Make Your Diabetic Patients Walk

Long-term impact of different amounts of physical activity on type 2 diabetes

Chiara Di Loreto, md
Carmine Fanelli, md
Paola Lucidi, md
Giuseppe Murdolo, md
Arianna De Cicco, md
Natascia Parlanti, md
Anna Ranchelli, md
Cristina Fatone, md
Chiara Taglioni, md
Fausto Santeusanio, md
Pierpaolo De Feo, md

OBJECTIVE — To establish the impact of different amounts of increased energy expenditure on type 2 diabetes care.

RESEARCH DESIGN AND METHODS — Post hoc analysis of long-term effects of different amounts of increased energy expenditure (metabolic equivalents [METS] per hour per week) through voluntary aerobic physical activity was performed in 179 type 2 diabetic subjects (age 62 ± 1 years [mean ± SE]) randomized to a physical activity counseling intervention. Subjects were followed for 2 years and divided into six groups based on their increments in METs per hour per week: group 0 (no activity, $n = 28$), group 1–10 (6.8 ± 0.3, $n = 27$), group 11–20 (17.1 ± 0.4, $n = 31$), group 21–30 (27.0 ± 0.5, $n = 27$), group 31–40 (37.5 ± 0.5, $n = 32$), and group >40 (58.3 ± 1.8, $n = 34$).

RESULTS — At baseline, the six groups did not differ for energy expenditure, age, sex, diabetes duration, and all parameters measured. After 2 years, in group 0 and in group 1–10, no parameter changed; in groups 11–20, 21–30, 31–40, and >40, HbA_{1c}, blood pressure, total serum cholesterol, triglycerides, and estimated percent of 10-year coronary heart disease risk improved ($P < 0.05$). In group 21–30, 31–40, and >40, body weight, waist circumference, heart rate, fasting plasma glucose, serum LDL and HDL cholesterol also improved ($P < 0.05$). METs per hour per week correlated positively with changes of HDL cholesterol and negatively with those of other parameters ($P < 0.001$). After 2 years, per capita yearly costs of medications increased ($P = 0.008$) by $393 in group 0, did not significantly change in group 1–10 ($206, $P = 0.09$), and decreased in group 11–20 (−$196, $P = 0.01$), group 21–30 (−$593, $P = 0.009$), group 31–40 (−$660, $P = 0.003$), and group >40 (−$579, $P = 0.001$).

CONCLUSIONS — Energy expenditure >10 METs · h^{-1} · $week^{-1}$ obtained through aerobic leisure time physical activity is sufficient to achieve health and financial advantages, but full benefits are achieved with energy expenditure >20 METs · h^{-1} · $week^{-1}$.

Diabetes Care **28:1295–1302, 2005**

From the Department of Internal Medicine, Section of Internal Medicine, Endocrine and Metabolic Sciences, University of Perugia, Perugia, Italy.

Address correspondence and reprint requests to Prof. Pierpaolo De Feo, DIMI, Via E. Dal Pozzo, 06126 Perugia, Italy. E-mail: defeo@dimisem.med.unipg.it.

Received for publication 29 November 2004 and accepted in revised form 15 January 2005.

Abbreviations: CHD, coronary heart disease; FPG, fasting plasma glucose; MET, metabolic equivalent; NHS, National Health Service.

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

© 2005 by the American Diabetes Association.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

See accompanying editorial, p. 1524.

Western and developing countries face two serious health problems: the rising prevalence of obesity and diabetes and the fact that people no longer need to be physically active in their daily lives (1–4). Many studies have shown that regular physical activity improves quality of life, reduces the risk of mortality from all causes (1–4), and is particularly advantageous in subjects with impaired glucose tolerance (5,6) or type 2 diabetes (7–12). Physical activity counseling can motivate most diabetic subjects to increase their levels of voluntary energy expenditure (9–11), but, at present, the relationship between amounts of physical activity and long-term beneficial effects in type 2 diabetes care is unknown. The American Diabetes Association emphasizes the benefits of regular physical activity in the prevention and treatment of type 2 diabetes, referring to proposals given to the general population by several scientific societies (1–4,12). These recommendations advise individuals to engage in ≥30 min moderate-intensity physical activity on most (preferably all) days of the week. To maintain long-term weight loss, data from several studies suggest that more exercise (60–75 min/day) is needed (1,12,13).

As no long-term studies have been performed in type 2 diabetic subjects, the influence of different amounts of energy expenditure on diabetes care remains to be established. This study examines the 2-year impact of different increments in energy expenditure on several physiological and biochemical outcomes, on direct medical costs, and on direct and indirect social costs in a group of type 2 diabetic subjects who were randomized to an exercise counseling intervention (9). Our data show that 2 years' counseling resulted in remarkable cost saving; health benefits and financial advantages were significantly related with increased amounts of energy expenditure.

RESEARCH DESIGN AND METHODS

— Eligibility criteria included diagnosis of type 2 diabetes of at

least 2 years and age >40 years before recruitment. Patients who had illnesses that could seriously reduce life expectancy or cause cardiac, liver, or renal failure were excluded. All eligible patients consecutively attending our outpatient diabetes clinic over a period of 3 months (October 1999 to January 2000) were recruited. After obtaining written informed consent, 182 patients (age 62 ± 0.7 years, 88 men and women, diabetes duration 7.6 ± 0.3 years) were randomized to the study, which closed on December 2002. The details of the intervention have been reported elsewhere (9). Briefly, it consisted of a first counseling session of at least 30 min conducted by a physician and designed to advise on physical activity, followed 1 month later by a telephone call made by the same doctor and then by 15-min sessions every 3 months in the outpatient clinic for a total of seven maintenance visits; the duration of the study was 2 years. Patients were treated for diabetes and other diseases according to accepted international guidelines. The diet suggested to all patients contained 55% of calories from complex carbohydrates, 30% from fat, and 15% from protein. Overweight and obese patients were given a diet with a negative balance of ~300 kcal/day, including in the calculation the energy expenditure due to voluntary physical activity.

Levels of voluntary physical activity were assessed every 3 months with the Modifiable Activity Questionnaire (14) and calculated as the product of the duration (hours times weeks) of the various activities weighted by an estimate of metabolic equivalent (MET) of each activity (5). The outcome of the intervention was the consistent achievement of an energy expenditure >10 METs · h^{-1} · $week^{-1}$ through moderate intensity (3–6 METs) aerobic leisure time physical activity. Subjects were instructed to exercise at moderate intensity (40–60% of heart rate reserve) between 3 and 6 METs (15). On a daily basis, all patients were asked to record type, intensity, and duration of performed physical activities. Their written reports were examined and discussed with the physician every 3 months. At the end of the study, we collected the detailed reports of 104 weeks from each patient. Most subjects (94%) varied their weekly amounts of energy expenditure <10 METs · h^{-1} · $week^{-1}$. If larger fluctuations in energy expenditure were reported, subjects were transferred into the next group with higher energy expenditure (see STATISTICAL ANALYSIS).

At each session, all subjects underwent measurements of body weight, BMI, waist circumference, resting heart rate, and blood pressure according to NHANES procedures (16). Plasma glucose and HbA_{1c} were measured as previously described (9), serum total cholesterol and triglycerides were measured using a colorimetric assay (Menarini Diagnostics, Florence, Italy), serum HDL cholesterol was measured using a direct enzymatic method (Menarini Diagnostics, Florence, Italy), and LDL cholesterol was calculated using the Friedewald formula (17). Coronary heart disease (CHD) risk was estimated using Framingham risk tables (18).

Costs were generally calculated using standard unit costs of the resources used, averaged on the year 2000 costs of resources in Italy (tables produced by Italian National Institute of Statistics and by Umbria region). Cost analysis included direct medical costs and direct and indirect social costs and is reported in U.S. dollars per capita per year, adjusted to year 2000. Direct medical costs include expenses for medications and other costs usually paid by the National Health Service (NHS), e.g., counseling intervention (hourly rate of physicians $49), laboratory testing, hospitalization, and outpatient care. Direct social costs include the value of the time that participants spent in practicing physical activity, cost of related items (shoes, fitness equipment, etc.), transportation to exercise places, and admission to health clubs. Indirect social costs include time that participants reported as lost from work or usual activities as a result of counseling visits, illness, or injury; each day lost to morbidity was valued at $100. Sensitive analysis was performed to estimate the economic impact of a less effective physical activity counseling. For this purpose we assumed that instead of 125 of 179 (69%), only 90 of 179 (50%) or 60 of 179 (33%) diabetic subjects achieved the target of the intervention (>10 METs · h^{-1} · $week^{-1}$). The 35 and the 65 subjects not reaching the target in the 50 and 33% simulation were equally distributed between groups 0 and 1–10 and equally subtracted from the other four groups.

Statistical analysis

Data obtained over the last year before study entry (basal) and the last year of intervention were analyzed using NCSS 2004 (Kaysville, UT). The primary end point of the study was the estimated 10-year CHD risk. Secondary end points were body weight, BMI, waist circumference, fasting plasma glucose (FPG), HbA_{1c}, systolic and diastolic blood pressure, heart rate, total cholesterol, LDL and HDL cholesterol, and triglycerides. Additional end points were medical and social costs. Results are presented as the means ± SE and 95% CI. Analysis of change from baseline values for each continuous variable were analyzed using paired samples *t* tests. The average rate of change for each variable was calculated using linear regressions according to the least-squares method. To assess the impact of different amounts of energy expenditure, a post hoc analysis was performed on the 179 subjects, dividing them into six groups. Ten METs · h^{-1} · $week^{-1}$ of energy expenditure was chosen as criterion to form the groups because this amount of energy expenditure was the target of the intervention (9) and roughly corresponds to the recommendations of several scientific societies (1–4,12). The 179 subjects were divided into the six following groups: group 0 (no activity, $n = 28$), group 1–10 (6.8 ± 0.3 METs · h^{-1} · $week^{-1}$, $n = 27$), group 11–20 (17.1 ± 0.4, $n = 31$), group 21–30 (27.0 ± 0.5, $n = 27$), group 31–40 (37.5 ± 0.5, $n = 32$), and group >40 (58.3 ± 1.8, $n = 34$), including all the subjects who achieved change in energy expenditure >40 METs · h^{-1} · $week^{-1}$. Analysis was conducted using ANOVA with post hoc analysis (Tukey's test), and proportions were analyzed using the McNemar test. A P value <0.05 indicated significant differences. To maintain an overall type I error rate of 5% ($\alpha = 0.05$), P values were corrected according to the modified Bonferroni procedure proposed by Finner (19), which is more powerful than the traditional Bonferroni approach for multiple test adjustments.

RESULTS — Originally, 182 patients were randomized to the intervention. Three patients did not complete the study. One dropped out of the follow-up, and two died of causes unrelated to physical activity. Data analysis refers to 179 patients who were divided into six groups

Table 1—*Effects of physical activity counseling on energy expenditure (METs per hour per week); body weight; BMI; waist circumference; FPG; HbA_{1c}; systolic and diastolic blood pressure; resting heart rate; serum total, LDL, and HDL cholesterol; serum triglycerides; and 10-year CHD risk in 179 type 2 diabetic subjects divided into six groups on the basis of different amounts of energy expenditure*

	Group 0 (n = 28) A		Group 1–10 (n = 27) B		Group 11–20 (n = 31) C	
	Basal	Change	Basal	Change	Basal	Change
Energy expenditure (METs · h^{-1} · $week^{-1}$)	0.3 ± 0.2	0.6 ± 0.3 (0.0–1.1)	0.3 ± 0.2	6.30 ± 0.4 (5.7–7.2)*	0.4 ± 0.2	17.1 ± 0.4 (16–17.9)
Weight (kg)	80.8 ± 2.0	0.8 ± 0.5 (−0.3 to 1.9)	82.0 ± 2.6	0.6 ± 0.7 (−0.8 to 1.9)	81.3 ± 2.9	0.1 ± 0.3 (−0.6 to 0.8)
BMI ($kg/m^{2)}$	29.5 ± 0.6	0.3 ± 0.2 (−0.1 to 0.7)	29.1 ± 0.6	0.3 ± 0.3 (−0.3 to 0.8)	28.9 ± 0.4	0.03 ± 0.1 (−0.2 to 0.3)
Waist circumference (cm)	97.3 ± 1.6	1.0 ± 0.7 (−0.5 to 2.5)	99.7 ± 2.4	1.0 ± 0.9 (−0.8 to 2.9)	100.6 ± 1.8	−0.9 ± 0.4 (−1.7 to −0.1)
FPG (mmol/l)	9.1 ± 0.4	1.6 ± 2.9 (−7.5 to 4.3)	9.4 ± 0.5	−0.02 ± 0.3 (−0.6 to 0.6)	9.2 ± 0.3	−0.39 ± 0.2 (−0.8 to 0.1)
HbA_{1c} (%)	7.3 ± 0.2	0.03 ± 0.01 (−0.1 to 0.2)	7.6 ± 0.3	−0.06 ± 0.09 (−0.2 to 0.1)	7.7 ± 0.2	−0.4 ± 0.1 (−0.6 to −0.3)†
Maximum blood pressure (mmHg)	147 ± 2	−1.8 ± 0.9 (−3.6 to 0.1)	145 ± 3	−1.5 ± 0.9 (−3.3 to 0.3)	143 ± 3	−6.4 ± 2.4 (−11 to −1.5)*
Minimum blood pressure (mmHg)	91 ± 3	−4.6 ± 2.5 (−9.8 to 0.6)	87 ± 1	−2.4 ± 0.9 (−4.3 to −0.5)	85 ± 1	−2.9 ± 1.6 (−4.6 to −1.2)†
Heart rate (bpm)	81 ± 1	1.1 ± 0.7 (−0.4 to 2.4)	79 ± 2	0.5 ± 0.9 (−1.4 to 2.4)	80 ± 1	−0.9 ± 0.4 (−1.7 to −0.1)
Total cholesterol (mmol/l)	5.7 ± 0.1	−0.1 ± 0.05 (−0.3 to 0.1)	5.5 ± 0.1	−0.1 ± 0.1 (−0.4 to 0.1)	5.6 ± 0.2	−0.3 ± 0.1 (−0.4 to −0.1)†
LDL cholesterol (mmol/l)	3.6 ± 0.1	−0.1 ± 0.1 (−0.3 to 0.3)	3.4 ± 0.2	−0.2 ± 0.1 (−0.5 to 0.1)	3.6 ± 0.2	−0.1 ± 0.1 (−0.2 to 0.1)
HDL cholesterol (mmol/l)	1.0 ± 0.1	0.1 ± 0.1 (−0.1 to 0.1)	1.0 ± 0.1	0.1 ± 0.1 (−0.1 to 0.1)	1.0 ± 0.1	0.1 ± 0.1 (−0.1 to 0.2)
Triglycerides (mmol/l)	2.3 ± 0.1	0.1 ± 0.1 (−0.1 to 0.2)	2.2 ± 0.1	0.1 ± 0.1 (−0.1 to 0.2)	2.4 ± 0.1	−0.5 ± 0.1 (−0.7 to −0.2)†
10-year CHD risk (%)	24.4 ± 1.9	0.1 ± 0.3 (−0.6 to 0.7)	21.3 ± 1.8	−0.3 ± 0.5 (−1.2 to 0.6)	22.5 ± 1.6	−2.6 ± 0.6 (−3.9 to −1.3)†

Data are means ± SE and means (95% CI). *$P < 0.05$, †$P < 0.01$ vs. basal. Between-group comparisons are reported in the last two columns. Significant differences are followed by post hoc results (e.g., ABC vs. F means that groups A, B, and C are not different from each other but they are all different compared with group F).

based on their change in increments in energy expenditure (METs per hour per week): group 0 (no activity, n = 28), group 1–10 (6.8 ± 0.3, n = 27), group 11–20 (17.1 ± 0.4, n = 31), group 21–30 (27.0 ± 0.5, n = 27), group 31–40 (37.5 ± 0.5, n = 32), and group >40 (58.3 ± 1.8, n = 34). Group 0 and group 1–10 (31% of the entire population) did not reach the study target (constant energy expenditure >10 METs · h^{-1} · $week^{-1}$), which was achieved by the subjects in the other four groups (69% of the entire population).

Age, diabetes duration, male-to-female ratio, and baseline levels of energy expenditure through voluntary physical activity did not differ in the six groups (Table 1). The intervention increased energy expenditure through voluntary physical activity by 26 ± 2 METs · h^{-1} · $week^{-1}$ ($P < 0.0001$) in the whole group (Table 2). As referred during the regular (every 3 months) ambulatory visits, the different amounts of physical activity practiced by the subjects in the six groups was not conditioned by associated diseases but was the result of only the subjects' free choice to use exercise to improve their state of health.

Group 0

There was no significant change in any of the parameters, except for a significant increase ($P < 0.01$) in medical costs (drugs) and indirect social costs for a total of \$828 · $capita^{-1}$ · $year^{-1}$ after 2 years' follow-up (Tables 1 and 3).

Group 1–10

There was no significant change in any of the health parameters examined and no significant change in medical or indirect social costs after 2 years (Tables 1 and 3).

Group 11–20

There were significant reductions in HbA_{1c} ($P < 0.0001$), systolic ($P = 0.0286$) and diastolic ($P < 0.003$) blood pressure, total cholesterol ($P < 0.0001$), triglycerides ($P < 0.0001$), and 10-year CHD risk ($P = 0.0003$). These results were associated with significant drops in medical ($P = 0.0159$) and social costs ($P = 0.011$), for a total saving ($P < 0.0001$) of \$386 · $capita^{-1}$ · $year^{-1}$ after 2 years' follow-up (Tables 1 and 3).

Group 21–30

There were significant ($P < 0.0001$) reductions in body weight, BMI, waist circumference, FPG, HbA_{1c}, systolic ($P = 0.048$) and diastolic (0.0156) blood pressure, heart rate, total and LDL ($P = 0.0229$) cholesterol, and triglycerides; an ~4% reduction in 10-year CHD risk; and a significant ($P < 0.0001$) increase in HDL cholesterol. These results were asso-

Table 1—*Continued*

Group 21–30 (n = 27) D		Group 31–40 (n = 32) E		Group >40 (n = 34) F		Between-group comparisons	
Basal	Change	Basal	Change	Basal	Change	P	Post hoc analysis
0.7 ± 0.3	27.0 ± 0.5 (25.9–28)†	0.9 ± 0.4	37.5 ± 0.5 (36–38.5)†	0.8 ± 0.3	58.3 ± 1.8 (54.3–62)†	0.000	All groups differ
81.9 ± 2.2	−2.2 ± 0.2 (−2.6 to −1.7)†	83.1 ± 1.7	−3.0 ± 0.3 (−3.6 to −2.4)	79.8 ± 2.0	−3.2 ± 0.3 (−3.7 to −2.7)†	0.268	—
29.3 ± 0.4	−0.8 ± 0.1 (−0.9 to −0.6)†	29.4 ± 0.5	−1.0 ± 0.1 (−1.2 to −0.8)†	29.7 ± 0.4	−1.2 ± 0.1 (−1.4 to −1.0)†	0.256	—
100.0 ± 2.2	−3.8 ± 0.3 (−4.4 to −3.1)†	100.1 ± 1.8	−5.5 ± 0.4 (−6.3 to −4.7)†	97.3 ± 1.6	−7.1 ± 0.5 (−8.1 to −6.2)†	0.000	ABC vs. F
9.1 ± 0.2	−1.2 ± 0.2 (−1.7 to −0.7)†	9.3 ± 0.3	−1.6 ± 0.3 (−2.0 to −1.2)†	8.8 ± 0.2	−1.5 ± 0.1 (−1.8 to −1.3)†	0.000	A vs. F, B vs. DEF, C vs. EF
7.6 ± 0.2	−0.9 ± 0.07 (−1.0 to −0.7)†	7.7 ± 0.2	−1.1 ± 0.1 (−1.3 to −0.9)†	7.6 ± 0.2	−1.0 ± 0.1 (−1.2 to −0.9)†	0.001	B vs. EF
143 ± 3	−5.6 ± 2.7 (−11 to −0.1)*	142 ± 3	−6.6 ± 1.0 (−8.6 to −4.4)†	146 ± 3	−9.1 ± 0.6 (−10.3 to −8)†	0.061	—
86 ± 1	−4.8 ± 1.8 (−8.5 to −1.1)*	84 ± 1	−5.3 ± 0.7 (−6.8 to −3.9)*	86 ± 1	−7.1 ± 1.0 (−9.1 to −5.0)†	0.000	A vs. EF, B vs. EF
79 ± 2	−3.8 ± 0.3 (−4.4 to −3.1)†	79 ± 2	−5.6 ± 0.4 (−6.3 to −4.7)†	76 ± 2	−7.0 ± 0.5 (−8.1 to −6.2)†	0.000	A vs. EF, B vs. F, C vs. F
5.4 ± 0.2	−0.3 ± 0.1 (−0.4 to −0.2)†	5.5 ± 0.1	−0.2 ± 0.1 (−0.3 to −0.1)†	5.6 ± 0.2	−0.3 ± 0.1 (−0.4 to −0.2)†	0.314	—
3.3 ± 0.2	−0.1 ± 0.1 (−0.3 to −0.1)*	3.4 ± 0.1	−0.2 ± 0.1 (−0.3 to −0.1)*	3.6 ± 0.2	−0.2 ± 0.1 (−0.3 to −0.1)†	0.376	—
0.1 ± 0.1	0.1 ± 0.1 (0.1 to 0.2)†	0.1 ± 0.1	0.3 ± 0.1 (0.2 to 0.4)*	1.0 ± 0.1	0.2 ± 0.1 (0.1 to 0.2)†	0.000	ABC vs. EF
2.4 ± 0.1	−0.6 ± 0.1 (−0.8 to −0.5)	2.3 ± 0.1	−0.6 ± 0.1 (−0.8 to −0.5)†	2.2 ± 0.1	−0.8 ± 0.1 (−0.9 to −0.6)†	0.000	AB vs. CDEF
22.9 ± 1.7	−3.7 ± 0.7 (−5.2 to −2.2)†	24.6 ± 1.7	−4.8 ± 1.0 (−6.8 to −2.8)†	21.1 ± 1.5	−4.3 ± 1.0 (−6.3 to −2.4)*	0.000	A vs. CDEF

ciated with significant ($P < 0.0001$) decreases in medical and social costs for a total saving of ~\$1,452 · capita^{-1} · year^{-1} after 2 years' follow-up (Tables 1 and 3).

Groups 31–40 and >40

There were significant ($P < 0.0001$) reductions in body weight, BMI, waist circumference, FPG, HbA_{1c}, systolic and diastolic blood pressure, heart rate, total and LDL ($P = 0.012$) cholesterol, and triglycerides; a 4–5% reduction in 10-year CHD risk; and a significant ($P < 0.0001$) increase in HDL cholesterol. These results were associated with significant ($P < 0.0001$) drops in medical and social costs, for a total saving of ~\$2,000 · capita^{-1} · year^{-1} after 2 years' follow-up (Tables 1 and 3).

Entire intervention group

There were significant ($P < 0.0001$) reductions in body weight, BMI, waist circumference, FPG, HbA_{1c}, systolic and diastolic blood pressure, heart rate, total and LDL cholesterol, and triglycerides; an ~3% reduction in 10-year CHD risk; and a significant ($P < 0.0001$) increase in HDL cholesterol. These results were associated with significant ($P < 0.0001$) drops in medical and social costs, for a

Table 2—*Effects of physical activity counseling on energy expenditure (METs per hour per week), body weight; BMI; waist circumference; FPG; HBA_{1c}; systolic and diastolic blood pressure; resting heart rate; serum total, LDL, and HDL cholesterol; serum triglycerides; and 10-year CHD risk in the entire group of 179 type 2 diabetic subjects*

	Basal	Change
Energy expenditure (METs · h^{-1} · week^{-1})	0.6 ± 0.2	26.0 ± 1.7 (21–28)*
Weight (kg)	81.6 ± 0.8	−1.3 ± 0.2 (−1.6 to −0.8)*
BMI (kg/m^2)	29.3 ± 0.2	−0.4 (−0.6 to −0.3)*
Waist (cm)	99.8 ± 0.8	−2.7 (−3.4 to −2.1)*
FPG (mmol/l)	9.1 ± 0.1*	−0.8 (−1.0 to −0.7)*
HbA_{1c} (%)	7.6 ± 0.1	−0.6 ± 0.1 (−0.7 to −0.5)*
Maximum blood pressure (mmHg)	144 ± 1	−5.4 ± 0.6 (−6.7 to −4.0)*
Minimum blood pressure (mmHg)	87 ± 1	−4.6 ± 1.0 (−5.7 to −3.5)*
Heart rate (bpm)	79 ± 2	−2.8 ± 0.5 (−3.5 to −2.2)*
Total cholesterol (mmol/l)	5.6 ± 0.1	−0.2 ± 0.1 (−0.3 to −0.1)*
LDL cholesterol (mmol/l)	3.5 ± 0.1	−0.2 ± 0.1 (−0.3 to −0.1)*
HDL cholesterol (mmol/l)	1.0 ± 0.1	0.1 ± 0.1 (0.2–0.1)*
Triglycerides (mmol/l)	2.3 ± 0.1	−0.4 ± 0.1 (−0.5 to −0.4)*
10-year CHD risk (%)	22.8 ± 0.7	−2.7 ± 1.0 (−3.4 to −2.1)†

Data are means ± SE and means (95% CI). *$P < 0.01$, †$P < 0.05$ vs. basal.

Table 3—*Effects of physical activity counseling on costs for medical prescriptions, other direct health system costs, direct and indirect social costs, and total costs in 179 type 2 diabetic subjects with different amounts of energy expenditure (METs per hour per week)*

	Drugs		Other health care	
	Basal	Change	Basal	Change
Group 0 (n = 28) A	1,173 ± 44	393 (111 ± 675)*	1,456 ± 77	123 (−25 ± 271)
Group 1–10 (n = 28) B	1,207 ± 52	206 (−34 ± 446)	1,541 ± 67	−7 (−15 ± 1)
Group 11–20 (n = 28) C	1,087 ± 43	−196 (−342 ± −50)*	1,384 ± 86	−92 (−191 ± 7)
Group 21–30 (n = 28) D	1,085 ± 39	−593 (−1,025 ± −161)*	1,414 ± 59	−296 (−518 ± −74)*
Group 31–40 (n = 28) E	1,177 ± 56	−660 (−1,078 ± −242)*	1,543 ± 73	−588 (−1,011 ± −165)*
Group >40 (n = 28) F	1,087 ± 45	−579 (−905 ± −253)*	1,645 ± 84	−794 (−1,241 ± −347)*
All 179 subjects	1,134 ± 55	−259 (−422 ± −96)*	1,528 ± 73	−298 (−521 ± −75)*
50% simulation	1,177 ± 63	−101 (−180 ± −6)*	1,580 ± 75	−207 (−362 ± −52)*
33% simulation	1,175 ± 71	77 (−41 ± 195)	1,571 ± 79	−91 (−200 ± 18)
Between-group comparisons P		<0.001		<0.001
Post hoc analysis		A vs. CDEF, B vs. CDEF, C vs. E		ABC vs. DEF, D vs. F

Data are means ± SE and means (95% CI). Sensitive analysis assumes that instead of 125 of 179 (69%) only 90 of 179 (50%) or 60 of 179 (33%) diabetic subjects achieved the target of the intervention (>10 METs · h^{-1} · $week^{-1}$). *$P < 0.05$ vs. basal, costs in U.S. dollars per capita per year. Between-group comparisons are reported in the last two rows. Significant differences are then followed by post hoc results (e.g., A vs. CDEF means that group A is different from groups C–F; CDEF are not different from each other).

total saving of \$855 · $capita^{-1}$ · $year^{-1}$ after 2 years' follow-up.

Amounts of energy expenditure (METs per hour per week) were inversely related ($P < 0.0001$) with changes in body weight ($r = 0.62$), BMI ($r = 0.62$), waist circumference ($r = 0.77$), FPG ($r = 0.52$), HbA_{1c} ($r = 0.70$), systolic ($r = 0.33$) and diastolic ($r = 0.23$, $P = 0.023$) blood pressure, resting heart rate ($r = 0.76$), triglycerides ($r = 0.56$), and percent 10-year CHD risk ($r = 0.39$) and positively related with changes in HDL cholesterol ($r = 0.39$, $P < 0.0001$). Accordingly, on average, for every increase of 1 MET · $hour^{-1}$ · $week^{-1}$, body weight decreased by 0.08 kg, BMI by 0.03 kg/m^2, waist circumference by 0.16 cm, FPG by 0.03 mmol/l, HbA_{1c} by 0.02%, systolic blood pressure by 0.14 mmHg, diastolic blood pressure by 0.08 mmHg, blood pressure resting heart rate by 0.16 bpm, serum triglycerides by 0.014 mmol/l, and percent 10-year CHD risk by 0.08%; HDL increased by 0.004 mmol/l.

Costs were significantly ($P < 0.0001$) related to energy expenditure. METs per hour per week were inversely related with medical prescription costs ($r = 0.51$, −\$18), other medical costs ($r = 0.33$, −\$23), indirect social costs ($r = 0.40$, −\$36), and total costs ($r = 0.60$, −\$66) and positively related with direct social costs ($r = 0.44$, \$13). In 2 years, a 3-mile daily walk is estimated to reduce drug costs by \$550, other medical costs by \$700, indirect social costs by \$1,100, and total costs by \$2,000 and to increase direct social costs by \$400. Reduction in costs for insulin had a major impact on medication costs. In fact, after 2 years, the number of subjects on insulin therapy fell by 25% (before 59 of 179, after 44 of 179, $P = 0.0003$). There was a significant ($P < 0.0001$) inverse correlation between METs per hour per week and daily units of insulin ($r = 0.38$, −0.35 IU/day), suggesting that over 2 years, a 3-mile daily walk reduces insulin dosage by ~11 units/day.

Sensitive analysis

The 50% compliance model (90 of 179 achieving >10 METs · h^{-1} · $week^{-1}$) predicted significant reductions in medical and social costs with expected total savings of ~\$500 · $capita^{-1}$ · $year^{-1}$ after 2 years. The 33% compliance model (60 of 179 achieving the target) predicted no significant change in medical and social costs after 2 years (Table 3).

CONCLUSIONS — This study demonstrates that physical activity is an effective cost-saving tool in the care of type 2 diabetes. Two years' individual exercise counseling of a randomized population of type 2 diabetic subjects provided valuable health benefits and financial advantages for the NHS and the individual patient. These results confirm that the advice of several scientific societies (1–4,12) recommending ≥30 min moderate-intensity physical activity (>10 METs · h^{-1} · $week^{-1}$) on most days, if not every day, is also valid for type 2 diabetic subjects and demonstrate a significant dose-response relationship.

Post hoc analysis showed that energy expenditure must be >10 METs · h^{-1} · $week^{-1}$ for significant beneficial effects. In fact, energy expenditure ranging between 11 and 20 METs · h^{-1} · $week^{-1}$ significantly reduced HbA_{1c}, total cholesterol, triglycerides, and blood pressure, with a 2.6 ± 0.6% reduction of 10-year CHD risk. These benefits occurred in the absence of any significant weight loss, suggesting that regular aerobic physical activity improves glucose control, lipid profile, and blood pressure independently of weight reduction. This conclusion concurs with results of a meta-analysis examining the effects of exercise on glucose control in type 2 diabetes (8) and on blood pressure in general population (20). However, from our data, it is not possible to rule out that changes in body composition, like a selective loss of visceral fat, contributed to the observed effects. Regarding the effects of exercise on body weight, our results, based on anthropometric measurements (body weight, waist circumference), confirm that visceral fat is a very sensitive target of physical activity (waist circumference vs. energy expenditure: $r = -0.77$) and that to induce long-term losses of body weight, increments in energy expenditure

Table 3—*Continued*

Direct social		Indirect social		Total costs	
Basal	Change	Basal	Change	Basal	Change
14 ± 1.0	10 (−6 ± 26)	1,444 ± 90	302 (51 ± 553)*	4,253 ± 289	828 (224 ± 1,432)*
12 ± 0.8	50* (9 ± 91)	1,356 ± 105	−24 (−71 ± 23)	4,116 ± 311	224 (−29 ± 477)
15 ± 1.2	152 (41 ± 263)*	1,281 ± 68	−250 (−438 ± −62)*	3,767 ± 235	−386 (−663 ± −109)*
11 ± 0.7	199 (48 ± 350)*	1,491 ± 93	−762 (−1,394 ± −130)*	4,001 ± 280	−1,452 (−2,364 ± −540)*
16 ± 1.2	256 (88 ± 424)*	1,434 ± 73	−909 (−1,551 ± −267)*	4,169 ± 228	−1,902 (−3,217 ± −587)*
14 ± 0.9	300 (83 ± 517)*	1,468 ± 80	−997 (−1,601 ± −393)*	4,214 ± 247	−2,070 (−3,325 ± −815)*
14 ± 1.3	168 (41 ± −269)*	1,412 ± 78	−466 (−809 ± −123)*	4,087 ± 235	−855 (−1,520 ± −190)*
14 ± 1	133 (30 ± 236)*	1,440 ± 82	−303 (−539 ± −67)*	4,210 ± 266	−478 (−817 ± −139)*
13 ± 1.1	87 (9 ± 165)*	1,411 ± 82	−106 (−191 ± −21)*	4,170 ± 246	−34 (−80 ± 12)
	<0.001		<0.001		<0.001
	AB vs. F, A vs. E		AB vs. DEF, C vs. EF		AB vs. DEF, C vs. EF

>20 METs · h^{-1} · $week^{-1}$ are required (1,12,13).

Constant energy expenditure >20 METs · h^{-1} · $week^{-1}$ is needed to decrease body weight, BMI, waist circumference, heart rate, and LDL cholesterol and to augment HDL cholesterol. This amount of energy expenditure induces greater reductions in HbA_{1c}, total cholesterol, triglycerides, and blood pressure, leading to an ~4–5% decrease in the 10-year CHD risk. The results in our type 2 diabetic subjects confirm reports of prospective studies in the general population that show an inverse linear dose response between amount of physical activity and all-cause mortality, total cardiovascular disease, and CHD incidence and mortality (1–4,21). This dose-response relationship demonstrates that full beneficial outcomes of exercise are obtained by the most physically active diabetic subjects. Differences in caloric intake among groups might have contributed to the final results. To control for differences in energy balance, all overweight and obese patients were given a diet with a negative balance of 300 kcal/day, including in the calculation the energy expenditure due to voluntary physical activity (9). Thus, the fact that despite greater caloric intakes, subjects of groups with increased energy expenditure had greater beneficial effects emphasizes the effectiveness of regular exercise in the management of type 2 diabetes.

As has been shown in the general population (2), the health benefits of exercise tend to become less evident in patients when the increase in energy expenditure is beyond a certain level, as was indicated by benefit analysis in groups with >20 METs · h^{-1} · $week^{-1}$ (Table 1). Since the threshold for full benefits was observed in group 21–30 (average energy expenditure 27 METs · h^{-1} · $week^{-1}$), we recommend a target of 27 METs · h^{-1} · $week^{-1}$ as a reasonable target of energy expenditure for previously sedentary type 2 diabetic subjects. This goal corresponds to a 3-mile (~5-km) daily walk (1 h/day at a pace of 3 mph or 45 min/day at a pace of 4 mph), which, according to our results, might be expected over 2 years to reduce body weight by 2.4 kg, BMI by 0.9 kg/m^2, waist circumference by 4.8 cm, FPG by 0.9 mmol/l, HbA_{1c} by 1.5%, systolic and diastolic blood pressure by 10 and 7 mmHg, respectively, resting heart rate by 5 bpm, triglycerides by 0.4 mmol/l, and 10-year CHD risk by 2.4% and to augment HDL cholesterol by 0.12 mmol/l. However, it must be emphasized that greater amounts of energy expenditure resulted in added improvements in anthropometric and biochemical markers of the metabolic syndrome, as is clearly shown by the group comparisons reported in Table 1. Subjects in groups with energy expenditure of 31–40 and/or >40 METs · h^{-1} · $week^{-1}$ had significantly greater beneficial effects than the subjects in groups with energy expenditure <20 METs · h^{-1} · $week^{-1}$. Brisk walking was the most common form of leisure time physical activity practiced by our type 2 diabetic subjects; however, it cannot always be recommended. To subjects affected by peripheral neuropathy or lower-limb complications, we suggested exercises with reduced physical impact like stationary cycling, water gym, or swimming.

Cost analysis indicates remarkable financial savings (Table 3). Over 2 years, prescription costs, which were usually medication for diabetes, hypertension, and dyslipidemia, were reduced by $259 and other health care costs by $298 · $capita^{-1}$ · $year^{-1}$ in the entire group, even allowing for the costs of counseling, which took a physician 75 min over the first year and 60 min over the second. Our physical activity counseling performed in type 2 diabetic subjects appears more convenient than the approach used for lifestyle intervention in the Diabetes Prevention Program in subjects with impaired glucose tolerance (5). However, comparison of medical and social costs must be done with caution considering that in the U.S., the cost of medical care is generally higher than in Italy.

Our physical activity counseling model is simple and reproducible (9,10) but requires physician training in the use of the social cognitive approach, which adds costs that were not included in the present calculations. In our study, counseling was conducted by physically active physicians who were highly motivated and obtained a 69% compliance rate after 2 years (9). Lower rates of long-term compliance might have been achieved in other settings. For this reason, Table 3 reports a sensitive analysis simulating compliance rates of 50 and 33%. Interestingly, physical activity counseling remains financially advantageous, even when only one of two or three diabetic subjects reaches the target of >10 METs · h^{-1} · $week^{-1}$. In fact, although the 33% compliance rate model does not significantly reduce costs versus baseline, it remains cost saving compared with sedentary diabetic sub-

jects whose health costs increased over 2 years by \$516 · capita^{-1} · year^{-1}. Again, compared with this latter group, even small amounts of energy expenditure (1–10 METs · h^{-1} · week^{-1}) save money as shown by the lack of increase over 2 years in costs for medical prescriptions in group 1–10 (Table 3). Furthermore, savings with our cost analysis, limited as they are to a 2-year time frame, are largely underestimated because long-term benefits related to the significant reduction in CHD risk (22) are not taken into account.

Post hoc subgroup cost analysis shows that as with the health benefits, the greatest financial benefits are achieved by groups with energy expenditure >20 METs · h^{-1} · week^{-1} (average energy expenditure: 27 METs · h^{-1} · week^{-1}). Money saving tends to become less evident when the increase in energy expenditure is beyond a certain level. In subjects with highest energy expenditure (group >40), savings due to lower medical costs and indirect social costs are partially counterbalanced by the increased costs of physical activity, i.e., exercise apparel, footwear, and gym costs. Thus, also from the financial point of view, recommending energy expenditure amounts of 27 METs · h^{-1} · week^{-1} appears to be an appropriate target for previously sedentary type 2 diabetic subjects.

In conclusion, the present study confirms the long-term efficacy of a program of physical activity counseling (9–11), confirms the beneficial effects of exercise on cardiovascular risk factors (1–4,11), and demonstrates that health benefits are associated with remarkable savings in the NHS care of type 2 diabetes. The present data strongly support the need for, and convenience of, instituting physical activity programs as an essential part of therapy for type 2 diabetes. Our diabetic subjects practiced only aerobic activities at moderate intensity, and most of them chose fitness walking. It remains to be established whether exercise at higher intensities (>6 METs) and mixed aerobic/anaerobic exercise might have provided additional benefits. In addition, future studies are required to establish if type 2 diabetic subjects have individual differences in metabolic responses to regular exercise and the extent to which genetic heterogeneity might affect the variability in training response (23,24).

References

1. Klein S, Sheard NF, Pi-Sunyer X, Daly A, Wylie-Rosett J, Kulkarni K, Clark NG, American Diabetes Association, North American Association for the Study of Obesity, American Society for Clinical Nutrition: Weight management through lifestyle modification for the prevention and management of type 2 diabetes: rationale and strategies. *Diabetes Care* 27: 2067–2073, 2004
2. Centers for Disease Control and Prevention and the American College of Sports Medicine: Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA* 273:402–407, 1995
3. Task Force on Community Preventive Services: Increasing physical activity: a report on recommendations of the Task Force on Community Preventive Services. *MMWR Recomm Rep* 50:1–14, 2001
4. Thompson PD, Buchner D, Pina IL, Balady GJ, Williams MA, Marcus BH, Berra K, Blair SN, Costa F, Franklin B, Fletcher GF, Gordon NF, Pate RR, Rodriguez BL, Yancey AK, Wenger NK: American Heart Association Council on Clinical Cardiology Subcommittee on Exercise, Rehabilitation, and Prevention, American Heart Association Council on Nutrition, Physical Activity, and Metabolism Subcommittee on Physical Activity: Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). *Circulation* 107:3109–3116, 2003
5. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM, Diabetes Prevention Program Research Group: Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 346:393–403, 2002
6. Tuomiletho J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, Keinanen-Kiuaanniemi S, Laasko 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
7. Horton ES: Role and management of exercise in diabetes mellitus. *Diabetes Care* 11:201–211, 1988
8. Boulé N, Haddad E, Kenny G, Wells G, Sigal R: Effects of exercise on glycemic control and body mass in type 2 diabetes: a meta-analysis of controlled clinical trials. *JAMA* 286:1218–1227, 2001
9. Di Loreto C, Fanelli C, Lucidi P, Murdolo G, De Cicco A, Parlanti N, Santeusanio F, Brunetti P, De Feo P: Validation of a counseling strategy to promote the adoption and the maintenance of physical activity by type 2 diabetic subjects. *Diabetes Care* 26:404–408, 2003
10. Smith SA, Vickers KS: A counseling strategy was better than usual care for adopting and maintaining physical activity in type 2 diabetes (Letter). *ACP Journal Club* 139:69, 2003
11. Kirk A, Mutrie N, MacIntyre P, Fisher M: Effects of a 12-month physical activity counselling intervention on glycaemic control and on the status of cardiovascular risk factors in people with type 2 diabetes. *Diabetologia* 47:821–832, 2004
12. Sigal RJ, Kenny JP, Wassermann DH, Castaneda-Sheppa G: Physical activity/exercise and type 2 diabetes. *Diabetes Care* 27: 2518–2539, 2004
13. Jakicic JM, Marcus BH, Gallagher KI, Napolitano M, Lang W: Effect of exercise duration and intensity on weight loss in overweight, sedentary women. *JAMA* 290:1323–1330, 2001
14. Kirska AM, Caspersen CJ: Introduction to a collection of a physical activity questionaries. *Med Sci Sports Exerc* 29:S5–S9, 1997
15. General principles of exercise prescription. In *ACSM's Guidelines for exercise testing and prescription.* 6th ed. American College of Sports Medicine, Baltimore, MD, Lippincott, Williams & Wilkins, 2000, p. 137–164
16. National Health and Nutrition Examination Survey: NHANES 1999–2000 data files. Available from http://www.cdc.gov/nchs/about/major/nhanes/nhanes99_00.htm. Accessed October 2004
17. Friedewald N, Nevy R, Frederickson D: Estimation of the concentration of LDL cholesterol in plasma without the use of preparative ultracentrifuge. *Clin Chem* 18: 499–502, 1972
18. Lloyd-Jones DM, Larson MG, Beiser A, Levy DSO: Lifetime risk of developing coronary heart disease. *Lancet* 353:89–92,1999
19. Finner H: On a monotonicity problem in step-down multiple test procedures. *J Am Stat Assoc* 88:920–923, 1993
20. Whelthon SP, Chin A, Xin X, He J: Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. *Ann Intern Med* 136:493–503, 2002
21. Haennel RG, Lemire F: Physical activity to prevent cardiovascular disease: how much is enough? *Can Fam Physician* 48: 65–71, 2002
22. The Centers for Disease Control and Pre-

vention: Leads from the morbidity and mortality weekly report, Atlanta, GA: Public Health Focus: physical activity and the prevention of coronary heart disease. *JAMA* 270: 1529–1530, 1993

23. Bouchard C, Rankinen T: Individual differences in response to regular physical activity. *Med Sci Sports Exerc* 33:S446–S451, 2001
24. Bouchard C, An P, Rice T, Skinner JS, Wilmore JH, Gagnon J, Perusse L, Leon AS, Rao DC: Familial aggregation of VO_{2max} response to exercise training: results from the HERITAGE Family Study. *J Appl Physiol* 87:1003–1008, 1999