Intensive Lifestyle Changes Are Necessary to Improve Insulin Sensitivity

A randomized controlled trial

KIRSTEN A. MCAULEY, MBCHB[1]
SHEILA M. WILLIAMS, BSC[2]
JIM I. MANN, DM, PHD[1]
AILSA GOULDING, PHD, FACN[3]
ALEX CHISHOLM, PHD[1]
NOELA WILSON, PHD [4]
GRETCHEN STORY, BPHED[1]
REBECCA T. MCLAY, MSC[1]
MICHELLE J. HARPER, BSC[1]
IANTHE E. JONES, MSC[3]

OBJECTIVE — The extent to which lifestyle must be altered to improve insulin sensitivity has not been established. This study compares the effect on insulin sensitivity of current dietary and exercise recommendations with a more intensive intervention in normoglycemic insulin-resistant individuals.

RESEARCH DESIGN AND METHODS — Seventy-nine normoglycemic insulin-resistant (determined by the euglycemic insulin clamp) men and women were randomized to either a control group or one of two combined dietary and exercise programs. One group (modest level) was based on current recommendations and the other on a more intensive dietary and exercise program. Insulin sensitivity was measured using a euglycemic insulin clamp, body composition was measured using dual-energy X-ray absorptiometry, and anthropometry and aerobic fitness were assessed before and after a 4-month intervention period. Four-day dietary intakes were recorded, and fasting glucose, insulin, and lipids were measured.

RESULTS — Only the intensive group showed a significant improvement in insulin sensitivity (23% increase, $P = 0.006$ vs. 9% in the modest group, $P = 0.23$). This was associated with a significant improvement in aerobic fitness (11% increase in the intensive group, $P = 0.02$ vs. 1% in the modest group, $P = 0.94$) and a greater fiber intake, but no difference in reported total or saturated dietary fat.

CONCLUSIONS — Current clinical dietary and exercise recommendations, even when vigorously implemented, did not significantly improve insulin sensitivity; however, a more intensive program did. Improved aerobic fitness appeared to be the major difference between the two intervention groups, although weight loss and diet composition may have also played an important role in determining insulin sensitivity.

Diabetes Care 25:445–452, 2002

Lifestyle intervention reduces the risk of progression from impaired glucose tolerance (IGT) to type 2 diabetes (1). It is widely assumed that current advice regarding physical activity (2) and dietary modification (3) is sufficient (presumably mediated via an improvement in insulin sensitivity) to reduce the risk of type 2 diabetes. All the large intervention trials either underway or completed have focused on intervention in subjects with IGT (1,4,5). However, it appears that once abnormal glucose levels have developed, significant β-cell dysfunction has already occurred, and there is less chance of improving insulin sensitivity (6).

Intervention before IGT has developed may offer the best opportunity to reduce progression to IGT and type 2 diabetes. Although increased physical activity and dietary modification have been shown to improve insulin sensitivity, there are no data that clearly show the extent of lifestyle change required. This study is the first to compare two levels of practical lifestyle intervention in normoglycemic insulin-resistant individuals on insulin sensitivity, one based on current recommendations (modest) and the other on a more intensive dietary and exercise program. This will help to answer the important question as to whether more aggressive lifestyle intervention is more beneficial. In this study, participants were randomized to either a control group or one of two intervention groups.

RESEARCH DESIGN AND METHODS

Eligibility

A total of 440 volunteers responded to local advertisements. Participants were eligible to be screened if they met the following criteria: aged 25–70 years, able and willing to take part in a dietary and exercise program (7), and no personal history of diabetes or any major medical condition, psychiatric illness, or drug or alcohol dependence. Those on warfarin or oral steroids were excluded, but those on other medications were included if they had been treated for >6 months and were unlikely to alter the medication during the intervention period. Screening involved measurement of fasting glucose, insulin, and triglycerides. Those with fasting glucose <6.1 mmol/l and poor insulin sensitivity ($n = 140$) based on our published prediction equation (8) were eligible for a euglycemic insulin clamp. Those

From the [1]Department of Human Nutrition, Otago University, Dunedin, New Zealand; the [2]Department of Preventive and Social Medicine, Otago University, Dunedin, New Zealand; the [3]Department of Medical and Surgical Sciences, Otago University, Dunedin, New Zealand; and the [4]Life in New Zealand Activity and Health Research Unit, Otago University, Dunedin, New Zealand.

Address correspondence and reprint requests to Dr. Kirsten McAuley, Department of Human Nutrition, Otago University, P.O. Box 56, Dunedin, New Zealand. E-mail: kirsten.mcauley@stonebow.otago.ac.nz.

Received for publication 23 May 2001 and accepted in revised form 6 December 2001.

Abbreviations: DXA, dual-energy X-ray absorptiometry; Gbw, glucose infused for total body weight; Gffm, glucose infused for fat-free mass; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; VLCD, very low–calorie diet.

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

with an insulin sensitivity index ≤4.2 G · $mU^{-1} \cdot l^{-1}$ (G = glucose infused in mg · $kg^{-1} \cdot min^{-1}$) were invited to enter the intervention study. This cutoff represented the lowest 25th centile of a lean population (BMI <27 kg/m^2). Seventy-nine Caucasian men and women were eligible and gave informed consent for the study, which was approved by the Otago Ethics Committee. Screening and recruitment occurred between February 1999 and August 2000. Participants were randomized to the three groups in blocks of nine (so that entry to the study could be staggered) after stratification for sex and degree of insulin sensitivity.

Dietary intervention

The modest dietary program was intended to reflect present dietary advice, and the intensive diet aimed to achieve an even lower total and saturated fat intake, lower dietary cholesterol, and a higher fiber intake. The modest program aimed to achieve a diet in which <32% of total energy was from fat, ~11% was from saturated fat, 14% was from monounsaturated fat, 7% was from polyunsaturated fat, 50% was from carbohydrates, and 18% was from protein. Cholesterol targets were <200 mg per day and dietary fiber >25 g per day. The intensive diet aimed for <26% of total energy from fat, <6% from saturated fat, 13% from monounsaturated fat, 7% from polyunsaturated fat, 55% from carbohydrates, and 18% from protein. Cholesterol targets were <140 mg/day and dietary fiber >35 g/day. In addition to these macronutrient goals, foods rich in nutrients believed to enhance insulin sensitivity were specified for each diet (9); the modest and intensive groups were required to have three or seven such foods daily, respectively. Study foods included low glycemic index foods, fish, nuts, seeds, grains, pasta, rice, fruit, vegetables, legumes, and low-fat dairy foods. The diets were individually prescribed and based on each participant's usual intake or an energy level designed to lead to gradual and sustained weight reduction. Compliance was assessed by a 4-day diet record at baseline, 2 months, and 4 months and by a daily record sheet, where type and amount of recommended foods were recorded. Diet records were analyzed using Diet Cruncher for Macintosh (Version 1.1.0; Marshall-Seeley, Dunedin, New Zealand), which used food composition data from the New Zealand Institute for Crop and Food Research (10). No modifications were made to the database. Foods not in the database were coded so that the same substitutions were made throughout, and participants were asked to supply recipes so that individual ingredients were entered and analyzed in the appropriate quantity. Some food was supplied free of charge (cereals, low fat spread, and canola oil), and all dietary information, including lists of suitable foods, sample eating plans, foods to be avoided, cooking and preparation advice, and recipes, was provided.

Exercise intervention

At baseline, assessment of recent participation in physical activity was based on the Life in New Zealand validated questionnaire (11). The individually designed exercise program was planned to incorporate 30 min of activity 5 days/week (at different intensities, depending on group) and took into account preferred activities. An exercise consultant exercised with each participant in an individual or group situation at least once per week to ensure that appropriate activities were chosen and that motivation and compliance were enhanced. The modest exercise intervention program was based on current health promotion recommendations for activity, which do not specify heart rate targets (2). The intense exercise intervention program aimed to meet the 1990 American College of Sports Medicine guidelines for developing and maintaining cardiorespiratory and muscular fitness (12). Participants were encouraged to train five times per week for at least 20 min per session at an intensity of 80–90% of age-predicted maximum heart rate. A gym membership was provided for participants in the intensive program to encourage participation in vigorous activity and involvement in resistance training at least twice per week. Type and duration of physical activity was recorded by participants for both intervention groups on a daily sheet (collected weekly). The control group was asked to continue their usual diet and exercise during the 4-month experimental period.

Clinical visits

At the time of the euglycemic insulin clamp study, fasting blood samples were taken for lipid measurements, and anthropometry and blood pressure measurements were repeated. Participants were randomized to one of the three groups, and within 1 week, they had a dual-energy X-ray absorptiometry (DXA) scan and an exercise test. All of these measures constituted baseline data. Intervention was commenced as soon as all baseline measures were collected. Participants in the intervention groups were seen by the researchers weekly for a weight measurement and a brief dietary and exercise assessment. If participants did not attend, they were contacted by phone, their progress was discussed, and a further appointment was made. At each monthly interval, participants in the intervention groups had the following measurements: weight, waist, and hip measurements, blood pressure, a fasting blood test for glucose, an insulin and lipid profile, and a 1-mile walk test. No contact was made with the control group until the end of the 4-month period, when baseline measures were repeated on all participants.

Methodology for outcome measures

The procedure for measuring waist and hip circumference, blood pressure, fasting insulin, glucose, and lipids has been previously described (8). Weight was measured using the same set of calibrated electronic scales, and all participants were weighed without shoes or heavy clothing. The last 50% of participants recruited had an oral glucose tolerance test (OGTT), which involved ingestion of a solution containing 75 g dextrose after a 10-h overnight fast, followed by a venous blood glucose drawing at 120 min (13). Body composition was measured using DXA, which is a sensitive test to quantitate changes in lean and fat mass in vivo (14) and to assess regional fat distribution (15). Total body scans were obtained on the same Lunar DPXL (Lunar, Madison, WI) scanner at baseline and at the end of the study on all participants weighing <120 kg, using patient positioning and scan speeds recommended by the manufacturer. All scans were analyzed with software package l.35 (Lunar). Coefficients of variation were 2.6% for fat mass, 2.5% for total body fat percentage, <3% for regional fat measures, and 0.88% for lean mass (15).

Insulin sensitivity was measured using the euglycemic insulin clamp, infusing insulin (Actrapid) at 40 mU · m^{-2} · min^{-1} and maintaining the blood glucose levels as close to 4.5 mmol/l as possible

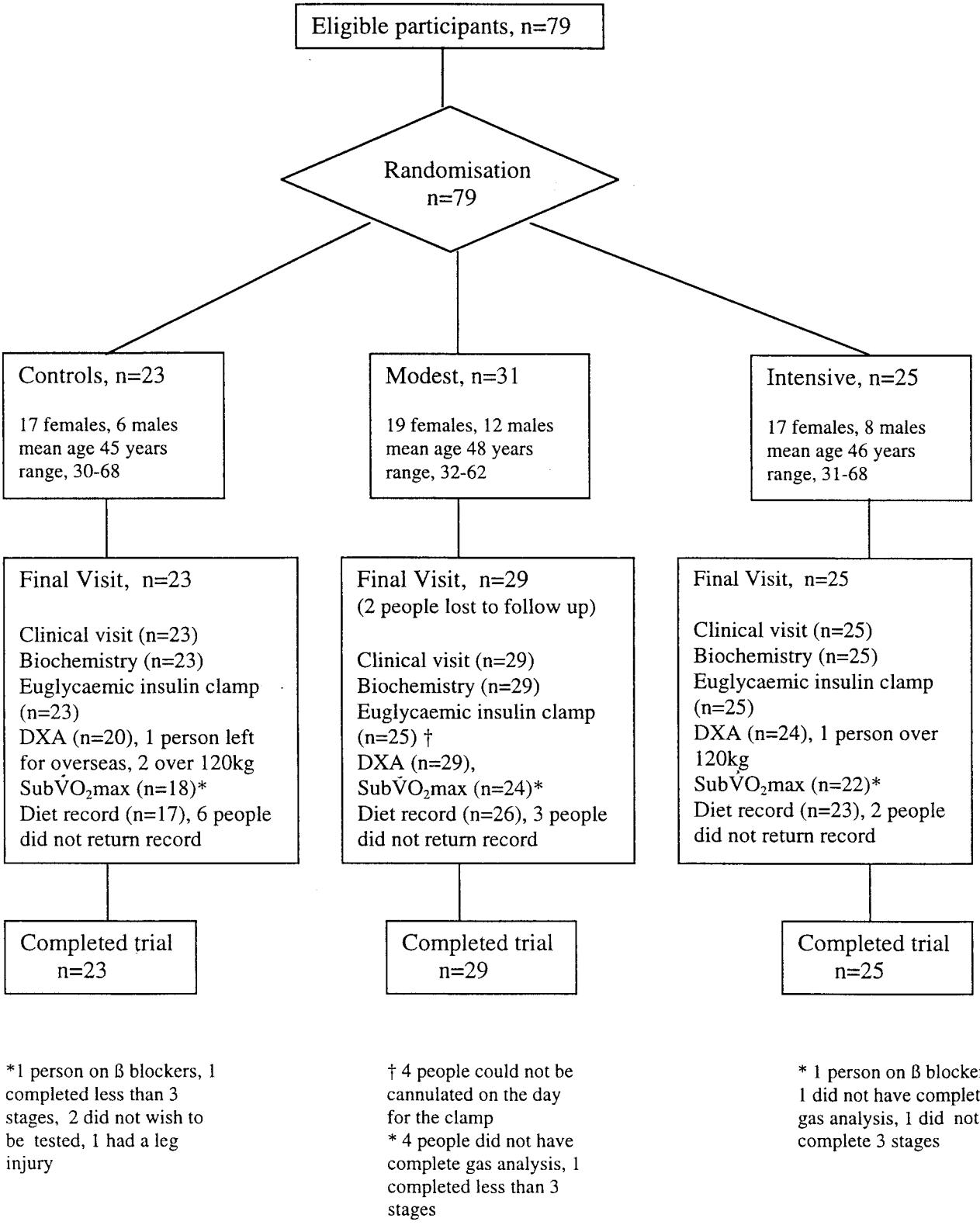

Figure 1—*Flow chart of randomized controlled intervention trial.*

(8). The extent to which adipose tissue contributes to glucose disposal is controversial; therefore, we have expressed the glucose infused (G) for total body weight (Gbw) and glucose infused for fat-free mass (Gffm) calculated from the DXA (Gffm = Gbw · weight^{-1} · lean body mass^{-1}) in mg · kg^{-1} · min^{-1}. Gbw and Gffm are reported alone and divided by

Table 1—*Baseline and final measures for DXA and euglycemic insulin clamp measures for the control (C), modest (M), and intensive (I) intervention groups*

	Group	Baseline mean (SD)	Final mean (SD)	*Adjusted difference	95% CI of difference	*P* value for adjusted difference
Total fat (kg)	C	44.1 (8.7)	43.5 (8.3)			
	M	39.0 (10.1)	35.6 (10.7)	−3.0	−4.8, −1.2	0.001
	I	35.7 (10.4)	31.4 (10.2)	−4.1	−6.0, −2.1	0.000
Truncal fat (kg)	C	24.0 (4.4)	23.7 (4.1)			
	M	21.2 (5.4)	19.2 (6.1)	−1.8	−3.0, −0.6	0.003
	I	18.7 (5.6)	16.1 (5.2)	−2.6	−3.9, −1.3	0.000
Lean mass (kg)	C	52.0 (8.2)	51.2 (7.8)			
	M	52.4 (9.7)	52.2 (9.6)	0.7	−0.3, 1.7	0.19
	I	50.2 (9.0)	50.2 (9.3)	0.7	−0.3, 1.8	0.18
Average insulin (mU/l)	C	160.3 (32.1)	151.1 (21.8)			
	M	155.2 (19.3)	145.2 (15.9)	−4.9	−15.8, 5.9	0.37
	I	166.1 (35.9)	143.0 (20.7)	−9.2	−20.1, 1.6	0.10
Gbw ($mg \cdot kg^{-1} \cdot min^{-1}$)	C	4.2 (1.0)	4.8 (0.9)			
	M	4.6 (1.3)	5.4 (1.5)	0.2	−0.4, 0.9	0.47
	I	5.1 (1.6)	6.3 (2.1)	0.7	0.0, 1.4	0.04
Gffm ($mg \cdot kg^{-1} \cdot min^{-1}$)	C	8.4 (2.2)	9.1 (1.8)			
	M	8.4 (2.2)	9.2 (2.1)	0.1	−0.9, 1.1	0.88
	I	8.9 (2.4)	10.4 (3.1)	0.9	−0.1, 1.9	0.09
Gbw/i ($G \cdot mU^{-1} \cdot l^{-1}$)	C	2.7 (0.9)	3.2 (0.7)			
	M	3.0 (0.8)	3.8 (1.3)	0.4	−0.3, 1.0	0.23
	I	3.2 (1.0)	4.4 (1.6)	0.9	0.3, 1.6	0.006
Gffm/i ($G \cdot mU^{-1} \cdot l^{-1)}$	C	5.4 (2.0)	6.2 (1.5)			
	M	5.4 (1.3)	6.5 (1.8)	0.3	−0.6, 1.3	0.50
	I	5.5 (1.7)	7.4 (2.4)	1.2	0.2, 2.2	0.02

*Adjusted for baseline variables. Gbw/i, glucose infused for body weight/average plasma insulin Gffm/i, glucose infused for fat-free mass/average plasma insulin.

the average insulin (i) level during the final 60 min of the test (Gbw/i and Gffm/i), in $G \cdot mU^{-1} \cdot l^{-1}$. A $\dot{V}O_{2max}$ test was considered inappropriate in sedentary overweight adults; therefore, aerobic fitness was estimated using a submaximal walk test on a motorized treadmill (Quinton Series 90 Q65; Quinton Instrument, Seattle, WA) based on a modified Bruce protocol (16). The test was terminated when the target heart rate (75% of age-predicted maximum) was reached or exercise could not be continued. Those on β-blocker medication were excluded. Minute ventilation (V_E), oxygen consumption ($\dot{V}O_2$), and carbon dioxide production ($\dot{V}CO_2$) were measured by open spirometry/indirect calorimetry (Sensormedics Metabolic Cart 2900Z BXB; Sensormedics, Anaheim, CA). The gas analyzer was calibrated before each test with standard mixtures. The average heart rate and $\dot{V}O_2$ were calculated for the last minute of each 3-min stage. A stage was included if the subject completed >2 min. If heart rates were <100 bpm, then only stages in which heart rate increased at least 5 bpm compared with the previous stage were used in the estimated $\dot{V}O_{2max}$. Heart rate was plotted against $\dot{V}O_2$, and the predicted $\dot{V}O_{2max}$ was determined by extrapolation to the estimated maximal heart rate. Exercise tests were excluded from this analysis if less than three stages had been completed or when there was incomplete gas collection.

Statistical methods

Sample size calculations were based on an estimate of the SD of the log-transformed insulin sensitivity index (Gffm/i), which was 0.25. Thus, a sample size of 25 in the three groups would give an 80% chance of detecting a 20% improvement in Gffm/i using the 5% level of significance. Regression analysis with the baseline measure as a covariate was used to compare the treatment groups with the control group. STATA statistical software Version 7.0 (Stata, College Station, Texas) was used. All major end points were assessed without knowledge of treatment groups.

RESULTS — The age and sex of the groups are included in Fig. 1, which also shows the progress of participants through the trial, including dropouts and those not completing each outcome measure. Five subjects were smokers and continued to smoke over the 4-month intervention. Of those who had an OGTT, two had a 2-h glucose value ≥7.8 mmol/l.

Insulin sensitivity changed significantly in the intensive group only (Table 1). This occurred in parallel with reductions in weight, waist circumference, BMI, systolic and diastolic blood pressure (Table 2), total and truncal fat (Table 1), increased reported dietary fiber, and increased aerobic fitness (Table 3). Both groups reduced intakes of total energy, total fat, saturated fat, and cholesterol. Attendance to supervised exercise sessions was similar for both intervention groups (>70%), and compliance based on self-reported daily tick sheets was high, with both groups meeting the exercise targets of 5 days/week.

Table 2—*Baseline and final measures for clinical and biochemical variables for the control (C), modest (M), and intensive (I) intervention groups*

	Group	Baseline mean (SD)	Final mean (SD)	*Adjusted difference	95% CI of difference	*P* value for adjusted difference
Weight (kg)	C	102.8 (15.3)	101.5 (15.1)			
	M	94.8 (12.6)	90.6 (12.2)	−3.4	−5.4, −1.3	0.002
	I	91.1 (16.2)	85.9 (15.4)	−4.7	−6.9, −2.4	0.000
Waist (cm)	C	113.7 (9.7)	112.2 (10.9)			
	M	106.1 (9.8)	102.2 (9.2)	−3.5	−6.5, −0.5	0.02
	I	100.9 (12.1)	97.2 (11.0)	−4.1	−7.4, −0.9	0.01
Waist-to-hip ratio	C	0.92 (0.08)	0.92 (0.08)			
	M	0.92 (0.08)	0.92 (0.07)	0.00	−0.02, 0.02	0.93
	I	0.90 (0.07)	0.89 (0.06)	−0.01	−0.03, 0.02	0.53
BMI (kg/m^2)	C	36.5 (4.3)	36.1 (4.4)			
	M	33.9 (4.4)	32.4 (4.4)	−1.2	−2.0, −0.4	0.002
	I	32.5 (5.2)	30.6 (4.7)	−1.7	−2.5, −0.9	0.000
Systolic BP (mmHg)	C	133 (15)	138 (18)			
	M	133 (13)	128 (14)	−10	−17, −2	0.01
	I	137 (18)	126 (17)	−15	−23, −7	0.000
Diastolic BP (mmHg)	C	85 (7)	84 (8)			
	M	84 (9)	77 (10)	−6	−10, −2	0.008
	I	87 (11)	78 (9)	−7	−11, −2	0.003
Glucose (mmol/l)	C	5.2 (0.6)	5.2 (0.5)			
	M	5.2 (0.6)	5.1 (0.6)	−0.1	−0.3, 0.2	0.61
	I	5.1 (0.8)	5.0 (0.6)	−0.1	−0.4, 0.2	0.47
Insulin (mIU/l)	C	24.7 (15.5)	21.2 (14.2)			
	M	17.5 (11.7)	16.5 (11.1)	−0.9	−5.9, 4.2	0.73
	I	17.0 (7.9)	12.9 (5.4)	−4.1	−9.3, 1.1	0.12
Total cholesterol (mmol/l)	C	5.4 (1.0)	5.3 (0.8)			
	M	5.8 (1.2)	5.3 (1.2)	−0.2	−0.6, 0.3	0.44
	I	5.8 (0.9)	5.3 (0.8)	−0.2	−0.7, 0.2	0.35
HDL cholesterol (mmol/l)	C	1.04 (0.22)	1.08 (0.19)			
	M	1.05 (0.33)	0.96 (0.24)	−0.12	−0.23, −0.00	0.04
	I	1.06 (0.31)	1.00 (0.33)	−0.09	−0.21, 0.03	0.12
Triglycerides (mmol/l)	C	1.66 (0.65)	1.57 (0.72)			
	M	1.78 (0.75)	1.63 (0.69)	−0.02	−0.34, 0.28	0.86
	I	1.73 (0.60)	1.52 (0.72)	−0.10	−0.42, 0.22	0.54
LDL cholesterol (mmol/l)	C	3.7 (0.8)	3.5 (0.7)			
	M	3.9 (1.1)	3.6 (1.1)	−0.0	−0.4, 0.4	0.92
	I	4.0 (0.7)	3.6 (0.7)	−0.1	−0.5, 0.3	0.75

*Adjusted for baseline values. BP, blood pressure.

CONCLUSIONS — Resistance to the action of insulin is an important precursor of IGT and type 2 diabetes (17). It is widely believed that current dietary and exercise recommendations will improve insulin sensitivity to an extent great enough to reduce the risk of type 2 diabetes. However, the evidence that such relatively modest lifestyle changes will improve insulin sensitivity is limited. We have compared the effect on insulin sensitivity of a modest lifestyle change (reflecting current public health promotion messages) with a more intensive program. The intensive program resulted in an appreciable improvement in insulin sensitivity when compared with the control group (23% when infused glucose was expressed for total body weight, 16% when expressed for lean mass). Indeed, the effect of the intervention may have been underestimated because insulin sensitivity tended to improve in the control group. In contrast, the tendency toward improved insulin sensitivity in the modest group did not differ appreciably from that of the control subjects. These findings have profound implications for public health because it appears that current advice, even when vigorously implemented, did not significantly influence a major underlying abnormality of type 2 diabetes in this study. When compared with the control group, participants in both the modest and the intensive group reduced total and truncal fat and waist circumference without reducing lean mass. These changes were accompanied by statistically significant reductions in systolic and diastolic blood pressure. Fasting insulin and triglyceride levels were also lower after the intervention, but not significantly so, perhaps because levels tended to also fall in the control group. HDL cholesterol was lower in both groups after the inter-

Table 3—*Baseline and final measures for dietary and exercise variables for the control (C), modest (M), and intensive (I) intervention groups*

	Group	Dietary targets	Baseline mean	Final mean	*Adjusted difference	95% CI of difference	*P* value for adjusted difference
Energy (kcal)	C		2,288	2,121			
	M		1,954	1,546	−408	−125, −690	0.005
	I		1,982	1,726	−242	−530, −46	0.098
Total fat (%)	C		33 (6)	35 (8)			
	M	32	32 (6)	24 (7)	−11	−15, −7	0.000
	I	26	35 (5)	27 (5)	−9	−12, −5	0.000
Saturated fat (%)	C		14 (3)	16 (5)			
	M	11	14 (4)	9 (3)	−7	−10, −5	0.000
	I	6	15 (3)	9 (2)	−7	−9, −5	0.000
Carbohydrate (%)	C		47 (6)	46 (8)			
	M	50	48 (7)	54 (7)	7	3, 11	0.001
	I	55	47 (6)	51 (5)	5	1, 9	0.02
Protein (%)	C		17 (4)	16 (3)			
	M	18	17 (3)	20 (4)	4	1, 6	0.002
	I	18	16 (2)	19 (4)	3	1, 6	0.01
Alcohol (g)	C		3.5	5.0	1		
	M		4.4	4.5	−1.0	−4.4, 2.5	0.58
	I		2.0	4.1	−2.1	−5.8, 1.5	0.24
Cholesterol (mg)	C		284.2	266.5			
	M	200†	240.2	142.3	−118.9	−177.0, −60.7	0.000
	I	140†	240.7	155.3	−105.6	−164.8, −46.3	0.001
Fiber (g/24 h)	C		24.5	21.7			
	M	25†	24.2	26.9	5.4	−0.4, 11.2	0.07
	I	35†	23.7	30.2	8.9	2.9, 14.9	0.004
Predicted $V_{O_{2max}}$ ($ml \cdot min^{-1} \cdot kg^{-1}$)	C		29 (6)	32 (7)			
	M		32 (9)	35 (9)	0	−3, 3	0.94
	I		30 (5)	37 (7)	4	1, 7	0.02
Stage‡	C		3.8	3.9			
	M		3.8	4.3	0.4	0.1, 0.7	0.005
	I		3.8	4.4	0.5	0.2, 0.9	0.001
Heart rate (bpm)§	C		137	132			
	M		135	127	−4	−10, 3	0.25
	I		140	124	−10	−16, −4	0.002

*Adjusted for baseline values; †per day; ‡stage using the modified Bruce protocol; §heart rate given for some stage pre- and postintervention.

vention, perhaps due to weight loss and restriction of dietary fat. Although the change in body composition, blood pressure, and metabolic variables was more marked in the intensive than the modest group, the differences were not striking and did not achieve statistical significance. Failure to demonstrate more marked differences in these measures between the two interventions groups may be due to the fact that the two groups made fairly similar dietary changes with regard to important dietary variables other than dietary fiber, which increased to a greater extent in the intensive group. On the other hand, measures of aerobic physical fitness ($V_{O_{2max}}$ and heart rate) differed appreciably between the two intervention groups. The standard advice of exercise for 30 min at least five times weekly (with no specific advice regarding intensity) appeared to have little effect, whereas the advice given to the intensive group has appreciably influenced all measures of aerobic fitness. As this is the main aspect of the intervention program that appears to differ significantly between the two intervention groups, it seems likely that this is one of the major factors accounting for the improved insulin sensitivity observed among those in the intensive program.

There is no doubt that weight loss leads to a reduction in resistance to the action of insulin (18,19). However, in this study, the difference in weight loss on the two programs did not achieve statistical significance. Goodpaster et al. (18) achieved a 15-kg weight loss and a 24% increase in insulin sensitivity in 32 obese men and women maintained on a very low–calorie diet (VLCD). However, such an approach is neither a practical option for widespread adoption, nor is it desirable. The VLCD was associated with a loss in lean body mass of 2.1 kg in women and 4.6 kg in men. Ross et al. (20) found either diet- or exercise-induced weight loss achieved a similar improvement in insulin sensitivity when the amount of total fat loss was also similar. Information regarding the effect of specific foods or nutrients independent of weight change is sparse. Saturated fatty acids (especially palmitic acid), reduced levels of α-linolenic acid, a low ratio of n-3 to n-6 fatty acids, and a high proportion of dihomoγlinolenic acid

have been shown to be positively correlated with insulin resistance (21,22). In the only carefully controlled intervention trial, Vessby et al. (232) found a 10% reduction in insulin sensitivity when monounsaturated fatty acids were replaced by saturated fatty acids. However, this effect appeared to operate only when total fat intake was <38% total energy.

Aerobic exercise has been shown to improve insulin sensitivity (23), but there is less information regarding the precise level or frequency required. Yamanouchi et al. (24) compared two groups of hospitalized obese people with diabetes, all of whom made similar dietary changes. One group walked 4,500 steps per day, the other 19,200 steps per day. The glucose infusion rate during a euglycemic insulin clamp did not improve in the modest exercise group but increased 34% in the group that walked further. Although the latter group also achieved greater weight reduction, multiple regression analysis showed that only the effect of walking was significant on measures of insulin action. Similar findings have been made earlier by Bogardus et al. (25), who demonstrated that obese diabetic subjects on diet only did not improve glucose infusion rates, but diet and exercise (at 75% $V_{O_{2max}}$) did. In this study, weight loss was the same for both groups. The Da Qing IGT and Diabetes Study found a similar reduction in those converting to diabetes on a diet only, exercise only, or combined program. They concluded that the efficacy of the diet was similar to that of exercise, and there was no additional benefit of combination therapy, despite a greater reduction in BMI (1). The recent results of the Finnish Diabetes Prevention Study showed that after a mean follow-up of 3.2 years, a combined diet and exercise program reduced conversion from IGT to type 2 diabetes from 23% in the control group to 11% in the intervention group (4). Thus, existing data do not enable us to determine the component of our intensive exercise program that accounted for the improvement in insulin sensitivity. However, our data do suggest that an intervention program that does not include a substantial increase in physical activity in addition to modest weight loss may not produce an appreciable improvement in insulin sensitivity. Furthermore, the level of physical activity required is greater than that currently recommended for the general population.

These data have important public health implications in countries with high rates of type 2 diabetes, and they have a bearing on intervention trials involving people with IGT. In those who have already developed IGT and are prescribed modest exercise as part of their program, it appears that a substantial number will still go on to develop type 2 diabetes (1). The greatest benefit of lifestyle intervention may be seen when instituted in insulin-resistant individuals who have not yet developed IGT and who have achieved an improved level of aerobic fitness.

Acknowledgments— This study was funded by the Health Research Council, Otago University, and the Otago Diabetes Research Trust, New Zealand.

Many thanks to Maggie Oakley and Ashley Duncan for technical assistance.

References

1. Pan X, Li G, Hu Y, Wang J, Yang W, An Z, Hu Z, Lin J, Xiao J, Cao H, Liu P, Jiang X, Jiang Y, Wang J, Zheng H, Zhang H, Bennett P, Howard B: Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. *Diabetes Care* 20:537–544, 1997
2. Pate R, Pratt M, Blair SN, Haskell WL, Macera CA, Bouchard C, Buchner D, Ettinger W, Heath GW, King AC, et al.: Physical activity and public health: a recommendation from the Centres for Disease Control and Prevention and the American College of Sports Medicine. *JAMA* 273:402–407, 1995
3. Krauss RM, Eckel RH, Howard B, Appel LJ, Daniels SR, Deckelbaum RJ, Erdman JW Jr, Kris-Etherton P, Goldberg IJ, Kotchen TA, Lichtenstein AH, Mitch WE, Mullis R, Robinson K, Wylie-Rosett J, St Jeor S, Suttie J, Tribble DL, Bazzarre TL: Revision 2000: a statement for healthcare professionals from the Nutrition Committee of the American Heart Association. *J Nutr* 131:132–146, 2001
4. Tuomilehto J, Lindstrom J, Eriksson J, Valle T, Hamalainen H, Ilanne-Parikka P, Keinanen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M: Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 344:1343–1350, 2001
5. The Diabetes Prevention Program Research Group: The Diabetes Prevention Program: design and methods for a clinical trial in the prevention of type 2 diabetes. *Diabetes Care* 22:623–631, 1999
6. Proietto J, Andrikopoulos S, Rosella G, Thorburn A: Understanding the pathogenesis of type 2 diabetes. Can we get off the metabolic merry-go-rounds? *Aust N Z J Med* 25:870–875, 1995
7. Thomas S, Reading J, Shepard R: Revision of the physical activity readiness questionnaire (PAR-Q). *Can J Sport Sci* 1996: 338–345, 1996
8. McAuley K, Williams S, Mann J, Walker R, Lewis-Barned N, Temple L, Duncan A: Diagnosing insulin resistance in the general population. *Diabetes Care* 24:460–464, 2001
9. Riccardi G, Rivellese AA: Dietary treatment of the metabolic syndrome: the optimal diet. *Br J Nutr* 83 (Suppl. 1):S143–S148, 2000
10. New Zealand Institute of Crop and Food Research: *The New Zealand Food Composition Database*. Palmerston North, New Zealand, New Zealand Institute of Crop and Food Research, 1993
11. Hopkins W, Wilson N, Russell D: Validation of the physical activity instrument for the Life in New Zealand national survey. *Am J Epidemiol* 133:73–82, 1991
12. American College of Sports Medicine Position Stand: The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness in healthy adults. *Med Sci Sports Exerc* 22:265–274, 1990
13. Alberti K, Zimmet P: Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and Classification of Diabetes Mellitus Provisional Report of a WHO Consultation. *Diabet Med* 15:539–553, 1998
14. Going S: Detection of small changes in body composition by dual-energy X-ray absorptiometry. *Am J Clin Nutr* 57:845–850, 1993
15. Taylor R, Keil D, Gold E, Williams S, Goulding A: Body mass index, waist girth, and waist-to-hip ratio as indexes of total and regional adiposity in women: evaluation using receiver operating characteristic curves. *Am J Clin Nutr* 67: 44–49, 1998
16. McInnis K, Balady G: Comparison of submaximal exercise responses using the Bruce vs modified Bruce protocols. *Med Sci Sports Exerc* 26:103–107, 1994
17. DeFronzo R, Ferrannini E: Insulin resistance: a multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diabetes Care* 14:173–194, 1991
18. Goodpaster BH, Kelley DE, Wing RR, Meier A, Thaete FL: Effects of weight loss on regional fat distribution and insulin sensitivity in obesity. *Diabetes* 48:839–847, 1999
19. Markovic T, Jenkins A, Campbell L,

Furler S, Kraegen E, Chisholm D: The determinants of glycemic responses to diet restriction and weight loss in obesity and NIDDM. *Diabetes Care* 21:687–694, 1998
20. Ross R, Dagnone D, Jones P, Smith H, Paddags A, Hudson R, Janssen I: Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men: a randomized, controlled trial. *Ann Intern Med* 133:92–103, 2000
21. Storlien L, Baur L, Kritetos A, Pan D, Cooney G, Jenkins A, Calvert G, Campbell L: Dietary fats and insulin action. *Diabetologia* 39:621–631, 1996
22. Vessby B, Tengblad S, Lithell H: Insulin sensitivity is related to the fatty acid composition of serum lipids and skeletal muscle phospholipids in 70 year old men. *Diabetologia* 37:1044–1050, 1994
23. Borghouts L, Keizer H: Exercise and insulin sensitivity: a review. *Int J Sports Med* 21:1–12, 2000
24. Yamanouchi K, Shinozaki T, Chikada K, Nishikawa T, Ito K, Shimizu S, Ozawa N, Suzuki Y, Maeno H, Kato K, Oshida Y, Sato Y: Daily walking combined with diet therapy is a useful means for obese NIDDM patients not only to reduce body weight but also to improve insulin sensitivity. *Diabetes Care* 18:775–778, 1995
25. Bogardus C, Ravussin E, Robbins D, Wolfe R, Horton E, Sims E: Effects of physical training and diet therapy on carbohydrate metabolism in patients with glucose intolerance and non-insulin-dependent diabetes mellitus. *Diabetes* 33: 311–318, 1984