Cardiorespiratory Fitness, Glycemic Status, and Mortality Risk in Men

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OBJECTIVE— To determine the association of baseline cardiorespiratory fitness to all-cause mortality across the range of blood glucose levels.

RESEARCH DESIGN AND METHODS— Data from a prospective study of 8715 men (average age 42 yr), followed for an average of 8.2 yr (range 1–15 yr), were analyzed. Cardiorespiratory fitness was assessed by maximal-exercise treadmill testing. Men with evidence of clinical vascular disease or who did not achieve 85% of their age-predicted maximum heart rate during exercise testing were excluded from analyses.

RESULTS— Age-adjusted death rates increased with higher levels of fasting blood glucose. Regardless of glycemic status, fit men had lower age-adjusted all-cause death rates than their less fit counterparts. For men with fasting blood glucose ≥7.8 mM or physician-diagnosed non-insulin-dependent diabetes mellitus (NIDDM), the age-adjusted death rates per 10,000 person-yr of follow-up in unfit and fit subjects were 82.5 and 45.9, respectively. The age-adjusted relative risk of death due to all causes was significantly elevated in the lower-fitness group within each of three glycemic status levels: fasting blood glucose <6.4 mM; relative risk (RR) = 1.93 (95% confidence interval [95% CI] 1.15–3.26); fasting blood glucose 6.4–7.8 mM; RR = 3.42 (95% CI 2.27–5.15); and fasting blood glucose ≥7.8 mM or with NIDDM, RR = 1.80 (95% CI 1.25–2.58). Multivariate analyses, controlling for risk factors of mortality (age, resting systolic blood pressure, serum cholesterol, body mass index, family history of heart disease, follow-up interval, and smoking habit) showed a higher risk of death due to all causes for unfit compared with fit men. Multivariate risks of death associated with low fitness, compared with higher fitness (RR), in the three glycemic status groups were: fasting blood glucose <6.4 mM, RR = 1.38 (95% CI 1.09–1.74); fasting blood glucose 6.4–7.8 mM, RR = 1.61 (95% CI 0.91–2.86); and fasting blood glucose ≥7.8 mM or with NIDDM, RR = 1.92 (95% CI 0.75–4.90).

CONCLUSIONS— These data suggest that risk of death increases with less-favorable glycemic status, and that cardiorespiratory fitness may attenuate the forces of impaired carbohydrate metabolism on mortality from any cause.

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RECEIVED FOR PUBLICATION 14 MAY 1991 AND ACCEPTED IN REVISED FORM 6 SEPTEMBER 1991.

Diabetes mellitus is a disease that increases the risk of human mortality, particularly that due to coronary heart disease (1). Less-severe forms of impaired carbohydrate metabolism (ICM) are not only the best predictors of future incidence of diabetes (2–5) but also have been postulated as conditions that may increase the risk for death due to all causes and to cardiovascular disease in particular. However, studies on this issue have provided conflicting evidence (6–10).

Higher levels of physical activity and cardiorespiratory fitness, on the other hand, are believed to reduce the risk of death due to all causes, cardio vascular disease, and perhaps some cancers (11–14). Furthermore, data from both animals (15,16) and humans (17–20) show that higher levels of exercise and fitness may favorably affect glucose homeostasis. Thus, high levels of physical activity and fitness might be beneficial in improving the mortality experience of people with ICM. Although this rationale provides the basis for exercise and increased physical fitness as a widely accepted clinical treatment for hyperglycemia and diabetes mellitus, long-term effects of exercise and fitness in these patients are virtually unknown. It is partly for this reason that, after critically evaluating the results of available studies, a recent National Institutes of Health Consensus Development Conference (21) expressed skepticism as to the overall benefits of exercise training for people with non-insulin-dependent diabetes mellitus (NIDDM).

It is possible that regular physical activity might benefit patients with ICM even if glycemic control is not improved, but no data are available on this issue. The purpose of this study is to report the results of an investigation into the association of baseline cardiorespiratory fitness to subsequent all-cause mortality in men across the range of glycemic control.

RESEARCH DESIGN AND METHODS — Subjects in this study were 8715 male patients (age 20–84 yr) of a preventive medicine clinic in Dallas, Texas, who were examined at baseline between 1971 and 1982; 190 (age 21–79 yr) subsequently died. All subjects were free of exercise and resting electrocardiographically determined coronary heart disease, self-reported history of myocardial infarction, stroke, or hypertension at baseline. Furthermore, patients who reported being treated with insulin were also excluded.

A complete preventive medical examination was given to all subjects after an overnight fast. Medical history and demographic information, health habits, anthropometry, blood chemistry analysis, blood pressures, electrocardiography, and a cardiorespiratory fitness determination by maximal-exercise treadmill testing were included as part of the examination. Serum glucose in these subjects was measured after a 12-h overnight fast. Specifically, serum glucose was measured with the hexokinase–glucose-6-phosphate dehydrogenase enzymatic method. Other specific procedures and protocols have been reported previously (13,22–23).

There are several distinct dimensions to physical fitness (24), but we refer to cardiorespiratory fitness (measured by time on maximal-exercise treadmill test) as the fitness variable throughout this study. Maximal O_2 uptake, the most widely accepted measure of cardiorespiratory fitness, was estimated by the total duration of time in which a subject was able to complete a maximal-exercise treadmill test (25). Treadmill speed was begun at 88 m/min. A 0% grade was maintained for the 1st min of the test. The grade was increased to 2% the 2nd min of the test and was subsequently raised 1% each minute of the test up to the 25th min. After this time, the speed of the treadmill was increased 5.4 m/min until test termination. Patients were encouraged to give maximal effort on the test and those who did not reach at least 85% of their age-predicted maximal heart rate (220-age) were excluded from further study. Total duration of this test is highly correlated with measured O_2 uptake in healthy men (26).

Quintile cutoff points were defined from the population age-group–specific distribution of treadmill times. Physically unfit men (n = 1365) were defined as those in the bottom 20% of the treadmill time distribution; all others were categorized as fit (n = 7350). Previous work from our group has identified individuals in the 1st quintile as being at significantly increased risk of death, relative to more-fit people (13).

Glycemic status was defined from values measured from fasting blood glucose and self-report of physician-diagnosed diabetes mellitus. Glucose tolerance tests were not available for these patients. Three levels of blood glucose profile were created concordant with the recommendations of the National Diabetes Data Group (27): group 1, fasting blood glucose <6.4 mM; group 2, fasting blood glucose 6.4–7.8 mM; and group 3, fasting blood glucose ≥7.8 mM or a reported personal history of NIDDM. All cases of insulin-dependent diabetes mellitus were excluded from these analyses. The number of men in each of the three groups were 8108, 509, and 98, respectively.

Study subjects were followed for mortality events from their baseline visit through 1985. The average length of follow-up was slightly >8 yr, and the total follow-up experience in this cohort was 64,784 person-yr. Mortality follow-up used various sources to achieve a 94% vital status ascertainment rate. Official death certificates were obtained for most (88%) decedents, and causes of death were coded by a nosologist with the *International Classification of Diseases*, 9th revision (ICD-9).

Mortality rates were computed for each of the two fitness categories within the three glycemic groups and were age-adjusted by the direct method with the total follow-up in each category as the standard. Multivariate estimation of relative risks (RR) with logistic regression was used to examine the independent effects of cardiorespiratory fitness as a risk factor for all-cause mortality in each glycemic control group after adjustment for potential confounding variables of mortality.

RESULTS — The data in Table 1 are baseline descriptive information and risk-factor status of each of the three glycemic groups. Means and 95% confidence intervals (CI) for continuous data and percentage distributions of smoking status are presented. Variables in Table 1 generally show an unfavorable trend across the three groupings. Specifically, mean age, weight, body mass index (BMI), blood pressure, and cholesterol are higher in men with higher levels of fasting blood glucose. Mean time on treadmill (cardiorespiratory fitness) is incrementally lower with higher levels of fasting blood glucose.

All-cause mortality rates by glycemic status within each of the two fitness groupings are shown in Fig. 1. Fit men with fasting blood glucose <6.4 mM had the lowest age-adjusted death rate (21.4/10,000 person-yr), although the highest death rate was in those men who were unfit and had a fasting blood glucose of 6.4–7.8 mM (101.6/10,000 person-yr). A significant linear trend of increasing death rates across glycemic status groups was seen in the fit men (slope = 18.2, 95% CI = 3.3–33.1). The unfit men also demonstrated an increasing slope (2.8), but CIs around this estimate included unity (−15.2–20.7). Moreover, within each class of glycemic status, those who were fit had lower mortality rates than those who were unfit. Note that those men who were fit and were in the most unfavorable glycemic control category

Table 1—*Descriptive information and risk-factor status by glycemic status (Cooper Clinic healthy men, 1971–1985)*

	<6.4 mM (N = 8108)		6.4–7.8 mM (N = 509)		≥7.8 mM or NIDDM (N = 98)	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
Age (yr)	41.7	41.5–41.9	46.0	45.1–46.8	47.3	45.6–49.0
Weight (kg)	80.7	80.5–81.0	85.7	84.5–87.1	87.3	84.0–90.6
Body mass index (kg/m^2)*	25.5	25.4–25.6	27.2	26.8–27.6	28.0	27.0–29.0
Systolic blood pressure (mmHg)	119.5	119.2–119.8	126.6	125.3–127.9	128.3	125.0–131.6
Diastolic blood pressure (mmHg)	79.3	79.1–79.5	83.6	82.8–84.4	83.7	81.9–85.5
Treadmill time (s)	1022.1	1016.1–1028.1	876.5	853.2–899.8	794.2	741.2–847.2
Total cholesterol (mM)	5.42	5.40–5.45	5.87	5.77–5.97	5.94	5.72–6.17
Glucose (mM)	5.39	5.38–5.40	6.80	6.78–6.83	9.40	8.68–10.11
Follow-up (yr)	8.2	8.1–8.3	9.6	9.3–9.9	9.1	8.5–9.8
Current smoker (%)	22.8		20.4		27.5	

CI, confidence interval.
*Missing heights for 47 men and were unable to calculate body mass index for 37 in group 1, 6 in group 2, and 4 in group 3.

(≥7.8 mM or NIDDM) had an age-adjusted all-cause mortality rate (45.9/10,000 person-yr) that approximated that of those who were classified as unfit and had fasting blood glucose <6.4 mM (41.5/10,000 person-yr). The age-adjusted RR of death due to all causes was significantly elevated in the low-fitness group within each of the three glycemic status categories: group 1, RR = 1.93 (95% CI 1.15–3.26); group 2, RR = 3.42 (95% CI 2.27–5.15); and group 3, RR = 1.80 (95% CI 1.25–2.58).

There were 105 deaths due to ischemic cardiovascular disease (ICD-9 390–448) in these men. Eighty-two deaths occurred in group 1, 13 in group 2, and 10 in group 3. Death rates per 10,000 person-yr of observation in those men who were unfit at baseline in each of the three ascending fasting blood glucose groups are shown in Fig. 2. A pattern similar to that of the all-cause mortality rates is seen in both fit and unfit men. However, the cardiovascular disease death rate in men who were unfit and in group 3 is lower than in similar men who were fit. Two deaths occurred in this category. The age-adjusted RR of death due to cardiovascular disease was significantly elevated in the low-fitness group within two of the three glycemic groups: group 1, RR = 2.54 (95% CI 1.26–5.13); group 2, RR = 2.98 (95% CI 1.77–5.02); and group 3, RR = 0.67 (95% CI 0.40–1.11).

The data in Table 2 are mortality information by separate exposures of other risk factors stratified by each of the three glycemic status groups. In general, similar associations are observed across the three levels of glycemic control. Higher blood pressure and cholesterol, cigarette smoking, and lower cardiorespiratory fitness were associated with higher risk of death in each of the three groups. Little association was seen for BMI in the two lower glycemic status groups. A significant protective association was noted for higher BMI in the highest glycemic status group, although there was a lower RR in each of the three groups. This estimate (highest glycemic control category) is based on a total of two deaths in the higher BMI group.

Multiple logistic regression was used to estimate the risk of all-cause mortality in the low-fitness group relative to the high-fitness group for each of the three glycemic control categories (Table 3). The RR estimates for the three groups within each glycemic control category are adjusted for simultaneous associations with age, BMI, glucose, systolic blood pressure, serum total cholesterol, smoking habit, family history of heart disease, and follow-up interval. In those men whose fasting blood glucose value was <6.4 mM, the risk of all-cause mortality in the lower 20% of the fitness distribution, relative to the other 80%, was 1.38. Men with elevated blood glucose (6.4–7.8 mM) and who were in the low-fitness group had an RR of death of 1.61. Finally, men with blood glucose values ≥7.8 mM or a history of NIDDM were at a 92% increased risk of all-cause mortality if they were unfit. The 95% CIs around risk estimates for the two higher blood glucose categories included unity.

Multivariate estimates of the RR of cardiovascular disease death in the

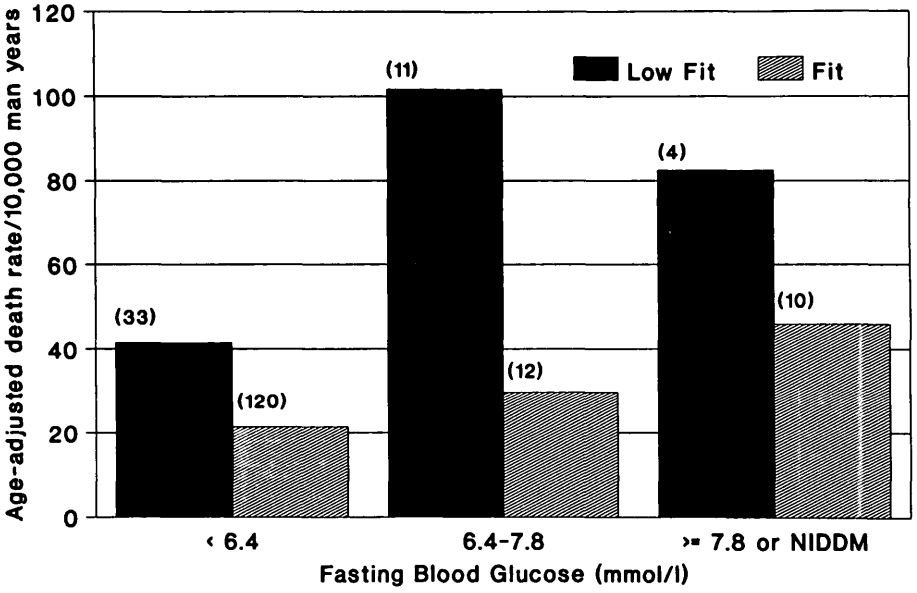

Figure 1—*Age-adjusted all-cause death rates/10,000 person-yr of observation by fitness grouping within glycemic status (Cooper Clinic men, 1971–1985). Numbers of deaths on which each rate is based are in parentheses above bars.*

low-fitness men at baseline was elevated in each of the three glycemic control groups. Estimates were: group 1, 1.62 (95% CI 1.21–2.18); group 2, 1.43 (95% CI 0.69–3.00), and group 3, 1.80 (95% CI 0.67–4.82).

Multivariate analyses were also conducted with cardiorespiratory fitness values treated as a continuous variable rather than as two categorical variables. After adjustment for the potential confounding variables, results similar to those above were observed. Per minute of lower treadmill time, RR estimates for all-cause mortality in each of the three glycemic control categories were: group 1, 1.09 (95% CI 1.04–1.14); group 2, 1.20 (95% CI 1.04–1.38); and group 3, 1.28 (95% CI 0.98–1.67). Comparable values for risk of cardiovascular disease death per minute of lower treadmill time in the three glycemic control categories were: group 1, 1.09 (95% CI 1.02–1.16); group 2, 1.14 (95% CI 0.94–1.38); and group 3, 1.25 (95% CI 0.96–1.64).

CONCLUSIONS— The data presented suggest a direct association between glycemic status and all-cause mortality. Men with lower levels of fasting blood glucose died at lower rates than their less glucose-tolerant counterparts. Furthermore, at each level of glycemic control, fit men had a lower risk of dying during the follow-up than unfit men. The increased risk appears to hold after multivariate adjustment for age and other confounding factors, although in some cases, these increased risks are not statistically different from unity, perhaps due to fewer deaths in some categories. This apparent relationship of cardiorespiratory fitness to mortality in ICM men is quite similar to that seen in men with a normal glucose profile. Thus, cardiorespiratory fitness is a substantial effect modifier of the observed relationship between blood glucose level and all-cause mortality in this group of men.

This study, the first to our knowledge to investigate the association between cardiorespiratory fitness and mortality across the spectrum of glycemic control and on a population basis, suggests that higher levels of cardiorespiratory fitness may attenuate the adverse impact of hyperglycemia and clinical diabetes mellitus on subsequent all-cause mortality. Indeed, the data suggest that fit men with blood glucose levels ≥7.8 mM or with NIDDM are at similar risk of death to those men who are unfit and who have a normal blood glucose profile. Because cardiorespiratory fitness can be improved by regular physical activity, these findings (although not conclusive) seem to support the use of physical activities that increase cardiorespiratory fitness as a cornerstone to the effective management of patients with abnormal blood glucose profiles or NIDDM.

The biological mechanisms through which this association may be operating are of interest. One explanation may be that increased cardiorespiratory fitness is working through its effects on other risk factors for death. Indeed, after controlling for the potential confounding factors, differences in death rates between unfit and fit men were attenuated from the differences seen with age adjustment only. Nonetheless, low-fitness men in group 2 (fasting blood glucose 6.4–7.8 mM) were still 61% more likely to die than their high-fitness counterparts, and the low-fitness men in group 3 (fasting blood glucose ≥7.8 mM or NIDDM) were 92% more likely to die than similarly classified fit men.

Higher levels of physical activity and cardiorespiratory fitness favorably alter or associate with more favorable levels of many of the variables that were controlled for in these analyses (23), and these factors are more prevalent in people with higher levels of blood glucose and those individuals who develop diabetes (28). Therefore, it is plausible that some of the beneficial effects of higher levels of cardiorespiratory fitness observed in the age-ad-

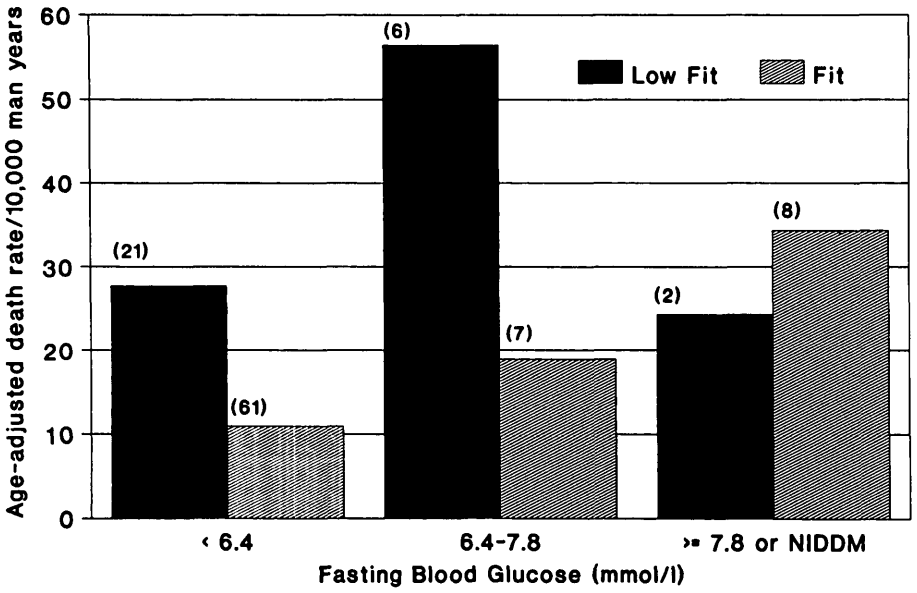

Figure 2—*Age-adjusted cardiovascular disease death rates/10,000 person-yr of observation by fitness grouping within glycemic status (Cooper Clinic men, 1971–1985). Numbers of deaths on which each rate is based are in parentheses above bars.*

justed rates is through beneficial effects on these or other factors that may not have been completely controlled for or were not available for analysis in this study (i.e., insulin sensitivity, adiposity or fat distribution, platelet aggregability, coronary perfusion, and propensity toward ventricular arrhythmias). Physically fit people may also have larger, more muscular hearts and could, therefore, be more likely to survive acute myocardial infarctions.

There are several possible limitations to our study, one of which is the method of classifying these men into exposure groups. The National Diabetes Data Group recommends two fasting plasma glucose determinations and sometimes an oral glucose tolerance test to correctly diagnose individuals as having diabetes mellitus or impaired glucose tolerance (27). Our measure of glycemic status was a single fasting plasma glucose value. Thus, the presence of false-positives and false-negatives cannot be ruled out. Although such misclassification is possible, our investigation of the mortality experience across the range of fasting plasma glucose levels would seem to minimize the problem, especially given the trends of increasing death rates across glycemic categories.

Instability in some death rates in these analyses is an issue. There was a total of four deaths (2 due to cardiovascular disease) in the unfit men whose fasting glucose values were ≥7.8 mM or who had NIDDM. This may help explain why the death rates (all cause and cardiovascular disease) were greater in low-fitness men with fasting glucose values 6.4–7.8 mM compared with the ≥7.8 mM or NIDDM category. The instability is further evidenced by the wide CIs around the risk estimates in this group (Table 3). The choice to maintain the clinically relevant categories for analyses was more important than having equivalent representation among groupings.

The maximal heart rate and disease history exclusions were made to help ensure that the group under study was apparently healthy (other than possible NIDDM). This means that associations similar to those reported here in people who happen to be afflicted with one or more of the exclusion criteria are unknown. Despite the exclusions, there is still a possibility that people with subclinical disease were not excluded and that disease may be in the causal pathway affecting (lowering) fitness levels. Other analyses have shown no difference in the association between fitness level and the risk of mortality between people with a short-term follow-up (<3 yr) and a longer-term follow-up (≥3 yr) (13). Although this does not definitively rule out the presence of subclinical disease, it would indicate that such an effect is not biasing the mortality results.

Our study population was largely from middle to upper socioeconomic classes and was generally well-educated, who chose to come to a preventive medicine clinic for an elective medical evaluation. However, the study group was similar on key physiological variables when compared with other representative samples of North-American men (29). Blood pressures, estimates of maximal O_2 uptake, and body weight were similar to those of men in the Lipid Research Clinics Prevalence Study and the Canada Fitness Survey. Moreover, total cholesterol was actually slightly higher, on the average, in our subjects than in the Lipid Research Clinics data, and the prevalence of ICM was similar to that estimated for all U.S. men (30).

Although physical activity was not directly analyzed in these analyses, it is possible to estimate the amount of exercise necessary to move from the low-fitness group (lower 20%) to the higher-fitness group. For example, the estimated maximal O_2 uptake for a 40- to 49-yr-old man in this study who was in the lower 20% of the fitness distribution would be <32 ml $\cdot$ kg^{-1} $\cdot$

Table 2—*Age-adjusted all-cause mortality rates and relative risks of death by glycemic status and other risk-factor levels (Cooper Clinic healthy men, 1971–1985)*

	Deaths	Follow-up (person-yr)	Age-adjusted death rates*/ 10,000 person-yr	Relative risk	95% confidence interval
Glycemic status <6.4 mM					
Fitness					
High	120	54,670	21.4	1.0	
Low	33	10,114	41.5	1.9	1.2–3.3
Systolic blood pressure (mmHg)					
<140	127	58,977	22.3	1.0	
≥140	26	5806	27.7	1.2	0.7–2.2
Age (yr)					
<50	88	52,098	13.4	1.0	
≥50	65	12,688	10.0	0.7	0.3–1.7
Cholesterol (mM)					
<6.24	88	50,341	18.3	1.0	
≥6.24	65	14,441	41.4	2.3	1.3–3.9
Smoking					
No	102	51,136	19.3	1.0	
Yes	51	13,648	42.9	2.2	1.3–3.7
Body mass index (kg/m^2)					
<27.4	126	51,004	24.3	1.0	
≥27.4	27	13,779	19.8	0.8	0.4–1.4
Family history coronary heart disease					
No	122	51,237	24.9	1.0	
Yes	31	13,546	19.4	0.8	0.4–1.4
Glycemic status 6.4–7.8 mM					
Fitness					
High	12	3621	29.7	1.0	
Low	11	1268	101.6	3.4	2.3–5.1
Systolic blood pressure (mmHg)					
<140	14	3828	38.4	1.0	
≥140	9	1059	76.4	2.0	1.3–2.9
Age (yr)					
<50	9	3350	18.4	1.0	
≥50	14	1537	28.6	1.5	0.9–2.8
Cholesterol (mM)					
<6.24	11	2998	39.0	1.0	
≥6.24	12	1889	58.2	1.5	1.0–2.2
Smoking					
No	14	3959	35.5	1.0	
Yes	9	925	96.3	2.7	1.8–4.0
Body mass index (kg/m^2)					
<27.4	15	2954	50.8	1.0	
≥27.4	8	1933	48.0	0.9	0.6–1.4
Family history coronary heart disease					
No	17	3324	83.9	1.0	
Yes	6	1563	31.4	0.4	0.2–0.6

Table 2—*Continued.*

	Deaths	Follow-up (person-yr)	Age-adjusted death rates*/10,000 person-yr	Relative risk	95% confidence interval
Glycemic status ≥7.8 mM or non-insulin-dependent diabetes mellitus					
Fitness					
High	10	2016	45.9	1.0	
Low	4	669	82.5	1.8	1.2–2.6
Systolic blood pressure (mmHg)					
<140	10	2278	43.9	1.0	
≥140	4	407	98.4	1.8	1.2–2.5
Age (yr)					
<50	5	1839	18.6	1.0	
≥50	9	846	33.5	1.8	1.0–3.2
Cholesterol (mM)					
<6.24	5	1568	31.2	1.0	
≥6.24	9	1116	81.3	2.6	1.7–3.9
Smoking					
No	7	1948	34.2	1.0	
Yes	7	737	103.5	3.0	2.1–4.5
Body mass index (kg/m^2)					
<27.4	12	1905	63.0	1.0	
≥27.4	2	780	25.6	0.4	0.2–0.6
Family history coronary heart disease					
No	9	1751	53.0	1.0	
Yes	5	934	48.5	0.9	0.6–1.3

* Adjusted to population distribution of age.

min^{-1} (<12.016 min on the treadmill). Based on available data from studies performed at this and other research centers, it is likely that 30 or 40 min of moderate-intensity exercise (e.g., a brisk walk) 3–5 days/wk would be sufficient to improve to, or maintain, the moderate fitness level in this study.

Although the exact exercise prescription necessary for good health is unknown, this and other studies suggest that the amount of cardiorespiratory fitness necessary to obtain health benefits appears not to be that attainable only by elite athletes but rather is attainable by most men without a substantial investment in either time or intensity. Clinicians are urged to relay this message to their patients when appropriate.

Acknowledgments— This study was supported by a grant from the American Diabetes Association and by U.S. Public Health Service Research Grant AG-06945 from the National Institutes of Health National Institute on Aging.

We thank Drs. Andrea Kriska, Ralph S.

Table 3—*Age- and multivariate-adjusted risks of death by glycemic status in low-fitness men relative to high-fitness men (Cooper Clinic healthy men, 1971–1985)*

	Age		Multivariate*	
Glycemic status	Relative risk	95% Confidence interval	Relative risk	95% Confidence interval
<6.4 mM	1.9	1.2–3.3	1.38	1.09–1.74
6.4–7.8 mM	3.4	2.3–5.1	1.61	0.91–2.86
≥7.8 mM	1.8	1.2–2.6	1.92	0.75–4.90

*Adjusted for associations with age, serum cholesterol, resting systolic blood pressure, age, body mass index, smoking habit, family history of heart disease, and follow-up interval.

Paffenbarger, Jr., and Larry Gibbons for constructive criticism on an earlier draft of this manuscript. Laura Becker assisted with manuscript preparation. We also thank the physicians and patients at the Cooper Clinic, Dallas, TX, for ongoing cooperation and support.

References

1. West KM: Epidemiology of Diabetes and Its Vascular Lesions. New York, Elsevier, 1978
2. Kadowaki T, Miyake Y, Hagura R, Ahanuma Y, Kajinuma H, Kuzuya N, Takaku F, Kosaka K: Risk factors for worsening to diabetes in subjects with impaired glucose tolerance. *Diabetologia* 26:44–49, 1984
3. Keen H, Jarrett RJ, McCartney P: The ten-year follow-up of the Bedford Survey (1962–1972): glucose tolerance and diabetes. *Diabetologia* 22:73–78, 1982
4. King H, Zimmet P, Raper LR, Balkau B: The natural history of impaired glucose tolerance in the Micronesian population of Nauru: a six-year follow-up study. *Diabetologia* 26:39–43, 1984
5. Jarrett RJ, Keen H, Fuller JH, McCartney M: Worsening to diabetes in men with impaired glucose tolerance ("borderline diabetes"). *Diabetologia* 16:25–30, 1979
6. Stenhouse NS, Murphy BP, Welborn TA: Busselton population study: risk associated with asymptomatic hyperglycemia. *J Chronic Dis* 32:693–98, 1979
7. Stamler R, Stamler J, Lindberg HA, Marquardt J, Berkson DM, Paul O, Lepper M, Dyer A, Stevens E: Asymptomatic hyperglycemia and coronary heart disease in middle-aged men in two employed populations in Chicago. *J Chronic Dis* 32:805–15, 1979
8. Fuller JH, Shipley MJ, Rose G, Jarrett RJ, Keen H: Coronary-heart disease risk and impaired glucose tolerance: the Whitehall Study. *Lancet* 1:1373–76, 1980
9. Pan W-H, Cedres LB, Liu K, Dyer A, Schoenberger JA, Shekelle RB, Stamler R, Smith D, Collette P, Stamler J: Relationship of clinical diabetes and asymptomatic hyperglycemia to risk of coronary heart disease mortality in men and women. *Am J Epidemiol* 123:504–16, 1986
10. Jarrett RJ, McCartney P, Keen H: The Bedford Survey: ten-year mortality rates in newly diagnosed diabetics, borderline diabetics, and normoglycemic controls and risk indices for coronary heart disease in borderline diabetics. *Diabetologia* 22:79–84, 1982
11. Paffenbarger RS Jr, Hyde RT, Wing AL, Hsieh C: Physical activity, all-cause mortality, and longevity of college alumni. *N Engl J Med* 314:605–13, 1986
12. Morris JN, Everitt MG, Pollard R, Chave SPW, Semmence AM: Vigorous exercise in leisure time: protection against coronary heart disease. *Lancet* 2:1207–10, 1980
13. Blair SN, Kohl HW III, Paffenbarger RS Jr, Clark DG, Cooper KH, Gibbons LW: Physical fitness and all-cause mortality: a prospective study of healthy men and women. *JAMA* 262:2395–401, 1989
14. Ekelund L-G, Haskell WL, Johnson JL, Whaley FS, Criqui MH, Sheps DS: Physical fitness as a predictor of cardiovascular mortality in asymptomatic North American men: the Lipid Research Clinics Mortality Follow-up Study. *N Engl J Med* 319:1379–84, 1988
15. Galbo H, Hedeskov K, Capito K, Vinten J: The effects of physical training on insulin secretion of rat pancreatic islets. *Acta Physiol Scand* 111:75–79, 1981
16. Richard D, LeBlanc J: Effects of physical training and food restriction on insulin secretion and glucose tolerance in male and female rats. *Am J Clin Nutr* 33: 2588–94, 1980
17. Seals DR, Hagberg JM, Allen WK, Hurley BF, Dalsky GP, Ehsani AA, Holloszy JO: Glucose tolerance in young and older athletes and sedentary men. *J Appl Physiol Respir Environ Exercise Physiol* 56:1521–25, 1984
18. Miller WJ, Sherman WM, Ivy JL: Effect of strength training on glucose tolerance and post-glucose insulin response. *Med Sci Sports Exercise* 16:539–43, 1984
19. Rogers MA, Yamamoto C, King DS, Hagberg JM, Ehsani AA, Holloszy JO: Improvement in glucose tolerance after 1 wk of exercise in patients with mild NIDDM. *Diabetes Care* 11:613–18, 1988
20. Trovati M, Carta Q, Cavalot F, Vitali S, Banaudi C, Lucchina PG, Fiocchi F, Emanuelli G, Lenti G: Influence of physical training on blood glucose control, glucose tolerance, insulin secretion, and insulin action in non-insulin-dependent diabetic patients. *Diabetes Care* 7:416–20, 1984
21. National Institutes of Health: Consensus development conference on diet and exercise in non-insulin-dependent diabetes mellitus. *Diabetes Care* 10:639–44, 1987
22. Blair SN, Goodyear NN, Gibbons LW, Cooper KH: Physical fitness and incidence of hypertension in healthy normotensive men and women. *JAMA* 252:487–90, 1984
23. Blair SN, Cooper KH, Gibbons LW, Gettman LR, Lewis S, Goodyear N: Changes in coronary heart disease risk factors associated with increased treadmill time in 753 men. *Am J Epidemiol* 118:352–59, 1983
24. Caspersen CJ, Powell KE, Christenson GM: Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep* 100:126–31, 1985
25. Balke B, Ware RW: An experimental study of physical fitness in Air Force personnel. *U S Armed Forces Med J* 10: 676–88, 1959
26. Pollock ML, Bohannon RL, Cooper KH, Ayers JJ, Ward A, White SR, Linnerud AC: A comparative analysis of four protocols for maximal stress testing. *Am Heart J* 92:39–46, 1976
27. National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes* 28:1039–57, 1979
28. Haffner SM, Stern MP, Hazuda HP, Mitchell BD, Patterson JK: Cardiovascular risk factors in confirmed prediabetic individuals. *JAMA* 263:2893–98, 1990

29. Blair SN, Kannel WB, Kohl HW, Goodyear NN, Wilson PWF: Surrogate measures of physical activity and physical fitness: evidence for sedentary traits of resting tachycardia, obesity, and low vital capacity. *Am J Epidemiol* 129:1145–56, 1989
30. Harris MI, Hadden WC, Knowler WC, Bennett PH: Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in U.S. population aged 20–74 yr. *Diabetes* 36:523–34, 1987