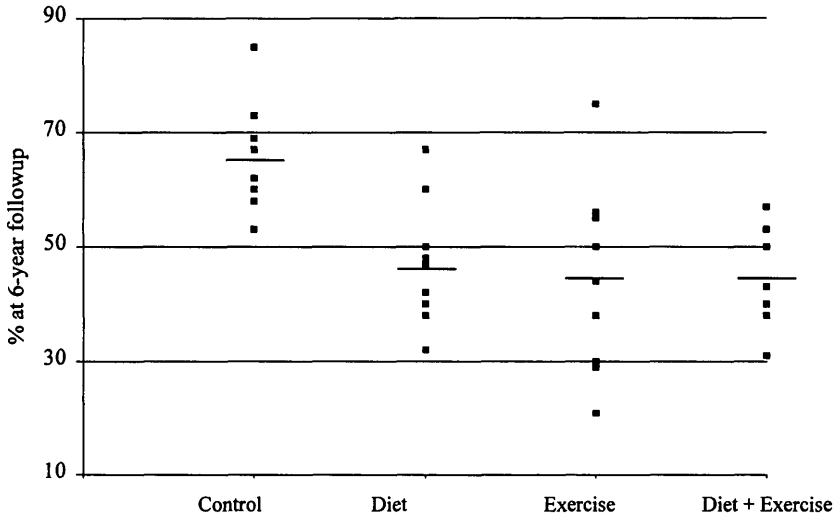

Figure 1—*Mean rate of diabetes for each clinic at 6-year follow-up, by intervention group. Means (± SD) were control, 66 ± 10; diet, 47 ± 11; exercise, 45 ± 9; and diet plus exercise, 44 ± 17.*

to BMI, leading to the possibility of different effects of the interventions in lean and overweight individuals, the incidence of diabetes was evaluated separately in those who had BMI at baseline <25 or ≥25 kg/m² (Tables 4 and 5, Fig. 2). Incidence rates of diabetes in the control group of overweight participants were higher than those in the control group of lean subjects (17.2 vs. 13.3/100 person-years [$P < 0.05$]). On the other hand, in both BMI categories, compared with the corresponding control groups, there were significantly lower incidence rates of diabetes in the intervention groups (except the lean diet group): 8.3 (diet) (NS), 5.1 (exercise) ($P < 0.01$), and 6.8 (diet plus exercise) ($P < 0.05$) for the lean groups; and 11.5, 10.8, and 11.4, respectively ($P < 0.05$ for all), for the overweight groups. The relative decrease in rate of development of diabetes in the active treatment groups (compared with the control group) was similar in the overweight and lean strata. Those who developed diabetes lost weight, and the change was significant in the lean and obese groups. When weight change was added to the model, the conclusions were not changed (data not shown).

Influence of type of intervention and baseline characteristics on the development of diabetes

When the three intervention strategies were compared with the control group in a proportional hazards model, there was an overall reduction in the incidence of diabetes of 33% in the diet-only group ($P < 0.03$), 47% in the exercise-only group ($P < 0.0005$), and 38% in the diet-plus-exercise group ($P < 0.005$) (Table 6). Inclusion of clinic as a variable did not change the results and had a nonsignificant effect ($P = 0.65$). Because plasma glucose level and BMI both influenced the incidence of NIDDM in subjects with IGT, the effects of intervention after adjustment for these baseline factors was examined. Only modest changes in the effects of intervention were seen in the risk reductions of 31, 46, and 42% for diet, exercise, and diet plus exercise, respectively. Baseline physical activity was not predictive of the development of NIDDM in any model. The interaction terms, BMI * Fasting plasma glucose and Diet * Exercise, were not significant (data not shown).

Changes in diet and exercise

Baseline caloric intake and diet composition were similar in all four intervention groups. After 6 years of follow-up, estimated caloric intake appeared lower in the diet and diet-plus-exercise groups, but these differences did not reach statistical significance. Analysis of calorie composition showed a slightly lower proportion of carbohydrates and proteins and a slightly higher proportion of fat at follow-up, but the differences were not statistically significant. Physical exercise, expressed in units per day, was significantly higher at baseline in the diet-plus exercise group than in the control group. At the 6-year follow-up, average units per day of exercise were significantly higher than at baseline in the exercise and in the diet-plus-exercise groups (Table 7).

CONCLUSIONS — This study has demonstrated in a large group of men and women with IGT, identified by screening, that institution of a lifestyle intervention over a 6-year period led to a significant decrease in the incidence of diabetes. Groups randomized by clinic to receive diet, exercise, or both had incidence rates 25–50% below that of the control group. The differences were significant if outcome was either assessed using the WHO criteria for diabetes or defined as unequivocal elevation of fasting glucose to ≥140 mg/dl (≥7.8 mmol/l).

Table 4—*Baseline and follow-up data in lean participants*

	Control	Diet	Exercise	Diet + exercise
n	50	55	57	46
Baseline				
Age (years)	46.4 ± 9.8	43.3 ± 9.8	42.2 ± 8.87	44.5 ± 8.7
Sex (M/F)	32/18	30/25	36/21	25/21
BMI (kg/m²)	22.4 ± 1.7	21.8 ± 1.9	21.7 ± 1.7	22.3 ± 2.1
Fasting plasma glucose (mmol/l)	5.35 ± 0.86	5.50 ± 0.94	5.40 ± 0.79	5.48 ± 0.83
2-h glucose (mmol/l)	9.09 ± 0.97	8.91 ± 0.92	8.91 ± 0.72	9.02 ± 0.94
6-year follow-up				
BMI (kg/m²)	22.8 ± 2.4	21.9 ± 2.3	21.8 ± 1.9	22.8 ± 2.5
Change in BMI	0.6 ± 1.8	0.8 ± 1.5	0.2 ± 1.5	0.4 ± 2.2
Fasting plasma glucose (mmol/l)	7.22 ± 2.58	7.06 ± 6.33	6.11 ± 1.72	6.43 ± 1.83
2-h glucose (mmol/l)	11.87 ± 4.31	10.34 ± 5.83	9.43 ± 3.50	11.02 ± 3.99
Diabetes *n* (%)	30 (60.0)	21 (38.2)	15 (26.3)	16 (34.8)
Incidence (100 person-years)	13.3	8.3	5.1	6.8
95% CI	8.9–17.7	4.9–11.7	2.6–7.6	3.6–10.0
P value		NS	< 0.01	0.05

Data are means ± SD. Baseline BMI <25 kg/m².

Table 5—*Baseline and follow-up data in overweight participants*

	Control	Diet	Exercise	Diet + exercise
n	83	75	84	80
Baseline				
Age (years)	46.6 ± 8.9	45.7 ± 9.0	45.6 ± 8.2	44.4 ± 9.4
Sex (M/F)	41/42	29/46	45/39	45/35
BMI (kg/m²)	28.5 ± 2.9	28.3 ± 2.2	27.9 ± 2.2	28.6 ± 2.7
Fasting plasma glucose (mmol/l)	5.63 ± 0.78	5.64 ± 0.68	5.70 ± 0.83	5.80 ± 0.75
2-h glucose (mmol/l)	8.98 ± 0.83	9.02 ± 0.94	8.83 ± 0.83	9.16 ± 0.89
6-year follow-up				
BMI (kg/m²)	27.5 ± 2.4	27.1 ± 2.7	27.0 ± 2.4	27.0 ± 2.7
Change in BMI	−0.9 ± 2.9	−1.1 ± 2.0	−0.9 ± 1.6	−1.6 ± 1.6
Fasting plasma glucose (mmol/l)	7.83 ± 2.59	6.87 ± 2.24	7.31 ± 2.43	7.59 ± 3.06
2-h glucose (mmol/l)	12.77 ± 4.11	10.64 ± 4.09	11.24 ± 4.06	11.22 ± 4.50
Diabetes *n* (%)	60 (72.3)	36 (48.0)	43 (51.2)	42 (52.5)
Incidence (100 person-years)	17.2	11.5	10.8	11.4
95% CI	13.3–21.3	8.0–15.0	7.8–13.8	8.1–14.6

Data are means ± SD. Baseline BMI ≥25 kg/m².

The present study was performed in community health clinic settings using both group sessions and individual counseling to deliver the interventions. Diet information was reviewed at 3- to 6-month intervals using an abbreviated food frequency instrument. Diet assessment was facilitated by the limited number of foods available and the generally regular eating habits of this population. Nevertheless, the dietary assessment methods were not capable of thoroughly assessing dietary changes and the assessments were carried out by interviewers who were not masked as to the intervention. The data suggest, however, that calorie consumption did decrease somewhat in the dietary intervention groups, although the differences did not reach statistical significance, perhaps reflecting the low precision of dietary assessment methods. The distribution of calories did not appear to change significantly in any of the groups. Of interest, in the relatively lean people (those with a BMI <25 kg/m²), significant decreases in the incidence of diabetes (except in the diet arm) were achieved despite the fact that subjects who developed diabetes showed an overall increase in weight. In fact, individuals with BMI <25 kg/m² and IGT may have significant amounts of abdominal fat and should possibly have been given weight-loss goals as well. In assessing occupational physical activity, mode of transportation had a substantial impact on total activity because private automobiles are not commonly available in Da Qing. Emphasis was placed on increasing rates of leisure activity, primarily walking. Activity levels appear to have increased in all three groups, but the follow-up interview could not be performed in a fully masked manner. Nevertheless, measured differences reached statistical significance only in the exercise and diet-plus-exercise groups. Baseline physical activity was somewhat different in the four groups, but baseline physical activity did not predict development of NIDDM when baseline physical activity was included in the multivariate analysis. Using "intention to treat" analysis, we did not observe any significant differences among the efficacies of the three active intervention strategies. Nevertheless, the risk ratios, after adjustment for baseline BMI and glucose, suggest that the efficacy of diet was similar to that of exercise, and there was no additional benefit of combining the interventions.

The reduced incidence of diabetes observed in the intervention groups in this study is consistent with the current understanding of the etiology of NIDDM. In most subjects, NIDDM and IGT are associated with insulin resistance. Resistance to insulin-mediated glucose disposal in the major glucose-utilizing tissue, such as muscle, is thought to lead to gradually increasing glucose concentrations, which result in progressive increasing compensatory insulin secretion and eventually to subsequent β-cell failure (2). Longitudinal studies of the development of NIDDM have shown conclusively that hyperinsulinemia and direct measurement of insulin-mediated glucose disposal are significant independent predictors of the development of NIDDM (12). The interventions of diet and exercise used in this study are both known to influence insulin resistance. Exercise increases insulin-mediated glucose disposal in muscle (18). Although lowering dietary fat content has not been shown conclusively in humans to influence insulin-mediated glucose disposal, hypocaloric diets leading to weight loss are associated with improved insulin-mediated glucose disposal, lowered insulin responses, and reduction of glycemia (19). It is thus likely that these interventions, by reducing

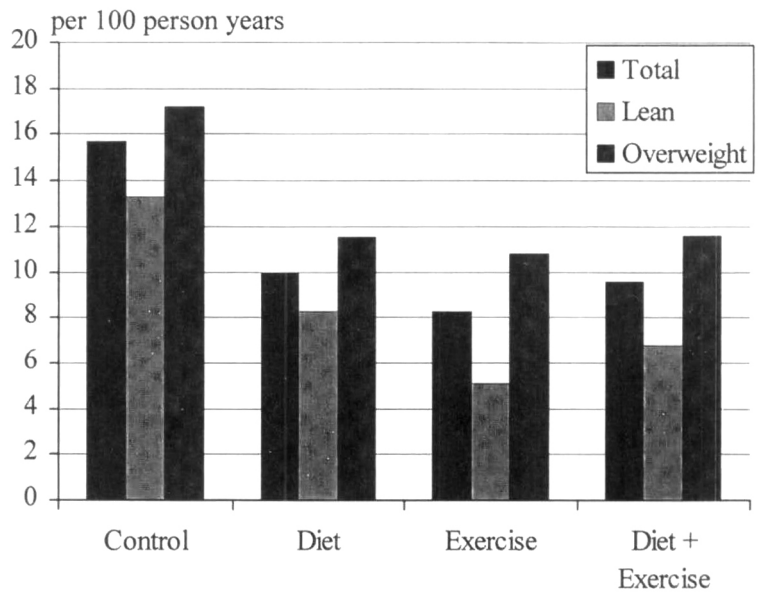

Figure 2—*Incidence of diabetes at or before 6-year evaluation. Lean subjects constituted 39.2% of the total sample (37.6% of the control group, 42.3% of the diet group, 40.4% of the exercise group, and 39.2% of the diet-plus-exercise group).*

Table 6—*Proportional hazard analyses of effects of interventions on the incidence of NIDDM*

Independent variable (n = 530)	β	SE	P value	Relative risk
Unadjusted				
Diet	–0.39	0.17	0.021	0.67
Exercise	–0.63	0.17	0.000	0.53
Diet plus exercise	–0.48	0.17	0.005	0.62
Model including fasting plasma glucose and BMI				
FPG (mmol/l)	0.02	0.00	0.001	1.02
BMI (kg/m^2)	0.49	0.02	0.002	1.05
Diet	–0.38	0.17	0.028	0.69
Exercise	–0.62	0.17	0.000	0.54
Diet plus exercise	–0.55	0.17	0.001	0.58

Unadjusted model includes three variables. The model including fasting plasma glucose and BMI is adjusted for baseline levels.

insulin resistance, slow the progression of glucose intolerance and thereby perhaps arrest or delay β-cell deterioration. The extent to which these effects can be sustained and how long this progression can be delayed or interrupted, are not known. Continued follow-up is planned to address these issues.

To our knowledge, this is the first randomized controlled clinical trial to demonstrate significant reduction in the incidence of diabetes in individuals with IGT. In the earlier Bedford (7) and Whitehall (5) studies, neither diet nor oral antidiabetic agents influenced the incidence of subsequent diabetes in individuals with IGT. Sartor et al. (6) randomized men with IGT into three groups that received diet therapy. One group also was treated with tolbutamide. In 10 years, when analyzed on an intent-to-treat basis, the incidence rate for diabetes was not significantly lower in the tolbutamide group. A more recent nonrandomized study in Sweden investigated moderate weight reduction and increased physical activity in individuals with early NIDDM and IGT and showed that these interventions were associated with an improvement in glucose tolerance and reduced mortality in the intervention groups (14).

Several questions can be raised concerning these results. The first concerns the analysis of individual subjects according to treatment group because individuals were actually assigned to clinics that then administered the same type of intervention to all subjects. Differences in treatment groups were fairly consistent across clinics providing the same type of intervention. Indeed, the mean incidence rates by clinic (Fig. 1, Table 3) indicate that when analyzed on the basis of clinic rather than individual, the same pattern of reduced incidence of diabetes occurred in clinics providing the active interventions, as compared with those providing the control treatment. These are the same differences as are found when the individual subject was the unit of analysis.

Another issue concerns the generalizability of these results. The residents of Da Qing migrated from many areas of China at the time the oil industry was initiated there in 1959. It seems probable that their health is now likely to be reasonably representative of that of the general working population of the People's Republic of China. It has been estimated that there will be 980,000 new cases of diabetes per year in China in the twenty-first century (20) and a total of 290 million people with diabetes by 2010 (21). These figures are likely to increase even more with rising affluence, increasingly sedentary lifestyles, and a more abundant food supply. In fact, the prevalence of NIDDM among Chinese residents of Mauritius approaches 12% among people aged 25 years and over (22). Thus, intervention in individuals with IGT could significantly reduce the incidence of diabetes and thereby have a major impact on the public health burden of diabetes in China in the near future.

Further studies are needed in other ethnic and socioeconomic groups to develop the most appropriate intervention strategies and test the generalizability of the results. This has now been initiated in the U.S., where the National Institutes of Health has begun to examine diabetes prevention strategies in several ethnic groups. Although lifestyle interventions must be tailored for specific populations and the best means to do so will certainly vary widely in different countries and ethnic communities, the results of the present study provide evidence that interventions aimed at lifestyle changes in individuals with IGT can successfully reduce the overall rate of diabetes.

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Table 7—*Diet intake and exercise by intervention group*

	Control subjects		Diet		Exercise		Diet + exercise	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Total calories	2,327 ± 693	2,228 ± 695	2,485 ± 804	2,359 ± 835	2,455 ± 629	2,359 ± 721	2,404 ± 758	2,162 ± 678
Carbohydrate (%)	58 ± 12	57 ± 12	60 ± 11	59 ± 12	59 ± 10	58 ± 10	60 ± 11	58 ± 12
Protein (%)	11 ± 2	11 ± 2	11 ± 2	11 ± 2	11 ± 2	12 ± 7	11 ± 2	11 ± 3
Fat (%)	26 ± 8	27 ± 8	26 ± 8	27 ± 8	25 ± 8	27 ± 10	25 ± 8	27 ± 9
Alcohol (g/day)	6 ± 9	5 ± 9	3 ± 7	3 ± 8	5 ± 8	5 ± 9	4 ± 9	4 ± 9
Exercise (U/day*)	2.4 ± 1.8	2.5 ± 1.9	2.0 ± 2.2	1.7 ± 1.9	3.4 ± 2.8†	4.0 ± 3.0	3.1 ± 2.4†	3.9 ± 2.3‡

Data are means ± SD. *For nonoccupational physical activity. $P < 0.05$ compared with controls (†) or baseline (‡) by a multivariate analysis with change between follow-up and baseline as the dependent variable and other measured components as independent variables.

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