

Exercise Type and Intensity in Relation to Coronary Heart Disease in Men

Mihaela Tanasescu, MD

Michael F. Leitzmann, MD

Eric B. Rimm, ScD

Walter C. Willett, MD

Meir J. Stampfer, MD

Frank B. Hu, MD

MULTIPLE EPIDEMIOLOGIC studies have shown an inverse relationship between physical activity and risk of coronary heart disease (CHD). Sedentary individuals have almost twice the risk of CHD as those performing high-intensity exercise.^{1,2} However, the optimal level of exercise for preventing CHD is unclear. In some studies, the reduction in risk from increased levels of activity appeared to be linear up to a certain level above which there was no further benefit; in others, the effect was restricted to the highest categories of total energy expenditure.³ In addition, the effect of walking is still under debate and the effect of weight training is unknown. In this study, we assessed the association between the amount, types, and intensity of exercise in relation to risk of CHD in a large cohort of men.

METHODS

Study population

The Health Professionals' Follow-up Study (HPFS) began in 1986 when 51 529 US health professionals (dentists, optometrists, pharmacists, podiatrists, osteopaths, and veterinarians), aged 40 through 75 years, answered a detailed questionnaire that included a comprehensive diet survey, lifestyle assessment (including questions on leisure-time physical activity), and medical history. Follow-up questionnaires were sent

Context Studies have shown an inverse relationship between exercise and risk of coronary heart disease (CHD), but data on type and intensity are sparse.

Objective To assess the amount, type, and intensity of physical activity in relation to risk of CHD among men.

Design, Setting, and Participants A cohort of 44 452 US men enrolled in the Health Professionals' Follow-up Study, followed up at 2-year intervals from 1986 through January 31, 1998, to assess potential CHD risk factors, identify newly diagnosed cases of CHD, and assess levels of leisure-time physical activity.

Main Outcome Measure Incident nonfatal myocardial infarction or fatal CHD occurring during the follow-up period.

Results During 475 755 person-years, we documented 1700 new cases of CHD. Total physical activity, running, weight training, and rowing were each inversely associated with risk of CHD. The RRs (95% confidence intervals [CIs]) corresponding to quintiles of metabolic equivalent tasks (METs) for total physical activity adjusted for age, smoking, and other cardiovascular risk factors were 1.0, 0.90 (0.78-1.04), 0.87 (0.75-1.00), 0.83 (0.71-0.96), and 0.70 (0.59-0.82) ($P < .001$ for trend). Men who ran for an hour or more per week had a 42% risk reduction (RR, 0.58; 95% CI, 0.44-0.77) compared with men who did not run ($P < .001$ for trend). Men who trained with weights for 30 minutes or more per week had a 23% risk reduction (RR, 0.77; 95% CI, 0.61-0.98) compared with men who did not train with weights ($P = .03$ for trend). Rowing for 1 hour or more per week was associated with an 18% risk reduction (RR, 0.82; 95% CI, 0.68-0.99). Average exercise intensity was associated with reduced CHD risk independent of the total volume of physical activity. The RRs (95% CIs) corresponding to moderate (4-6 METs) and high (6-12 METs) activity intensities were 0.94 (0.83-1.04) and 0.83 (0.72-0.97) compared with low activity intensity (< 4 METs) ($P = .02$ for trend). A half-hour per day or more of brisk walking was associated with an 18% risk reduction (RR, 0.82; 95% CI, 0.67-1.00). Walking pace was associated with reduced CHD risk independent of the number of walking hours.

Conclusions Total physical activity, running, weight training, and walking were each associated with reduced CHD risk. Average exercise intensity was associated with reduced risk independent of the number of MET-hours spent in physical activity.

JAMA. 2002;288:1994-2000

www.jama.com

in 1988, 1990, 1992, 1994, 1996, and 1998 to update information on potential risk factors and to identify newly diagnosed cases of CHD and other illnesses. We excluded from the current analysis men with a diagnosis of cardiovascular disease (myocardial infarction [MI], angina, and/or coronary revascularization and stroke) and cancer other than nonmelanoma skin cancer prior to 1986. Men with a CHD event during the follow-up were excluded from analyses

in the subsequent intervals. Men who reported difficulty in climbing stairs or walking were excluded from analysis at

Author Affiliations: Departments of Nutrition (Drs Tanasescu, Leitzmann, Rimm, Willett, Stampfer, and Hu) and Epidemiology (Drs Leitzmann, Rimm, Willett, and Stampfer), Harvard School of Public Health; the Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, and Harvard Medical School (Drs Rimm, Willett, Stampfer, and Hu).

Corresponding Author and Reprints: Mihaela Tanasescu, MD, Nutrition Department, Loma Linda University, Nichol Hall, Room 1120, Loma Linda, CA 92350 (e-mail: mtanases@hsph.harvard.edu).

each time point starting from 1988. Thus, 44452 men remained for our analyses.

Assessment of Physical Activity

Leisure-time physical activity was assessed every 2 years between 1986 and 1996, using the question: "During the past year what was your average time per week spent at each activity?" The average weekly time spent on walking or hiking outdoors, jogging (<6 mph), running (≥ 6 mph), bicycling, lap swimming, tennis, squash or racquetball, calisthenics, or rowing was recorded beginning in 1986. Heavy outdoor work was added in 1988 and weight training in 1990. Walking pace, categorized as casual (≤ 2 mph), normal (2-2.9 mph), brisk (3-3.9 mph), or striding (≥ 4 mph), was also recorded. The time spent at each activity in hours per week was multiplied by its typical energy expenditure, expressed in metabolic equivalent tasks (METs),⁴ then summed over all activities, to yield a MET-hour score. One MET, the energy expended by sitting quietly, is equivalent to 3.5 mL of oxygen uptake per kilogram of body weight per minute, or to 1 kcal/kg of body weight per hour. Vigorous activities were defined as those requiring 6 METs or more: jogging, running, bicycling, lap swimming, tennis, squash or racquetball, and rowing. Nonvigorous activities (<6 METs) include walking, heavy outdoor work, and weight training.

We created a measure of average exercise intensity for each individual by dividing the total weekly volume of exercise in MET-hours by the total weekly hours spent in physical activity.

The validity and reproducibility of the physical activity questionnaire were assessed in 1991 when 238 participants in the HPFS completed a 1-week activity diary at 4 periods corresponding to different seasons throughout a year.⁵ The questionnaire showed good time integration when levels of activity were compared with the average of the 4 single-week physical activity diaries administered during the 4 seasons. The correlation between scores of physical activity from the diaries and from the questionnaire was 0.65 for total physical activity and 0.58

for vigorous activity. The correlation between questionnaire-derived vigorous activity and resting pulse rate was -0.45 ; the correlation between vigorous activity and pulse rate after a self-administered step test was -0.41 .⁵ In a subsample of participants in the HPFS ($n=466$), high-density lipoprotein cholesterol levels increased by 2.4 mg/dL (0.06 mmol/L) for each increment of 20 MET-h/wk ($P<.001$).⁶

CHD End Points

Combined end points for the analysis were fatal CHD and nonfatal MI occurring between the return of the 1986 questionnaire and January 31, 1998. Self-reported MIs were confirmed by a review of medical records based on World Health Organization criteria that included characteristic symptoms with either typical electrocardiographic changes or elevations of cardiac enzymes. Probable cases of MI (no available records but confirmed by hospitalization and information from telephone interview/letter) were also included in the analysis after ensuring that results were not appreciably different from those including definite cases alone.

Deaths were reported by next of kin, work associates, and postal authorities. In case of persistent nonresponse, the National Death Index was used to identify deceased cohort members. Fatal CHD was confirmed by reviewing medical records or autopsy reports with the permission of the next of kin. The cause listed on the death certificate was not sufficient alone to confirm a coronary death. Sudden deaths (ie, deaths within 1 hour of symptom onset in men without known disease that could explain death) were included in the fatal CHD category. For subjects with multiple end points, follow-up ended with onset of the first event.

Data Analysis

Person-months of follow-up accumulated starting with the date of return of the 1986 questionnaire until occurrence of a CHD end point, death, or the end of the study period (January 31, 1998), whichever came first.

In our main analyses, we used the cumulative average of physical activity levels from all available questionnaires up to the start of each 2-year follow-up interval.⁷ For example, the level of physical activity reported on the 1986 questionnaire was related to the incidence of CHD from 1986 through 1988, and the level of average activity reported on the 1986 and 1988 questionnaires was related to the incidence from 1988 through 1990. Additional analyses were performed using baseline levels of activity and simple updated levels of physical activity in which CHD was predicted only from the most recent questionnaire.

Participants were divided into quintiles of total volume of physical activity (total MET-hours), walking, and vigorous activity. We used informative increments for exercise intensity, walking pace, and specific sport activities. Tests for trend were calculated by assigning the median values to increasing categories of activity. Relative risks (RRs) were initially calculated adjusting for age. Cox proportional hazard models were then used to estimate RRs of CHD over each 2-year follow-up interval using the cumulative average of the reported levels of activity on prior questionnaires, adjusting for other potential confounders.⁸ We also analyzed cumulative, simple-updated, and baseline (1986) activity as categorical and continuous variables. We corrected RRs corresponding to increments of simple-updated and baseline physical activity using the method of Rosner et al.⁹

All multivariate models included the following covariates unless otherwise specified: alcohol intake (nondrinker, or consuming 0.1-4.9, 5-30, or >30 g/day), smoking (never, past, or currently smoking 1-14, 15-24, or ≥ 25 cigarettes/day), family history of MI, use of vitamin E supplements, history of diabetes, hypertension, and hypercholesterolemia at baseline, and quintiles of dietary intake of *trans* fatty acids, polyunsaturated fat, fiber, and folate. In secondary analyses we additionally controlled for body mass index (BMI; calculated as participant's weight in kilograms divided by the square of partici-

Table 1. Age-Standardized Characteristics According to Weekly Level of Total Physical Activity at Baseline (1986)*

Characteristic	Quintile of Physical Activity, MET-hours per Week				
	1	2	3	4	5
Median (range)	1.2 (0-2.9)	5.0 (3.0-7.9)	12.1 (8.0-17.7)	24.1 (17.8-34.5)	49.1 (34.6-69.2)
BMI, mean	26.2	26.0	25.5	25.1	24.8
Current smoking, %	14.3	10.9	9.1	7.1	6.6
Hypertension, %	22.3	21.6	20.4	18.7	17.1
High serum cholesterol, %	10.5	10.3	11.1	10.5	10.3
Family history of MI, %	12.0	12.0	11.9	11.3	12.7
Vitamin E supplement use, %	16.0	18.0	20.3	21.1	22.6
Total fat intake, % of total kcal	33.5	32.8	32.2	31.6	30.6
Polyunsaturated fat intake, % of total kcal	5.9	6.0	6.0	6.0	5.9
Saturated fat intake, % of total kcal	11.7	11.4	11.0	10.7	10.4
<i>Trans</i> fatty acid intake, % of total kcal	1.36	1.32	1.27	1.21	1.16
Dietary fiber intake, mean, g/d	18.4	19.9	20.7	21.6	23.0
Alcohol intake, mean, g/d	10.9	11.1	11.3	11.6	12.3

*MET indicates metabolic equivalent; BMI, body mass index; and MI, myocardial infarction.

pant's height in meters and stratified into 3 categories: ≤ 25 , 25-29.9, ≥ 30) to estimate how this potential intermediate factor would affect the RRs. The interaction between physical activity and obesity was assessed by the difference in -2 log likelihood between the model containing the interaction with obesity in 2 categories ($BMI < 30$, $BMI \geq 30$) and the main effects model.

In a secondary analysis, we performed a propensity analysis¹⁰ in which we used logistic regression modeling to predict the highest as opposed to the lowest quintile of physical activity. Demographic, clinical, and dietary variables were included in the propensity model. We used the resulting propensity scores to match men from the 2 groups.

RESULTS

We examined physical activity in relation to other potential risk factors for CHD at baseline (TABLE 1). Physically more active men tended to have lower BMIs, lower intakes of total fat and saturated fat, higher intakes of fiber and alcohol, a higher prevalence of vitamin E supplement use, and a lower prevalence of smoking and hypertension.

During 475 755 person-years of follow-up, we documented 1700 new cases of CHD. The age-adjusted RRs across quintiles of total physical activity decreased monotonically and were modestly attenuated after adjustment for alcohol consumption, smoking, family history of MI before age 50 years, and nutrient intake (polyunsaturated fat, *trans* fatty acids, folic acid, fiber, and vitamin E supplements (TABLE 2). The association was further attenuated by additionally adjusting for baseline presence of hypertension, diabetes, and high cholesterol levels. The RR comparing extreme quintiles was 0.70 (95% confidence interval [CI], 0.59-0.82) ($P < .001$ for trend). When the same analysis was performed using simple updated and baseline physical activity, the corresponding RRs were 0.70 (95% CI, 0.59-0.82; $P < .001$ for trend) and 0.77 (95% CI, 0.66-0.91; $P < .001$ for trend). Adjustment for current BMI did not appreciably alter these results.

In the secondary analysis of propensity-matched men, those who were at the highest quintile of activity still had a reduced CHD risk compared with those in the lowest quintile (adjusted RR, 0.73; 95% CI, 0.60-0.88).

When physical activity was modeled as a continuous variable, every 50 MET-h/wk increase of cumulatively updated physical activity was associated with a 26% reduction in risk of CHD (RR, 0.74; 95% CI, 0.65-0.85). The corresponding RRs were 0.79 (95% CI, 0.71-0.88) for simple-updated activity and 0.77 (95% CI, 0.67-0.89) for baseline physical activity. The association was strengthened considerably after correction for measurement error (for simple update: RR, 0.45 [95% CI, 0.28-0.72]; for baseline physical activity: RR, 0.49 [95% CI, 0.30-0.81]).

When analyzed separately, exercise intensity (low = 1-4 METs; moderate = 4-6 METs; high = 6-12 METs) was related to reduced risk of CHD (Table 2). To assess if exercise intensity is related to CHD risk independent of exercise volume, we added the average intensity to the model containing the total volume of exercise. The multivariate RRs corresponding to moderate and high exercise intensity were 0.94 (95% CI, 0.83-1.04) and 0.83 (95% CI, 0.72-0.97), respectively, compared with that for low exercise intensity ($P = .02$ for trend). When assessed as a continuous variable, exercise intensity was related to a reduction in risk of 4% for each 1-MET increase independent of the total exercise volume.

In supplementary analyses, we assessed the association between changes in exercise intensity and risk of CHD. Compared with men who maintained a low intensity of exercise (< 4 METs over 2-year intervals), men who maintained a high level of intensity (≥ 6 METs) had an RR of 0.72 (95% CI, 0.55-0.93), and those who increased intensity from low to high over time had an RR of 0.88 (95% CI, 0.70-1.12).

To address the possibility that men with subclinical disease reduced their amount of physical activity thereby biasing our results, we excluded men who drastically reduced their levels of activity (> 20 MET-h/wk) from one questionnaire to the next. The RRs across quintiles of physical activity, adjusted for alcohol consumption, smoking, family history of MI before age 50 years,

nutrient intake (polyunsaturated fat, *trans* fatty acids, folic acid, fiber, vitamin E supplements), and baseline presence of hypertension, high cholesterol levels, and diabetes, were 1.0, 0.91 (95% CI, 0.79-1.05), 0.87 (95% CI, 0.74-1.04), 0.81 (95% CI, 0.68-0.97), and 0.66 (95% CI, 0.56-0.80) ($P<.001$ for trend).

We evaluated the effect of physical activity across different subgroups defined by established risk factors for CHD (smoking status, alcohol consumption, obesity, presence of hypertension, family history of MI, age, and presence of hypercholesterolemia). Inverse associations were observed in all subgroups (smokers and nonsmokers, drinkers and nondrinkers, hypertensives and nonhypertensives, men with or without family history of MI before age 50 years, men younger than 65 or 65 years and older, men with or without high cholesterol levels, and men with BMIs lower than 25 or between 25 and 30, with the exception of obese men [BMI>30]). However, the interaction between obesity status and physical activity was not statistically significant ($P=.09$).

We further assessed the effect of activity type on CHD risk (TABLE 3). Running, jogging, rowing, and racquet sports (tennis and racquetball) were associated with reduced risk in age-adjusted analyses. In multivariate analyses including previously mentioned covariates plus all activities, running and rowing remained significant predictors of CHD. Running for one or more hours per week was associated with a 42% risk reduction (RR, 0.58; 95% CI, 0.44-0.77) and rowing for one or more hours per week was associated with an 18% risk reduction (RR, 0.82; 95% CI, 0.68-0.99) compared with men who did not engage in these activities. Cycling and swimming were not associated with risk.

We performed separate analyses on the effect of resistance training (weight training and strength machines) on risk of CHD starting from 1990 when these activities were first assessed. Compared with men who did not perform resistance training, the RRs for men who performed resistance training for less than 30 minutes or for 30 or more minutes per week were 0.83 (95% CI, 0.67-1.02) and 0.65 (95% CI, 0.51-0.81), re-

spectively ($P<.001$ for trend). In multivariate analyses that also controlled for other types of physical activity, weight training for 30 minutes or more per week was associated with a significant 23% risk reduction (RR, 0.77; 95% CI, 0.61-0.98; $P=.03$ for trend) (TABLE 4).

Walking was the most frequent form of exercise in this cohort, with 58% of men reporting at least 1 hour of walking per week, while 48% reported at least 1 hour of weekly vigorous activity. When analyzing the effect of walking and walking parameters on CHD events, we restricted the study population to men who reported less than 1 hour of weekly vigorous exercise (<6 MET-h/wk) to minimize the confounding effect of high-intensity activity. Total walking volume was associated with reduced risk of CHD in age-adjusted analysis. In multivariate analysis, risk of CHD was reduced only for men in the highest quintile, corresponding to 14.75 MET-h/wk (approximately 3.5 h/wk or a half hour per week of brisk walking) or more, with an 18% reduction in risk of CHD (RR, 0.82; 95% CI, 0.67-1.00; $P=.04$ for trend) (TABLE 5). Walking pace was significantly associated with reduced risk in

Table 2. Relative Risk for Coronary Heart Disease Associated With Weekly MET-Hours of Physical Activity and Average Exercise Intensity, 1986-1998*

Model	Cumulatively Updated Volume of Physical Activity by Quintile, MET-h/wk					P Value for Trend
	Quintile 1 0-6.32	Quintile 2 6.33-14.49	Quintile 3 14.50-25.08	Quintile 4 25.09-41.98	Quintile 5 ≥41.99	
Cases, No. (person-years)	432 (93 317)	370 (94 036)	336 (93 466)	294 (91 189)	268 (103 767)	
Age-adjusted	Reference	0.85 (0.74-0.98)	0.78 (0.67-0.92)	0.72 (0.62-0.83)	0.58 (0.49-0.68)	<.001
Multivariate model 1†	Reference	0.90 (0.78-1.03)	0.84 (0.73-0.98)	0.80 (0.68-0.92)	0.65 (0.56-0.77)	<.001
Multivariate model 2‡	Reference	0.90 (0.78-1.04)	0.87 (0.75-1.00)	0.83 (0.71-0.96)	0.70 (0.59-0.82)	<.001
Multivariate model 3§	Reference	0.93 (0.80-1.06)	0.90 (0.78-1.05)	0.87 (0.71-1.01)	0.74 (0.63-0.87)	<.001
Multivariate model 4	Reference	0.90 (0.78-1.04)	0.88 (0.76-1.01)	0.84 (0.72-0.98)	0.72 (0.61-0.85)	<.001
Model	Average Exercise Intensity, METs			P Value for Trend		
	Low (1-3.9)	Moderate (4-5.9)	High (≥6)			
Cases, No. (person-years)	482 (88 374)	911 (251 489)	307 (135 892)			
Age-adjusted	Reference	0.83 (0.74-0.93)	0.68 (0.59-0.79)	<.001		
Multivariate model 1†	Reference	0.88 (0.78-0.98)	0.75 (0.65-0.87)	<.001		
Multivariate model 2‡	Reference	0.91 (0.81-1.02)	0.79 (0.68-0.92)	.002		
Multivariate model 3§	Reference	0.93 (0.83-1.04)	0.82 (0.71-0.97)	.01		
Multivariate model 4	Reference	0.94 (0.83-1.04)	0.83 (0.74-0.97)	.02		

*All values are relative risk (95% confidence interval) unless otherwise specified.

†Adjusted for alcohol consumption, smoking, family history of myocardial infarction, and nutrient intake (polyunsaturated fat, *trans* fatty acids, folic acid, fiber, vitamin E supplements).

‡Adjusted for covariates in model 1 and for the presence of diabetes, high cholesterol levels, and hypertension at baseline.

§Adjusted for the covariates in model 2 and for BMI.

||Adjusted for the covariates in model 2, with physical activity volume in MET-hours per week and intensity in METs included in the same model.

Table 3. Multivariate Relative Risk of Coronary Heart Disease by Subtypes of Activity*

Activity	Duration of Activity, h/wk				P Value for Trend
	0	<.05†	0.5-1	≥1	
Running					
Cases, No. (person-years)	1511 (362 192)	111 (51 674)	24 (14 486)	54 (47 585)	
Age-adjusted	Reference	0.72 (0.59-0.88)	0.63 (0.42-0.94)	0.47 (0.35-0.61)	<.001
Multivariate‡	Reference	0.87 (0.70-1.07)	0.79 (0.52-1.21)	0.58 (0.44-0.77)	<.001
Jogging					
Cases, No. (person-years)	1392 (343 179)	198 (83 816)	44 (20 957)	66 (27 984)	
Age-adjusted	Reference	0.76 (0.65-0.88)	0.69 (0.51-0.93)	0.73 (0.57-0.93)	.002
Multivariate‡	Reference	0.86 (0.73-1.01)	0.85 (0.62-1.16)	0.93 (0.72-1.21)	.51
Rowing					
Cases, No. (person-years)	1107 (271 110)	356 (117 403)	109 (37 931)	128 (49 492)	
Age-adjusted	Reference	0.82 (0.73-0.93)	0.76 (0.62-0.92)	0.69 (0.57-0.82)	<.001
Multivariate‡	Reference	0.91 (0.80-1.03)	0.88 (0.72-1.08)	0.82 (0.68-1.00)	.04
Cycling					
Cases, No. (person-years)	983 (252 729)	408 (126 099)	118 (37 745)	191 (59 363)	
Age-adjusted	Reference	0.98 (0.87-1.10)	0.91 (0.75-1.10)	0.92 (0.78-1.07)	.21
Multivariate‡	Reference	1.07 (0.95-1.21)	1.06 (0.87-1.29)	1.07 (0.91-1.25)	.50
Swimming					
Cases, No. (person-years)	1409 (388 393)	195 (60 693)	25 (9829)	71 (16 822)	
Age-adjusted	Reference	0.97 (0.83-1.12)	0.69 (0.46-1.02)	1.08 (0.85-1.37)	.95
Multivariate‡	Reference	1.01 (0.87-1.18)	0.74 (0.50-1.10)	1.21 (0.95-1.54)	.29
Racquet sports					
Cases, No. (person-years)	1400 (359 072)	108 (43 584)	35 (15 890)	157 (57 391)	
Age-adjusted	Reference	0.97 (0.80-1.19)	0.80 (0.57-1.12)	0.84 (0.72-1.00)	.04
Multivariate‡	Reference	1.08 (0.88-1.32)	0.93 (0.67-1.31)	0.99 (0.84-1.17)	.83

*All values are relative risk (95% confidence interval) unless otherwise specified.

†Does not include zero.

‡Adjusted for alcohol consumption, smoking, family history of myocardial infarction, high-intensity activity, and nutrient intake (polyunsaturated fatty acids, trans fatty acids, folic acid, fiber, and vitamin E supplements), as well as for baseline diabetes, high cholesterol levels, and hypertension, and all other types of physical activity.

Table 4. Relative Risks of Coronary Heart Disease Associated With Weight Training, 1990-1998*

	Duration of Activity, h/wk			P Value for Trend
	0	<0.5†	≥0.5	
Cases, No. (person-years)	1011 (210 126)	96 (29 672)	90 (41 877)	
Age-adjusted	Reference	0.83 (0.67-1.02)	0.65 (0.51-0.81)	<.001
Multivariate model 1‡	Reference	0.88 (0.70-1.11)	0.69 (0.56-0.89)	.001
Multivariate model 2§	Reference	0.99 (0.78-1.25)	0.77 (0.61-0.98)	.03

*All values are relative risk (95% confidence interval) unless otherwise specified.

†Does not include zero.

‡Adjusted for alcohol consumption, smoking, family history of myocardial infarction, and nutrient intake (polyunsaturated fat, trans fatty acids, folic acid, fiber, and vitamin E supplements).

§Adjusted for covariates in model 1 and for other activities.

age-adjusted and multivariate models. When analyzed in the same multivariate model with walking MET-hours and compared with walking at an easy pace, the RRs corresponding to normal pace (2-3 mph), brisk pace (3-4 mph), and very brisk pace (≥4 mph) were 0.72 (95% CI, 0.54-0.94), 0.61 (95% CI, 0.45-0.81), and 0.51 (95% CI, 0.31-0.84), respectively (P<.001 for trend). Thus, walking pace is related to reduced CHD risk over and above the effect of walk-

ing volume. Time spent walking and walking MET-hours were not materially related to risk in analyses that controlled for walking pace.

COMMENT

In this prospective study, increased total physical activity was associated with reduced risk of CHD in a dose-dependent manner. This inverse association was not explained by other known coronary risk factors, including BMI. Exer-

cise intensity was associated with an additional risk reduction. Running, weight training, and rowing were each associated with reduced risk. Walking pace was strongly related to reduced risk independent of walking MET-hours.

The strengths of the current study include the prospective design, the large size of the cohort, detailed information on exposure and covariates, the extensive follow-up time, the strict and uniform criteria for coronary events, and the relative homogeneity of socioeconomic status among subjects. Men with cancer and previous CHD at baseline, as well as men with physical impairment, were excluded from the main analyses. These exclusions are likely to have minimized potential bias related to preexisting disease. Furthermore, when we excluded men who greatly reduced their levels of physical activity in the last 2 years, we obtained similar results.

One limitation of our study was self-report of physical activity. Although our

questionnaire was validated against diary and biomarkers, some misclassification is inevitable and random misclassification usually results in bias toward the null. Our results corrected for measurement error illustrated this point. Because of the observational nature of this study, we cannot completely rule out the possibility of residual and unmeasured confounding and cannot draw a causal relationship simply based on these data. However, the magnitude and consistency of the observed association, together with evidence from randomized trials on cardiovascular risk factors, strongly suggest protective effects of increasing physical activity against CHD.

When we analyzed specific activities such as swimming and cycling, our findings were limited by their low range of exposure. For example, only 2% of the cohort spent more than 1 h/wk swimming and only 7% spent more than 1 h/wk cycling. We also suspect that some participants performed these sports at lower than typical intensity (eg, 7 METs) or spent less than reported time in actual exercise.

Walking is the most common leisure activity among US men and women,¹¹ and it offers an alternative to high-intensity exercise in older populations. Current guidelines recommend 30 minutes of moderate-intensity activity on

most, and preferably all, days of the week to prevent CHD and other chronic diseases.^{12,13} However, few studies have assessed the effect of moderate-intensity activity on risk of CHD. Some studies suggest that exercise must be vigorous to reduce CHD risk,^{14,15,16} while others show benefit from moderate ranges of total physical activity without further risk reduction from high levels of exercise.^{17,18} More recently, several studies have shown that increasing walking is associated with reduced incidence of coronary events. In a study among 1645 men and women aged 65 years or older, LaCroix et al¹⁹ observed that walking more than 4 h/wk was associated with lower risk of hospitalization for cardiovascular disease. In the Honolulu Heart Program,²⁰ walking less than 0.25 miles/d and 0.25 to 1.5 miles/d was associated with RRs of 2.3 (95% CI, 1.3-4.1) and 2.1 (95% CI, 1.2-3.6), respectively, compared with walking more than 1.5 miles/d. Manson et al²¹ also showed an inverse relationship between walking and the risk of CHD in the Nurses' Health Study. The multivariate RRs for walking, across quintiles of walking (≤ 0.5 , 0.6-2.0, 2.1-3.8, 3.9-9.9 and ≥ 10 MET-hours/week), were 1.0, 0.78 (95% CI, 0.57-1.06), 0.88 (95% CI, 0.65-1.21), 0.70 (95% CI, 0.51-0.95), and 0.65 (95% CI, 0.47-0.91), respectively.

Other data show null or marginal results for the effect of walking on risk of CHD. In the Harvard Alumni Health Study,²² the trend of reduced CHD risk with increasing levels of walking was not significant. The authors attributed this result to a threshold effect, to the imprecise measurement of moderate activities, or to the difficulty in achieving high enough energy expenditure from moderate exercise. Also, in the Atherosclerosis Risk in Communities (ARIC) study,²³ frequent walking and the composite score of light activities were not associated with significant reductions in CHD risk.

We found an inverse relationship between walking and risk of CHD, but the association was significant only for the highest quintile in multivariate analysis. Also, walking pace was strongly associated with risk, suggesting that intensity of walking was more important than time spent. Only 2 previous studies, both in women, have investigated the independent association of walking pace with risk of CHD. In the Nurses' Health Study, walking pace was associated with CHD risk independent of the number of MET-hours spent walking,²¹ while in the Women's Health Study, time spent walking, but not walking pace, was related to risk.²⁴ It has also been reported that time spent walking may be less validly reported than usual walking pace.²⁴ Brisk and very brisk

Table 5. Relative Risk for Coronary Heart Disease Associated With Walking and With Walking Pace Among Men Who Did Not Perform Vigorous Exercise Regularly (ie, <1 h/wk)*

	Walking, MET-h/wk					P Value
	Quintile 1 0-1.19	Quintile 2 1.20-3.49	Quintile 3 3.50-6.99	Quintile 4 7.00-14.74	Quintile 5 ≥ 14.75	
Cases, No. (person-years)	215 (49 592)	228 (51 111)	190 (46 185)	221 (44 519)	203 (47 775)	
Age-adjusted	Reference	0.97 (0.81-1.17)	0.86 (0.70-1.04)	0.95 (0.78-1.15)	0.74 (0.61-0.90)	.002
Multivariate model 1†	Reference	1.00 (0.83-1.21)	0.90 (0.74-1.10)	1.02 (0.84-1.23)	0.82 (0.67-1.00)	.04
Multivariate model 2‡	Reference	1.03 (0.85-1.25)	0.96 (0.78-1.17)	1.10 (0.90-1.34)	0.90 (0.73-1.10)	.27
	Usual Walking Pace, mph				P Value	
	<2	2 to 3	3 to 4	≥ 4		
Cases, No. (person-years)	102 (11 950)	611 (124 571)	316 (92 620)	28 (10 040)		
Age-adjusted	Reference	0.66 (0.53-0.81)	0.52 (0.41-0.65)	0.45 (0.29-0.68)	$<.001$	
Multivariate model 1†	Reference	0.74 (0.60-0.91)	0.60 (0.45-0.79)	0.50 (0.30-0.83)	$<.001$	
Multivariate model 2‡	Reference	0.72 (0.54-0.94)	0.61 (0.45-0.81)	0.51 (0.31-0.84)	$<.001$	

*All values are relative risk (95% confidence interval) unless otherwise specified. MET indicates metabolic equivalent.

†Adjusted for alcohol consumption, smoking, family history of myocardial infarction, and nutrient intake (polyunsaturated fat, trans fatty acids, folic acid, fiber and vitamin E supplements), as well as for baseline diabetes, high cholesterol levels, and hypertension.

‡Adjusted for covariates in model 1 and with walking volume in MET-hours per week and walking pace included in the same model.

walking correspond to moderate exercise while walking at an easy or moderate pace represents low-intensity activity. Therefore, our findings lend some support to current recommendations for regular moderate exercise. Nonetheless, as shown in our analyses on total physical activity, performing the same number of MET-hours at a higher intensity is associated with further risk reduction. Hence, while moderate exercise like brisk walking is associated with reduced risk, greater risk reduction can be obtained with more intense exercise.

Mechanisms that are likely to explain the effect of physical activity on risk of CHD are multiple: direct action on the heart (increased myocardial oxygen supply, improved myocardial contraction, and electrical stability), increased high-density lipoprotein cholesterol levels, decreased low-density lipoprotein cholesterol levels, lowered blood pressure, decreased blood coagulability, and increased insulin sensitivity.²⁵ Moderate-intensity activities are associated with improvements in lipoprotein profile²⁶ and glucose control,²⁷ but frequent sessions to achieve a total high-energy expenditure may be required.²⁸ The additional risk reduction observed with higher intensity may be due to its effect on aerobic fitness, which is a strong predictor of CHD risk,^{29,30} and to energy balance.

A novel finding of our study was the significant reduction in CHD risk from resistive-type activities (ie, weight training and use of strength machines). Previous prospective studies have not directly assessed this relationship, but there is increasing evidence for the beneficial effects of strength training on CHD risk factors. Weight training increases fat-free mass and possibly resting metabolic rate,³¹ improves glycemic control,³² and may improve lipoprotein profile³³ and reduce hypertension.³⁴ Currently, strength training is recommended primarily for elderly persons and individuals with cardiovascular disease¹² as a means of improving overall musculoskeletal function. More research is needed to address whether inclusion of strength training recommendations for CHD prevention is warranted.

In conclusion, our study confirms a significant inverse dose-response relationship between total physical activity and risk of CHD. Additionally, we found that running, rowing, and weight training were related to reduced CHD risk. Intensity of physical activity was related to reduced risk, as reflected by the inverse association of walking pace and overall exercise intensity with CHD incidence. Thus, increasing total volume of activity, increasing intensity of aerobic exercise from low to moderate and from moderate to high, and adding weight training to the exercise program are among the most effective strategies to reduce the risk of CHD in men.

Author Contributions: Study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical expertise: Tanasescu, Leitzmann, Rimm, Willett, Stampfer, and Hu.

Obtained funding: Rimm, Willett, Hu.

Administrative, technical, or material support: Rimm, Willett, Stampfer, Hu.

Study supervision: Rimm, Willett, Hu.

Funding/Support: This work was supported by research grants CA 55075 and HL 35464 from the National Institutes of Health.

REFERENCES

- Berlin JA, Colditz GA. A meta-analysis of physical activity in the prevention of coronary heart disease. *Am J Epidemiol*. 1990;132:612-628.
- Francis K. Physical activity in the prevention of cardiovascular disease. *Phys Ther*. 1996;76:456-468.
- Wannamethee SG, Shaper AG. Physical activity in the prevention of cardiovascular disease: an epidemiological perspective. *Sports Med*. 2001;31:101-114.
- Ainsworth BE, Haskell WL, Leon AS, et al. Compendium of physical activities. *Med Sci Sports Exerc*. 1993;25:71-80.
- Chasan-Taber S, Rimm EB, Stampfer MJ, et al. Reproducibility and validity of a self-administered physical activity questionnaire for male health professionals. *Epidemiology*. 1996;7:81-86.
- Fung TT, Hu FB, Yu J, et al. Leisure-time physical activity, television watching, and plasma biomarkers of obesity and cardiovascular disease risk. *Am J Epidemiol*. 2000;152:1171-1178.
- Hu FB, Stampfer MJ, Rimm E, et al. Dietary fat and coronary heart disease. *Am J Epidemiol*. 1999;149:531-540.
- Therneau TM. Extending the Cox model. In: Lin DY, Fleming TR, eds. *Proceedings of the First Seattle Symposium in Biostatistics: Survival Analysis*. Heidelberg, Germany: Springer Verlag; 1997:51-84.
- Rosner B, Willett WC, Spiegelman D. Correction of logistic regression relative risk estimates and confidence intervals for systematic within-person measurement error. *Stat Med*. 1989;8:1051-1069; discussion 1071-1073.
- D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Stat Med*. 1998;17:2265-2281.
- Crespo CJ, Keteyian SJ, Heath GW, Sempos CT. Leisure-time physical activity among US adults. *Arch Intern Med*. 1996;156:93-98.
- NIH Consensus Development Panel on Physical Activity and Cardiovascular Health. Physical activity and cardiovascular health. *JAMA*. 1996;276:241-246.
- Pate RR, Pratt M, Blair SN, et al. Physical activity and public health. *JAMA*. 1995;273:402-407.
- Morris JN, Clayton DG, Everitt MG, Semmence AM, Burgess EH. Exercise in leisure time: coronary attack and death rates. *Br Heart J*. 1990;63:325-334.
- Lakka TA, Venalainen JM, Rauramaa R, et al. Relation of leisure-time physical activity and cardiorespiratory fitness to the risk of acute myocardial infarction. *N Engl J Med*. 1994;330:1549-1554.
- Mensink GB, Deketh M, Mul MD, Schuit AJ, Hoffmeister H. Physical activity and its association with cardiovascular risk factors and mortality. *Epidemiology*. 1996;7:391-397.
- Shaper AG, Wannamethee G, Weatherall R. Physical activity and ischaemic heart disease in middle-aged British men. *Br Heart J*. 1991;66:384-394.
- Leon AS, Connett J. Physical activity and 10.5 year mortality in the Multiple Risk Factor Intervention Trial (MRFIT). *Int J Epidemiol*. 1991;20:690-697.
- LaCroix AZ, Leveille SG, Hecht JA, Grothaus LC, Wagner EH. Does walking decrease the risk of cardiovascular disease hospitalizations and death in older adults? *J Am Geriatr Soc*. 1996;44:113-120.
- Hakim AA, Curb JD, Petrovitch H, et al. Effects of walking on coronary heart disease in elderly men: the Honolulu Heart Program. *Circulation*. 1999;100:9-13.
- Manson JE, Hu FB, Rich-Edwards JW, et al. A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. *N Engl J Med*. 1999;341:650-658.
- Sesso HD, Paffenbarger RS Jr, Lee IM. Physical activity and coronary heart disease in men. *Circulation*. 2000;102:975-980.
- Folsom AR, Arnett DK, Hutchinson RG, Liao F, Clegg LX, Cooper LS. Physical activity and incidence of coronary heart disease in middle-aged women and men. *Med Sci Sports Exerc*. 1997;29:901-909.
- Lee IM, Rexrode KM, Cook NR, Manson JE, Buring JE. Physical activity and coronary heart disease in women. *JAMA*. 2001;285:1447-1454.
- Paffenbarger RS, Lee IM. Exercise and fitness. In: Manson JE, Ridker PM, Gaziano JM, Hennekens CH, eds. *Prevention of Myocardial Infarction*. New York, NY: Oxford University Press; 1996:172-202.
- Hardman AE, Hudson A. Brisk walking and serum lipid and lipoprotein variables in previously sedentary women. *Br J Sports Med*. 1994;28:261-266.
- Walker KZ, Piers LS, Putt RS, Jones JA, O'Dea K. Effects of regular walking on cardiovascular risk factors and body composition in normoglycemic women and women with type 2 diabetes. *Diabetes Care*. 1999;22:555-561.
- Drygas W, Kostka T, Jegier A, Kunski H. Long-term effects of different physical activity levels on coronary heart disease risk factors in middle-aged men. *Int J Sports Med*. 2000;21:235-241.
- Williams PT. Physical fitness and activity as separate heart disease risk factors: a meta-analysis. *Med Sci Sports Exerc*. 2001;33:754-761.
- Prakash M, Myers J, Froelicher VF, et al. Clinical and exercise test predictors of all-cause mortality. *Chest*. 2001;120:1003-1013.
- Poehlman ET, Melby C. Resistance training and energy balance. *Int J Sport Nutr*. 1998;8:143-159.
- Poehlman ET, Dvorak RV, DeNino WF, Brochu M, Ades PA. Effects of resistance training and endurance training on insulin sensitivity in nonobese, young women. *J Clin Endocrinol Metab*. 2000;85:2463-2468.
- Prabhakaran B, Dowling EA, Branch JD, Swain DP, Leutholtz BC. Effect of 14 weeks of resistance training on lipid profile and body fat percentage in premenopausal women. *Br J Sports Med*. 1999;33:190-195.
- Hurley BF, Roth SM. Strength training in the elderly. *Sports Med*. 2000;30:249-268.