in younger adults (Kohrt et al. 1991). The interrelationships of age, $\dot{V}O_2$max, and training status are evident when the loss in $\dot{V}O_2$max with age is compared for active and sedentary individuals (Figure 3-5).

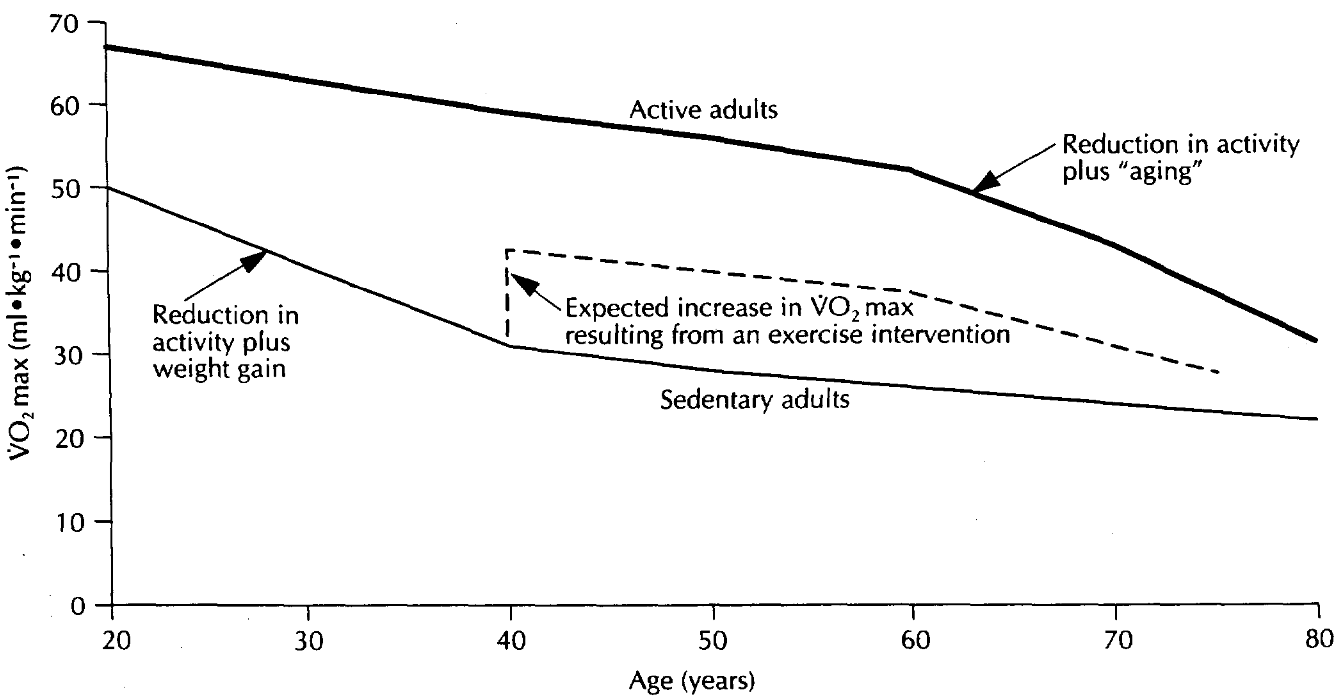
When the cardiorespiratory responses of an older adult are compared with those of a young or middle-aged adult at the same absolute submaximal rate of work, stroke volume for an older person is generally lower and heart rate is higher from the attempt to maintain cardiac output. Because this attempt is generally insufficient, the A-$\bar{v}O_2$ difference must increase to provide the same submaximal oxygen uptake (Raven and Mitchell 1980; Thompson and Dorsey 1986). Some researchers have shown, however, that cardiac output can be maintained at both submaximal and maximal rates of work through a higher stroke volume in older adults (Rodeheffer et al. 1984).

The deterioration in physiological function normally associated with aging is, in fact, caused by a combination of reduced physical activity and the aging process itself. By maintaining an active lifestyle, or by increasing levels of physical activity if previously sedentary, older persons can maintain relatively high levels of cardiovascular and metabolic function, including $\dot{V}O_2$max (Kohrt et al. 1991), and of skeletal muscle function (Rogers and Evans 1993). For example, Fiatarone and colleagues (1994) found an increase of 113 percent in the strength of elderly men and women (mean age of 87.1 years) following a 10-week training program of progressive resistance exercise. Cross-sectional thigh muscle area was increased, as was stair-climbing power, gait velocity, and level of spontaneous activity. Increasing endurance and strength in the elderly contributes to their ability to live independently.

Differences by Sex

For the most part, women and men who participate in exercise training have similar responses in cardiovascular, respiratory, and metabolic function (providing that size and activity level are normalized). Relative increases in $\dot{V}O_2$max are equivalent

Figure 3-5. Changes in $\dot{V}O_2$ max with aging, comparing an active population and sedentary population (the figure also illustrates the expected increase in $\dot{V}O_2$ max when a previously sedentary person begins an exercise program)



Adapted, by permission, from Buskirk ER, Hodgson JL. *Federation Proceedings* 1987.

for women and men (Kohrt et al. 1991; Mitchell et al. 1992). Some evidence suggests that older women accomplish this increase in $\dot{V}O_2max$ mainly through an increase in the A-$\bar{v}O_2$ difference, whereas younger women and men have substantial increases in stroke volume, which increases maximal cardiac output (Spina et al. 1993). With resistance training, women experience equivalent increases in strength (Rogers and Evans 1993; Holloway and Baechle 1990), although they gain less fat-free mass due to less muscle hypertrophy.

Several sex differences have been noted in the acute response to exercise. At the same absolute rate of exercise, women have a higher heart rate response than men, primarily because of a lower stroke volume. This lower stroke volume is a function of smaller heart size and smaller blood volume. In addition, women have less potential to increase the A-$\bar{v}O_2$ difference because of lower hemoglobin content. Those differences, in addition to greater fat mass, result in a lower $\dot{V}O_2max$ in women, even when normalized for size and level of training (Lewis, Kamon, Hodgson 1986).

Conclusions

1. Physical activity has numerous beneficial physiologic effects. Most widely appreciated are its effects on the cardiovascular and musculoskeletal systems, but benefits on the functioning of metabolic, endocrine, and immune systems are also considerable.
2. Many of the beneficial effects of exercise training—from both endurance and resistance activities—diminish within 2 weeks if physical activity is substantially reduced, and effects disappear within 2 to 8 months if physical activity is not resumed.
3. People of all ages, both male and female, undergo beneficial physiologic adaptations to physical activity.

Research Needs

1. Explore individual variations in response to exercise.
2. Better characterize mechanisms through which the musculoskeletal system responds differentially to endurance and resistance exercise.
3. Better characterize the mechanisms by which physical activity reduces the risk of cardiovascular disease, hypertension, and non-insulin-dependent diabetes mellitus.
4. Determine the minimal and optimal amount of exercise for disease prevention.
5. Better characterize beneficial activity profiles for people with disabilities.

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Chapter 4

The Effects of Physical Activity on Health and Disease

Contents

Contents, *continued*

CHAPTER 4

THE EFFECTS OF PHYSICAL ACTIVITY ON HEALTH AND DISEASE

Introduction

This chapter examines the relationship of physical activity and cardiorespiratory fitness to a variety of health problems. The primary focus is on diseases and conditions for which sufficient data exist to evaluate an association with physical activity, the strength of such relationships, and their potential biologic mechanisms. Because most of the research to date has addressed the health effects of endurance-type physical activity (involving repetitive use of large muscle groups, such as in walking and bicycling), this chapter focuses on that type of activity. Unless otherwise specified, the term physical activity should be understood to refer to endurance-type physical activity. Less well studied are the health effects of resistance-type physical activity (i.e., that which develops muscular strength); when this type of physical activity is discussed, it is specified as such. Much of the research summarized is based on studies having only white men as participants; it remains to be clarified whether the relationships described here are the same for women, racial and ethnic minority groups, and people with disabilities.

Physical activity is difficult to measure directly. Three types of physical activity measures have been used in observational studies over the last 40 years. Most studies have relied on self-reported level of physical activity, as recalled by people prompted by a questionnaire or interview. A more objectively measured characteristic is cardiorespiratory fitness (also referred to as cardiorespiratory endurance) which is measured by aerobic power (see Chapter 2 for more information on measurement issues). Some studies have relied on occupation to classify people according to how likely they were to be physically active at work.

Epidemiologic studies of physical activity and health have compared the activity levels of people who have or develop diseases and those who do not. Cohort studies follow populations forward in time to observe how physical activity habits affect disease occurrence or death. In case-control studies, groups of persons who have disease and separate groups of people who do not have disease are asked to recall their previous physical activity. Cross-sectional studies assess the association between physical activity and disease at the same point in time. Clinical trials, on the other hand, attempt to alter physical activity patterns and then assess whether disease occurrence is modified as a result.

Results from epidemiologic studies can be used to estimate the relative magnitude or strength of an association between physical activity and a health outcome. Two such measures used in this chapter are risk ratio (RR) and odds ratio (OR). For these measures, an estimate of 1.0 indicates no association, when the risk of disease is equivalent in the two groups being compared. RR or OR estimates greater than 1.0 indicate an increase in risk; those less than 1.0 indicate a decreased risk. Confidence intervals (CI) reported with estimates of association indicate the precision of the estimate, as well as its statistical significance. When the CI range includes 1.0, the effect is considered likely to have occurred by chance; therefore the estimate of association is not considered statistically significantly different from the null value of 1.0.

Overall Mortality

Persons with moderate to high levels of physical activity or cardiorespiratory fitness have a lower mortality rate than those with sedentary habits or low cardiorespiratory fitness. For example, compared with people who are most active, sedentary people experience between a 1.2-fold to a 2-fold increased risk of dying during the follow-up interval (Slattery and Jacobs 1988; Slattery, Jacobs, Nichaman 1989; Leon and Connett 1991; Stender et al. 1993; Sandvik et al. 1993; Chang-Claude and Frentzel-Beyme 1993; Kaplan et al. 1987; Arraiz, Wigle, Mao 1992; Paffenbarger et al. 1993).

Associations are generally stronger for measured cardiorespiratory fitness than for reported physical activity (Blair, Kohl, Paffenbarger 1989). Blair, Kohl, and Barlow (1993) showed that low levels of cardiorespiratory fitness were strongly associated with overall mortality for both women (RR = 5.35; 95% CI, 2.44–11.73) and men (RR = 3.16; 95% CI, 1.92–5.20). The association with physical inactivity was weaker for men (RR = 1.70; 95% CI, 1.06–2.74), and there was no association for women (RR = 0.95; 95% CI, 0.54–1.70).

Though cardiorespiratory fitness may be the better indicator of regular physical activity, the level of reported physical activity has been associated with reduced all-cause mortality. Paffenbarger, Lee, and Leung (1994) evaluated several types of recalled activity (walking, stair climbing, all sports, moderate-level sports, and total energy expended in activity per week) as predictors of all-cause mortality among male Harvard alumni. Among these men, the relative risk of death within the follow-up period was reduced to 0.67 with walking 15 or more kilometers per week (reference group, < 5 kilometers/week), to 0.75 with climbing 55 or more flights of stairs per week (reference group, < 20 flights/week), to 0.63 with involvement in moderate sports (reference group, no involvement), and to 0.47 with 3 or more hours of moderate sports activities per week (reference group, < 1 hour/week). Most importantly, there was a significant trend of decreasing risk of death across increasing categories of distance walked, flights of stairs climbed, and degree of intensity of sports play.

Researchers have also examined age-specific effects of different levels of physical activity on all-cause mortality. Kaplan and colleagues (1987) have shown that physical activity level has an effect on death rates among both older and younger persons. Data from a study of 9,484 Seventh-Day Adventist men aged 30 years or older in 1958 who were followed through 1985 indicated that both moderate and intense levels of activity reduced overall risk of death even late in life (Lindsted, Tonstad, Kuzma 1991). Both moderate and vigorous levels of activity were equally protective at age 50 years. The protective effect of high levels of activity lasted only until age 70, but the protective effect for moderate activity lasted beyond age 80.

The studies cited thus far in this section assessed physical activity or cardiorespiratory fitness at baseline only and then followed up for mortality. A stronger test for a causal relationship is to examine the effect that changing from lower to higher levels of physical activity or cardiorespiratory fitness has on subsequent mortality. Two large studies provide such evidence. Among middle-aged Harvard male alumni who were sedentary in 1962 or 1966, those who took up moderately intense sports activity during the study's 11 years of follow-up had a 23 percent lower death rate (RR = 0.77; 95% CI, 0.58–0.96) than those who remained sedentary (Paffenbarger et al. 1993). (By comparison, men who quit smoking during the interval had a 41 percent decrease in death rate [RR = 0.59; 95% CI, 0.43–0.80].) Men 45–84 years of age who took up moderately intense sports extended their longevity on average by 0.72 years; added years of life were observed in all age groups, including men 75–84 years of age (Paffenbarger et al. 1993).

Similar reductions in death rates with increases in cardiorespiratory fitness were reported for men in the Aerobics Center Longitudinal Study. Blair and colleagues (1995) reported a reduction in death rates among healthy men (aged 20–82 years) who improved their initially low levels of cardiorespiratory fitness. The men performed two maximal exercise tests an average of 4.8 years apart; follow-up for mortality after the second test occurred an average of 4.7 years later. Among men in the bottom fifth of the cardiorespiratory fitness distribution, those who improved to at least a moderate fitness level had a 44 percent lower death rate than their peers who remained in the bottom fifth (RR = 0.56; 95% CI, 0.41–0.75). After multivariate adjustment, those who became fit had a significant 64 percent reduction in their relative mortality rate. In comparison, men who stopped smoking reduced their adjusted RR by about 50 percent.

Conclusions

The data reviewed here suggest that regular physical activity and higher cardiorespiratory fitness decrease overall mortality rates in a dose-response fashion. Whereas most studies of physical activity and health address specific diseases and health conditions, the studies in this chapter provide more insight into the biologic mechanisms by which mortality rate reduction occurs.

Cardiovascular Diseases

Despite a progressive decline since the late 1960s, cardiovascular diseases (CVDs), including coronary heart disease (CHD) and stroke, remain major causes of death, disability, and health care expenditures in the United States (NCHS 1994; Gillum 1994). In 1992, more than 860,000 deaths in the United States were attributed to heart disease and stroke (DHHS 1994). High blood pressure, a major risk factor for CVD, affects about 50 million Americans (National Institutes of Health [NIH] 1993), including an estimated 2.8 million children and adolescents 6–17 years of age (Task Force on Blood Pressure Control in Children 1987). The prevalence of CVD increases with age and is higher among African Americans than whites. The majority of population-based research in the area of physical activity and health has focused on some aspect of CVD.

Cardiovascular Diseases Combined

Most of the reported studies relating physical activity to CVD have reported CVD mortality as an endpoint; two also reported on nonfatal disease, and one reported on CVD hospitalization (Table 4-1). Seven cohort studies evaluated the association between level of physical activity and the risk of total CVD (Kannel and Sorlie 1979; Paffenbarger et al. 1984; Kannel et al. 1986; Lindsted, Tonstad, Kuzma 1991; Arraiz, Wigle, Mao 1992; Sherman et al. 1994; LaCroix et al. 1996). All relied on a single point-in-time estimate of physical activity, in some cases assessed as long as 26 years before the end of the observational period, and four had follow-up periods of ≥ 14 years. Four of the seven studies found both an inverse association and a dose-response gradient between level of physical activity and risk of CVD outcome (Kannel and Sorlie 1979; Paffenbarger et al. 1984; Kannel et al. 1986; LaCroix et al. 1996). One study among men found an inverse association among the moderately active group but less of an effect in the vigorously active group (Lindsted, Tonstad, Kuzma 1991). One study of women 50–74 years of age found no relationship of physical activity with CVD mortality (Sherman et al. 1994).

Five large cohort studies have related cardiorespiratory fitness to the risk of CVD mortality (Arraiz, Wigle, Mao 1992; Ekelund et al. 1988; Blair, Kohl, Paffenbarger 1989; Sandvik et al. 1993; Blair et al. 1995), but only one provided a separate analysis for women (Blair, Kohl, Paffenbarger 1989). Each of these studies demonstrated an inverse dose-response relationship between level of cardiorespiratory fitness and CVD mortality. Three of the five studies relied on a maximal or near-maximal exercise test to estimate cardiorespiratory fitness. One study (Blair et al. 1995) demonstrated that men with low cardiorespiratory fitness who became fit had a lower risk of CVD mortality than men who remained unfit.

Taken together, these major cohort studies indicate that low levels of physical activity or cardiorespiratory fitness increase risk of CVD mortality. Findings seem to be more consistent for studies of cardiorespiratory fitness, perhaps because of its greater precision of measurement, than for those of reported physical activity. The demonstrated dose-response relationship indicates that the benefit derived from physical activity occurs at moderate levels of physical activity or cardiorespiratory fitness and increases with increasing levels of physical activity or higher levels of fitness.

Coronary Heart Disease

Numerous studies have examined the relationship between physical activity and CHD as a specific CVD outcome. Reviews of the epidemiologic literature (Powell et al. 1987; Berlin and Colditz 1990; Blair 1994) have concluded that physical activity is strongly and inversely related to CHD risk. Although physical exertion may transiently increase the risk of an acute coronary event among persons with advanced coronary atherosclerosis, particularly among those who do not exercise regularly (Mittleman et al. 1993; Willich et al. 1993; Siscovick et al. 1984), physically active people have a substantially lower overall risk for major coronary events.

Table 4-1. Population-based studies of association of physical activity or cardiorespiratory fitness with total cardiovascular diseases

Study	Population	Definition of physical activity or cardiorespiratory fitness	Definition of cardiovascular disease
Physical activity			
Kannel and Sorlie (1979)	1,909 Framingham (MA) men and 2,311 women aged 35–64 years at 14-year follow-up	Physical activity index based on hours per day spent at activity-specific intensity	CVD fatal and nonfatal in men (n = 140 deaths, n = 435 total cases) and women (n = 101 deaths)
Paffenbarger et al. (1984)	16,936 US male college alumni who entered college between 1916 and 1950; followed from 1962–1978	Physical activity index estimated from reports of stairs climbed, city blocks walked, and sports played each week	Death due to CVD (n = 640)
Kannel et al. (1986)	1,166 Framingham (MA) men aged 45–64 years; 24-year follow-up	Physical activity index based on hours per day at activity-specific intensity; occupational physical activity classified by physical demand of work	Death due to CVD (n = 325)
Lindsted, Tonstad, Kuzma (1991)	9,484 Seventh-Day Adventist men aged ≥ 30 years; 26-year follow-up	Self-report to single physical activity question	Death due to CVD (ICD-8 410–458) (n = 410)
Arraiz, Wigle, Mao (1992)	Stratified probability sample of Canadians aged 30–69 years, conducted in 1978–1979; 7-year follow-up	Physical activity index summarizing frequency, intensity, and duration of leisure-time activity and household chores	Death due to CVD (n = 256)
Sherman et al. (1994)	1,404 Framingham (MA) women aged 50–74 years; 16-year follow-up	Physical activity index based on hours per day spent at activity-specific intensity	CVD incidence (n = 994) and mortality (n = 303)
LaCroix et al. (1996)	1,645 HMO members age ≥ 65 years; 4.2-year average follow-up	Hours of walking per week	CVD hospitalization (ICD-9 390–448) (n = 359)
Cardiorespiratory fitness			
Ekelund et al. (1988)	3,106 North American men aged 30–69 years; 8.5-year average follow-up	Submaximal aerobic capacity estimated from exercise test	Death due to CVD (ICD-8 390–458) (n = 45)
Blair et al. (1989)	10,244 men and 3,120 women aged ≥ 20 years; 8.1-year average follow-up	Maximal aerobic capacity estimated by exercise test	Death due to CVD (ICD-9 390–448) in men (n = 66) and women (n = 7)

Main findings	Dose response*	Adjustment for confounders and other comments
Inverse association between physical activity index and CVD mortality for both men and women	Yes	Control for several confounding variables; statistical significance only for men after multivariate adjustment
Inverse association; relative to highest category (2,000+ kcal/week), relative risk estimates were 1.28 and 1.84, respectively	Yes	Significant dose-response after adjusting for age, smoking, and hypertension prevalence
Inverse association; for physical activity index, age-adjusted RR relative to high activity category = 1.62 for low activity, 1.30 for moderate; for occupational activity, age-adjusted RR relative to heavy physical demand category = 1.34 for sedentary, 1.26 for light, 1.09 for medium	Yes	Inverse association constant across all analyses; inverse association maintained after multivariate analyses
Inverse association relative to inactive group; moderately active RR = 0.79 (95% CI, 0.58–1.07), highly active RR = 1.02 (95% CI,0.66–1.58)	No	No statistical significance after controlling for sociodemographic variables, BMI, and dietary pattern
Null association across categories of physical activity index	No	Point estimates adjusted for age, BMI, sex, and smoking
Null association across quartiles of physical activity index	No	No statistical significance after controlling for several clinical and sociodemographic confounding variables
Inverse association; compared with walking 4 hrs/week, RR = 0.90 (95% CI 0.69–1.17) for walking 1–4 hrs/week; RR = 0.73 (95% CI 0.55–0.96) for walking > 4 hrs/week	Yes	Multivariate analysis adjusted for age, sex, functional status, BMI, smoking, chronic illnesses, and alcohol
Inverse association; adjusted risk estimate of 2.7-fold increased risk of CVD death for a 35 beat/min increase in heart rate for stage II of exercise test	Yes	Extensive control for clinical and sociodemographic confounding influences
Inverse association; for men, age-adjusted RR for lowest 20% compared with upper 40% = 7.9; for middle 40% = 2.5; for women, 9.2 and 3.6	Yes	Significant linear dose-response association; adjusted for age

Table 4-1. *Continued*

Study	Population	Definition of physical activity or cardiorespiratory fitness	Definition of cardiovascular disease
Arraiz, Wigle, Mao (1992)	Stratified probability sample of Canadians aged 30–69 years, conducted in 1978–1979; 7-year follow-up	Submaximal aerobic capacity estimated from home step test	Death due to CVD (n = 37)
Sandvik et al. (1993)	1,960 Norwegian men aged 40–59 years; average 16-year follow-up	Maximal aerobic capacity estimated by exercise test	Death due to CVD (n = 144)
Blair et al. (1995)	9,777 US men aged 20–82 years with 2 evaluations; 5.1-year average follow-up	Maximal aerobic capacity estimated by exercise test	Death due to CVD (ICD-9 390–449.9) (n = 87)

Thirty-six studies examining the relationship of physical activity level to risk of CHD have been published since 1953 (Table 4-2). Studies published before 1978 predominantly classified physical activity level by job title or occupational activities. Studies thereafter usually defined activity level by recall of leisure-time activity or by such activity combined with occupational activity. These later studies were also able to control statistically for many potentially confounding variables in addition to age. Most of these studies focused on men in the age ranges associated with increasing risk of CHD (30–75 years); only four included women. Although in several studies, CHD mortality was the sole outcome variable, most included both fatal and nonfatal disease. All but one (Morris et al. 1973) were cohort studies; lengths of follow-up from baseline assessment ranged from 4 to 25 years. All studies related a single baseline estimate of physical activity level to risk of CHD during the follow-up period.

Some study populations have had more than one follow-up assessment for CHD. For example, three follow-up assessments (at 10, 12, and 23 years) have been reported for men in the Honolulu Heart Program (Yano, Reed, McGee 1984; Donahue et al. 1988; Rodriguez et al. 1994). Each represented follow-up further removed from the original determination of physical activity. Thus, the diminishing effect seen over time might indicate changing patterns of physical activity—and thereby a lessening of validity of the original physical activity classification (Table 4-2). Oddly, in the 12-year follow-up, the reduction in CHD risk observed among both active middle-aged men (RR = 0.7) and active older men (RR = 0.4) when compared with their least active counterparts was not diminished by bivariate adjustment for serum cholesterol, body mass index (BMI), or blood pressure (Donahue et al. 1988). In the 23-year follow-up, however, the reduction in CHD risk among active men (RR = 0.8) was greatly diminished by simultaneous adjustment for serum cholesterol, BMI, blood pressure, and diabetes (RR = 0.95), leading the authors to conclude that the beneficial effect of physical activity on CHD risk is likely mediated by the beneficial effect of physical activity on these other factors (Rodriguez et al. 1994). These reports thus illustrate not only the problem of lengthy follow-up without repeated assessments of physical activity but also the problem of lack of uniformity in adjustment for potential confounding factors, as well as the underlying, thorny problem of adjustment for multiple factors that may be in the causal pathway between physical activity and disease. Studies have in fact varied greatly in the extent to which they have controlled for potential confounding and in the factors selected for adjustment.

Although early studies were not designed to demonstrate a dose-response gradient between physical

Main findings	Dose response*	Adjustment for confounders and other comments
Inverse association; relative to highest fitness level, persons in "moderate" and "low" categories had risks of 0.8 (95% CI, 0.1–7.6) and 5.4 (95% CI, 1.9–15.9), respectively	No	Point estimates adjusted for age, BMI, sex, and smoking
Inverse association; relative to men in lowest fitness quartile, multivariate adjusted RR in quartiles 2, 3, and 4 were 0.59, 0.45, and 0.41, respectively	Yes	Extensive control for confounding influences
Inverse association; relative to men who remained unfit (lowest 20% of distribution), those who improved had an age-adjusted RR of 0.48 (95% CI, 0.31–0.74)	Yes	For each minute of improvement in exercise test time, adjusted CVD mortality risk was reduced 8.6%

Abbreviations: BMI = body mass index (wt [kg] /ht [m]^2); CVD = cardiovascular disease; CI = confidence interval; HMO = health maintenance organization; ICD = International Classification of Diseases (8 and 9 refer to editions); RR = relative risk.

*A dose-response relationship requires more than 2 levels of comparison. In this column, "NA" means that there were only 2 levels of comparison; "No" means that there were more than 2 levels but no dose-response gradient was found; "Yes" means that there were more than 2 levels and a dose-response gradient was found.

activity level and CHD, most found an inverse association: more active persons were found to be at lower risk of CHD than their more sedentary counterparts. Of the 17 recent studies that found an inverse relationship and were able to examine dose-response relationships, 13 (76 percent) demonstrated an inverse dose-response gradient between level of physical activity and risk of CHD, whereas 2 showed a dose-response gradient only for some subgroups.

The relationship between cardiorespiratory fitness and risk of CHD was examined in seven cohort studies (follow-up range, 4–20 years). All but two (Lie, Mundal, Erikssen 1985; Erikssen 1986) used estimates of aerobic power based on submaximal exercise testing. None of these studies included women. Similar to the studies of physical activity and CHD, these all related a single baseline assessment of cardiorespiratory fitness to risk of CHD during the follow-up period. Most controlled statistically for possible confounding variables. All seven studies showed an inverse association between cardiorespiratory fitness and CHD. Of the six studies that had more than two categories of cardiorespiratory fitness, all demonstrated an inverse dose-response gradient.

Two recent meta-analyses of studies of physical activity and CHD have included independent scoring for the quality of the methods used in each study (Powell et al. 1987; Berlin and Colditz 1990). Both concluded that studies with higher-quality scores tended to show higher relative risk estimates than those with lower-quality scores. In the Berlin and Colditz quantitative meta-analysis, the pooled relative risk for CHD—comparing risk for the lowest level of physical activity with risk for the highest level—was 1.8 among the studies judged to be of higher quality. In contrast, the pooled relative risk for the studies with low-quality scores was in the null range.

CVD Risk Factors in Children

Because CHD is rare in children, the cardiovascular effects of physical activity in children are assessed through the relationship of physical activity with CHD risk factors such as elevated low-density lipoprotein cholesterol (LDL-C), lowered high-density lipoprotein cholesterol (HDL-C), and elevated blood pressure. The presence of CHD risk factors in children is of concern because of evidence that atherosclerosis begins in childhood (Stary 1989), that presence of CHD in adults is related to elevated blood

Table 4-2. Population-based studies of association of physical activity or cardiorespiratory fitness with coronary heart disease

Study	Population	Definition of physical activity or cardiorespiratory fitness	Definition of coronary heart disease
Physical activity			
Morris et al. (1953)	31,000 male employees of London Transport Executive aged 35–64 years	Occupational classification of job duties: sedentary drivers and active conductors	First clinical episode of CHD
Morris and Crawford (1958)	3,731 case necropsy studies (decedents aged 45–70 years) conducted in Scotland, England, and Wales	Physical activity at work defined by coding of last known job title before death (light, active, heavy)	Necropsy evaluation of IMF among persons dying from noncoronary causes
Taylor et al. (1962)	191,609 US white male railroad industry employees aged 40–64 years	Physical activity at work defined by job title for clerks, switchmen, and section men	Death due to arteriosclerotic disease (ICD 420, 422) in 1955–1956
Kahn (1963)	2,240 Postal Service employees in the Washington, D.C., Post Office between 1906 and 1940; followed through December 1961	Physical activity at work defined by job title for clerks and carriers	Death due to CHD
Morris et al. (1966)	667 London bus conductors and drivers aged 30–69 years; 5-year follow-up	Occupational classification of job duties as sedentary drivers and active conductors	Incidence of CHD (n = 47)
Cassel et al. (1971)	3,009 male residents of Evans County, Georgia, aged over 40 years in 1960–1962; 7.25-year average follow-up	Occupational classification of job duties as active or sedentary	Incidence of CHD (n = 337)
Morris et al. (1973)	British male executive grade civil servants aged 40–60 years; 232 heart attack case-patients and 428 matched controls	48-hour recall of leisure-time physical activities; activities defined as capable of reaching 7.5 kcal/min were defined as vigorous	First CHD attack (fatal and nonfatal)
Brunner et al. (1974)	5,288 male and 5,229 female residents of 58 Israeli kibbutzim aged 40–69 years; 15-year follow-up	Work types classified as sedentary or nonsedentary	Fatal and nonfatal CHD, males (n = 281) and females (n = 70)

Main findings	Dose response*	Adjustment for confounders and other comments
Inverse association; relative to men whose main job responsibility was driving buses, conductors had an age-adjusted risk of first coronary episode of 0.70	NA	No control for confounding; results were similar in subgroup of men who died of CHD-associated conditions
Inverse association; RR for IMF for persons in light occupations was 1.97 relative to heavy group; active group rate was intermediate	Yes	No control for confounding; one of few pathology studies
Inverse association; RR for arteriosclerotic disease among clerks was 2.03 relative to that for section men; risk estimate for switchmen was 1.46	Yes	No control for confounding; specific analyses were consistent with overall results
Inverse and null associations; among employees classified by their original occupational category, the age-adjusted risk for CHD death for clerks relative to carriers was 1.26	NA	No control for confounding; extensive efforts made to consider and evaluate job transfers
Inverse association; age-adjusted risk of CHD incidence among drivers was 1.8 relative to that for conductors	NA	Medical evaluation data used to control for confounding variables
Inverse association; age-adjusted risk of CHD among sedentary, nonfarm occupations relative to that for active nonfarm occupations was 1.8	NA	Data also available on black residents; comparisons between sedentary and active occupations not possible
Inverse association; RR estimate for first attack among vigorous group = 0.33 compared with nonvigorous group	NA	Only study to analyze 48-hour recall of leisure-time physical activity (5-minute intervals)
Inverse association; risk for CHD incidence among those engaged in sedentary work compared with that for nonsedentary peers was 2.52 for men and 3.28 for women	NA	No differences in serum cholesterol and body weight between groups

Table 4-2. *Continued*

Study	Population	Definition of physical activity or cardiorespiratory fitness	Definition of coronary heart disease
Paffenbarger and Hale (1975)	6,351 San Francisco Bay Area longshoremen aged 35–74 years; followed for 22 years, from 1951 to death or to age 75	Work-years according to required energy output: heavy (5.2–7.5 kcal/min), moderate (2.4–5.0 kcal/min), and light (1.5–2.0 kcal/min)	CHD death (ICD-7 420) (n = 598)
Paffenbarger et al. (1977)	3,686 San Francisco Bay Area longshoremen aged 35–74 years; followed for 22 years, from 1951 to death or to age 75	Work-years according to required energy output: high (5.2–7.5 kcal/min), intermediate (2.4–5.0 kcal/min), and light (1.5–2.0 kcal/min)	CHD death (ICD-7 420) (n = 395)
Rosenman, Bawol, Oscherwitz (1977)	2,065 white male San Francisco Bay Area federal employees aged 35–59 years; 4-year follow-up	Occupational physical activity; estimated caloric expenditure for work and nonwork activity	Fatal and nonfatal CHD (n = 65)
Chave et al. (1978)	3,591 British male executive-grade civil servants aged 40–64 years; 8.5-year average follow-up from 1968 to 1970	48-hour leisure-time physical activity recall; activities capable of reaching 7.5 kcal/min defined as vigorous	Fatal and nonfatal first CHD attack (n = 268)
Paffenbarger, Wing, Hyde (1978)	16,936 Harvard male alumni aged 35–74 years; followed up for 6–10 years	Physical activity index based on self-report of stairs climbed, blocks walked, and strenuous sports play	Fatal and nonfatal first heart attack (n = 572)
Morris et al. (1980)	17,944 British male executive grade civil servants aged 40–64 years; 8.5-year average follow-up from 1968 to 1970	48-hour recall of leisure-time physical activities; activities defined as capable of reaching 7.5 kcal/min were defined as vigorous	Fatal and nonfatal first heart attack (n =1,138)
Salonen et al. (1982)	3,829 women and 4,110 men aged 30–59 years from Eastern Finland; 7-year follow-up	Dichotomous assessment of occupational and leisure-time physical activity (low/high)	Fatal acute ischemic heart disease (ICD-8, 410–412) (n = 89 men and 14 women) and acute myocardial infarction (ICD-8, 410–411) (n = 210 men and 63 women)
Pomrehn et al. (1982)	61,922 deaths from 1964–1978 among Iowa men aged 20 to 64 years	Occupational classification; farmers vs. nonfarmers	Death from ischemic heart disease

Main findings	Dose response*	Adjustment for confounders and other comments
Inverse association; relative to heavy category, age-adjusted RR of CHD death was 1.70 in moderate and 1.80 in light categories	Yes	No control for confounding variables; efforts made to evaluate job changes in the cohort over time
Inverse association overall, inverse for younger birth cohorts and null for older cohorts; relative to high category, age-adjusted RRs of CHD death were 1.8 in intermediate and 1.60 in light categories	No/Yes	Dose response noted in age-adjusted rates only for two younger groups; two older groups exhibited no association
Null association	No	Relatively short-term follow-up
Inverse association; risk of CHD attack among men reporting nonvigorous exercise relative to men reporting vigorous exercise was 2.2	NA	Preliminary report of further data of Morris et al. 1980
Inverse association; age-adjusted RR of first heart attack for men who expended fewer than 2,000 kcal/week was 1.64 compared with men who expended 2,000 or more kcal/week	Yes	History of athleticism not associated with lower risk unless there was also current energy expenditure
Inverse association; age-adjusted risk of CHD attack among men reporting nonvigorous exercise relative to those reporting vigorous exercise was 2.2	NA	Increased risk similar for fatal and nonfatal attacks
Inverse association; RR of acute myocardial infarction for men and women with low levels of physical activity at work = 1.5 (90% CI, 1.2–2.0) for men and 2.4 (90% CI, 1.5–3.7) for women	NA	No associations with leisure-time physical activity; extensive adjustment for confounding
Farm men had significantly less mortality than expected from the experience in the general population of Iowa men (SMR = 0.89)	NA	No adjustment for confounding

Table 4-2. *Continued*

Study	Population	Definition of physical activity or cardiorespiratory fitness	Definition of coronary heart disease
Garcia-Palmieri et al. (1982)	8,793 Puerto Rican men aged 45–64 years; followed for up to 8.25 years	Usual 24-hour physical activity index based on hours/day at specific intensity	CHD incidence other than angina pectoris (n = 335)
Paffenbarger et al. (1984)	16,936 US male college alumni who entered college between 1916 and 1950; followed from 1962 to 1978	Physical activity index estimated from reports of stairs climbed, city blocks walked, and sports played each week	Death due to CHD (n = 441)
Yano, Reed, McGee (1984)	7,705 Hawaiian men of Japanese ancestry aged 45–68 years with no history of heart disease; 10-year follow-up	Self-report of 24-hour habitual physical activity in 1965–1968	Incident cases of fatal and nonfatal CHD (n = 511)
Menotti and Seccareccia (1985)	99,029 Italian male railroad employees aged 40–59 years; 5-year follow-up	Occupational physical activity (heavy, moderate, sedentary)	Fatal myocardial infarction (n = 614)
Kannel et al. (1986)	1,166 Framingham (MA) men aged 45–64 years; 24-year follow-up	Physical activity index based on hours per day at activity-specific intensity; occupational physical activity classified by physical demand of work	Death due to CHD (n = 220)
Lapidus and Bengtsson (1986)	1,462 Swedish women aged 38–60 years; follow-up between 1968 and 1981	Physical activity at work and during leisure hours, lifetime, and during previous years	Nonfatal myocardial infarction and angina pectoris
Leon et al. (1987)	12,138 North American men at high risk for CHD, aged 35–57 years; 7-year average follow-up	Leisure-time physical activity index; energy expenditure (minutes/week)	Fatal and nonfatal CHD (n = 781; 368 fatal)
Pekkanen et al. (1987)	636 apparently healthy Finnish men aged 45–64 years, followed for 20 years from 1964 baseline	Occupational and transport/ recreational physical activity (high or low)	Death due to CHD (n = 106)
Sobolski et al. (1987)	2,109 Belgian men aged 40–55 years in 1976–1978; 5-year follow-up	Occupational and leisure-time physical activity (4 categories each)	Incident cases of fatal and nonfatal myocardial infarction and sudden death (n = 36)

Main findings	Dose response*	Adjustment for confounders and other comments
Inverse association; physical activity index was significantly related to lower risk of CHD in urban as well as rural men	Yes	Significant inverse relationship for CHD after multivariate adjustment
Inverse association; relative to highest category of index (2,000+ kcal/week), risk estimates in next two lower categories were 1.28 and 1.84, respectively	Yes	Significant dose-response after adjusting for age, smoking, and hypertension prevalence
Inverse association; significant only for all CHD; no significant association for various subtypes	NA	Adjusted for age, blood pressure, cholesterol, BMI, serum glucose, vital capacity, etc.
Inverse association; relative to sedentary, men in moderate and heavy occupational activity had RRs of 0.97 and 0.64, respectively	Yes	Adjusted for age
Inverse association; age-adjusted RR (relative to high category) = 1.38 (low), 1.21 (moderate); for occupational activity, age-adjusted RR (relative to heavy category) = 1.27 (sedentary), 1.22 (light), 0.99 (medium)	Yes	Inverse association constant across all analyses and maintained after controlling for multivariate confounding
Inverse association only for leisure-time physical activity; RR = 2.8 (95% CI, 1.2–6.5) comparing low leisure-time physical activity with all other categories	NA	Adjusted for age
Inverse association; multivariate adjusted risk estimate (relative to low activity tertile) was 0.90 (95% CI, 0.76–1.06) for more active and 0.83 (95% CI, 0.70–0.99) for most active	Yes	Dose response for fatal and nonfatal cases combined but not for CHD death or sudden death separately
Inverse association; adjusted RR for men in low physical activity group was 1.30 ($p = 0.17$)	NA	Association limited to second half of follow-up period
Null association for both leisure-time and occupational physical activity	No	One of two studies to simultaneously evaluate associations of physical activity, fitness, and CHD

Table 4-2. *Continued*

Study	Population	Definition of physical activity or cardiorespiratory fitness	Definition of coronary heart disease
Donahue et al. (1988)	7,644 Hawaiian men of Japanese ancestry aged 45–64 years with no history of heart disease; 12-year follow-up	Self-report of 24-hour habitual physical activity in 1965–1968; 3-point scale defined by tertiles of distribution	Incident cases of fatal and nonfatal CHD (n = 444)
Salonen et al. (1988)	15,088 Eastern Finnish men and women aged 30–59 years; 6-year follow-up	Self-reported leisure-time and occupational physical activity (4 levels collapsed into 2 categories each)	Death due to CHD (ICD-8 410–414) (n = 102 90 men, 12 women)
Johansson et al. (1988)	7,495 Göteburg men aged 47–55 years at entry; 11.8-year average follow-up	Physical activity at work and physical activity during leisure time (4-point scale for each)	Incident cases of fatal and nonfatal CHD
Slattery, Jacobs, Nichaman (1989)	3,043 US male railroad employees; followed for 17–20 years	Leisure-time physical activity index (kcal/week)	Death due to CHD (ICD-8 410–414)
Morris et al. (1990)	9,376 British male middle grade executives aged 45–64 years; 9.3-year average follow-up	Leisure-time physical activity reported over previous 4 weeks; energy expenditure values ascribed to reported activities	Fatal and nonfatal CHD (ICD-8 410–414) (n = 474)
Lindsted, Tonstad, Kuzma (1991)	9,484 Seventh-Day Adventist men aged ≥ 30 years; 26-year follow-up	Self-report to single physical activity question	Ischemic heart disease mortality (ICD-8 410–414) (n = 1,351)
Shaper and Wannamethee (1991)	7,735 British men aged 40–59 years; 8.5-year follow-up	Self-report of physical activity at baseline; 6-point scale	Fatal and nonfatal heart attack (n = 488)
Seccareccia and Menotti (1992)	1,712 men from Northern and Central Italy, aged 40–59 years, initially examined in 1960; 25-year follow-up	Occupational physical activity (self-report): sedentary, moderate, and heavy	Death due to CHD
Hein, Suadicani, Gyntelberg (1992)	4,999 Copenhagen men aged 40–59 years; 17-year follow-up from 1970/1971	Leisure-time physical activity (4-point scale)	Fatal myocardial infarction (ICD-8 410–414) (n = 266)

Main findings	Dose response*	Adjustment for confounders and other comments
Inverse association; RR among active men relative to sedentary men was 0.69 (95% CI, 0.53–0.88) for men aged 45–64 and 0.43 (95% CI, 0.19–0.99) for older men aged 65–74	Yes	Adjusted for age, alcohol use, and smoking; bivariate adjustment for cholesterol, BMI, and blood pressure did not alter findings; follow-up to Yano, Reed, McGee (1984)
Inverse association; occupational: adjusted RR among inactive was 1.3 (95% CI, 1.1–1.6) relative to active; adjusted RR of CHD among leisure-time active was 1.2 (95% CI, 1.0–1.5)	NA	Point estimate for low leisure-time physical activity was adjusted toward the null after consideration of other CHD risk factors
Null association between physical activity at work and CHD risk; inverse association (not statistically significant) between leisure-time physical activity and CHD	No	Extensive control for confounding variables; ancillary analysis on postinfarction patients also yielded null association
Inverse association; adjusted risk estimate (relative to highest physical activity category) was 1.28 for sedentary group (not statistically significant)	Yes	Adjusted for age, smoking, cholesterol, and blood pressure
Inverse association; age-adjusted RR for 3 episodes per week of vigorous physical activity relative to sedentary group was 0.36	Yes	No adjustment for confounding; association only noted for vigorous physical activity
Null association; risk estimates of CHD death exhibited a U-shaped relationship with increasing physical activity levels	No	Possible protective association among moderate activity group
Inverse association only for 2 activity levels; RR compared with sedentary for increasing physical activity levels: occasional 0.9 (95%CI, 0.5–1.3), light 0.9 (95% CI, 0.6–1.4), moderate 0.5 (95% CI, 0.2–0.8), moderately vigorous 0.5 (95% CI, 0.3–0.9), and vigorous 0.9 (95% CI, 0.5–1.8)	No	No clear linear trend
Inverse association; age-adjusted RR for moderate and heavy categories compared with that for sedentary group was 0.69 and 0.58, respectively	Yes	Inverse association remained statistically significant after adjustment for confounding
Inverse association; relative to more active men (categories 2–4 of index), least active men had an adjusted RR of CHD of 1.59 (95% CI, 1.14–2.21)	No	One of two studies to simultaneously evaluate activity and fitness in relation to CHD mortality

Table 4-2. *Continued*

Study	Population	Definition of physical activity or cardiorespiratory fitness	Definition of coronary heart disease
Shaper, Wannamethee, Walker (1994)	5,694 British men aged 40–59 years; 9.5-year follow-up	Self-report of physical activity at baseline; 6-point scale data analyzed by hypertensive status	Fatal and nonfatal heart attack (n = 311; 165 normotensive, 146 hypertensive)
Rodriguez et al. (1994)	7,074 Hawaiian men of Japanese ancestry aged 45–68 years; 23-year follow-up	Self-report of 24-hour habitual physical activity in 1965–1968	Incident cases of fatal and nonfatal CHD (n = 340)
Cardiorespiratory fitness			
Peters et al. (1983)	2,779 male Los Angeles County public safety employees aged < 55 years; 4.8-year average follow-up	Submaximal aerobic capacity estimated from cycle ergometer test; age-specific median split used to determine low/high fitness	Incident cases of fatal and nonfatal myocardial infarction (n = 36)
Lie, Mundal, Erikssen (1985)	2,014 Norwegian employed men aged 40–59 years; 7-year follow-up	Near maximal cycle ergometer exercise test; total work in quartiles	Incident cases of fatal and nonfatal CHD
Erikssen (1986)	1,832 Norwegian men aged 40–59 years; 7-year average follow-up	Near maximal cycle ergometer exercise test; total work in quartiles	Incident cases of fatal and nonfatal myocardial infarction and CHD death
Sobolski et al. (1987)	2,109 Belgian men aged 40–55 years in 1976–1978; 5-year follow-up	Submaximal aerobic capacity estimated from cycle ergometry test	Incident cases of fatal and nonfatal myocardial infarction and sudden death (n = 36)
Ekelund et al. (1988)	3,106 North American men aged 30–69 years; 8.5-year average follow-up	Submaximal aerobic capacity estimated from exercise test	Death due to CHD (ICD-8 410–414)
Slattery et al. (1988)	2,431 US male railroad employees; 17- through 20-year follow-up	Submaximal exercise heart rate on standard (3 min) treadmill test evaluation	Death due to CHD (ICD-8 410–414)
Hein, Suadicani, Gyntelberg (1992)	4,999 Copenhagen men aged 40–59 years; 17-year follow-up from 1970/1971	Submaximal aerobic capacity estimated from cycle ergometer exercise test	Fatal myocardial infarction (ICD-8 410–414) (n = 266)