Physical Fitness and All-Cause Mortality

A Prospective Study of Healthy Men and Women

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We studied physical fitness and risk of all-cause and cause-specific mortality in 10 224 men and 3120 women who were given a preventive medical examination. Physical fitness was measured by a maximal treadmill exercise test. Average follow-up was slightly more than 8 years, for a total of 110 482 person-years of observation. There were 240 deaths in men and 43 deaths in women. Age-adjusted all-cause mortality rates declined across physical fitness quintiles from 64.0 per 10 000 person-years in the least-fit men to 18.6 per 10 000 person-years in the most-fit men (slope, −4.5). Corresponding values for women were 39.5 per 10 000 person-years to 8.5 per 10 000 person-years (slope, −5.5). These trends remained after statistical adjustment for age, smoking habit, cholesterol level, systolic blood pressure, fasting blood glucose level, parental history of coronary heart disease, and follow-up interval. Lower mortality rates in higher fitness categories also were seen for cardiovascular disease and cancer of combined sites. Attributable risk estimates for all-cause mortality indicated that low physical fitness was an important risk factor in both men and women. Higher levels of physical fitness appear to delay all-cause mortality primarily due to lowered rates of cardiovascular disease and cancer.

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PHYSICAL activity is inversely associated with morbidity and mortality from several chronic diseases. The apparently protective effect of a more active life is seen for occupational activity and death from cardiovascular disease[1] and colon cancer,[2] and for leisure-time physical activity and cardiovascular disease.[3-5] Higher levels of leisure-time physical activity are associated with increased longevity in college alumni.[6] These associations of sedentary habits to health appear to be independent of confounding by other well-established risk factors.[7] Furthermore, the relationship of physical fitness (an attribute) to physical activity (a behavior) and disease rates is controversial,[8-10] and it is uncertain whether physical activity sufficient to increase physical fitness is required for health benefits.

For editorial comment see p 2437.

In contrast to physical activity, published studies on physical fitness and mortality are few, typically with fewer than 20 000 person-years of follow-up, and usually limited to men. Physical activity is an important determinant of physical fitness[9]; so to some extent, fitness is an objective marker for habitual physical activity. Physical fitness can be measured more objectively than physical activity, and thus may be more useful clinically. Research studies that include the measurement of physical fitness may provide additional insight into the contribution of a physically active way of life to decreased risk of morbidity and mortality.

Here, we report all-cause and cause-specific mortality by physical fitness categories in men and women followed up for 110 482 person-years, or an average of more than 8 years.

SUBJECTS AND METHODS

Subjects

The 13 344 study participants comprised 10 224 men and 3120 women who received a preventive medical examination at the Cooper Clinic in Dallas, Tex, during 1970 to 1981. Patients were included in the study if they were residents of the United States at their first clinic visit, had a complete examination, and achieved at least 85% of their age-predicted maximal heart rate on a treadmill exercise test at the baseline clinic visit. Patients not achieving this maximal heart rate standard were presumed to be more likely to have preexisting disease or be receiving medication with β-blockers. These conditions would be associated with poorer treadmill test performance and higher risk of death during follow-up. Thus, excluding patients with these characteristics is a conservative decision that reduces the chance of finding a spurious inverse relationship between fitness and mortality. At baseline, all patients had no personal history of heart attack, hypertension, stroke, or diabetes; no resting electrocardiographic (ECG) abnormalities; and no abnormal responses on the exercise ECG.

Clinical Examination

The baseline examination was given after an overnight fast of at least 12 hours and after patients gave their informed consent. The examination was a complete preventive medical evaluation that included a personal and family health history, a physical examination, a questionnaire on demographic characteristics and health habits, anthropometry, resting ECG, blood chemistry tests, blood pressures, and a maximal treadmill exercise test. Examination methods and procedures followed a standard manual of operations and have been described further in earlier reports.[11,12] All patients were free of known chronic disease as determined by the following criteria: no personal history of heart attack, hypertension, stroke, or diabetes; no resting ECG abnormalities; and no abnormal responses on the exercise ECG.

Physical fitness was measured by a maximal treadmill exercise test.[13] Treadmill speed was set initially at 88 m/min. The grade was 0% for the first minute, 2% the second minute, and increased 1% each minute until 25 minutes. After 25 minutes, the grade did not change and speed was increased 5.4 m/min each minute until test termination. Patients were given encouragement to give maximal effort. Total treadmill test time in seconds was the variable used in analysis. Treadmill time from this protocol is highly correlated with measured maximal oxygen

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uptake in men[14] ($r=.92$) and women[15] ($r=.94$), which is the most widely accepted index of cardiorespiratory fitness.

Patients were assigned to physical fitness categories based on their age, sex, and maximal time on the treadmill test. Treadmill-time quintiles were determined for each age and sex group. Individuals with a treadmill time in the first quintile were assigned to the low-fit group. Those with scores in the second through the fifth quintiles constituted fitness groups 2 through 5, respectively. Thus, assignment to a fitness category was based on age and sex norms of treadmill performance rather than by an absolute fitness standard. (Treadmill-time quintile cutoff points for each age group for men and women may be obtained from us.)

Cigarette-smoking status was determined from the medical questionnaire. Patients who reported smoking at present or within the 2 years preceding the baseline examination were designated as current smokers. This conservative definition for smoking was adopted because many smokers may have quit temporarily in preparation for their preventive medical examination, and mortality risk for recent quitters is similar to continuing smokers.[16] Results from the smoking analyses were essentially unchanged when current smoking was defined as cigarette smoking at baseline or during the year preceding the examination.

Height and weight were measured on a standard physician's scale, and body mass index was calculated (kilograms per meter squared). Blood pressure was measured by the auscultatory method with a mercury sphygmomanometer, diastolic pressure being recorded as the disappearance of sound. Serum samples were analyzed for cholesterol and glucose by automated techniques.

Table 1.—Baseline Characteristics of Surviving and Deceased Male and Female Patients, Aerobics Center Longitudinal Study, 1970 to 1981

	Men				Women			
	Surviving (n=9984)		Deceased (n=240)		Surviving (n=3077)		Deceased (n=43)	
	$\bar{x}$	SD	$\bar{x}$	SD	$\bar{x}$	SD	$\bar{x}$	SD
Age, y	41.5	9.3	49.8	11.6	40.8	9.9	51.7	14.5
(95% confidence limits)	(41.3, 41.7)		(48.3, 51.3)		(40.4, 41.1)		(47.4, 56.0)	
Weight, kg	81.9	12.1	83.2	13.3	59.9	10.2	60.7	9.4
(95% confidence limits)	(81.7, 82.1)		(81.5, 84.9)		(59.5, 60.3)		(57.9, 63.5)	
Height, cm	178.8	6.3	180.1	22.1	164.3	5.6	164.1	5.6
(95% confidence limits)	(178.7, 178.9)		(177.3, 182.9)		(164.1, 165.0)		(162.4, 165.8)	
Body mass index	25.6	3.3	25.8	3.4	22.2	3.5	23.2	3.7
(95% confidence limits)	(25.5, 25.7)		(25.4, 26.2)		(22.1, 22.3)		(22.1, 24.3)	
Treadmill time, s	1017	281	811	354	691	240	489	250
(95% confidence limits)	(1011, 1022)		(766, 856)		(682, 699)		(414, 564)	
Follow-up, y	8.4	2.9	6.5	4.0	8.2	2.9	6.5	3.8
(95% confidence limits)	(8.3, 8.5)		(6.0, 7.0)		(8.1, 8.3)		(5.4, 7.6)	
Total cholesterol level, mmol/L	5.45	1.0	6.05	1.20	5.20	0.95	6.05	1.0
(95% confidence limits)	(5.43, 5.47)		(5.90, 6.20)		(5.17, 5.23)		(5.7, 6.3)	
Systolic blood pressure, mm Hg	120.4	13.1	126.1	17.1	112.2	14.0	124.1	19.5
(95% confidence limits)	(120.1, 120.6)		(124.0, 128.3)		(111.7, 112.7)		(118.3, 129.9)	
Diastolic blood pressure, mm Hg	79.7	9.1	82.4	11.2	74.5	9.1	79.2	9.4
(95% confidence limits)	(79.5, 79.9)		(81.0, 83.8)		(74.2, 74.8)		(76.4, 82.0)	
Current smoker, %	28.5		47.5		21.2		32.6	

Mortality Surveillance

Study subjects were followed up for mortality from their first clinic visit through 1985. The average length of follow-up was slightly more than 8 years, and the total follow-up experience for the cohort was 110 482 person-years. Several follow-up methods were used. Decedents were identified by reports from family, friends, and business associates; responses to appointment reminders; and other mailings from the clinic. The entire cohort was sent a case-finding and disease-identifying questionnaire in 1982.[11] Nonrespondents were followed-up via the Social Security Administration files, the Department of Motor Vehicles in the subject's state of residence, and a nationwide credit bureau network. The National Death Index has been used since it was established in 1979 to search for possible matches in this cohort. Finally, individuals with unknown vital status and with a Dallas-area address were checked in local telephone directories. Follow-up has been difficult since patients come from all 50 states and are mobile and since a significant portion of the follow-up occurred prior to the establishment of the National Death Index. Despite these limitations, vital status has been ascertained for 95% of the cohort.

There have been 283 deaths in the study group. Official death certificates were obtained from the states. The underlying cause and up to four contributing causes of death were coded by a nosologist according to the *International Classification of Diseases, Ninth Edition, Revised.*

Data Analysis

A total of 283 deaths were identified in the cohort over the average of approximately 8 years of follow-up. Mortality rates per 10 000 person-years of follow-up were computed for each of the five fitness categories and age-adjusted by the direct method, using the total experience in the population as the standard. Age differences were adjusted by the following groupings: 20 to 39, 40 to 49, 50 to 59, and 60 or more years. These rates were then used to compute relative risks (RR) of death for each fitness quintile as well as for examination of the role other variables played in confounding the relationship between fitness and mortality. Attributable risk percentages (etiologic fractions) for those groups exposed to adverse characteristics were calculated as were population-based estimates of attributable risks.[17]

Multiple logistic regression was used to estimate RRs of death among the fitness quintiles after control for associated confounding risk factors.[18] Interval estimation was used to calculate confidence intervals (CIs) around point estimates of risk.

RESULTS

Patients in this study are from middle to upper socioeconomic strata; approximately 70% are college graduates. Most are employed in professional, executive, or white-collar positions. More than 99% are white. Baseline characteristics on selected demographic and clinical variables are shown in Table 1. Decedents were somewhat older, less physically fit, and had less favorable risk profiles.

Table 2 shows the age-adjusted all-cause death rates by physical fitness categories in men and women. Relative risks of death with the 95% CIs are shown with the most-fit quintile as the reference category. Less-fit individuals had a higher risk of death than the more-fit men and women. Increased RR for all-cause mortality was significantly higher for the least-fit quintile in men, and for the two least-fit quintiles in women. The 95% CIs for the test for linear trend across fitness categories did not include 1.0 in either men or women.

Univariate age-adjusted RR for all-cause mortality for several important clinical and life-style variables for men and women are presented in Table 3.

Table 2.—Age-Adjusted All-Cause Death Rates per 10 000 Person-Years of Follow-up (1970 to 1985) by Physical Fitness Groups in Men and Women in the Aerobics Center Longitudinal Study

Fitness Group	Person-Years of Follow-up	No. of Deaths	Age-Adjusted Rates per 10 000 Person-Years	Relative Risk	95% Confidence Limits
Men					
1 (low)	14515	75	64.0	3.44*	2.05, 5.77
2	16898	40	25.5	1.37	0.76, 2.50
3	17287	47	27.1	1.46	0.81, 2.63
4	18792	43	21.7	1.17	0.63, 2.17
5 (high)	17557	35	18.6	1.00	...
Women					
1 (low)	4916	18	39.5	4.65†	2.22, 9.75
2	5329	11	20.5	2.42	1.09, 5.37
3	5053	6	12.2	1.43	0.60, 3.44
4	5522	4	6.5	0.76	0.27, 2.11
5 (high)	4613	4	8.5	1.00	...

*Test for linear trend, slope = −4.5; 95% confidence limits, −7.1, −1.9.
†Test for linear trend, slope = −5.5; 95% confidence limits, −9.2, −1.9.

Table 3.—Relative Risk for All-Cause Mortality for Selected Clinical and Life-style Variables, Men and Women in the Aerobics Center Longitudinal Study

Variable	Prevalence in Person-Years, %	Relative Risk	95% Confidence Limits
Men			
Serum cholesterol level ≥6.20 mmol/L	19.4	2.21	1.72, 2.85
Systolic blood pressure ≥140 mm Hg	6.9	1.74	1.20, 2.52
Body mass index ≥27.2	22.8	0.85	0.62, 1.17
Current smoker or quit in past 2 y	27.5	2.60	2.03, 3.33
Either parent died of coronary heart disease	20.0	1.60	1.16, 2.20
Serum glucose level ≥6.7 mmol/L	4.9	2.74	1.93, 3.89
Women			
Serum cholesterol level ≥6.20 mmol/L	11.2	2.69	1.50, 4.84
Systolic blood pressure ≥140 mm Hg	3.9	3.24	1.52, 6.89
Body mass index ≥26.9	6.6	1.84	0.80, 4.25
Current smoker or quit in past 2 y	21.6	2.08	1.10, 3.91
Either parent died of coronary heart disease	19.5	1.50	0.72, 3.14
Serum glucose level ≥6.7 mmol/L	1.4	3.73	1.29, 10.75

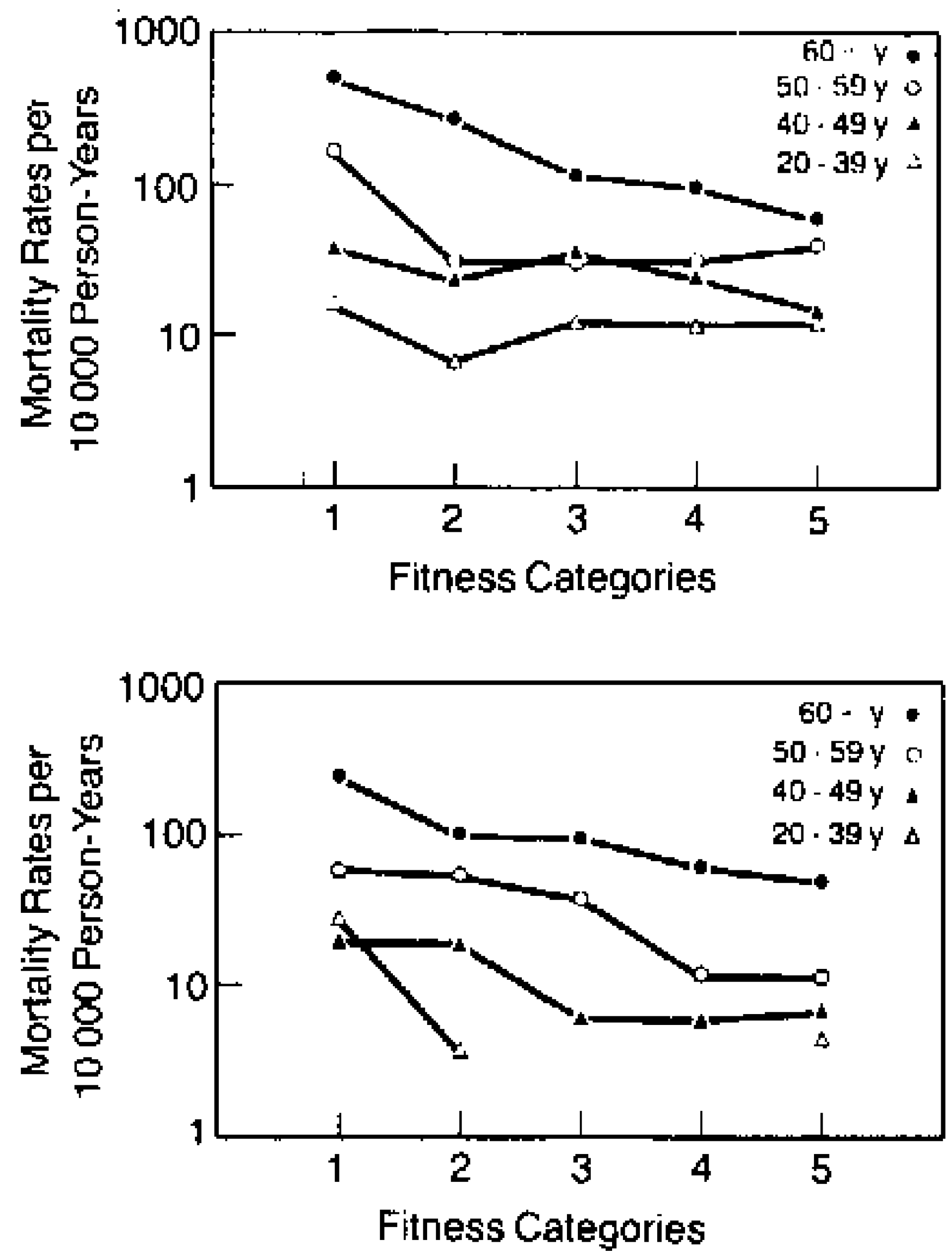

Fig 1.—Age-specific, all-cause death rates per 10 000 person-years of follow-up in 10 224 men (top) and 3120 women (bottom) in the Aerobics Center Longitudinal Study, by physical fitness quintiles as determined by maximal treadmill exercise tests.

The findings show an increased risk, as expected, for all variables except body mass index, which shows a trend in the expected direction only in women.

Multiple logistic analyses were done to estimate RR of death in the fitness categories while adjusting for potential confounding. The dependent measure was all-cause mortality and the model included physical fitness and all variables in Table 3. All variables were included, although overweight for height in both men and women and parental history of coronary heart disease (CHD) in women were not statistically significantly associated with mortality in univariate analyses. The RRs (95% CI) of low physical fitness for all-cause mortality for each quintile (Q1 to Q4) compared with the most-fit quintile were as follows: Q1 = 1.53 (1.23 to 1.89), Q2 = 1.03 (0.81 to 1.30), Q3 = 1.12 (0.89 to 1.40), and Q4 = 1.03 (0.81 to 1.28) for men; and Q1 = 1.98 (1.13 to 3.47), Q2 = 1.45 (0.80 to 2.62), Q3 = 1.07 (0.55 to 2.09), and Q4 = 1.07 (0.55 to 2.23) for women. A more pronounced dose-response gradient was seen when length of follow-up (as a continuous variable) was added to the model. Relative risks (95% CI) for the four less-fit quintiles relative to the most-fit quintile were as follows: Q1 = 1.82 (1.38 to 2.40), Q2 = 1.33 (1.0 to 1.78), Q3 = 1.29 (0.97 to 1.71), and Q4 = 1.06 (0.78 to 1.44) for men; and Q1 = 3.92 (1.39 to 11.04), Q2 = 3.01 (1.05 to 8.65), Q3 = 2.06 (0.66 to 6.22), and Q4 = 1.55 (0.49 to 4.91) for women. Several interaction terms among the independent variables were tested, and the assumption of no interaction on a multiplicative scale was not violated.

Subclinical disease could cause poor performance on the treadmill and also lead to elevated death rates in patients presumed to be healthy at baseline. Mortality rates in both short- and long-term follow-up were examined to test the hypothesis that preexisting disease was confounding the relationship between fitness and mortality. Logistic regression analyses were done for two subgroups as follows: the first 3 years of follow-up and for extended follow-up after 3 years. The dependent measure was all-cause mortality. *Low fitness* again was defined as the first quintile of the fitness distribution. Other independent variables in the analyses were those in Table 3, to control for possible confounding. Adjusted RRs for all-cause mortality in low-fit men were as follows: follow-up less than or equal to 3 years, 1.60 (95% CI, 1.18 to 2.16); and follow-up greater than 3 years, 1.45 (95% CI, 1.08 to 1.96). Corresponding values for women were as follows: less than or equal to 3 years, 1.47 (95% CI, 0.74 to 2.94); and greater than 3 years, 3.00 (95% CI, 1.06 to 8.51). The elevated RR in later follow-up suggests that the relationship between fitness and mortality is not likely to be due entirely to confounding by subclinical disease.

Age-specific, all-cause mortality rates across fitness categories are shown in Fig 1. The upper panel presents data for men, and the lower, for women. In both analyses, the decline in death rates with higher levels of fitness is more pronounced in the older individuals. The small number of deaths in the younger women leads to unstable estimates of the death rate in this group.

Table 4 shows cause-specific death rates by fitness categories in men and women. The fitness quintiles were collapsed into three groups for these analyses due to smaller numbers of deaths

Table 4.—Age-Adjusted Cause-Specific Death Rates per 10 000 Person-Years of Follow-up (1970 to 1985) by Physical Fitness Groups in Men and Women in the Aerobics Center Longitudinal Study

			Age-Adjusted Death Rates per 10 000 Person-Years			Trend (Linear)	
			Fitness Groups				
Underlying Cause of Death*	N	% of Total	1	2 to 3	4 to 5	Slope	95% Confidence Interval
			Men				
All-causes	240	100	64.0	26.3	20.3	−10.5	−15.8, −5.2
Cardiovascular disease (*ICD-9*, 390-448)	66	27.5	24.6	7.8	3.1	−6.0	−8.8, −3.3
Cancer (*ICD-9*, 140-208)	64	26.7	20.3	7.3	4.7	−3.5	−6.2, −0.7
Accidents/external (*ICD-9*, 800-999)	44	18.3	4.8	5.8	5.4	−0.4	−1.6, 2.4
All other (specified)	46	19.2	11.0	3.7	5.5	0.1	−2.2, 2.5
All other (nonspecified)	20	8.3	8.7	1.3	1.7	−0.4	−2.0, 1.2
			Women				
All-causes	43	100	39.5	16.4	7.4	−11.6	−18.7, −4.6
Cardiovascular disease (*ICD-9*, 390-448)	7	16.3	7.4	2.9	0.8	−2.3	−5.1, 0.5
Cancer (*ICD-9*, 140-208)	18	41.9	16.3	9.7	1.0	−7.5	−11.8, −3.3
Accidents/external (*ICD-9*, 800-999)	5	11.6	3.9	1.0	1.8	−0.1	−3.0, 2.6
All other (specified)	7	16.3	7.9	0.9	1.9	−0.4	−3.3, 2.5
All other (nonspecified)	6	14.0	5.2	2.0	0.8	−1.3	−3.7, 1.1

*Coded from official death certificates by *International Classification of Diseases, Ninth Edition, Revised*, (*ICD-9*).

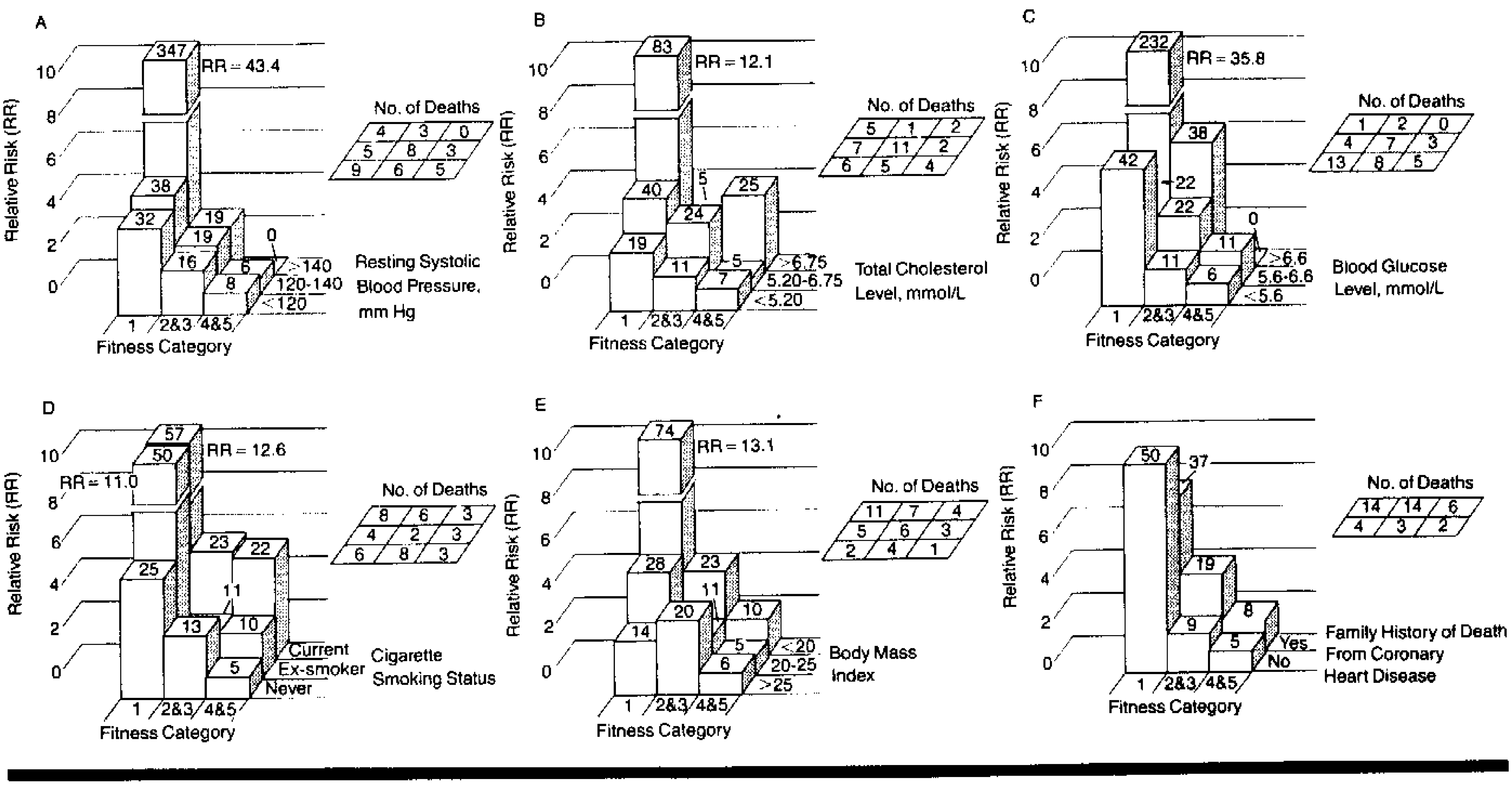

Fig 2.—Relative risks of all-cause mortality in 3120 women in the Aerobics Center Longitudinal Study, by physical fitness categories and blood pressure (A), serum cholesterol level (B), serum glucose level (C), smoking habits (D), body mass index (E), and parental history of coronary heart disease (F). Each bar represents the relative risk based on age-adjusted, all-cause death rates per 10 000 person-years of follow-up, with the relative risk of the front-right cell set at 1.0. Numbers on top of the bars are the all-cause death rates per 10 000 person-years of follow-up for each cell. The number of deaths in each cell is shown in the parallelograms.

in the specific causes. There are few deaths for the specific causes in women, which leads to unstable estimates of rates; these results should be interpreted cautiously. Death rates for cardiovascular disease and cancer show a strong gradient across fitness groups in both men and women, while none is seen for other causes of death.

The RRs for all-cause mortality by cross-tabulations of fitness groups and other clinical and life-style variables are presented in Figs 2 and 3. In these stereograms, the back-left cell shows the RR for the presumed highest-risk group (eg, low fit and high systolic blood pressure). The lowest-risk group (referent) is in the front-right cell of the fig-

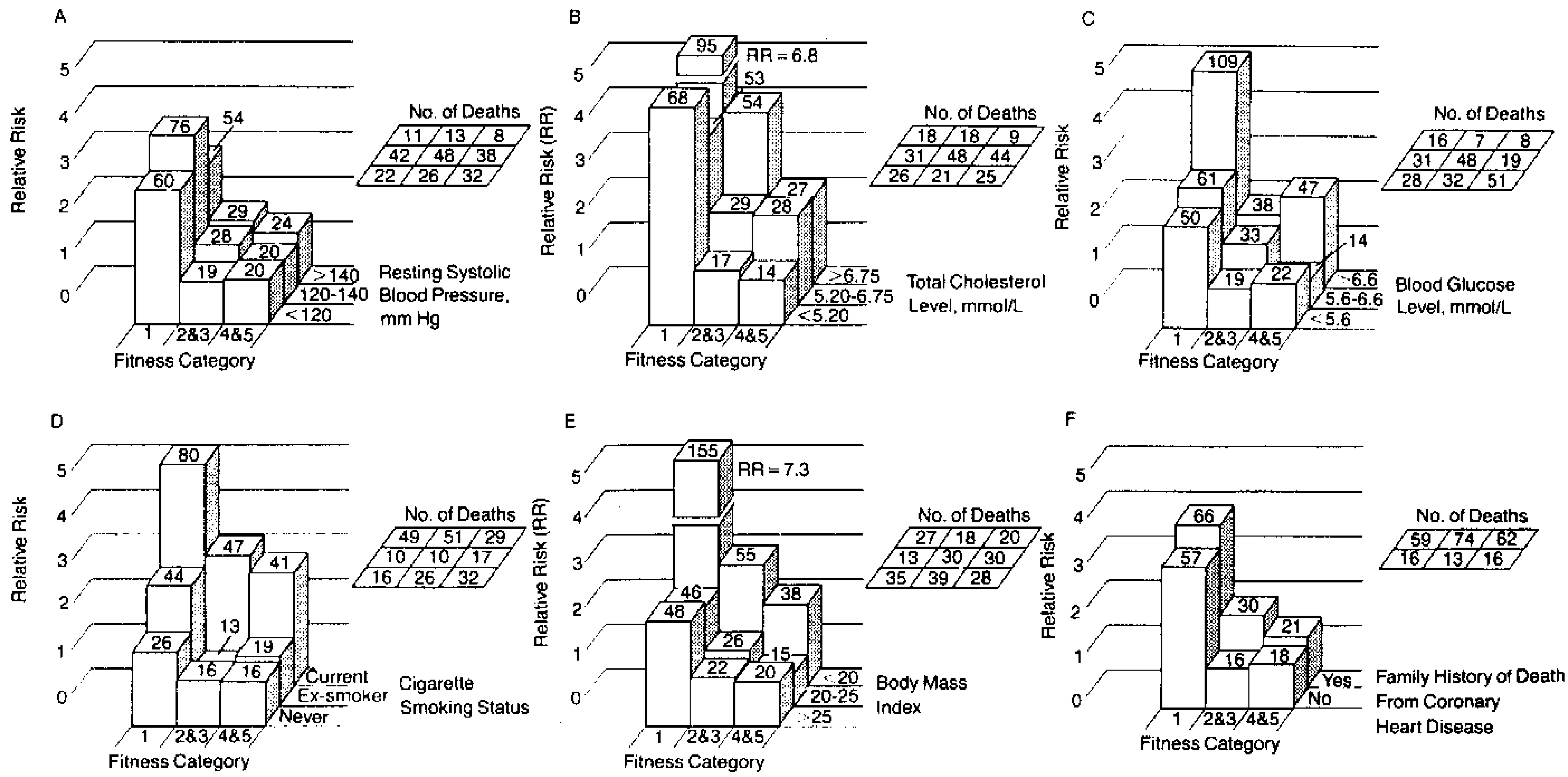

Fig 3.—Relative risks of all-cause mortality in 10 224 men in the Aerobics Center Longitudinal Study, by physical fitness categories and blood pressure (A), serum cholesterol level (B), serum glucose level (C), smoking habits (D), body mass index (E), and parental history of coronary heart disease (F). Each bar represents the relative risk based on age-adjusted all-cause death rates per 10 000 person-years of follow-up, with the relative risk of the front-right cell set at 1.0. Numbers on top of the bars are the all-cause death rates per 10 000 person-years of follow-up for each cell. The number of deaths in each cell is shown in the parallelograms.

ures. Cutoff points for the clinical and behavioral risk factors in these analyses were established somewhat arbitrarily, so as to provide an adequate number of person-years in each cell for analysis. Increased risk of death in low-fit men and women is clearly illustrated in these stereograms, and this pattern generally holds across risk strata for the other variables. In several cases, notably stereograms for men on blood pressure and cholesterol level, high-fit patients at the highest level of either blood pressure or cholesterol have a lower risk than unfit patients with low blood pressure or cholesterol level. For example, fit but hypercholesterolemic men have double the risk (death rate of 27 per 10 000 person-years compared with 14 per 10 000 person-years) of the fit men with lower cholesterol levels, but these fit, hypercholesterolemic men have only a little more than one third the risk (death rate of 27 per 10 000 person-years compared with 68 per 10 000 person-years) of unfit men with low cholesterol levels.

The various analyses presented thus far were based on physical fitness quintiles. To present the results in a more clinically useful format, all-cause death rates calculated by metabolic equivalents (MET) and maximal oxygen uptake values are shown in Fig 4. The MET values are multiples of resting metabolic rate (work metabolic rate/resting metabolic rate). One MET is equal to an oxygen uptake of $3.5\,mL \cdot kg^{-1} \cdot min^{-1}$. In Fig 4, METs and maximal oxygen uptake values are estimated maximal scores achieved during the maximal treadmill test. Age-adjusted mortality rates for men and women are shown. Perhaps the asymptote is a reasonable value to establish an optimal physical fitness level, which occurs in these data at approximately 9 METs ($32.5\ mL \cdot kg^{-1} \cdot min^{-1}$) in women and 10 METs ($35\ mL \cdot kg^{-1} \cdot min^{-1}$) in men. We calculated age-specific, all-cause death rates for men and women across MET categories (not shown). The rates, especially for women, were unstable, presumable due to small numbers in several cells. Although interpretation of these data is difficult and risky, it appears that the asymptote occurs at approximately the same point for each age, 9 METs for women and 10 METs for men.

The results presented here support the hypothesis that a low level of physical fitness is an important risk factor for all-cause mortality in both men and women. The relative importance of low fitness level and other characteristics for risk of death for exposed individuals and from a population-disease–burden

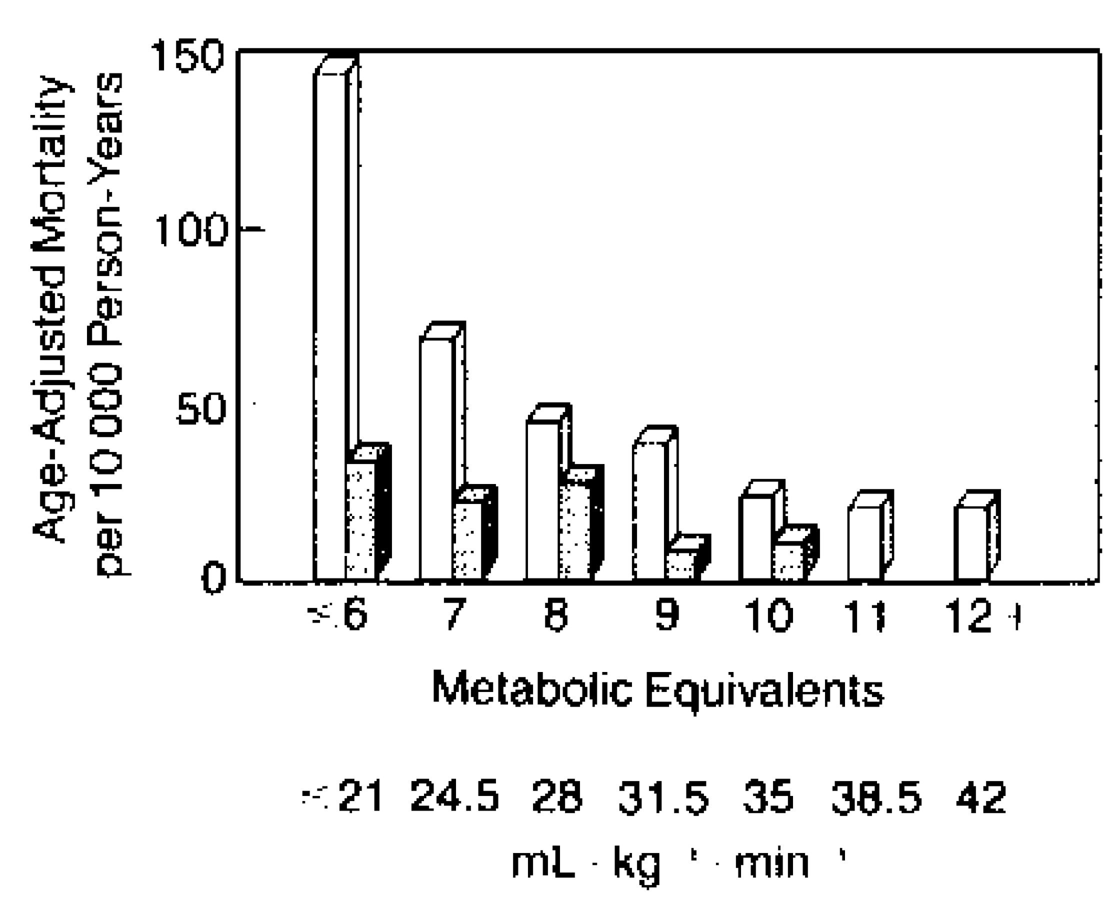

Fig 4.—Age-adjusted, all-cause mortality rates per 10 000 person-years of follow-up by physical fitness categories in 3120 women and 10 224 men in the Aerobics Center Longitudinal Study. Physical fitness categories are expressed here as maximal metabolic equivalents (work metabolic rate/resting metabolic rate) achieved during the maximal treadmill exercise test. One metabolic equivalent equals $3.5\,mL \cdot kg^{-1} \cdot min^{-1}$. The estimated maximal oxygen uptake for each category is shown also.

perspective is seen in Table 5. In these analyses, low fitness level (least-fit quintile) is compared with the top four quintiles. The individual attributable risk of a characteristic depends on both the RR and the prevalence of the characteristic. The individual attributable

Table 5.—Individual and Population Attributable Risks of All-Cause Mortality for Selected Characteristics, Men and Women in the Aerobics Center Longitudinal Study

Characteristic	Prevalence in Person-Years, %	Relative Risk (95% Confidence Limits)	Attributable Risk,* %	
			Individual	Population
Men				
Lowest fitness quintile compared with all others	17.1	1.58 (1.32, 1.89)	36.7	9.0
Current smoker or quit in past 2 y	27.5	1.08 (0.90, 1.28)	7.4	2.1
Serum cholesterol level ≥6.20 mmol/L	19.4	1.65 (1.39, 1.97)	39.3	11.2
Systolic blood pressure ≥140 mm Hg	6.9	1.36 (1.05, 1.77)	26.5	2.4
Either parent died of coronary heart disease	20.0	1.56 (1.26, 1.92)	35.8	10.1
Serum glucose level ≥6.7 mmol/L	4.9	1.58 (1.21, 2.08)	36.7	2.8
Women				
Lowest fitness quintile compared with all others	19.3	1.94 (1.30, 2.88)	48.4	15.3
Current smoker or quit in past 2 y	21.6	1.13 (0.84, 1.84)	11.5	2.7
Serum cholesterol level ≥6.20 mmol/L	11.2	1.68 (1.09, 2.60)	40.5	7.1
Systolic blood pressure ≥140 mm Hg	3.9	2.23 (1.27, 3.90)	55.1	4.6
Either parent died of coronary heart disease	19.6	1.14 (0.73, 1.77)	12.3	2.7
Serum glucose level ≥6.7 mmol/L	1.4	3.31 (1.63, 6.72)	69.8	3.1

*Adjusted for age and other characteristics in the table

risks in Table 5 show the estimated benefit for individuals who might change a characteristic from a high-risk to a low-risk category. For example, a man with high cholesterol level might reduce his risk by 39% if he lowered it. An unfit woman might reduce her risk of dying by almost 50% if she became fit.

The population-attributable risks show the percentage of deaths in the study group that might have been prevented if beneficial changes in the population occurred for each characteristic. If all unfit persons became fit, reductions in death rates of 9.0% in men and 15.3% in women might be expected.

COMMENT

The results presented herein show a strong and graded association between physical fitness and mortality due to all causes, cardiovascular disease, and cancer. The findings are consistent for men and women and hold after adjustment for age, serum cholesterol level, blood pressure, smoking habit, fasting blood glucose level, family history of CHD, and length of follow-up. Strengths of the study are a maximal exercise test, participants free of known chronic disease at baseline, wide range of physical fitness, objective end points (mortality), a large sample (13 344 men and women) with extensive follow-up experience (85 049 person-years of observation for men and 25 433 for women), and a large enough sample of women to permit meaningful analyses. We believe that this is the only study of physical fitness and health that meets all these criteria.

Cardiovascular Disease

There are four published studies on low physical fitness and increased risk of fatal and nonfatal CHD in men[19-22] and five on fatal CHD.[22-26] It is difficult to compare results among studies due to different methods and definitions of unfit groups, but the RR of fatal and nonfatal CHD in unfit men is approximately 2.0 in the various studies.[19-22] These results generally hold in multivariate analyses with adjustment for confounders. Studies on fitness and fatal CHD show a range of RR from 1.4 to approximately 5.0 when comparing least-fit to most-fit men.[23-26] The age-adjusted RR for cardiovascular disease death in our study was approximately 8.0 in both men and women (Table 4) when the least-fit quintile was compared with quintiles 4 and 5. This value is somewhat higher than the results of Lie et al[25] (RR = 4.8), and is considerably greater than the findings of Slattery and Jacobs[24] (RR = 1.5). Our results are comparable with the results of Ekelund et al[26] for cardiovascular disease death (RR = 8.5) in men.

The RRs reported here are higher than the average RR in studies of physical activity and CHD (approximately 2.0 as calculated by Powell et al[7]). The high RR for low-fitness and all-cause, cardiovascular disease, and cancer mortality in our study may be related to the objective measurement of fitness afforded by the treadmill tests. Perhaps physical activity has a stronger relationship with mortality than has been detected by present methods of activity assessment, but is reflected by the objective physical fitness measure.

Physical fitness and CHD in women has not been thoroughly studied. The studies on physical *activity* and CHD in women are conflicting, with approximately 50% showing no advantage in the active group.[7] Many of the physical activity questionnaires used in epidemiologic studies were developed and validated primarily on men. Many women may undertake considerable physical activity in child care and household activities. If previous questionnaires misclassify more women than men on physical activity, studies on sedentary habits and disease in women would be more likely to show no association. The objective measure of physical fitness shows similar associations to disease in women and men in the present study.

All-Cause Mortality

All-cause mortality rates show a strong inverse association across fitness groups in both men and women in the present study. The RRs for the least-fit quintile compared with the most-fit quintile were 3.44 in men and 4.65 in women. The major reduction in all-cause death rates in our study occurs between the first and second quintile. There is some further decline, especially in women in the middle part of the fitness distribution, and only marginally continued reduction in death rates in the most-fit individuals. This finding has clinical and public health importance. The MET values (Fig 4) associated with a plateau in death rates are attainable by most men and women who engage regularly in moderate exercise. A brisk walk of 30 to 60 minutes each day will be sufficient to produce the fitness standard (9 METs for women and 10 METs for men) illustrated in Fig 4 for most men and women. These findings are also important from a public health perspective; approximately 30% of US adults are quite sedentary,[27] and the prevalence of low fitness levels is correspondingly high.

Other possible confounders must be considered. Subclinical disease at the baseline examination could negatively affect treadmill performance and increase risk of dying during follow-up. It seems unlikely that this could account entirely for the relationship between fitness and mortality since early and late follow-up analyses gave similar results. The possibility of undetected serious disease in the cohort at baseline is diminished by having the results of the maximal exercise test. Patients who did not achieve at least 85% of their predicted maximal heart rate were excluded from this analysis, as were patients who had an abnormal exercise ECG. The strong dose-response gradient also supports a causal inference.

There are several possible biologic mechanisms to account for reduced mortality risk in fit individuals. High physical fitness is associated with several important metabolic and hematologic variables, and these issues are discussed in some detail by Ekelund et al.[26] There probably are beneficial indirect effects of fitness on mortality risk; in addition, there may be important direct effects on the myocardium. For example, a fit individual has better left ventricular function and is perhaps better able to survive a myocardial infarction.

Physical fitness at baseline was objectively measured by a maximal exercise test. Change in fitness after baseline produces misclassification during follow-up, but this weakens the relationship between fitness and mortality rather than strengthening it.

Physical fitness has both genetic and environmental determinants. It is well established that exercise training improves physical fitness, typically by 15% to 20% in middle-aged men and women.[28] Earlier reports suggested in 1971 that approximately 90% of the interindividual variation in maximal aerobic power could be explained by heredity,[29] but more recent studies place the genetic component at approximately 30%.[30] Athletes presumably have genetic advantages in terms of physical fitness. However, Paffenbarger et al[4] reported that it is physical activity as an adult, not college athleticism, that is associated with a reduced risk of death in Harvard alumni. Many other CHD risk factors have a genetic component but this does not alter their validity or causal influence.

The representativeness of our population must be considered. These patients are relatively well educated and come from middle and upper socioeconomic strata. On key clinical variables such as serum cholesterol levels, triglyceride levels, and blood pressure, however, they are quite similar to the participants of other large epidemiologic studies such as the Lipid Research Clinics Prevalence Study and surveys done by the National Center for Health Statistics.[31] Nonetheless, our results must be generalized with caution.

In summary, the results reported here show a strong, graded, and consistent inverse relationship between physical fitness and mortality in men and women. The findings seem not to be due to confounding by age or other risk factors. Moderate levels of physical fitness that are attainable by most adults appear to be protective against early mortality. The specificity of this effect is evidence that it is largely limited to reduced rates of cardiovascular disease and cancer deaths in the more-fit men and women. The strength of the associations and the high prevalence of sedentary habits and low physical fitness levels produce high attributable risk estimates and suggest that these characteristics constitute an important public health problem that deserves remedial attention.

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