CHAPTER 4
THE EFFECTS OF PHYSICAL ACTIVITY ON HEALTH AND DISEASE

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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 $\geq$ 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)

Main findings	Dose response*	Adjustment for confounders and other comments
Inverse association; statistically significant trend among nonhypertensive participants, U-shaped association among hypertensive participants	Yes/No	In hypertensive men, the protective effect of physical activity was eliminated with vigorous activity
Inverse association when adjusted only for age; null association when adjusted for cholesterol, blood pressure, BMI, diabetes, etc.	No	Follow-up report to that of Yano, Reed, McGee (1984) and Donahue et al. (1988)
Inverse association; RR for CHD incidence in low fitness group was 2.2 (95% CI, 1.1–4.7) compared with high fitness	NA	Similar results seen when men with electrocardiogram evidence of heart disease were excluded
Inverse association; point estimates and significance not reported	Yes	No adjustment for confounding variables
Inverse association; point estimates and significance not reported	Yes	No adjustment for confounding variables
Inverse association; RR for myocardial infarction and sudden death in low fit group was 1.6 relative to high fit	Yes	One of two studies to simultaneously evaluate associations of activity, fitness, and CHD
Inverse association; adjusted risk estimate of 3.2-fold increased risk of CHD death for a 35 beat/min increase in heart rate for stage II of exercise test	Yes	Extensive control for confounding influences
Inverse association; adjusted risk estimate for highest heart rate response group relative to lowest was 1.20 (95% CI, 1.10–1.26)	Yes	Risk estimate attenuated substantially after adjustment for other CHD risk factors
Inverse association; relative to more fit men, least fit men had an adjusted risk of 1.46 (95% CI, 0.94–2.26)	Yes	One of two studies to simultaneously evaluate activity and fitness in relation to CHD mortality

Abbreviations: BMI = Body mass index (wt [kg] /ht [m]^2); CHD = coronary heart disease; CI = confidence interval; ICD = International Classification of Diseases (8 and 9 refer to editions); IMF = ischemic myocardial fibrosis; 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.

lipids in children (Lee, Lauer, Clarke 1986), and that CHD risk factor patterns persist from childhood to adulthood (Webber et al. 1991; Mahoney et al. 1991).

Recently, Armstrong and Simons-Morton (1994) reviewed the research literature on physical activity and blood lipids in children and adolescents, including over 20 observational and 8 intervention studies. They concluded that the cross-sectional observational studies did not demonstrate a relationship between physical activity level or cardiorespiratory fitness and total cholesterol, LDL-C, or HDL-C, especially when differences in body weight or fat were taken into account, suggesting that activity and body fat are not independently related to serum lipids. However, highly physically active or fit children and adolescents tended to have higher HDL-C than their inactive or unfit peers. The intervention studies generally showed favorable effects of exercise on LDL-C or HDL-C only in children and adolescents who were at high risk for CHD because of obesity, insulin-dependent diabetes mellitus, or having a parent with three or more CHD risk factors.

Alpert and Wilmore (1994) recently reviewed the research literature on physical activity and blood pressure in children and adolescents, including 18 observational and 11 intervention studies. These authors found evidence in studies of normotensive children and adolescents that higher levels of physical activity tended to be related to lower blood pressure. The associations were generally reduced in magnitude in those studies that adjusted for BMI, suggesting that lower body fat mass may at least partly explain why physical activity is related to lower blood pressure. Intervention studies tended to show that training programs lowered blood pressure by 1–6 mm Hg in normotensive children and adolescents, although the effects were inconsistent for boys and girls and for systolic and diastolic blood pressure. In hypertensive children and adolescents, physical activity interventions lowered blood pressure to a greater degree than in their normotensive peers (by approximately 10 mm Hg), although statistical significance was not always achieved because of small sample sizes.

Interpreting these studies on lipids and blood pressure in children and adolescents is hindered by several factors. Studies used a variety of physical activity categorizations, and the interventions covered a wide range of frequency, type, duration, and intensity, which were not all specified. The difficulties of assessing physical activity by self-report in children and adolescents, together with the highly self-selected population in the observational studies, may account for the less consistent findings on lipids and physical activity that were reported for children and adolescents than for adults. The relationship between dose of physical activity and amount of effect on blood pressure or serum lipids in children has not been adequately addressed.

Nonetheless, there appears to be some evidence, although not strong, of a direct relationship between physical activity and HDL-C level in children and adolescents. There is also evidence that increased physical activity can favorably influence the lipid profile in children and adolescents who are at high risk of CHD. Similarly, the evidence suggests that physical activity can lower blood pressure in children and adolescents, particularly in those who have elevated blood pressure.

Stroke

A major cardiovascular problem in developed countries, stroke (ischemic stroke and hemorrhagic stroke) is the third leading cause of death in the United States (NCHS 1994). Atherosclerosis of the extracranial and intracranial arteries, which triggers thrombosis, is thought to be the underlying pathologic basis of ischemic stroke. Cigarette smoking and high blood pressure are major risk factors for ischemic stroke, whereas high blood pressure is the major determinant of hemorrhagic stroke. The studies cited in this section examined the association between reported level of physical activity and stroke. No published studies have examined the association between cardiorespiratory fitness and stroke.

Fourteen population-based studies (four that include women) relate physical activity to risk of all types of stroke; these closely parallel the study designs and populations previously cited for CVD and CHD (Table 4-3). Thirteen of the studies were cohort studies (follow-up range, 5–26 years). Only eight found an inverse association. As with the earlier studies on CHD, the earlier studies of stroke did not permit a dose-response evaluation. Among later studies that could do so by virtue of design, half did not find a gradient. This outcome, coupled with some suggestion of a "U-shaped" association

in two studies (Menotti and Seccareccia 1985; Lindsted, Tonstad, Kuzma 1991), casts doubt on the nature of the association between physical activity and risk of both types of strokes combined.

Because of their different pathophysiologies, physical activity may not affect ischemic and hemorrhagic stroke in the same way; this issue requires more research. Only one study distinguished between ischemic and hemorrhagic stroke (Abbott et al. 1994). In this study, inactive men were more likely than active men to have a hemorrhagic stroke; physical activity was also associated with a lower risk of ischemic stroke in smokers but not in nonsmokers.

Thus the existing data do not unequivocally support an association between physical activity and risk of stroke.

High Blood Pressure

High blood pressure is a major underlying cause of cardiovascular complications and mortality. Organ damage and complications related to elevated blood pressure include left ventricular hypertrophy (which can eventually lead to left ventricular dysfunction and congestive heart failure), hemorrhagic stroke, aortic aneurysms and dissections, renal failure, and retinopathy. Atherosclerotic complications of high blood pressure include CHD, ischemic stroke, and peripheral vascular disease. Although rates of hypertension have been declining in the United States since 1960, nearly one in four Americans can be classified as being hypertensive (DHHS 1995).

Prospective observational studies relating physical activity level or cardiorespiratory fitness to risk of hypertension are summarized in Table 4-4. Several cohort studies have followed male college alumni after graduation. One found later development of hypertension to be inversely related to the reported number of hours per week of participation in sports or exercise while in college (Paffenbarger, Thorne, Wing 1968). In a later follow-up of the same cohort, using information on physical activity during mid-life, vigorous sports were associated with a 19–30 percent reduction in risk of developing hypertension over the 14-year period (Paffenbarger et al. 1991). Follow-up of a different cohort of male college alumni similarly showed the least active men to have a 30 percent increased risk of developing hypertension (Paffenbarger et al. 1983). In a study of 55- through 69-year-old women followed for 2 years, the most active women were found to have a 30 percent reduced risk of developing hypertension (Folsom et al. 1990).

One randomized trial for the primary prevention of hypertension has been conducted. A 5-year trial of a nutrition and physical activity intervention showed that the incidence of hypertension for the intervention group was less than half that of the control group (Stamler et al. 1989). Participants in the intervention group lost more weight than those in the control group, reduced more of their sodium and alcohol intake, and were more likely to become more physically active. Although the effects of the nutritional and physical activity components of this intervention cannot be separated, the study does show that the risk for developing hypertension among persons who are at high risk for the disease can be lowered by weight loss and improvements in dietary and physical activity practices.

Like physical inactivity, low cardiorespiratory fitness in middle age is associated with increased risk for high blood pressure. After adjustment for sex, age, baseline blood pressure, and body mass index, persons with low cardiorespiratory fitness had a 52 percent higher risk of later developing high blood pressure than their fit peers (Blair et al. 1984).

Taken together, the cohort studies show that physical inactivity is associated with an increased risk of later developing hypertension among both men and women. Three of the studies had more than two categories of physical activity for comparison, and each demonstrated a dose-response gradient between amount of activity and degree of protection from hypertension. Point estimates for quantification of risk suggest that those least physically active have a 30 percent greater risk of developing hypertension than their most active counterparts. Unfortunately, none of these studies was conducted in minority populations, which have a disproportionate burden of hypertensive disease (DHHS 1995).

Several randomized controlled trials have been conducted to determine the effects of exercise on blood pressure in people with elevated blood pressure levels. The reduction of elevated blood pressure is important for preventing stroke and CHD, for which high blood pressure is a risk factor with a dose-response relationship (NIH 1992). Thirteen

Table 4-3. Population-based studies of association of physical activity with stroke (CVA)

Study	Population	Definition of physical activity	Definition of stroke
Paffenbarger and Williams (1967)	> 50,000 US male college alumni aged 30–70years	Participation in college varsity athletics (yes/no)	Hemorrhagic and ischemic stroke death (n = 171)
Paffenbarger (1972)	3,991 US longshoremen aged 35 years and older; 18.5-year follow-up from 1951	Occupational activity (cargo handler or not)	Hemorrhagic and ischemic stroke death (n = 132)
Kannel and Sorlie (1979)	1,909 Framingham (MA) men aged 35–64 at 4th biennial examination; 14-year follow-up	Physical activity index based on hours per day spent at activity-specific intensity	Cerebrovascular accident (n = 87)
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 physical activity (low/high)	Cerebral stroke (ICD-8 430–437) morbidity and mortality among men (n = 71) and women (n = 56)
Herman et al. (1983)	132 hospitalized Dutch stroke case-patients and 239 age- and sex-matched controls; men and women aged 40–74 years	Leisure-time physical activity (greatest portion of one's lifetime) ranging from little to regular-heavy	Rapidly developed clinical signs of focal or global disturbance of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than vascular origin
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 stroke (n = 103)
Menotti and Seccareccia (1985)	99,029 Italian males railroad employees aged 40–59 years; 5-year follow-up	Classification of occupational physical activity (heavy, moderate, sedentary)	Fatal stroke (n = 187)
Lapidus and Bengtsson (1986)	1,462 Swedish women aged 38–60; follow-up between 1968 and 1981	Work and leisure physical activity assessed via 4-scales for lifetime and for the time before 1968 baseline	Fatal and nonfatal stroke (n = 13)
Menotti et al. (1990)	8,287 men aged 40–59 years in six of seven countries from Seven Countries Study; 20-year follow-up	Classification of occupational physical activity (heavy, moderate, sedentary)	Fatal stroke (cohort analysis)

Main findings	Dose response*	Adjustment for confounders and other comments
Inverse association; nondecedents were 2.2 times as likely to have participated in varsity sports than were decedents; hemorrhagic strokes = 2.1, occlusive strokes = 2.5	NA	Results adjusted for age only
Noncargo handlers were 1.11 times as likely as cargo handlers to die from stroke	NA	Results adjusted for age only
Inverse association between physical activity index and 14-year incidence of stroke	Yes	No statistical significance after controlling for several confounding variables
Inverse association with statistically significant RRs for men and women with low levels of physical activity at work were 1.5 (95% CI, 1.2–2.0) for men and 2.4 (95% CI, 1.5–3.7) for women	NA	Evidence for inverse association for low activity during leisure time, but no statistical significance after adjustment for other factors
Inverse association; relative to lowest physical activity category, risk estimates were 0.72 (95% CI, 0.37–1.42) for moderate and 0.41 (95% CI, 0.21–0.84) for high categories	Yes	Adjusted for a variety of potential confounding influences
Inverse association; relative to highest category of index (2,000+ kcal/week), risk estimates in next two lower categories were 1.25 and 2.71, respectively	Yes	Significant dose-response trend after adjusting for differences in age, cigarette smoking, and hypertension prevalence
Nonlinear "U" shape association; relative to sedentary category, men in moderate and heavy occupational activity categories had risks of 0.65 and 1.0, respectively	No	Age-adjusted only
Inverse association; women with low physical activity at work were 7.8 times as likely as others to have stroke (95% CI, 2.7–23.0); womenwith low physical activity leisure were 10.1 times as likely as others to have stroke (95% CI, 3.8–27.1)	NA	Age-adjusted only
Null association	No	No association after statistical adjustment for risk factors

Table 4-3. *Continued*

Study	Population	Definition of physical activity	Definition of stroke
Harmsen et al. (1990)	7,495 Swedish men aged 47–55 years at baseline examination; 11.8-year average follow-up	Physical activity at work and leisure hours (low, high)	Fatal stroke (all and subtypes) (n = 230)
Lindsted, Tonstad, Kuzma, (1991)	9,484 male Seventh-Day Adventists aged ≥ 30 years; 26-year follow-up	Self-report of physical activity level in 1960 (highly active, moderately active, low activity)	Fatal stroke (n = 410)
Wannamethee and Shaper (1992)	7,735 British men aged 40–59 years; 8.5-year follow-up	Self-report of physical activity at baseline; 6-point scale defined on the basis of type and frequency of activity	Fatal and nonfatal stroke (n = 128)
Abbott et al. (1994)	7,530 Hawaiian men of Japanese ancestry aged 45–68 years; 22-year follow-up	Self-report of 24-hour habitual physical activity in 1965–1968 (inactive, partially active, active)	Fatal and nonfatal neurologic deficit with sudden occurrence and remaining present for at least 2 weeks or until death (subtypes) (n = 537)
Kiely et al. (1994)	Four cohorts of Framingham (MA) men and women: cohort I—1,897 men aged 35–69 years; cohort II—2,299 women aged 35–68 years; cohort III—men aged 49–83 years; cohort IV—women aged 49–83 years; follow-up for cohorts I and II up to 32 years, for cohorts III and IV up to 18 years	Self-report of daily activity level; composite score formulated from index and categorized into high, medium, and low physical activity	Fatal and nonfatal first occurrence of atherothrombotic brain infarction, cerebral embolism, or other stroke (cohort I, n = 195; cohort II, n = 232; cohort III, n = 113; cohort IV, n = 140)

Main findings	Dose response*	Adjustment for confounders and other comments
Null association; relative to low physical activity category, slightly elevated estimates were observed for all strokes and subtypes for high activity group	No	No association after statistical adjustment for risk factors
Nonlinear "U" shape association; relative to low activity level, risk estimates were 0.78 (95% CI, 0.61–1.00) for moderate activity and 1.08 (95% CI, 0.58–2.01) for high activity	No	Adjusted for sociodemographic factors, BMI, and dietary pattern
Inverse association; statistically significant linear trend of lower risk of stroke with higher physical activity scale	Yes	Linear trend observed in men both with and without existing ischemic heart disease
Null association seen for all strokes and all subtypes for men aged 45–54 years	Yes, in older	No association of physical activity to risk of stroke in older smokers
Inverse association seen for all strokes and subtypes for men aged 55–68 years	No in younger	
Risk estimate relative to low physical activity group: cohort I—nonsignificant inverse association for medium group = 0.90 (0.62–1.31) and for high group = 0.84 (0.59–1.18); cohort II—nonsignificant nonlinear association for medium group = 1.21 (0.89–1.63) and for high group = 0.89 (0.60–1.31); cohort III—significant inverse association for medium group = 0.41 (0.24–0.69) and for high group = 0.53 (0.34–0.84); cohort IV—nonsignificant nonlinear association for medium group = 0.97 (0.64–1.47) and for high group = 1.21	 Yes, C I Yes, C I No, C II No, C II Yes, C III No, C IV	Control for many confounding factors; nonlinear association in women only (cohorts III and IV); suggestion of threshold relationship (cohort III)

Abbreviations: BMI = body mass index (wt [kg] /ht [m]^2); CVA = cerebrovascular accident; CI = confidence interval; 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.

Table 4-4. Population-based cohort studies of association of physical activity with hypertension

Study	Population	Definition of physical activity	Definition of hypertension
Paffenbarger, Thorne, Wing (1968)	7,685 men who attended the University of Pennsylvania between 1931 and 1940 and who responded to a questionnaire in 1962	Reported hours per week of participation in sports or exercise in college	Self-reported incidence of physician-diagnosed hypertension from mail-back health questionnaire (n = 671)
Paffenbarger et al. (1983)	14,998 US male college alumni who entered college between 1916 and 1950; followed from 1962–1972 (for 6–10 years)	Physical activity index (kcal/week) estimated from reports of stairs climbed, city blocks walked, and sports played each week, assessed by mail-back questionnaire in 1962 or 1966	Self-reported incidence of physician-diagnosed hypertension from mail-back health questionnaire (n = 681)
Blair et al. (1984)	4,820 US men and 1,219 US women patients of a preventive medical clinic aged 20–65 years at baseline	Maximal aerobic capacity estimated by exercise tests, categorized into "high" fitness (≥ 85th percentile) and "low" fitness	Self-reported incidence of physician-diagnosed hypertension (n = 240)
Stamler et al. (1989)	201 US men and women with diastolic blood pressure 85–89 mm Hg or 80–84 mm Hg (if overweight) were randomly assigned to control or nutritional/ hygienic intervention (including exercise)	Self-report of moderate physical activity	Initiation of hypertensive therapy or sustained elevation of diastolic blood pressure ≥ 90 mm Hg
Folsom et al. (1990)	41,837 Iowa women aged 55–69 years; 2-year follow-up	Self-reported frequency of leisure-time physical activity from mail-back survey	Self-reported incidence of physician-diagnosed hypertension
Paffenbarger et al. (1991)	5,463 male college alumni from the University of Pennsylvania	Self-report of physical activity from mail-back questionnaire in 1962	Self-reported incidence of physician-diagnosed hypertension from mail-back questionnaire in 1976 (n = 739)

Main findings	Dose response*	Adjustment for confounders and other comments
Inverse association; respondents who reported participation in sports or exercise fewer than 5 hours per week had a significantly increased age- and interval-adjusted risk of physician-diagnosed hypertension (RR = 1.30, $p < 0.01$)	NA	Adjustments for age and follow-up had little effect
Inverse association; alumni with < 2,000 kcal/week of energy expenditure had RR of 1.30 (95% CI, 1.09–1.55) of developing hypertension relative to others	Yes, especially in heavier men	Increased risk observed for less active alumni with stratification of student blood pressure, alumnus BMI, increase in BMI since college, and family history of hypertension
Patients in low fitness category were 1.52 times as likely (95% CI, 1.08–2.15) to develop hypertension as those in high fitness category	NA	Extensive control for confounding variables; no sex-specific analyses
Control group RR = 2.4 (90% CI, 1.2–4.8) of developing hypertension when compared with the intervention group	NA	Intervention was combined nutritional, weight loss, and physical activity
Inverse association; relative to women at low levels of physical activity, women at high and moderate levels had 30% and 10% lower age-adjusted risks of developing hypertension (RR high = 0.70, 95% CI, 0.6–0.9; RR moderate = 0.90, 95% CI, 0.7–1.1)	Yes	Adjustment for BMI, waist-to-hip ratio, cigarette smoking, and age eliminated the association with physical activity
Vigorous sports play in 1962 was associated with a 30% reduced risk of developing hypertension	Yes	Adjusted for age, BMI, weight gain since college, and parental history of hypertension

Abbreviations: BMI = body mass index (wt [kg] /ht $[m]^2$); CI = confidence interval; 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.

controlled trials of habitual activity and blood pressure were analyzed in a meta-analysis by Arroll and Beaglehole (1992), and nine randomized controlled trials of aerobic exercise using the lower extremities (e.g., walking, jogging, cycling) and blood pressure were analyzed in a meta-analysis by Kelley and McClellan (1994). The two meta-analyses independently concluded that aerobic exercise decreases both systolic and diastolic blood pressure by approximately 6–7 mm Hg. Some of the studies were conducted with persons with defined hypertension (> 140/90 mm Hg), and others were conducted with persons with high normal blood pressure. Most of the studies tested aerobic training of 60–70 percent maximum oxygen uptake, 3–4 times/week, 30–60 minutes per session.

Three trials have specifically examined the effect of different intensities of exercise on blood pressure. Hagberg et al. (1989) randomly assigned 33 hypertensive participants to a nonexercising control group and to two groups participating in different intensities of exercise (53 percent and 73 percent of $\dot{V}O_2$ max) for 9 months. Both exercise groups had comparable decreases in diastolic blood pressure (11–12 mm Hg), and the lower-intensity group had a greater decrease in systolic blood pressure than the higher-intensity group (20 mm Hg vs. 8 mm Hg). All the decreases were statistically significant when compared with the control group's blood pressure level, except the 8 mm Hg decrease in systolic blood pressure in the higher-intensity group. Matsusaki and colleagues (1992) randomly assigned 26 mildly hypertensive participants to two exercise intensities (50 percent $\dot{V}O_2$ max and 75 percent $\dot{V}O_2$ max) for 10 weeks. The pretest-to-posttest decreases in systolic and diastolic blood pressure in the lower-workload group were significant (9 mm Hg/6 mm Hg), but those in the higher-intensity group were not (3 mm Hg/5 mm Hg). Marceau and colleagues (1993) used a randomized crossover design to compare intensities of 50 percent and 70 percent $\dot{V}O_2$max training on 24-hour ambulatory blood pressure in persons with hypertension. A similar reduction in 24-hour blood pressure was observed for both training intensities (5 mm Hg decrease), but diurnal patterns of reduction were different.

These trials provide some evidence that moderate-intensity activity may achieve a similar, or an even greater, blood-pressure-lowering effect than vigorous-intensity activity. Because few studies have directly addressed the intensity question, however, the research base is not strong enough to draw a firm conclusion about the role of activity intensity in lowering blood pressure. It is not clear, for example, how the findings could have been affected by several issues, such as use of antihypertensive medications, changes in body weight, lack of direct intervention-control comparisons, dropout rates, and total caloric expenditure.

Biologic Plausibility

Multiple physiological mechanisms may contribute to the protective effects of physical activity against CVDs. Postulated mechanisms involve advantageous effects on atherosclerosis, plasma lipid/lipoprotein profile, blood pressure, availability of oxygenated blood for heart muscle needs (ischemia), blood clotting (thrombosis), and heart rhythm disturbances (arrhythmias) (Haskell 1995; Leon 1991a; Gordon and Scott 1991).

Other effects of activity that may be associated with modifications of CVD risk include reduced incidence of obesity, healthier distribution of body fat, and reduced incidence of non–insulin-dependent diabetes. These other effects are discussed in later sections of this chapter.

Atherosclerosis

Atherosclerosis begins when cholesterol is transported from the blood into the artery wall by lipoproteins, particularly LDL (Getz 1990; Yanowitz 1992). The formation of atherosclerotic plaques is increased at sites where the blood vessel lining is injured, which may occur in areas where blood flow is uneven (e.g., near the origin or branching of major vessels). An inflammatory reaction leads to the formation of atherosclerotic plaques in the wall of the artery.

In animal studies, exercise has been seen to protect against the effects of excess cholesterol and other contributors to the development of atherosclerosis (Kramsch et al. 1981). In addition, longitudinal studies of men with coronary artery disease have shown that endurance training, together with a cholesterol-lowering diet and interventions for other CVD risk factors, can help prevent the progression or reduce the severity of atherosclerosis in the coronary

arteries (Ornish et al. 1990; Schuler et al. 1992; Hambrecht et al. 1993; Haskell et al. 1994). There is also an inverse relationship between cardiorespiratory fitness and ultrasound-measured severity of atherosclerosis in neck arteries to the head (carotid arteries) (Rauramaa et al. 1995).

Plasma Lipid/Lipoprotein Profile

The relationships of physical activity to blood lipid and lipoprotein levels in men and women have been reviewed extensively (Leon 1991a; Krummel et al. 1993; Superko 1991; Durstine and Haskell 1994; Stefanick and Wood 1994). Of more than 60 studies of men and women, about half found that exercise training is associated with an increase in HDL. HDL, a lipid scavenger, helps protect against atherosclerosis by transporting cholesterol to the liver for elimination in the bile (Tall 1990). Cross-sectional studies show a dose-response relationship between the amount of regular physical activity and plasma levels of HDL (Leon 1991c). In these studies, the HDL levels of endurance-trained male and female athletes were generally 20 to 30 percent higher than those of healthy, age-matched, sedentary persons.

Moderate-intensity exercise training appears to be less likely to increase HDL levels in young to middle-aged women than men in the same age range (Leon 1991a; Kummel et al. 1993; Durstine and Haskell 1994). Moderate-intensity exercise was seen to increase HDL as much as more vigorous exercise in one randomized controlled trial of women (Duncan, Gordon, Scott 1991).

Studies have found that even a single episode of physical activity can result in an improved blood lipid profile that persists for several days (Tsopanakis et al. 1989; Durstine and Haskell 1994). Evidence also shows that exercise training increases lipoprotein lipase activity, an enzyme that removes cholesterol and fatty acids from the blood (Stefanick and Wood 1994). Exercise training also reduces elevated levels of triglycerides (Leon 1991c; Durstine and Haskell 1994), another blood lipid associated with heart disease.

Blood Pressure

The mechanisms by which physical activity lowers blood pressure are complicated (Leon 1991a; American College of Sports Medicine [ACSM] 1993; Fagard et al. 1990) and are mentioned only briefly here (see also Chapter 3). Blood pressure is directly proportional to cardiac output and total resistance in the peripheral blood vessels. An episode of physical activity has the immediate and temporary effect of lowering blood pressure through dilating the peripheral blood vessels, and exercise training has the ongoing effect of lowering blood pressure by attenuating sympathetic nervous system activity (Leon 1991a; ACSM 1993; Fagard et al. 1990). The reduced sympathetic activity may reduce renin-angiotensin system activity, reset baroreceptors, and promote arterial vasodilatation—all of which help control blood pressure. Improved insulin sensitivity and the associated reduction in circulating insulin levels may also contribute to blood pressure reduction by decreasing insulin-mediated sodium reabsorption by the kidney (Tipton 1984).

Ischemia

Clinical symptoms of atherosclerotic CHD occur when the heart muscle (myocardium) needs more oxygen than can be supplied from blood flowing through narrowed coronary arteries. This oxygen shortage leads to ischemia in the heart muscle—that is, to inadequate oxygenated blood for myocardial demand. Adaptations to a gradual reduction in blood flow may reduce the likelihood of myocardial ischemia. For example, new blood vessels may develop from other coronary arteries to provide an auxiliary blood supply (Cohen 1985). A person with advanced atherosclerotic CHD may remain free of symptoms at rest but may develop ischemic chest pain (angina pectoris) or electrocardiographic changes during physical exertion, which generally result from too high a myocardial oxygen demand for the blood supply available through partially occluded coronary arteries and collateral vessels (Smith and Leon 1992). Less commonly, angina pectoris may result from transient constriction (spasm) of a large coronary artery, generally at the site of an atherosclerotic plaque, or from spasm of small arterial vessels that have no evidence of plaque formation.

A recent review has summarized adaptations in the coronary circulation that are induced by endurance exercise training and that can decrease the likelihood of ischemia (Laughlin 1994). Data obtained primarily from research on animals have

demonstrated that exercise leads to a greater capacity to increase coronary blood flow and an improved efficiency of oxygen exchange between blood in the capillaries and the heart muscle cells. These functional changes are the result of a remodeled vascular structure, improved control of blood flow dynamics, and promotion of biochemical pathways for oxygen transfer.

The first and most consistent structural adaptation to exercise is an increase in the interior diameter of the major coronary arteries and an associated increase in maximal coronary blood flow (Leon and Bloor 1968, 1976; Scheuer 1982; Laughlin 1994). The second vascular adaptation is the formation of new myocardial blood vessels (capillaries and coronary arterioles) (Tomanek 1994; Leon and Bloor 1968). Animal studies also have shown that exercise training alters coronary vascular reactivity and thereby improves control of blood flow and distribution (Overholser, Laughlin, Bhatte 1994; Underwood, Laughlin, Sturek 1994). This adaptation may reduce the incidence of spasms in the proximal coronary arteries and arterioles (Laughlin 1994). In addition, exercise training results in a reduced workload on the heart due to both an increase in compliance of the heart and a relative reduction in peripheral resistance; together, these reduce myocardial oxygen demand (Jorgensen et al. 1977).

Thrombosis

An acute coronary event is usually initiated by disruption of an atherosclerotic plaque within an artery (Smith and Leon 1992). Platelet accumulation at the injury site initiates a cascade of processes leading to clot formation (thrombosis), which further reduces or completely obstructs coronary flow. A major obstruction of flow in a coronary artery may lead to the death of heart muscle (myocardial infarction) in the area served by that artery. These obstructions can, in addition, trigger potentially lethal disturbances in the rhythm of the heart (cardiac arrhythmia).

Thrombosis, usually occurring at the site of rupture or fissuring of an atherosclerotic plaque, is the precipitating event in the transition of silent or stable coronary artery disease to acute ischemic events, such as unstable angina, acute myocardial infarction, or sudden cardiac death, and in the occurrence of ischemic stroke (Davies and Thomas 1985; Falk 1985). Endurance training reduces thrombosis by enhancing the enzymatic breakdown of blood clots (fibrinolysis) and by decreasing platelet adhesiveness and aggregation (which helps prevent clot formation) (Kramsch et al. 1981; Leon 1991b).

Arrhythmia

Although persons with coronary artery disease have an increased risk of ventricular fibrillation (a life-threatening heart rhythm disturbance) during acute physical activity, persons with a healthy cardiovascular system do not incur this elevated risk (Siscovick et al. 1984; Mittleman et al. 1993; Willich et al. 1993; Thompson and Mitchell 1984; Thompson, Funk, et al. 1982; Haskell 1995; Dawson, Leon, Taylor 1979). Exercise training may reduce the risk of ventricular fibrillation in healthy persons and in cardiac patients by improving myocardial oxygen supply and demand and by reducing sympathetic nervous system activity (Leon 1991c). Evidence from epidemiologic studies shows that a physically active lifestyle reduces the risk of sudden cardiac death (Leon et al. 1987). A meta-analysis of studies that examined use of physical activity for cardiac rehabilitation showed that endurance exercise training reduced the overall risk of sudden cardiac death even among persons with advanced coronary atherosclerosis (O'Connor et al. 1989).

Conclusions

The epidemiologic literature supports an inverse association and a dose-response gradient between physical activity level or cardiorespiratory fitness and both CVD in general and CHD in particular. A smaller body of research supports similar findings for hypertension. The biological mechanisms for these effects are plausible and supported by a wealth of clinical and observational studies. It is unclear whether physical activity plays a protective role against stroke.

Cancer

Cancer, the second leading cause of death in the United States, accounts for about 25 percent of all deaths, and this percentage is increasing (NCHS 1996; American Cancer Society [ACS] 1996). The ACS has estimated that 1,359,150 new cases of

cancer and 554,740 cancer-related deaths will occur among Americans during 1996 (ACS 1996). Physical inactivity has been examined as an etiologic factor for some cancers.

Colorectal Cancer

Colorectal cancer has been the most thoroughly investigated cancer in epidemiologic studies of physical activity. To date, nearly 30 published studies have examined the association between physical activity and risk of developing colon cancer alone.

Studies that combined colon and rectal cancers as a single endpoint—colorectal cancer—are only briefly reviewed here because current research, summarized in this section, suggests that the relationship between physical activity and risk of colon cancer may be different from that for rectal cancer. Among nine studies that have examined the relationship between physical activity and colorectal cancer, one reported an inverse relationship (Wu et al. 1987), and three reported positive associations that were not statistically significant (Garfinkel and Stellman 1988; Paffenbarger, Hyde, Wing 1987 [for analysis of two cohorts]). One (Kune, Kune, Watson 1990) reported no significant associations, and in the four other studies (Albanes, Blair, Taylor 1989; Ballard-Barbash et al. 1990; Markowitz et al. 1992; Peters et al. 1989), the associations lacked consistency in subpopulations within the study, anatomic subsites of the large bowel, or measures of physical activity. Colorectal adenomas are generally thought to be precursors to colorectal cancers. A single study of colorectal adenomatous polyps has reported an inverse relationship between risk of adenomas and level of total physical activity (Sandler, Pritchard, Bangdiwala 1995). Another study of colorectal adenomas also found an inverse association, but only for running or bicycling, and only with one of two different comparison groups (Little et al. 1993).

Colon Cancer

Of the 29 studies of colon cancer, 18 used job title as the only measure of physical activity and thus addressed only occupational physical activity. These studies are a mix of mortality and incidence studies, and few have evaluated possible confounding by socioeconomic status, diet, and other possible risk factors for colon cancer. Nonetheless, findings from these 18 studies have been remarkably consistent: 14 studies (Brownson et al. 1989; Brownson et al. 1991; Chow et al. 1993; Dosemeci et al. 1993; Fraser and Pearce 1993; Fredriksson, Bengtsson, Hardell 1989; Garabrant et al. 1984; Gerhardsson et al. 1986; Kato, Tominaga, Ikari 1990; Lynge and Thygesen 1988; Marti and Minder 1989; Peters et al. 1989; Vena et al. 1985; Vena et al. 1987) reported a statistically significant inverse relationship between estimated occupational physical activity and risk of colon cancer. Four studies (Arbman et al. 1993; Vetter et al. 1992; Vlajinac, Jarebinski, Adanja 1987; Vineis, Ciccone, Magnino 1993) found no significant relationship between occupational physical activity and risk of colon cancer. The 18 studies were conducted in a variety of study populations in China, Denmark, Japan, New Zealand, Sweden, Switzerland, Turkey, and the United States.

Eleven studies assessed the association between leisure-time or total physical activity and colon cancer risk in 13 different study populations (Table 4-5). These studies either measured physical activity and tracked participants over time to ascertain colon cancer outcomes or compared recalled histories of physical activity among colon cancer patients with those among controls. In eight study populations, an inverse association was reported between physical activity and risk of colon cancer, and results were generally consistent for men and women. The three studies that examined the effect of physical activity during early adulthood (Polednak 1976; Paffenbarger, Hyde, Wing 1987; Marcus, Newcomb, Storer 1994) found no effect, which could indicate that the earlier activity did not affect risk of colon cancer later in life. In studies that used more than two categories of physical activity, 10 potential dose-response relationships between level of physical activity or cardiorespiratory fitness and colon cancer risk were evaluated. Five of these showed a statistically significant inverse dose-response gradient, one showed an inverse dose-response gradient that was not statistically significant, three showed no gradient, and one showed a positive relationship that was not statistically significant.

Two studies of colon adenomas (Giovannucci et al. 1995; Kono et al. 1991) reported an inverse relationship between leisure-time physical activity and risk of colon adenomas.

Table 4-5. Epidemiologic studies of leisure-time or leisure-time plus occupational physical activity* and colon cancer

Study	Population	Definition of physical activity	Definition of cancer
Polednak (1976)	Cohort of 8,393 former US college men	College athletic status; major, minor, and nonathlete	Colon cancer mortality (n = 107)
Paffenbarger, Hyde, Wing (1987)	Cohort of 51,977 male, 4,706 female former US college students	Sports play in college	Colon cancer incidence (n = 201)
	Cohort of 16,936 male US college alumni aged 35–74 years	Physical activity index (kcal/week)	Colon cancer mortality (n = 44)
Gerhardsson, Floderus, Norell (1988)	Cohort of 16,477 Swedish men and women twins aged 43–82 years	Categories of occupational and leisure-time activity	Colon cancer incidence
Slattery et al. (1988)	Cohort of Utah men (110 cases and 180 controls) and women (119 cases and 204 controls) aged 40–79 years	Occupational and leisure-time activity were both assessed by total energy expended	Colon cancer incidence
Severson et al. (1989)	Cohort of 7,925 Japanese men aged 46–65 years	Physical activity index from Framingham study and heart rate	Colon cancer incidence (n = 172)
Gerhardsson et al. (1990)	Swedish men (163 cases) and women (189 cases) and 512 controls; all ages	Categories of occupational and leisure-time activity	Colon cancer incidence
Whittemore et al. (1990)	North American Chinese men (179 cases and 698 controls) and women (114 cases and 494 controls) aged ≥ 20 years	Time per day spent sleeping/ reclining, sitting, in light or moderate activity, and in vigorous activity	Colon cancer incidence
	Asian Chinese men (95 cases and 678 controls) and women (78 cases and 618 controls) aged 20–79 years	Time per day spent sleeping/ reclining, sitting, in light or moderate activity, and in vigorous activity	Colon cancer incidence
Lee, Paffenbarger, Hsieh (1991)	Cohort of 7,148 male male US college alumni aged 30–79 years	Index of energy expenditure based on stair climbing, walking, and sports/recreation, assessed 2 times > 11 years apart	Colon cancer incidence

Main findings	Dose response†	Adjustment for confounders and other comments
No differences in mortality	No	None
Sports play ≥ 5 hrs/week relative to < 5 hrs/week: RR = 0.91; p = 0.60	NA	Adjusted for age (2 levels of activity)
Risk increased with physical activity index: p for trend = 0.45	No	Adjusted for age, BMI, and smoking
Least active relative to most active for work and leisure: RR = 3.6 (95% CI, 1.3–9.8)	NA	Adjusted for age and sex (2 levels of activity); adjustments for possible confounders said to not change results
High activity quartile relative to low activity quartile; men: OR total 0.70 (90% CI, 0.38–1.29); women: OR total 0.48 (90% CI, 0.27–0.87)	Yes	Adjusted for age, BMI, dietary fiber, and total energyintake; greater effect with intense activity; population-based
High activity tertile relative to low activity tertile: RR 0.71 (95% CI, 0.51–0.99); high heart rate relative to low: RR 1.37 (95% CI, 0.97–1.93)	No Yes	Adjusted for age, BMI
Low activity relative to high: work and leisure, RR = 1.8 (95% CI, 1.0–3.4)	Yes	Adjusted for age, sex, BMI, dietary intake of total energy, protein, fat, fiber, and browned meat surface; population-based
Sedentary relative to active: RR = 1.6 (95% CI, 1.1–2.4) for men, RR = 2.0(95% CI, 1.2–3.3) for women	NA	Adjusted for age (2 levels of activity); population-based; adjustment for diet had little effect on findings
Sedentary relative to active: RR = 0.85 (95% CI, 0.39–1.9) for men, RR = 2.5 (95% CI, 1.0–6.3) for women	NA	Adjusted for age (2 levels of activity); population-based; no effect of physical activity after adjustment for diet
Highly active relative to inactive: RR = 0.85 (90% CI, 0.6–1.1); high lifetime activity: RR = 0.5 (90% CI, 0.3–0.9)	No	Adjusted for age

Table 4-5. *Continued*

Study	Population	Definition of physical activity	Definition of cancer
Marcus, Newcomb, Storer (1994)	Wisconsin women aged up to 74 years, 536 cases and 2,315 controls	Total strenuous physical activity during ages 14–22 years	Colon cancer incidence
Giovannucci et al. (1995)	47,723 US male health professionals aged 40–75 years	Weekly recreational physical activity index based on 8 categories of moderate and vigorous activities	Colon cancer incidence (n = 201)
Longnecker et al. (1995)	US men aged > 30 years, 163 cases 703 controls	Leisure-time vigorous physical activity	Right-sided colon cancer incidence

Dietary factors may confound or modify the association between physical activity and colon cancer risk (Willett et al. 1990). Five of the studies in Table 4-5 controlled for dietary components in analyses and continued to observe a significant inverse association (Gerhardsson, Floderus, Norell 1988; Slattery et al. 1988; Gerhardsson et al. 1990; Giovannucci et al. 1995; Longnecker et al. 1995), and in one study (Whittemore et al.1990), adjustment for dietary intakes altered findings in one study population but not in the other.

Together, the research on occupational and leisure-time or total physical activity strongly suggests that physical activity has a protective effect against the risk of developing colon cancer.

Rectal Cancer

Many of the studies on physical activity and colon cancer risk also studied rectal cancer as a separate outcome. Of 13 studies that investigated occupational physical activity alone, 10 reported no statistically significant association with rectal cancer risk (Garabrant et al. 1984; Vena et al. 1985, 1987; Gerhardsson et al. 1986; Jarebinski, Adanja, Vlajinac 1988; Lynge and Thygesen 1988; Brownson et al. 1991; Marti and Minder 1989; Peters et al. 1989; Dosemeci et al. 1993), two reported significant inverse associations (Kato, Tominaga, Ikari 1990; Fraser and Pearce 1993), and one reported a significant direct association (i.e., increasing risk with increasing physical activity) (Arbman et al. 1993).

Six of the studies that investigated the association between leisure-time or total physical activity and the risk of developing rectal cancer failed to find a significant association (Gerhardsson, Floderus, Norell 1988; Severson et al. 1989; Gerhardsson et al. 1990; Kune, Kune, Watson 1990; Lee, Paffenbarger, Hsieh 1991; Longnecker et al. 1995). In another study, Whittemore and colleagues (1990) observed a statistically significant inverse association in one study population and no effect in the other. Paffenbarger, Hyde, and Wing (1987) found an inverse relationship in one cohort and a direct relationship in the other.

Taken together, study results on both occupational and leisure-time or total physical activity suggest that risk of rectal cancer is unrelated to physical activity.

Hormone-Dependent Cancers in Women

Of the epidemiologic studies examining the relationship between physical activity and hormone-dependent cancers in women, 13 have investigated the risk associated with breast cancer, two with ovarian cancer, four with uterine corpus cancer (mostly endometrial), and one with a combination of cancers. It should be noted that studies of physical activity in women have been especially prone to misclassification problems because they did not

Main findings	Dose response[†]	Adjustment for confounders and other comments
Any strenuous activity relative to none: RR = 1.0 (95% CI, 0.8–1.3)	No	Adjusted for age, family history, screening sigmoidoscopy, BMI; population based
Most active quintile compared with least active quintile, RR = 0.53 (95% CI, 0.32–0.88) p for trend = 0.03	Yes	Adjusted for age, BMI, parental history of colorectal cancer, history of endoscopic screening or polyp diagnosis, smoking, aspirin use, and diet
Vigorous activity ≥ 2 hours/week relative to none: RR = 0.6 (95% CI, 0.4–1.0)	Yes	Adjusted for BMI, family history, income, race, smoking, and intakes of alcohol, energy, fat, fiber, and calcium

Abbreviations: BMI = body mass index (wt [kg] /ht [m]^2); CI = confidence interval; OR = odds ratio; RR = relative risk.

[*]Excludes studies where only occupational physical activity was measured.
[†]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.

include household work and child care in their assessment. Studies of leisure-time or total physical activity and hormone-dependent cancers in women are summarized in Table 4-6.

Breast Cancer

Four of the 13 breast cancer studies considered only occupational physical activity. Two of those studies described significant inverse associations (Vena et al. 1987; Zheng et al. 1993), and two others reported no significant association (Dosemeci et al. 1993; Pukkala et al. 1993). Only two (Dosemeci et al. 1993; Pukkala et al. 1993) adjusted for socioeconomic status, and none gathered information about reproductive factors and thus could not control for those potential confounding variables.

The epidemiologic studies of leisure-time or total physical activity and breast cancer risk have yielded inconsistent results (Table 4-6). Of these 10 studies, two reported a significant inverse association (Bernstein et al. 1994; Mittendorf et al. 1995), three reported an inverse association that was not statistically significant (Frisch et al. 1985,1987; Friedenreich and Rohan 1995), three reported no relationship (Paffenbarger, Hyde, Wing 1987; Albanes, Blair, Taylor 1989; Taioli, Barone, Wynder 1995). The other two reported a direct association, although in one this did not reach statistical significance (Dorgan et al. 1994), and in the other it remained statistically significant (after adjustment for confounding) only for physical activity at age 30–39 years (Sternfeld et al. 1993).

Even among the studies that controlled for potential confounding by reproductive factors, findings were inconsistent (Bernstein et al. 1994; Dorgan et al. 1994; Sternfeld et al. 1993; Friedenreich and Rohan 1995; Mittendorf et al. 1995; Taioli, Barone, Wynder 1995). Results were inconsistent as well among studies that included primarily postmenopausal women (i.e., all but the study by Bernstein and colleagues [1994]).

Nonetheless, it is possible that physical activity during adolescence and young adulthood may protect against later development of breast cancer. Five of the studies cited here have examined this possibility. Among these five studies, two found a strong and statistically significant reduction in risk (Bernstein et al. 1994 [RR = 0.42]; Mittendorf et al. 1995 [RR = 0.5]), one found a nonsignificant reduction in risk (Frisch et al. 1985 [RR = 0.54]), and two found a null association (Paffenbarger, Hyde, Wing 1987; Taioli, Barone, Wynder 1995). These studies thus lend limited support to the hypothesis that physical activity during adolescence

Table 4-6. Epidemiologic studies of leisure-time or leisure-time plus occupational physical activity* and hormone-dependent cancers in women

Study	Population	Definition of physical activity	Definition of cancer
Breast cancer			
Frisch et al. (1985 and 1987)	Cohort of former US college athletes and nonathletes; 5,398 women aged 21–80 years	Athletic status during college	Breast cancer prevalence (n = 69)
Paffenbarger, Hyde, Wing (1987)	Cohort of former US college students, 4,706 women	Sports play during college	Breast cancer incidence and mortality
Albanes, Blair, Taylor (1989)	NHANES cohort: 7,413 women aged 25–74 years, in US	One question on nonrecreational activity, one on recreational activity	Breast cancer incidence (n = 122)
Sternfeld et al. (1993)	254 cases and 201 controls in an HMO	Age-specific recreational activity levels	Breast cancer incidence
Bernstein et al. (1994)	Women ≥ 40 years; 545 cases and 545 controls in California, US	Participation in several leisure-time activities after menarche	Breast cancer incidence in situ and invasive
Dorgan et al. (1994)	Framingham Study cohort: 2,307 women aged 35–68 years, Massachusetts, US	Physical activity index	Breast cancer incidence (n = 117)
Friedenreich and Rohan (1995)	Australian women aged 20–74 years; 451 cases and 451 controls (matched)	Recreational physical activity index	Breast cancer incidence
Mittendorf et al. (1995)	US women aged 17–74 years; 6,888 cases and 9,539 controls	Strenuous physical activity at ages 14–22 years	Breast cancer incidence
Taioli, Barone, Wynder (1995)	All ages in US; 617 cases; 531 controls	Leisure-time physical activity at ages 15–22 years	Breast cancer incidence
Ovarian cancers			
Mink et al. (1996)	Iowa Women's Health Study; cohort of 31,396 postmenopausal women	Categories of physical activity	Ovarian cancer incidence (n = 97)

Main findings	Dose response[†]	Adjustment for confounders and other comments
Nonathletes vs. athletes: RR = 1.86 (95% CI, 1.0–3.47)	NA	Adjusted for age, family history of cancer, age at menarche, number of pregnancies, oral contraceptive use, smoking, use of estrogen, leanness
Sports play of ≥ 5 relative to < 5 hours/week RR = 0.96 (p value = 0.92)	NA	Adjusted for age
Sedentary relative to most active: RR = 1.1 (95% CI, 0.6–2.0) for nonrecreational; RR = 1.0 (95% CI, 0.6–1.6) for recreational	No	Adjusted for age; adjustment for confounders had little effect on results; suggestive of variable effects by menopausal status
For activity from age 30–39, high activity quartile vs. low activity quartile, postmenopausal OR = 2.3 (95% CI, 1.03–5.04); premenopausal OR = 2.8 (95% CI, 0.98–5.18)	Yes (opposite direction)	Adjusted for age, menopausal status, and potential confounders
≥ 3.8 hours/week relative to 0 hours of leisure-time activity, RR = 0.42 (95% CI, 0.27–0.64)	Yes	Adjusted for age, race, neighborhood, age at menarche, age at first full-term pregnancy, number of full-term pregnancies, oral contraceptive use, lactation, family history of breast cancer, Quetelet index; population-based
High activity quartile relative to low activity quartile: RR = 1.6 (95% CI, 0.9–2.9)	Yes (opposite direction)	Adjusted for age, menopausal status, age at first pregnancy, parity, education, occupation, and alcohol
> 4,000 kcal/week in physical activity relative to none: RR = 0.73 (95% CI, 0.51–1.05)	Yes	Adjusted for BMI and energy intake; effects observed for premenopausal and postmenopausal cancer and for light and vigorous activity; population-based
≥ daily strenuous activity relative to none: RR = 0.5 (95% CI, 0.4–0.7)	Yes	Adjusted for age, parity, age at first birth, family history, BMI, prior breast disease, age at menopause, menopausal status, alcohol use, and menopausal status x BMI; population-based
> 1,750 kcal/week relative to none: RR = 1.1 (95% CI, 0.5–2.6)	No	Adjusted for age, education, BMI, age at menarche, and prior pregnancy; hospital-based
Most active relative to least active: RR = 1.97 (95% CI, 1.22–3.19)	Yes (opposite direction)	Adjusted for age, smoking, education, live births, hysterectomy, and family history

Table 4-6. *Continued*

Study	Population	Definition of physical activity	Definition of cancer
Endometrial cancers			
Levi et al. (1993)	Switzerland/Northern Italy; 274 cases and 572 controls aged 31–75	Categories of leisure-time and occupational activity	Endometrial cancer incidence
Shu et al. (1993)	Women in Shanghai, China aged 18–74 years, 268 cases and 268 controls	Occupational and nonoccupational physical activity index	Endometrial cancer incidence
Sturgeon et al. (1993)	US women aged 20–74 years; 405 cases and 297 controls	Recreational and nonrecreational activity categories	Endometrial cancer incidence
Combined set			
Frisch et al. (1985 and 1987)	Cohort of former US college athletes and nonathletes; 5,398 women aged 21–80 years	Athletic status during college	Cervix, uterus, ovary, vagina cancer prevalence (n = 37)

and young adulthood may be protective against later development of breast cancer.

Other Hormone-Dependent Cancers in Women

Too little information is available to evaluate the possible effect of physical activity on risk of ovarian cancer. Zheng and colleagues (1993) found no significant associations between occupational physical activity and risk of ovarian cancer. On the other hand, data from the Iowa Women's Health Study showed that risk of ovarian cancer among women who were most active was twice the risk among sedentary women (Mink et al. 1996).

Findings are limited for uterine corpus cancers as well. Zheng et al. (1993) found no relationship between physical activity and risk of cancer of the uterine corpus. Among the endometrial cancer studies, one (Levi et al. 1993) found a decreased risk associated with nonoccupational activity, and one (Sturgeon et al. 1993) found combined recreational and nonrecreational activity to be protective. Another study (Shu et al. 1993) found no protective effect of nonoccupational activity in any age group and a possible protective effect of occupational activity among younger women but not among older women.

In Frisch and colleagues' (1985) study of the combined prevalence of cancers of the ovary, uterus, cervix, and vagina, nonathletes were 2.5 times more likely than former college athletes to have these forms of cancer at follow-up. Because these cancers have different etiologies, however, the import of this finding is difficult to determine.

Thus the data are either too limited or too inconsistent to firmly establish relationships between physical activity and hormone-dependent cancers in women. The suggestive finding that physical activity in adolescence and early adulthood may protect against later development of breast cancer deserves further study.

Main findings	Dose response[†]	Adjustment for confounders and other comments
Sedentary relative to active for total activity: RR = 2.4 (95% CI, 1.0–5.8) to RR = 8.6 (95% CI, 3.0–25.3) for different ages	Yes	Adjusted for age, education, parity, menopausal status, oral contraceptive use, estrogen replacement, BMI, and caloric intake; hospital-based
Low average adult activity quartile relative to high quartile: occupational age ≤ 55 years RR = 2.5 (95% CI, 0.9–6.3), age > 55 years RR = 0.6 (no CI given); nonoccupational RR = 0.8 (95% CI, 0.5–1.3)	No	Adjusted for age, number of pregnancies, BMI, and caloric intake; possible modification of occupational activity by age; population-based
Sustained (lifetime) activity, inactive relative to active: recreational RR = 1.5 (95% CI, 0.7–3.2) nonrecreational RR = 1.6 (95% CI, 0.7–3.3)	No	Adjusted for age, study area, education, parity, oral contraceptive use, hormone replacement use, cigarette smoking, BMI, and other type of activity; recent activity also protective; population-based
Nonathletes vs. athletes: RR = 2.53 (95% CI, 1.17–5.47)	N/A	Adjusted for age, family history of cancer, age at menarche, number of pregnancies, oral contraceptive use, smoking, use of estrogen, leanness

Abbreviations: BMI = body mass index (wt [kg]/ht [m]^2); CI = confidence interval; HMO = health maintenance organization; NHANES = National Health and Examination Survey; OR = odds ratio; RR = relative risk.

[*]Excludes studies where only occupational physical activity was measured.

[†]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.

Cancers in Men

Prostate Cancer

Among epidemiologic studies of physical activity and cancer, prostate cancer is the second most commonly studied, after colorectal cancer. Results of these studies are inconsistent. Seven studies have investigated the association between occupational physical activity and prostate cancer risk or mortality. Two described significant inverse dose-response relationships (Vena et al. 1987; Brownson et al. 1991). Two showed a nonsignificant decreased risk with heavy occupational activity (Dosemeci et al. 1993; Thune and Lund 1994). In one publication that presented data from two cohorts, there was no effect in either (Paffenbarger, Hyde, Wing 1987). The remaining study (Le Marchand, Kolonel, Yoshizawa 1991) reported inconsistent findings by age: increasing risk with increasing activity among men aged 70 years or older and no relationship among men younger than age 70.

The 10 studies of leisure-time physical activity, or total physical activity, or cardiorespiratory fitness and risk of prostate cancer have also produced inconsistent results (Table 4-7). Two of the studies described significant inverse relationships (Lee, Paffenbarger, Hsieh 1992; Oliveria et al. 1996), although one of these (Lee, Paffenbarger, Hsieh 1992) observed this relationship only among men aged 70 years or older. Four studies found inverse relationships (Albanes, Blair, Taylor 1989; Severson et al. 1989; Yu, Harris, Wynder 1988; Thune and

Table 4-7. Epidemiologic studies of leisure-time or total physical activity or cardiorespiratory fitness and prostate cancer

Study	Population	Definition of physical activity or cardiorespiratory fitness	Definition of cancer
Physical activity			
Polednak (1976)	Cohort of 8,393 former US college men	College athletic status, major, minor, and nonathletes	Prostate cancer incidence (n = 124)
Paffenbarger, Hyde, Wing (1987)	Cohort of 51,977 US male former college students	Sports play	Prostate cancer incidence and mortality (n = 154)
	16,936 US male alumni aged 35–74 years	Physical activity index	Prostate cancer mortality (n = 36)
Yu, Harris, Wynder (1988)	US men, all ages, 1,162 cases and 3,124 controls	Categories of leisure-time aerobic exercise	Prostate cancer incidence
Albanes, Blair, Taylor (1989)	NHANES cohort of 5,141 US men aged 25–74 years	Categories of recreational and nonrecreational activity	Prostate cancer incidence
Severson et al. (1989)	Cohort of 7,925 Japanese men in Hawaii aged 46–65 years	Physical activity index from Framingham study and heart rate	Prostate cancer incidence
West et al. (1991)	Utah men aged 45–74 years, 358 cases and 679 controls	Categories of energy expended	Prostate cancer incidence
Lee, Paffenbarger, Hsieh (1992)	Cohort of US college alumni, 17,719 men aged 30–79 years	Physical activity index based on stair climbing, walking, playing sports	Prostate cancer incidence (n = 221)
Thune and Lund (1994)	Cohort of Norwegian 43,685 men	Recreational and occupational activity based on questionnaire; categories of occupational and leisure-time activity	Prostate cancer incidence (n = 220)
Cardiorespiratory Fitness			
Oliveria et al. (1996)	Cohort of 12,975 Texas men aged 20–80 years	Maximal exercise test	Prostate cancer incidence or mortality (n = 94)
	Cohort of 7,570 Texas men	Categories of weekly energy expenditure in leisure time	Prostate cancer incidence or mortality (n = 44)

Main findings	Dose response*	Adjustment for confounders and other comments
Major athletes relative to nonathletes, RR = 1.64 ($p < 0.05$)	No	None
Sports play ≥ 5 relative to < 5 hours/week, RR = 1.66; ($p < 0.05$)	NA	Adjusted for age (2 levels of activity)
Comparing ≥ 2,000 with < 500 kcal/week, RR = 0.57; $p = 0.33$	No	Adjusted for age, BMI, and smoking
Most sedentary relative to most active menduring leisure time, RR = 1.3 (95% CI, 1.0–1.6) for whites, RR = 1.4 (95% CI, 0.8–2.6) for blacks	Yes	Adjusted for age; in multivariate analysis, findings no longer significant for whites; hospital based
Least active relative to most active individuals, RR = 1.3 (95% CI, 0.7–2.4); for nonrecreational RR = 1.8 (95% CI, 1.0–3.3); for recreational RR = 1.8 (95% CI, 1.0–3.3)	No Yes No	Adjusted for age; further adjustment for confounders said to not affect results
Most active relative to least active men, RR = 1.05 (95% CI, 0.73–1.51); for occupation, RR = 0.77 (95% CI, 0.58–1.01); high heart rate relative to low, RR = 0.97 (95% CI, 0.69–1.36)	NA No NA	Adjusted for age, BMI
Overall no association found		For agressive tumors, physical activity was associated with increased risk, but this was not statistically significant
Men aged ≥ 70 years: comparing > 4,000 with < 1,000 kcal/week; RR = 0.53 (95% CI, 0.29–0.95); men aged < 70 years, RR = 1.21 (95% CI, 0.8–0.18)	No	Adjusted for age; no effect of activity at 2,500 kcal, the level found protective for colon cancer
Heavy occupational activity relative to sedentary, RR = 0.81 (95% CI, 0.50–1.30); regular training in leisure time relative to sedentary, RR = 0.87 (95% CI, 0.57–1.34)	No	Adjusted for age, BMI, and geographic region
Among men < 60 years, most fit relative to least fit, RR = 0.26 (95% CI, 0.10–0.63);	Yes	Adjusted for age, BMI, and smoking
among men > 60 years, no effect, RR not given	No	Adjusted for age, BMI, and smoking
≥ 3,000 kcal/week relative to < 1,000 kcal/week, RR = 0.37 (95% CI, 0.14–0.98)	No	Adjusted for age, BMI, and smoking

Abbreviations: BMI = body mass index (wt [kg]/ht $[m]^2$); CI = confidence interval; 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.

Lund 1994), but these were not statistically significant, and one of the four (Thune and Lund 1994) showed this relationship only for those aged 60 years or older. Two studies found that men who had been athletically active in college had significantly increased risks of later developing prostate cancer (Polednak 1976; Paffenbarger, Hyde, Wing 1987). One study found no overall association between physical activity and prostate cancer risk but found a higher risk (although not statistically significant) of more aggressive prostate cancer (West et al. 1991).

The two studies of the association of cardiorespiratory fitness with prostate cancer incidence were also inconsistent. Severson and colleagues (1989) found no association between resting pulse rate and subsequent risk of prostate cancer. Oliveria and colleagues (1996) found a strong inverse dose-response relationship between fitness assessed by time on a treadmill and subsequent risk of prostate cancer.

Thus the body of research conducted to date shows no consistent relationship between prostate cancer and physical activity.

Testicular Cancer

Two studies investigated physical activity and risk of developing testicular cancer; again, results are inconsistent. A case-control study in England found that men who spent at least 15 hours per week in recreational physical activity had approximately half the risk of sedentary men, and a significant trend was reported over six categories of total time spent exercising (United Kingdom Testicular Cancer Study Group 1994). A cohort study in Norway (Thune and Lund 1994) was limited by few cases. It showed no association between leisure-time physical activity and risk of testicular cancer, but heavy manual occupational activity was associated with an approximately twofold increase in risk, although this result was not statistically significant. Thus no meaningful conclusions about a relationship between physical activity and testicular cancer can be drawn.

Other Site-Specific Cancers

Few epidemiologic studies have examined the association of physical activity with other site-specific cancers (Lee 1994). The totality of evidence provides little basis for a suggestion of a relationship.

Biologic Plausibility

Because the data presented in this section demonstrate a clear association only between physical activity and colon cancer, the biologic plausibility of this relationship is the focus of this section. The alteration of local prostaglandin synthesis may serve as a mechanism through which physical activity may confer protection against colon cancer (Shephard et al. 1991; Lee 1994; Cordain, Latin, Beanke 1986). Strenuous physical activity increases prostaglandin F_2 alpha, which strongly increases intestinal motility, and may suppress prostaglandin E_2, which reduces intestinal motility and, released in greater quantities by colon tumor cells than normal cells, accelerates the rate of colon cell proliferation (Thor et al. 1985; Tutton and Barkla 1980). It has been hypothesized that physical activity decreases gastrointestinal transit time, which in turn decreases the length of contact between the colon mucosa and potential carcinogens, cocarcinogens, or promoters contained in the fecal stream (Shephard 1993; Lee 1994). This hypothesis could partly explain why physical activity has been associated with reduced cancer risk in the colon but not in the rectum. Physical activity may shorten transit time within segments of the colon without affecting transit time in the rectum. Further, the rectum is only intermittently filled with fecal material before evacuation. Despite these hypothetical mechanisms, studies on the effects of physical activity on gastrointestinal transit time in humans have yielded inconsistent results (Shephard 1993; Lee 1994).

Conclusions

The relative consistency of findings in epidemiologic studies indicates that physical activity is associated with a reduced risk of colon cancer, and biologically plausible mechanisms underlying this association have been described. The data consistently show no association between physical activity and rectal cancer. Data regarding a relationship between physical activity and breast, endometrial, ovarian, prostate, and testicular cancers are too limited or too inconsistent to support any firm conclusions. The suggestion that physical activity in adolescence and early adulthood may protect against later development of breast cancer clearly deserves further study.

Non–Insulin-Dependent Diabetes Mellitus

An estimated 8 million Americans (about 3 percent of the U.S. population) have been diagnosed with diabetes mellitus, and it is estimated that twice that many have diabetes but do not know it (Harris 1995). More than 169,000 deaths per year are attributed to diabetes as the underlying cause, making it the seventh leading cause of mortality in the United States (NCHS 1994). This figure, however, underestimates the actual death toll: in 1993, more than twice this number of deaths occurred among persons for whom diabetes was listed as a secondary diagnosis on the death certificate. Many of these deaths were the result of complications of diabetes, particularly CVDs, including CHD, stroke, peripheral vascular disease, and congestive heart failure. Diabetes accounts for at least 10 percent of all acute hospital days and in 1992 accounted for an estimated $92 billion in direct and indirect medical costs (Rubin et al. 1993). In addition, by age 65 years, about 40 percent of the general population has impaired glucose tolerance, which increases the risk of CVD (Harris et al. 1987).

Diabetes is a heterogeneous group of metabolic disorders that have in common elevated blood glucose and associated metabolic derangements. Insulin-dependent diabetes mellitus (IDDM, or type I) is characterized by an absolute deficiency of circulating insulin caused by destruction of pancreatic beta islet cells, thought to have occurred by an autoimmune process. Non–insulin-dependent diabetes mellitus (NIDDM, or type II) is characterized either by elevated insulin levels that are ineffective in normalizing blood glucose levels because of insulin resistance (decreased sensitivity to insulin), largely in skeletal muscle, or by impaired insulin secretion. More than 90 percent of persons with diabetes have NIDDM (Krall and Beaser 1989).

Nonmodifiable biologic factors implicated in the etiology of NIDDM include a strong genetic influence and advanced age, but the development of insulin resistance, hyperinsulinemia, and glucose intolerance are related to a modifiable factor: weight gain in adults, particularly in those persons in whom fat accumulates around the waist, abdomen, and upper body and within the abdominal cavity (this is also called the android or central distribution pattern) (Harris et al. 1987).

Physical Activity and NIDDM

Considerable evidence supports a relationship between physical inactivity and NIDDM (Kriska, Blair, Pereira 1994; Zimmet 1992; King and Kriska 1992; Kriska and Bennett 1992). Early suggestions of a relationship emerged from the observation that societies that had discontinued their traditional lifestyles (which presumably included large amounts of regular physical activity) experienced major increases in the prevalence of NIDDM (West 1978). Additional evidence for the importance of lifestyle was provided by comparison studies demonstrating that groups of people who migrated to a more technologically advanced environment had higher prevalences of NIDDM than their ethnic counterparts who remained in their native land (Hara et al. 1983; Kawate et al. 1979; Ravussin et al. 1994) and that rural dwellers had a lower prevalence of diabetes than their urban counterparts (Cruz-Vidal et al. 1979; Zimmet 1981; Taylor et al. 1983; King, Taylor, Zimmet, et al. 1984).

Many cross-sectional studies have found physical inactivity to be significantly associated with NIDDM (Taylor et al. 1983; Taylor et al. 1984; King, Taylor, Zimmet, et al. 1984; Dowse et al. 1991; Ramaiya et al. 1991; Kriska, Gregg, et al. 1993; Chen and Lowenstein 1986; Frish et al. 1986; Holbrook, Barrett-Connor, Wingard 1989). Cross-sectional studies that have examined the relationship between physical activity and glucose intolerance in persons without diabetes have generally found that after a meal, glucose levels (Lindgärde and Saltin 1981; Cederholm and Wibell 1985; Wang et al. 1989; Schranz et al. 1991; Dowse et al. 1991; Kriska, LaPorte, et al. 1993) and insulin values (Lindgärde and Saltin 1981; Wang et al. 1989; McKeigue et al. 1992; Feskens, Loeber, Kromhout 1994; Regensteiner et al. 1995) were significantly higher in less active than in more active persons. However, some cross-sectional studies did not find that physical inactivity was consistently associated with NIDDM in either the entire population or in all subgroups (King, Taylor, Zimmet, et al. 1984; Dowse et al. 1991; Kriska, Gregg, et al. 1993; Montoye et al. 1977; Taylor et al. 1983; Fisch et al. 1987; Jarrett, Shipley, Hunt 1986; Levitt et al. 1993; Harris 1991). For example, the Second National Health and Nutrition Examination Survey and the Hispanic Health and Nutrition Examination Survey found that higher

levels of occupational physical activity among MexicanAmericans were associated with less NIDDM (Harris 1991). However, in contrast to findings from the First National Health and Nutrition Examination Survey (Chen and Lewenstein 1986), this association was not found for either occupational or leisure-time physical activity among blacks or whites.

Two case-control studies have found physical inactivity to be significantly associated with NIDDM (Kaye et al. 1991; Uusitupa et al. 1985). One was a population-based nested case-control study, in which women aged 55–69 years who had high levels of physical activity were found to be half as likely to develop NIDDM as were same-aged women with low levels of physical activity (age-adjusted OR = 0.5; 95% CI, 0.4–0.7) (Kaye et al. 1991). Moderately active women had an intermediate risk (OR = 0.7; 95% CI, 0.5–0.9).

Prospective cohort studies of college alumni, female registered nurses, and male physicians have demonstrated that physical activity protects against the development of NIDDM (Table 4-8). A study of male university alumni (Helmrich et al. 1991) demonstrated that physical activity was inversely related to the incidence of NIDDM, a relationship that was particularly evident in men at high risk for developing diabetes (defined as those with a high BMI, a history of high blood pressure, or a parental history of diabetes). Each 500 kilocalories of additional leisure-time physical activity per week was associated with a 6 percent decrease in risk (adjusted for age, BMI, history of high blood pressure, and parental history of diabetes) of developing NIDDM. This study showed a more pronounced benefit from vigorous sports than from stair climbing or walking. In a study of female registered nurses aged 34–59 years, women who reported engaging in vigorous physical activity at least once a week had a 16 percent lower adjusted relative risk of self-reported NIDDM during the 8 years of follow-up than women who reported no vigorous physical activity (Manson et al. 1991). Similar findings were observed between physical activity and incidence of NIDDM in a 5-year prospective study of male physicians 40–84 years of age

Table 4-8. Cohort studies of association of physical activity with non–insulin-dependent diabetes mellitus (NIDDM)

Study	Population	Definition of physical activity	Definition of NIDDM
Helmrich et al. (1991)	Male college alumni	Leisure-time physical activity (walking, stair climbing, and sports)	Self-reported physician-diagnosed diabetes
Manson et al. (1991)	Female nurses	Single questions regarding number of times per week of vigorous activity	Self-reported diagnosed diabetes, confirmed by classic symptoms plus fasting plasma glucose ≥ 140 mg/dl; two elevated plasma glucose levels on two different occasions; hypoglycemic medication use
Manson et al. (1992)	Male physicians	Single questions regarding number of times per week of vigorous activity	Self-reported physician-diagnosed diabetes

(Manson et al. 1992). Although the incidence of diabetes was self-reported in these cohorts, concerns about accuracy are somewhat mitigated by the fact that these were studies of health professionals and college-educated persons. In these three cohort studies, two found an inverse dose-response gradient of physical activity and the development of NIDDM (Helmrich et al. 1991; Manson et al. 1992).

In a feasibility study in Malmo, Sweden, physical activity was included as part of an intervention strategy to prevent diabetes among persons with impaired glucose tolerance (Eriksson and Lindgärde 1991). At the end of 5 years of follow-up, twice as many in the control group as in the intervention group had developed diabetes. The lack of random assignment of participants, however, limits the generalizability of this finding. A study conducted in Daqing, China, also included physical activity as an intervention to prevent diabetes among persons with impaired glucose tolerance (Pan, Li, Hu 1995). After 6 years of follow-up, 8.3 cases per 100 person-years occurred in the exercise intervention group and 15.7 cases per 100 person-years in the control group.

It has been recommended that an appropriate exercise program may be added to diet or drug therapy to improve blood glucose control and reduce certain cardiovascular risk factors among persons with diabetes (American Diabetes Association 1990). Diet and exercise have been found to be most effective for controlling NIDDM in persons who have mild disease and are not taking medications (Barnard, Jung, Inkeles 1994). However, excessive physical activity can sometimes cause persons with diabetes (particularly those who take insulin for blood glucose control) to experience detrimental effects, such as worsening of hyperglycemia and ketosis from poorly controlled diabetes, hypoglycemia (insulin-reaction) either during vigorous physical activity or—more commonly—several hours after prolonged physical activity, complications from proliferative retinopathy (e.g., detached retina), complications from superficial foot injuries, and a risk of myocardial infarction and sudden death, particularly among older people with NIDDM and advanced, but silent, coronary atherosclerosis. These risks can be minimized by a preexercise medical evaluation and by taking proper precautions (Leon 1989, 1992). To

Main findings	Dose response*	Adjustment for confounder and other comments
0.94 (95% CI, 0.90–0.98) or 6% decrease in NIDDM for each 500 kcal increment	Yes	Adjusted for age, BMI, hypertension history, parental history of diabetes
0.84 (95% CI, 0.75–0.94) for ≥ 1 time per week vs. < 1 time per week vigorous activity	No	Adjusted for age, BMI, family history of diabetes, smoking, alcohol consumption, hypertension history, cholesterol history, family of history coronary heart disease
0.71 (95% CI, 0.54–0.94) for ≥ 1 time per week vs. < 1 time per week vigorous activity	Yes	Adjusted for age, BMI, smoking, alcohol consumption, reported blood pressure, hypertension history, cholesterol history, parental history of myocardial infarction

Abbreviations: BMI = body mass index (wt [kg]/ht $[m]^2$); CI = confidence interval.

*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.

reduce risk of hypoglycemic episodes, persons with diabetes who take insulin or oral hypoglycemic drugs must closely monitor their blood glucose levels and make appropriate adjustments in insulin or oral hypoglycemic drug dosage, food intake, and timing of physical activity sessions.

Biologic Plausibility

Numerous reviews of the short- and long-term effects of physical activity on carbohydrate metabolism and glucose tolerance describe the physiological basis for a relationship (Björntorp and Krotkiewski 1985; Koivisto, Yki-Järvinen, DeFronzo 1986; Lampman and Schteingart 1991; Horton 1991; Wallberg-Henriksson 1992; Leon 1992; Richter, Ruderman, Schneider 1981; Harris et al. 1987). During a single prolonged session of physical activity, contracting skeletal muscle appears to have a synergistic effect with insulin in enhancing glucose uptake into the cells. This effect appears to be related to both increased blood flow in the muscle and enhanced glucose transport into the muscle cell. This enhancement persists for 24 hours or more as glycogen levels in the muscle are being replenished. Such observations suggest that many of the effects of regular physical activity are due to the overlapping effects of individual physical activity sessions and are thus independent of long-term adaptations to exercise training or changes in body composition (Harris et al. 1987).

In general, studies of exercise training have suggested that physical activity helps prevent NIDDM by increasing sensitivity to insulin (Saltin et al. 1979; Lindgärde, Malmquist, Balke 1983; Krotkiewski 1983; Trovati et al. 1984; Schneider et al. 1984; Rönnemaa et al. 1986). These studies suggest that physical activity is more likely to improve abnormal glucose tolerance when the abnormality is primarily caused by insulin resistance than when it is caused by deficient amounts of circulating insulin (Holloszy et al. 1986). Thus, physical activity is likely to be most beneficial in preventing the progression of NIDDM during the earlier stages of the disease process, before insulin therapy is required. Evidence supporting this theory includes intervention programs that promote physical activity together with a low-fat diet high in complex carbohydrates (Barnard, Jung, Inkeles 1994) or programs that promote diet alone (Nagulesparan et al. 1981). These studies have shown that diet and physical activity interventions are much less beneficial for persons with NIDDM who require insulin therapy than for those who do not yet take any medication or those who take only oral medications for blood glucose control.

Cross-sectional studies also show that, compared with their sedentary counterparts, endurance athletes and exercise-trained animals have greater insulin sensitivity, as evidenced by a lower plasma insulin concentration at a similar plasma glucose concentration, and increased ^{121}I-insulin binding to white blood cells and adipocytes (Koivisto et al. 1979). Insulin sensitivity and rate of glucose disposal are related to cardiorespiratory fitness even in older persons (Hollenbeck et al. 1984). Resistance or strength-training exercise has also been reported to have beneficial effects on glucose-insulin dynamics in some, but not all, studies involving persons who do not have diabetes (Goldberg 1989; Kokkinos et al. 1988). Much of the effect of physical activity appears to be due to the metabolic adaptation of skeletal muscle. However, exercise training may contribute to improved glucose disposal and glucose-insulin dynamics in both adipose tissue and the working skeletal muscles (Leon 1989, 1992; Gudat, Berger, Lefèbvre 1994; Horton 1991).

In addition, exercise training may reduce other risk factors for atherosclerosis (e.g., blood lipid abnormalities and elevated blood pressure levels), as discussed previously in this chapter, and thereby decrease the risk of macrovascular or atherosclerotic complications of diabetes (Leon 1991a).

Lastly, physical activity may prevent or delay the onset of NIDDM by reducing total body fat or specifically intra-abdominal fat, a known risk factor for insulin resistance. As discussed later in this chapter, physical activity is inversely associated with obesity and intra-abdominal fat distribution, and recent studies have demonstrated that physical training can reduce these body fat stores (Björntorp, Sjöström, Sullivan 1979; Brownell and Stunkard 1980; Després et al. 1988; Krotkiewski 1988).

Conclusions

The epidemiologic literature strongly supports a protective effect of physical activity on the likelihood of developing NIDDM in the populations

studied. Several plausible biologic mechanisms exist to explain this effect. Physical activity may also reduce the risk of developing NIDDM in groups of people with impaired glucose tolerance, but this topic needs further study.

Osteoarthritis

Osteoarthritis, the most common form of arthritis, is characterized by both degeneration of cartilage and new growth of bone around the joint. Because its prevalence increases with age, osteoarthritis is the leading cause of activity limitation among older persons. The etiology of osteoarthritis is unknown, and the risk factors and pathogenesis of osteoarthritis differ for each joint group.

Whether an active lifestyle offers protection against the development of osteoarthritis is not known, but studies have examined the risk of developing it in relation to specific athletic pursuits. Cross-sectional studies have associated competitive—as opposed to recreational—running at high levels and for long periods with the development of osteoarthritis seen on x-rays (Marti and Minder 1989; Kujala, Kaprio, Sarna 1994; Kujala et al. 1995). On the other hand, both cross-sectional and cohort studies have suggested that persons who engage in recreational running over long periods of time have no more risk of developing osteoarthritis of the knee or hip than sedentary persons (Lane 1995; Lane et al. 1986, 1993; Panush et al. 1995; Panush et al. 1986; Panush and Lane 1994). There is also currently no evidence that persons with normal joints increase their risk of osteoarthritis by walking.

Studies of competitive athletes suggest that some sports—specifically soccer, football, and weight lifting—are associated with developing osteoarthritis of the joints of the lower extremity (Kujala, Kaprio, Sarna 1994; Kujala et al. 1995; Rall, McElroy, Keats 1964; Vincelette, Laurin, Lévesque 1972; Lindberg, Roos, Gärdsell 1993). Other competitive sports activities in which specific joints are used excessively have also been associated with the development of osteoarthritis. For example, baseball pitchers are reported to have an increased prevalence of osteoarthritis in the elbow and shoulder joint (Adams 1965; Bennett 1941). These studies are limited because they involve small sample sizes. Further confounding these studies is the high incidence of fractures, ligamentous and cartilage injuries, and other injuries to joints that occur with greater-than-average frequency among competitive participants in these sports. Because joint injury is a strong risk factor for the development of osteoarthritis, it may not be the physical activity but rather the associated injuries that cause osteoarthritis in these competitive athletes. In a study by Roos and colleagues (1994), soccer players who had not suffered knee injuries had no greater prevalence of osteoarthritis than did sedentary controls. Regular noncompetitive physical activity of the amount and intensity recommended for improving health thus does not appear harmful to joints that have no existing injury.

Physical Activity in Persons with Arthritis

Given the high prevalence of osteoarthritis among older people, it is important to determine whether persons with arthritis can safely exercise and be physically active. Experimental work with animals shows that use of injured joints inhibits tissue repair (Buckwalter 1995). More specifically, several studies have indicated that running accelerates joint damage in animal models where osteoarthritis has been experimentally induced (Armstrong et al. 1993).

In contrast, several short-term studies of human subjects have indicated that regular moderate-exercise programs, whether including aerobic or resistance training, relieve symptoms and improve function among people with both osteoarthritis and rheumatoid arthritis (Ettinger and Afable 1994; Allegrante et al. 1993; Fisher et al. 1991; Fisher et al. 1994; Fisher and Pendergast 1994; Puett and Griffin 1994). For example, it has been shown that after regular physical activity, persons with arthritis have a significant reduction in joint swelling (Minor et al. 1988). In other studies of persons with osteoarthritis, increased levels of physical activity were associated with improved psychosocial status, functional status, and physical fitness (Minor 1991; Minor and Brown 1993). Furthermore, regular physical activity of moderate intensity has been found to raise the pain threshold, improve energy level, and improve self-efficacy among persons with osteoarthritis (Minor et al. 1989; Chow et al. 1986; Holman, Mazonson, Lorig 1989).

Biologic Plausibility

The biologic effects of physical activity on the health and function of joints have not been extensively investigated, but some level of physical activity is necessary to preserve joint function. Because hyaline cartilage has no blood vessels or nerves, mature cartilage cells (chondrocytes) receive nourishment only from the diffusion of substances through the cartilage matrix from joint fluid. Physical activity enhances this process. In the laboratory, putting pressure on cartilage deforms the tissue, creating pressure gradients that cause fluid to flow and alter osmotic pressures within the cartilage matrix (Hall, Urban, Gehl 1991). The effect of such loading on the metabolism of chondrocytes is not well described, but when loading is performed within the physiologic range, chondrocytes increase proteoglycan synthesis (Grodzinsky 1993). In contrast, high-intensity loading and repetitive high-impact loads disrupt the cartilage matrix and inhibit proteoglycan synthesis (Lammi 1993).

The role of normal loading is confirmed by the effect of inactivity on articular cartilage. Immobility leads to decreased cartilage proteoglycan synthesis, increased water content, and decreased cartilage stiffness and thickness. Disuse may make the cartilage more vulnerable to injury, and prolonged disuse causes loss of normal joint function as the joint cavity is obliterated by fibrous tissue.

Studies of running on joint function in dogs with normal joints have confirmed that running does affect the proteoglycan and water content of cartilage and does not lead to degeneration of articular surfaces or to degenerative joint disease (Arokoski et al. 1993). In contrast, in dogs with injured joints, running has been shown to cause arthritis (Buckwalter 1995).

Conclusions

Physical activity is essential for maintaining the health of joints and appears to be beneficial for control of symptoms among people with osteoarthritis. Although there is no evidence that physical activity itself causes osteoarthritis, injuries sustained during competitive sports have been shown to increase the risk of developing osteoarthritis.

Osteoporosis

Osteoporosis is characterized by decreased bone mass and structural deterioration of bone tissue, leading to bone fragility and increased susceptibility to fractures. Because bone mass and strength progressively decline with advancing age, this disease primarily affects older persons (Cummings et al. 1985). Osteoporosis is more common among women than among men, for at least three reasons: women have lower peak bone mass than men, women lose bone mass at an accelerated rate after menopause when estrogen levels decline, and women have a longer life span than men.

The most common potential fracture sites are vertebrae of the chest and lower back, the distal radius (or wrist), the hips, and the proximal humerus (NIH 1984). Vertebral fractures can occur spontaneously or with minimal trauma (e.g., bending forward or coughing); once deformed, the vertebrae never return to their normal shape. These fractures may be asymptomatic and discovered only incidentally on a chest or spine x-ray. Accumulation of such vertebral fractures causes a bent-over or hunchbacked posture that is generally associated with chronic back pain and often with gastrointestinal and abdominal problems related to a lowering of the rib cage.

In the United States, fractures of the hip account for 250,000 of the 1.5 million fractures that are attributed each year to osteoporosis. Hip fractures are associated with more deaths (a 15–20 percent 1-year mortality rate), permanent disability, and medical and institutional care costs than all other osteoporotic fractures combined (Cummings et al. 1985; Rankin 1993). By age 90, about one-third of women and about one-sixth of men will have sustained a hip fracture.

In both men and women, the development of osteoporosis may be related to three factors: a deficient level of peak bone mass at physical maturity, failure to maintain this peak bone mass during the third and fourth decades of life, and the bone loss that begins during the fourth or fifth decade of life. Physical activity may positively affect all three of these factors.

Physical activity may play a substantial role in the development of bone mass during childhood and adolescence and in the maintenance of skeletal mass

as a young adult. This inference is partly based on findings that athletic young adults have a higher density of bone mineral than sedentary young adults (Kirchner, Lewis, O'Connor 1996; Grimston, Willows, Hanley 1993; Conroy et al. 1993; Nichols et al. 1994; Rubin et al. 1993), on reports that athletes have a differential density of bones according to the sport they train for (Robinson et al. 1995; Heinonen et al. 1995), and on evidence that increase in bone mass in university students is related to higher levels of physical activity (Recker et al. 1992).

Beyond this hypothesized function in youth, physical activity plays a well-established role throughout the life span in maintaining the normal structure and functional strength of bone. Prolonged bed rest or immobility causes rapid and marked reduction in bone mineral density (Krølner et al. 1983; Chesnut 1993; Donaldson et al. 1970). Of particular public health interest is the degree to which physical activity can prevent or slow the bone loss that begins occurring in women as a normal process after menopause. Cross-sectional studies of postmenopausal women have shown that bone mineral density is correlated with muscle strength (Sinaki et al. 1986; Sinaki and Offord 1988), physical activity (Sinaki and Offord 1988; Shimegi et al 1994; Jacobson et al. 1984; Talmage et al. 1986), and cardiorespiratory fitness (Pocock et al. 1986; Chow et al. 1986). Longitudinal studies of postmenopausal women have attributed increases in both cardiorespiratory fitness and bone mass to physical activity (Chow et al. 1987; Dalsky et al. 1988). There is some evidence that through physical activity, osteoporotic women can minimize bone loss or facilitate some gain in bone mineral content (Krølner et al. 1983; Kohrt et al. 1995). However, other studies have failed to show such benefits (Nelson et al. 1991; Sandler et al. 1989; Cavanaugh and Cann 1988). The intensity of the physical activity and the degree to which it stresses the bones may be crucial factors in determining whether bone mass is maintained. Thus it is likely that resistance exercise may have more pronounced effects than endurance exercise, although this has not yet been unequivocally established.

Several investigators have found that the positive effect of physical activity on the bones of both premenopausal and postmenopausal women depends on the presence of estrogen. In postmenopausal women, greater gain in bone density accrues when physical activity and estrogen replacement therapy occur simultaneously (Prince et al. 1991; Kohrt et al. 1995). In young, premenopausal women, however, excessive amounts of vigorous training may lead to a low estrogen level and secondary amenorrhea, with subsequent decreased bone mass and increased risk of stress fractures (Marcus et al. 1985; Drinkwater et al. 1984; Allen 1994).

The exercise-associated changes in bone mineral density observed over time among both premenopausal and postmenopausal women are much less pronounced than those differences observed cross-sectionally between active and sedentary persons (Drinkwater 1993). Cross-sectional studies demonstrate differences of 10–15 percent in bone mineral density at various sites (Aloia et al. 1988; Lane et al. 1986; Michel, Bloch, Fries 1989; Recker et al. 1992), whereas intervention studies show smaller gains of 1–5 percent (Krølner et al. 1983; Dalsky et al. 1988; Nelson et al. 1991; Pruitt et al. 1992; Drinkwater 1993). These differences may be due to differences in comparison groups, to follow-up duration insufficient to show large changes in bone mineral density, or to measurement at different skeletal sites. Still to be conducted are well-designed randomized clinical trials that are of sufficient size and duration to determine definitively the longitudinal effects of physical activity change or the differential effects of resistance and endurance activity on bone mineral density.

Biologic Plausibility

Bone is a dynamic tissue that is constantly remodeling its structure by resorption and formation. Physical activity, through its load-bearing effect on the skeleton, is likely the single most important influence on bone density and architecture (Lanyon 1996). Bone cells respond to mechanical loading by improving the balance between bone formation and bone resorption, which in turn builds greater bone mass (Lanyon 1987, 1993). The higher the load, the greater the bone mass; conversely, when the skeleton is unloaded (as with inactivity), bone mass declines. Glucose-6-phosphate, prostaglandins, and nitric oxide play a role in mediating the mechanical

loading effect on bone (Pitsillides et al. 1995; Turner et al. 1995; Tang et al. 1995). Because it is muscle that exerts the largest forces on bone during physical activity, the role of muscle mass and strength in maintaining skeletal integrity should be explored more fully.

Nonmechanical factors, such as age, hormonal milieu, nutritional intake, and medications, are increasingly being recognized as important determinants of the bone's response to mechanical loading (Lanyon 1996). The relative contributions of each of these factors are currently under study and are not yet clearly delineated. Animal studies confirm a difference in bone response to mechanical loading with age and by estrogen status (Turner, Takano, Owan 1995). The potential clinical relevance of this research is to better define the optimal amount and type of exercise for maintaining or increasing bone mass, particularly with aging or in the absence of estrogen replacement therapy after menopause.

Physical Activity and the Prevention of Fractures and Falling

Studies of physical activity in relation to hip fracture in women have generally found a lower risk of hip fracture among those who were more active. Three cohort studies have reported such a protective effect. One showed a statistically significant protective effect among those reporting the most recreational activity at baseline (Farmer et al. 1989), one showed inverse but not statistically significant associations for both work and leisure-time physical activity (Meyer, Tverdal, Falch 1993), and one showed a significant protective effect of walking for exercise (Cummings et al. 1995). Case-control studies have been more equivocal. One such study found a significant protective effect for two levels of past activity, but for recent activity only moderate amounts of activity showed a significant protective effect (Jaglal, Kreiger, Darlington 1993). Another case-control study showed inconsistent effects across a variety of physical activity classifications (Cumming and Klineberg 1994).

Nonskeletal factors that increase the risk of fractures due to falls include limitations in activities of daily living (e.g., dressing and feeding oneself); compromised gait, balance, reaction time, and muscle strength; impaired vision; medication use; and environmental hazards (Dunn et al. 1992; Gilligan, Checovich, Smith 1993; Tinetti, Speechley, Ginter 1988; Cummings et al. 1995). Various exercises may help prevent falls by improving muscle strength, functional capacity, gait, balance, and reaction time. Tinetti and colleagues (1994) showed a significant decrease in falls in the elderly concomitant with an improvement in balance and gait achieved through exercise. Province and colleagues (1995) demonstrated a protective effect against falls through general exercise and exercises designed to improve balance. Moreover, Fiatarone and colleagues (1994) have shown that even frail elderly persons who have multiple chronic diseases benefit substantially from resistance training. This well-controlled randomized trial demonstrated the importance of strength training in improving stair-climbing power, gait, and other measures of physical function. Moderate exercise-training techniques, such as tai chi chuan, have also been shown to decrease falling and to improve function in older adults by increasing or maintaining aerobic power, strength, and balance (Lai et al. 1995; Wolf et al. 1996; Wolfson et al. 1996).

Conclusions

Physical activity appears to build greater bone mass in childhood and early adolescence and to help maintain peak bone mass in adulthood. Among women after menopause, physical activity may protect against the rapid decline in bone mass, but findings are inconsistent in this regard, and it is unclear whether muscle-strengthening (resistance) activity may be more effective than endurance activity for this purpose. Estrogen replacement therapy has been shown conclusively to decrease bone loss after menopause, and there is evidence that this effect is enhanced with physical activity. However, it is not clear whether physical activity alone, in the absence of estrogen replacement therapy, can prevent bone loss.

Physical activity, including muscle-strengthening (resistance) exercise, appears to be protective against falling and fractures among the elderly, probably by increasing muscle strength and balance.

Obesity

Obesity, a major public health problem in the United States, plays a central role in the development of diabetes mellitus (West 1978) and confers an increased risk for CHD, high blood pressure, osteoarthritis, dyslipoproteinemia, various cancers, and all-cause mortality (Hubert et al. 1983; Bray 1985; Albanes 1987; Lee et al. 1993; Manson et al. 1995). The progressive weight gain often observed between the third and sixth decades of life may be partly explained by age-related changes: although energy intake tends to decline after the second decade of life, this decrease is insufficient to offset the greater decline in the amount of energy that most people expend throughout their adult years (Bray 1983; Federation of American Societies for Experimental Biology 1995). In addition to these age trends, population surveys indicate that the age-adjusted prevalence of overweight among adults in the United States has increased from about 25 percent in the 1970s to 33 percent in 1988–1991 (Kuczmarski et al. 1994). The increase is evident for all race and sex groups. This phenomenon is believed to be due to high rates of inactivity combined with easy access to energy-dense food (Blackburn and Prineas 1983).

Obesity, defined as an excess of adipose tissue, is difficult to measure in population-based studies. Most investigations have therefore either used a relative weight index, such as percent desirable weight (Metropolitan Life Insurance Company 1959), or have used BMI (defined by a ratio of weight to height) as a surrogate measure. Quetelet's index (weight [kg]/height[m]^2) has been the most frequently used BMI. Although these weight-height indices are strongly correlated with more direct measures of adiposity, such as underwater weighing, they have limitations: fatty tissue cannot be distinguished from muscle mass or edema, and associations between weight-height indices and adiposity may be nonlinear or may differ by age or ethnic group (Harrison et al. 1985; Garn, Leonard, Hawthorne 1986; Lillioja and Bogardus 1988). Despite these limitations, BMI has shown a monotonic association with mortality in several recent cohort studies (Lee et al. 1993; Manson et al. 1995; Willett et al. 1995).

Using nationally representative data, the CDC has defined overweight as a Quetelet's index at or above the 85th percentile for 20- to 29-year-olds ($\geq$ 27.3 kg/m^2 for women, $\geq$ 27.8 kg/m^2 for men), corresponding to 120–125 percent of desirable weight (NIH 1985; Kuczmarkski 1992; Kuczmarkski et al. 1994). The 95th percentile of Quetelet's index (32.3 kg/m^2 for women, 31.1 kg/m^2 for men), equivalent to a relative weight of approximately 145 percent, has been used to classify persons as severely overweight. Between 1976 and 1991, the mean weight of U.S. adults increased by 3.6 kg (almost 8 pounds), and 58 million American adults (33 percent) are now considered to be overweight (Kuczmarski et al. 1994).

Because substantial weight loss in adults is difficult to achieve and maintain (Dyer 1994), childhood obesity and its prevention have received increased attention. Overweight children are likely to remain overweight as adolescents and adults (Johnston 1985) and are subsequently at increased risk for high blood pressure, diabetes, CHD, and all-cause mortality (Abraham, Collins, Nordsieck 1971; Nieto, Szklo, Comstock 1992; Must et al. 1992). Moreover, paralleling the trend seen among adults, the prevalence of overweight among U.S. children and adolescents has increased substantially over the past decade (Shear et al. 1988; Troiano et al. 1995).

Physical Activity and Obesity

It is commonly believed that physically active people are less likely to gain weight over the course of their lives and are thus more likely to have a lower prevalence of obesity than inactive people; accordingly, it is also commonly believed that low levels of physical activity are a cause of obesity. Few data, however, exist to evaluate the truth of these suppositions.

Several cross-sectional studies report lower weight, BMI, or skinfold measures among people with higher levels of self-reported physical activity or fitness (DiPietro 1995; Ching et al. 1996; Williamson et al. 1993; French et al. 1994; Folsom et al. 1985; Dannenberg et al. 1989; Slattery et al. 1992; Gibbons et al. 1983; Voorrips et al. 1992). Prospective studies have shown less consistent results. French and colleagues (1994) reported an inverse association between leisure-time physical activity (either walking or engaging in high-intensity activity) and later weight gain, and Ching and colleagues (1996) found that physical activity was inversely related to the risk of becoming overweight. Klesges and colleagues (1992) reported that weight gain was

inversely associated with leisure-time physical activity among women but not among men. Williamson and colleagues (1993), however, found no association between physical activity and subsequent weight change. Williamson and colleagues (1993) and Voorrips and colleagues (1992) proposed that decreases in physical activity may be both a cause and a consequence of weight gain over a lifetime and that multiple measurements over time may be necessary to characterize the interrelationship. One cohort study that assessed changes in physical activity reported that among women, decreased physical activity performed as work was related to weight gain; no associations were found among men (Klesges et al. 1992).

The relationship between physical activity and obesity in children is still under investigation. Some studies comparing obese and nonobese children have shown higher physical activity levels in nonobese children (Johnson, Burke, Mayer 1956; Bullen, Reed, Mayer 1964); others have shown little or no relationship (Stefanik, Heald, Mayer 1959; Bradfield, Paulos, Grossman 1971). Somewhat inconsistent results have also been seen in cross-sectional studies, with several finding lower BMIs or skinfold measures among children with higher levels of physical activity or fitness (Wolf et al. 1993; Obarzanek et al. 1994; Strazzullo et al. 1988; Tell and Vellar 1988) and some smaller studies finding no association (Sallis et al. 1988; LaPorte et al. 1982). More recently, two longitudinal studies have reported inverse relationships between physical activity and triceps skinfold measures (Moore et al. 1995) and BMI (Klesges et al. 1995) in young children. A third longitudinal study (Ku et al. 1981) found a significant negative association between physical activity and percentage of body fat in boys but not in girls. Additional longitudinal studies of children, including measurement of changes in physical activity, will help clarify whether physical activity prevents the development of obesity.

Over the past two decades, several comprehensive review articles (Oscai 1973; Stefanick 1993; Thompson, Jarvie, et al. 1982; Wilmore 1983), as well as two meta-analyses (Ballor and Keesey 1991; Epstein and Wing 1980), have examined the impact of exercise training on body weight and obesity. These reviews conclude that 1) physical activity generally affects body composition and weight favorably by promoting fat loss while preserving or increasing lean mass; 2) the rate of weight loss is positively related, in a dose-response manner, to the frequency and duration of the physical activity session, as well as to the duration (e.g., months, years) of the physical activity program; and 3) although the rate of weight loss resulting from increased physical activity without caloric restriction is relatively slow, the combination of increased physical activity and dieting appears to be more effective for long-term weight regulation than is dieting alone (Brownell and Stunkard 1980; Kayman, Bruvold, Stern 1990).

Independent of its effect on body weight and total adiposity, physical activity may favorably affect fat distribution. Several large cross-sectional studies in Europe (Seidell et al. 1991), Canada (Tremblay et al. 1990), and the United States (Kaye et al. 1990; Slattery et al. 1992; Troisi et al. 1991; Wing et al. 1991) report an inverse association between energy expenditure from physical activity and several indicators of central body fat distribution, such as the waist-to-hip ratio or the waist-to-thigh-circumference ratio.

Biologic Plausibility

Increase in fat mass and the development of obesity occur when energy intake exceeds total daily energy expenditure for a prolonged period (Bray 1983; Leibel, Rosenbaum, Hirsch 1995). Total energy expenditure represents the sum of 1) resting energy expenditure for maintaining basic body functions (approximately 60 percent of total energy requirements); 2) the thermic effect of eating for digestion, absorption, transport, and deposition of nutrients (about 10 percent); and 3) nonresting energy expenditure, primarily in the form of physical activity (about 30 percent) (Leibel, Rosenbaum, Hirsch 1995). This third component, nonresting energy expenditure, is the most variable. Energy balance tilts to weight gain when disproportionately more energy is taken in; theoretically, about one pound (or 0.45 kg) of fat energy is stored for each 3,500 kilocalories of excess energy intake. By increasing nonresting energy expenditure, regular physical activity contributes to weight maintenance and weight reduction. Evidence supports the metabolic and

physiological benefits of incorporating physical activity into programs that prevent or manage obesity (Pi-Sunyer 1988; Leon 1989; Bouchard, Després, Tremblay 1993; DiPietro 1995; Ewbank, Darga, Lucas 1995).

Controversy exists over whether physical activity following a meal increases the thermic effect of food ingestion and whether physical activity before a meal reduces appetite. The evidence suggests that physical activity programs do not necessarily produce a compensatory increase in food intake in obese individuals (Woo, Garrow, Pi-Sunyer 1982a, 1982b). Moreover, daily physical activity may further assist in weight loss by partially reducing the decline in resting energy expenditure that occurs during dieting and associated weight loss (Lennon et al. 1985). This effect is plausible because endurance exercise and strength training may help preserve, to some degree, metabolically active, lean body mass, whereas caloric restriction does not (Hill, Drougas, Peters 1994; Ballor and Keesy 1991).

Because abdominal fat is more responsive than gluteal or lower-body fat to epinephrine stimulation (Wahrenberg, Bolinder, Arner 1991), physical activity may result in a more beneficial redistribution of body fat in both sexes (Bouchard, Després, Tremblay 1993). Further investigation, however, is needed to clarify the associations between gonadal hormone levels, baseline regional fat distribution, and exercise-related changes in weight and body fat distribution.

Conclusions

Physical activity is important for weight control. By using energy and maintaining muscle mass, physical activity is a useful and effective adjunct to dietary management for avoiding weight gain or losing weight. Physical activity appears to favorably affect distribution of body fat.

Mental Health

Mental disorders pose a significant public health burden in the United States. Some disorders, such as depression, are associated with suicide, which is currently the ninth leading cause of death among Americans (NCHS 1996). A major cause of hospitalization and disability, mental disorders cost $148 billion per year, about half of which is due to severe mental illness (National Advisory Mental Health Council 1993).

The annual prevalence of mental disorders in the United States population is high. Nearly three out of 10 persons 15–54 years of age who live in households report having had a mental disorder during the previous year (Regier et al. 1993; Kessler et al. 1994). The most frequently reported disorders are affective (mood) and anxiety disorders. More than one out of 10 adults suffers from a depressive disorder in any given year; between 13 and 17 percent suffer from an anxiety disorder. Women report a higher prevalence of affective and anxiety disorders than do men. Most people with mental disorders do not obtain any professional treatment; only one in five people with a disorder during the previous year has received help from a health service provider.

Mental disorders, mental illnesses, mental health, and psychological well-being relate to such factors as mood or affect, personality, cognition, and perception. Psychological constructs about these factors are interrelated with a person's physical health status and quality of life. In studies of the effects of physical activity on mental health, the most frequently studied outcomes include mood (anxiety, depression, negative affect, and to a lesser extent, positive affect), self-esteem, self-efficacy, and cognitive functioning. The general hypothesis is that people who are physically active or have higher levels of cardiorespiratory fitness have enhanced mood (less negative and greater positive affect), higher self-esteem, greater confidence in their ability to perform tasks requiring physical activity (i.e., greater self-efficacy), and better cognitive functioning than sedentary persons or those who are less physically fit. One National Institutes of Mental Health workshop (Morgan and Goldston 1987) and numerous recent reviews have been devoted to this literature (Brown 1990; LaFontaine et al. 1992; Landers and Petruzzello 1994; Martinsen and Stephens 1994; McAuley 1994; McDonald and Hodgdon 1991; Morgan 1994; North, McCullagh, Tran 1990; Plante and Rodin 1990; Raglin 1990; Sime 1990). The effects of physical activity on most mental disorders—including sleep and eating disorders, schizophrenia, dementia, personality disorders, and substance-related disorders—are not as well studied

(Dishman 1986; Taylor, Sallis, Needle 1985; Martinsen and Stephens 1994).

This section focuses primarily on the association of physical activity with anxiety and depression. Evidence related to other psychological factors, such as positive affect, self-esteem, self-efficacy, and cognitive functioning, is discussed later in this chapter in the "Health-Related Quality of Life" section.

Physical Activity and Mental Health

Epidemiologic research among men and women suggests that physical activity may be associated with reduced symptoms of depression (Ross and Hayes 1988; Stephens 1988; Stephens and Craig 1990; Farmer et al. 1988; Camacho et al. 1991), clinical depression (Weyerer 1992), symptoms of anxiety (Ross and Hayes 1988; Stephens 1988), and improvements in positive affect (Stephens 1988; Stephens and Craig 1990) and general well-being (Stephens 1988). In general, persons who are inactive are twice as likely to have symptoms of depression than are more active persons.

Most epidemiologic and intervention studies on the relationship of physical activity and mental health have used self-report questionnaires to assess symptoms of anxiety and depression among persons from the general population, although some studies have focused on patients diagnosed by clinicians. These questionnaires are useful for identifying persons experiencing mental distress (i.e., symptoms of anxiety or depression), but such identifications do not necessarily correspond to diagnoses of anxiety or depression by clinicians using standard interview criteria (Fechner-Bates, Coyne, Schwenk 1994).

The literature suggests that physical activity helps improve the mental health of both clinical and nonclinical populations. Physical activity interventions have benefited persons from the general population who report mood disturbance (Simons and Birkimer 1988; Wilfley and Kunce 1986), including symptoms of anxiety (Steptoe et al. 1989) and depression (Morgan et al. 1970), as well as patients who have been diagnosed with nonbipolar, nonpsychotic depression (Doyne et al. 1987; Klein et al. 1985; Martinsen, Medhus, Sandvik 1985). These findings are supported by a limited number of intervention studies conducted in community and laboratory settings (Brown 1990; Landers and Petruzzello 1994; Martinsen and Stephens 1994; McAuley 1994; Morgan 1994; Plante and Rodin 1990; Sime 1990). Intervention studies have primarily evaluated the effects of aerobic physical activities, such as brisk walking and running, on mental health; how other forms of physical activity, such as strength training, affect mental health requires further study.

The psychological benefits of regular physical activity for persons who have relatively good physical and mental health are less clear. Some intervention studies have found that physical activity provides mental health benefits to persons recruited from the community who are without serious psychological problems. These benefits included increases in general well-being (Cramer, Nieman, Lee 1991) and reductions in tension, confusion (Moses et al. 1989), and perceived stress and anxiety (King, Taylor, Haskell 1993). Other researchers have found that few (Brown et al. 1995; Blumenthal et al. 1989; King, Taylor, Haskell 1989) or no mental health benefits (Hughes, Casal, Leon 1986; Lennox, Bedell, Stone 1990) occurred among people without mental disorders who participated in physical activity interventions.

Most of these studies involved relatively small sample sizes. Furthermore, the participants had little opportunity to show improvement on objective and standardized mental health measures, since their baseline scores were already in the normal range or lower on measures of negative affect and were in the normal range or higher for positive affect. Even when no change was observed on objective measures, in some of these studies, participants reported feeling a subjective sensation of improved physical, psychological, or social well-being after participating in regular physical activity (Blumenthal et al. 1989; King, Taylor, Haskell 1993).

Psychological assessments that have been used in physical activity research have included state and trait measures. State measures, which reflect how a person feels "right now," are particularly useful in assessing changes in mood that occur before and after an intervention, such as a single episode of physical activity. Trait measures, which evaluate how a person "generally" feels, focus on personality characteristics that tend to be stable or sustained across the life span. Although physical activity training programs can result in sustained psychological

benefits, many people after a single session of physical activity report improvements in transient moods, such as reduced anxiety (Morgan 1979a; Roth 1989), and have temporary reductions in muscular tension (DeVries 1981; DeVries and Adams 1972). The reduction in anxiety may persist for 2 to 6 hours following a session of physical activity (Landers and Petruzzello 1994; Raglin and Morgan 1987). Regular daily physical activity is required to experience this calming effect on an ongoing basis. Some researchers have thus proposed that the episodic mental health benefits associated with physical activity may act as an important preventive measure that could lead to the maintenance of mental health over time (Morgan 1981; Morgan et al. 1980; Raglin 1990).

A number of epidemiologic studies of noninstitutionalized populations have evaluated the associations between self-reported levels of physical activity and mental health. These studies typically assessed retrospective self-reports of leisure-time physical activity during the previous several weeks or more. How these assessments relate to changes in cardiorespiratory fitness is unknown. The available evidence indicates, however, that increases in cardiorespiratory fitness are not necessary for psychological benefits to occur (Brown and Wang 1992; King, Taylor, Haskell 1989; Landers and Petruzzello 1994; Martinsen and Stephens 1994).

Cross-sectional epidemiologic or community population studies support an association between physical activity and psychological well-being in the general population. For example, in one cross-sectional study using data generated from a state telephone survey, researchers determined that adults (n = 401) who spent more time participating in regular exercise, sports, or other physical activities had fewer symptoms of depression and anxiety than persons reporting no physical activity or low levels of participation (Ross and Hayes 1988). These associations were similar for men and women and for older and younger adults. The cause-and-effect relationship, however, cannot be determined because physical activity and mood were measured at the same time.

In another cross-sectional study (Stephens 1988), secondary analyses of two Canadian surveys (n = 23,791 and 22,250 young people and adults) and two U.S. surveys (n = 3,025 and 6,913 adults) conducted between 1971 and 1981 associated physical activity with fewer symptoms of anxiety and depression and with higher positive mood and general well-being. These associations were observed in all four surveys, even though they used different measures of physical activity and mental health, and were strongest among women and among persons aged 40 years or older. However, one of the Canadian surveys found that women manifested higher positive affect when their energy expenditure scores were based on recreational activities only, rather than on a combination of recreational and household activities. Hence, mental health outcomes may depend on the type of physical activities being performed and perhaps on the setting in which they occur. This finding is important in that investigators have typically evaluated the mental health effects of recreational aerobic activities, such as running, rather than occupational and household activities.

A subsequent nationwide Canadian survey (Stephens and Craig 1990) of approximately 4,000 respondents aged 10 years and older found that persons who reported higher levels of total daily leisure-time energy expenditure had a more positive mood than persons reporting lower levels of expenditure. Persons aged 25 years and older demonstrated an inverse relationship between physical activity and symptoms of depression.

Although many cross-sectional studies suggest a positive association between physical activity and mental health, they do not necessarily indicate a cause-and-effect relationship. Persons who have good mental health may simply be more likely to be active. Another possibility is that physical activity and mental health vary together, in which case a third variable, such as chronic health conditions, would mediate this relationship.

Cohort studies provide additional insights into whether physical activity contributes to the primary prevention of mental health problems (Table 4-9). In one cohort study of 1,900 U.S. adults, a cross-sectional analysis of the baseline data revealed an association between depressive symptoms and little or no involvement in physical activity (Farmer et al. 1988). At 8-year follow-up, little or no recreational physical activity was found to be a significant predictor of increased depressive symptoms among white women who had reported few depressive symptoms

Table 4-9. Longitudinal population-based studies of physical activity as related to depressive symptoms

Study	Population	Definition of physical activity	Definition of cancer
Farmer et al. (1988)	NHANES I Follow-up Study participants, white adults, aged 25–77 years, 1975 baseline	Little or no exercise done for recreation at baseline	Depressive symptoms scores of (a) < 16 and (b) ≥ 16 at baseline
Camacho et al. (1991)	Alameda County, CA population study participants aged ≥ 20 years; or ever married, 1965 baseline	Self-reported frequency of involvement in active sports, swimming or walking, daily exercise, and gardening; (low = 0–4, moderate = 5–8, high = 9–14)	Depressive symptoms at 1974 follow-up
Weyerer (1992)	German population study participants aged ≥ 16 years at 1975–1979 baseline	Regular, occasional, or no exercise at baseline based on single question: How often do you currently exercise for sports?	Psychiatric interview assessed depression at follow-up (1980–1984)
Paffenbarger, Lee, Leung (1994)	Harvard alumni study participants, men aged 35–74 years, 1962 or 1966 baseline	(a) ≤ 1hour, 1–2 hours, 3+ hours of sports play/week at baseline (b) < 1,000 kcal, 1,000–2,499 kcal, or 2,500+ kcal/week at baseline	Physician-diagnosed depression at 1988 follow-up

Main findings	Dose response*	Adjustment for confounders and other comments
(a) Men: 1.3 (95% CI, 0.5–3.1) Women: 1.9 (95% CI, 1.1–3.2) (b) Men: 12.9 (95% CI, 1.7–98.9) Women: 2.0 (95% CI, 0.8–14.5)	NA	Odds ratio adjusted for age, education, chronic conditions, employment status, household income, physical activity apart from recreation at baseline, length of follow-up
Relative to high active, low active men: 1.76 (95% CI, 1.06–2.92) moderate active men: 1.46 (95% CI, 0.91–2.34) low active women: 1.70 (95% CI, 1.06–2.70) moderate active women: 1.00 (95% CI, 0.63–1.59)	 Yes No NA NA	Odds ratio adjusted for age, income, race, smoking status, alcohol consumption, relative weight for height, education, chronic conditions, physical symptoms/disability, stress events, isolation, feelings of anomie
Relative to regular exercise, men/no exercise: 1.15 (95% CI, 0.30–4.36) men/occasional exercise: 0.27 (95% CI, 0.03–2.35) women/no exercise: 0.70 (95% CI, 0.30–1.62) women/occasional exercise: 0.65 (95% CI, 0.26–1.61) Total/no exercise: 0.88 (95% CI, 0.44–1.77) Total/occasional exercise: 0.70 (95% CI, 0.30–1.50)	 NA No NA No NA No	Odds ratio adjusted for age, social class, and physical health
Relative to ≤ 1 hour of sports play/week, RR for 1–2 hours = 0.96, RR for 3+ hours = 0.73	Yes	Adjusted for age
Relative to < 1,000 kcal/week, RR for 1,000–2,499 kcal/week = 0.83 RR for 2,500 kcal/week = 0.72	Yes	

Abbreviations: CI = confidence interval; NA = not available; NHANES = National Health and Nutrition Examination Survey; 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.

at baseline. Among white men who had excessive depressive symptoms at baseline, low levels of recreational activity predicted continued depressive symptoms at follow-up.

A cross-sectional analysis (Camacho et al. 1991) of 1965 baseline data on 6,928 U.S. residents revealed an inverse association between physical activity (low, moderate, and high levels of participation in active sports, swimming or walking, doing exercises, or gardening) and depressive symptoms. Follow-up study of the men and women who had few depressive symptoms in 1965 showed that those who had low levels of physical activity were at greater risk than their highly active counterparts for having a high number of depressive symptoms in 1974.

A 23- through 27-year follow-up study of 10,201 Harvard alumni men revealed that level of physical activity reported at an initial interview in 1962 or 1966 was inversely related to self-reported physician-diagnosed depression in 1988 (Paffenbarger, Lee, Leung 1994). Physical activity in 1962 and 1966 was defined as the number of hours per week spent doing physical activities (e.g., golf, gardening, carpentry, tennis, swimming, brisk walking, jogging, or running); from this information, a physical activity index was computed as kilocalories of energy expended per week. In 1988, respondents were asked whether they had ever been told by a physician that they had health problems (e.g., CHD, emphysema), including depression, and to list the year of onset. Incidence of depression was determined by an attack first experienced (at a known age of the respondent) during the follow-up period. This study was unique in that the relationship between physical activity and deaths due to suicides was also evaluated. The incidence of suicide (as identified on death certificates) was largely unrelated to the 1962 or 1966 physical activity history of the college alumni. However, the relative risk of depression was 27 percent lower for men who had reported playing 3 or more hours of sports each week than for men who had reported playing none. In addition, men who had expended 1,000 to 2,499 kilocalories per week and those who had expended 2,500 kilocalories or more per week were at 17 percent and 28 percent less risk for depression, respectively, than men who had expended fewer than 1,000 kilocalories per week.

In a study of rural Europeans (n = 1,536), a cross-sectional association was observed between inactivity (no physical exercise or sports participation) and depression (diagnosed by research psychiatrists) (Weyerer 1992). However, low levels of physical activity at baseline were not a risk factor for depression at 5-year follow-up for men or women in this study.

Two of the epidemiologic studies reviewed above examined a possible dose-response relationship. In one study (Camacho et al. 1991), the baseline prevalence of symptoms of depression was higher for persons reporting low levels of physical activity than for highly active persons; the risk was intermediate for the moderately active group. At follow-up, the incidence of depressive symptoms revealed a significant difference only between persons in the lowest and highest activity groups. In the second study (Paffenbarger, Lee, Leung 1994), an inverse dose-response gradient was found between the baseline self-reported amount of physical activity calculated as kilocalories per week (< 1,000, 1,000–2,499, ≥ 2,500) and the follow-up incidence of physician-diagnosed depression. Men who at baseline had reported no hours of sports play per week had a similar follow-up incidence of depression as men who reported 1 to 2 hours of weekly play; but men who had participated in 3 or more hours of weekly play had a 27 percent lower risk for developing depression than the least active group.

The findings from these two studies provide limited support for a dose-response relationship between levels of physical activity and measures of depressive symptoms or depression. However, among some endurance athletes, mood disturbances (decreased vigor and increased fatigue, anxiety, and symptoms of depression) have been observed with overtraining; mood improved after training was tapered (Morgan et al. 1987). It is therefore conceivable that for the general population, too strenuous a physical activity regimen may lead to deleterious effects on mental health (Morgan 1979b, 1994; Polivy 1994; Raglin 1990). To date, research has not identified a threshold or an optimal frequency, duration, or intensity of physical activity necessary to improve mental health status.

Biologic Plausibility

Some researchers have proposed that exercise-induced changes in brain neuroreceptor concentrations of monoamines (norepinephrine, dopamine, or serotonin) (Ransford 1982) or endogenous opiates (endorphins and enkephalins) (Moore 1982) may help to favorably alter mood. The increased core body temperature that occurs from physical activity may also decrease muscle tension (DeVries 1981). Other hypothalamic, metabolic, hormonal, or cardiorespiratory changes that result from training may eventually be linked to enhanced mental health.

Psychosocial aspects of physical activity, such as having the opportunity for social interaction and support (Hughes, Casal, Leon 1986), experiencing increased feelings of self-mastery and self-efficacy (Simons et al. 1985; Hughes, Casal, Leon 1986), and experiencing relief from daily stressors (Bahrke and Morgan 1978), may improve mental health status in some people.

Conclusions

The literature reported here supports a beneficial effect of physical activity on relieving symptoms of depression and anxiety and on improving mood. There is some evidence that physical activity may protect against the development of depression, although further research is needed to confirm these findings.

Health-Related Quality of Life

For several decades, it has been recognized that health should not be defined simply as the absence of disease and disability; rather, health is now conceptualized by the World Health Organization as a positive state of physical, mental, and social well-being (World Health Organization 1947). This recognition has resulted in an increasing clinical, scientific, and public interest in the assessment and promotion of health-related quality of life (HRQL).

Kaplan and Bush (1982) introduced the term HRQL to capture the influence that health status and health care have on the quality of day-to-day life. Viewed as a multidimensional construct that represents a person's overall satisfaction with life, HRQL includes the following dimensions: cognitive, social, physical, and emotional functioning; personal productivity; and intimacy (Shumaker, Anderson, Czajkowski 1990). Rejeski, Brawley, and Shumaker (1996) have shown that physical activity has significant potential to influence HRQL. The most direct effects are likely in the areas of psychological well-being (e.g., self-concept, self-esteem, mood, and affect), perceived physical function (e.g., perceived ability to perform activities of daily living), physical well-being (e.g., perceived symptoms and perceived physical states, such as dyspnea, pain, fatigue, and energy), and, to a limited extent, cognitive function.

In a recent review, McAuley (1994) concluded that a positive association exists between physical activity habits and self-esteem in both young adults and children. The strength of this relationship increases when physical activity is personally valued and when measures of psychological well-being are specific rather than general. Among nonclinical and clinical samples of men and women, this association is observed both with the long-term effects of exercise training and with the immediate, short-term effects of a single episode of activity.

In a review of studies of middle-aged participants (mean age, 56.7 years), McAuley and Rudolph (1995) found correlations between involvement in physical activity and psychological well-being that were similar to those patterns observed among younger persons. Further, the strength of these relationships was directly related to the length of time that the participants had been involved in physical activity programs. This moderating effect requires cautious interpretation because of the possibility of selective adherence. There was little evidence that the relationship between physical activity and psychological well-being was affected by either sex or age. Finally, although a number of studies noted improvements in both the cardiorespiratory fitness and the psychological well-being of older adults, these improvements were not necessarily correlated (McAuley and Rudolph 1995). Involvement in physical activity may thus increase the psychological well-being of older adults independently of cardiorespiratory fitness (Brown and Wang 1992; King, Taylor, Haskell 1989; Landers and Petruzzello 1994; Martinsen and Stephens 1994; McAuley and Rudolph 1995).

Other data suggest that physical activity is related to perceived improvement in physical function in activities of daily living. However, there is a limit

to this effect, since sedentary people can usually do their daily tasks. Most research on this aspect of HRQL is thus confined to populations of people who, because of health problems, have restrictions in their activities of daily living. The growing body of literature on this topic indicates that patients whose physical function is compromised by heart disease (Ewart 1989) or arthritis (Fisher et al. 1993) experience improved daily function from increases in physical activity.

HRQL requires a number of different types of measurements; however, few studies on physical activity have used a multidimensional measurement scheme. Exceptions include a randomized clinical trial involving healthy elderly persons (Stewart, King, Haskell 1993) and a 2-year observational study of persons with chronic disease (Stewart et al. 1994). In the clinical trial, healthy persons who were assigned to endurance exercise had better self-reported ratings of their physical functioning and health (e.g., physical and role function, experiencing of pain, perception of health status) than control participants, yet endurance training brought no changes in self-reported energy/fatigue, psychological distress, or psychological well-being. By contrast, among persons with chronic diseases, physical activity was associated with improvement in both psychological well-being and physical function; however, the magnitude of these effects was highly dependent on the status of the patient's chronic disease. Participants who have lower levels of mental or physical health may have the most to gain from physical activity (Lennox, Bedell, Stone 1990; Morgan et al. 1970; Simons and Birkimer 1988; Rejeski et al. 1995), since they have more room to improve their health status than people already possessing good health.

A relatively small number of cross-sectional studies have shown a strong positive association between regular physical activity and cognitive and neuropsychological performance on tasks such as math, acuity, and reaction time (Dustman, Emmerson, Shearer 1994; Thomas et al. 1994). However, longer-term training studies (2 or more years) are required to confirm whether aerobic exercise has a pronounced effect on cognitive function. Also unclear are whether the effects of low-intensity physical activity are similar to those of aerobic exercise and whether objective measures of cognitive function can elucidate the perceived cognitive function of participants (Dustman, Emmerson, Shearer 1994).

Conclusions

Physical activity appears to improve psychological well-being. Among people compromised by ill health, physical activity appears to improve their ability to perform activities of daily living.

Adverse Effects of Physical Activity

Although physical activity has numerous health benefits, its potential adverse effects must also be considered. Listing the potential risks associated with physical activity is a straightforward matter. It is much more difficult to determine how commonly they occur among people who are physically active.

Types of Adverse Effects

Musculoskeletal Injuries

Acute stress from sudden forceful movement can cause strains, tears, and even fractures. For example, a vigorous swing of a baseball bat can lead to a dislocated shoulder. An attempt to accelerate forward in tennis can tear an Achilles tendon. Bending to retrieve an object can rupture an intervertebral disc. Injuries like these can result from any activity, exercise, or sport that features sudden movements, such as those that can occur in professional or amateur track and field, racquet sports, basketball, baseball, football, soccer, and golf. Collisions with equipment, other participants, and surfaces can also produce severe injury. Children and adolescents with developing bodies are at special risk of permanent physical damage if injury occurs to the growth plates of long bones or to other bone or connective tissue structures.

Activities that involve repetitive motions, sometimes with traumatic contact with a ground surface or ball, are associated with other musculoskeletal injuries. An extensive literature describes injuries related to jogging and running (Hoeberigs 1992; Rolf 1995; Van Mechelen 1992). Lower-extremity injuries appear to be the most common; of these,

the knee, ankle, and foot have the highest proportions of injuries (e.g., torn cartilage, tendinitis, plantar fasciitis, neuromas, and shinsplints). Injuries are also seen in excessive bicycling (e.g., ulnar nerve palsies, ischial bursitis [Cohen 1993; Mellion 1991; Pfeiffer and Kronisch 1995]), swimming (e.g., shoulder pain [Allegrucci, Whitney, Irrgang 1994; Johnson, Sim, Scott 1987]), racquet sports (e.g., epicondylitis [Kamien 1990]), aerobic dancing (e.g., shin pain and plantar fasciitis [Richie, Kelso, Bellucci 1985]), and rowing (e.g., back and knee injuries [Howell 1984]).

Metabolic Abnormalities

Severe exertion, particularly of prolonged duration and under hot or humid conditions, can lead to hyperthermia, electrolyte imbalance, and dehydration (England et al. 1982; Frizzell et al. 1986; Surgenor and Uphold 1994). Timely fluid intake and replacement, with proper electrolyte and caloric composition, can prevent or ameliorate such metabolic upsets. Hypothermia is a risk in many water sports and for any activities undertaken in cold weather (or even cool weather if inadequate clothing is worn). Extreme endurance training regimens can lead to endocrine system alterations, sometimes resulting in anovulation and amenorrhea in females, in association with a decrease in body weight below a critical lean mass, as well as with a decrease in bone mass (Shangold 1984). Hypoglycemia can occur in people with diabetes if they do not develop a routine of regular activity in conjunction with regular monitoring of their blood sugar (and adjustment of their medication accordingly).

Hematologic and Body Organ Abnormalities

Anemia is reported in athletes vigorously engaged in sports such as long-distance running; hemoglobinuria can occur secondary to breakage of red blood cells during the repetitive impact of distance running, and hematuria can occur when distance running traumatizes the bladder or other structures in the genitourinary system. Rhabdomyolysis, the leakage of contents of muscle cells, can occur as a result of strenuous activity, such as weight lifting or military basic training, and can lead to renal failure (Kuipers 1994; Sinert et al. 1994).

Hazards

Cyclists, runners, and walkers often face risks associated with travel on roadways—collisions with motor vehicles, injuries from falls secondary to uneven surfaces, and attacks by animals or humans. Skiers and skaters must contend with falls at high velocities. Baseball players may be struck by a thrown or batted ball or injured by a spike-soled shoe. Basketball and soccer entail collisions with other players and frequent falls to hard surfaces. Football, hockey, and boxing, by their very nature, are sports where sanctioned and moderately controlled interpersonal violence often leads to contusions, lacerations, musculoskeletal injury, and fractures, as well as to concussions and chronic disability (Kraus and Conroy 1984).

Infectious, Allergic, and Inflammatory Conditions

Swimming increases the risk of otitis externa ("swimmer's ear"). Overtrained athletes may have an increased risk of infections from immunosuppression (Newsholme and Parry-Billings 1994). Exertion may provoke asthmatic attacks, usually occurring after exercise in susceptible individuals (Anderson, Daviskas, Smith 1989).

Cardiac Events

As was discussed earlier in this chapter, regular physical activity improves cardiorespiratory fitness and reduces the risk of CVD mortality over the long term, although it can acutely increase risk for untoward cardiac events in the short term. Persons with compromised coronary circulation may develop angina or acute myocardial infarction during vigorous activity (Mittleman et al. 1993; Willich et al. 1993). Arrythmias may be precipitated by a combination of exertion and underlying heart disease, and some can lead to sudden death (Kohl et al. 1992; Koplan 1979; Siscovick et al. 1984; Thompson, Funk, et al. 1982). Compared with sedentary people who suddenly begin exercising vigorously, persons who exercise regularly have a lower risk of exercise-related sudden death, although even this group has a transient elevation of risk during and immediately after vigorous exercise (Kohl et al. 1992; Siscovick et al. 1984). Nonetheless, the net effect of regular physical activity is to decrease the risk of cardiac death.

Occurrence of Adverse Effects

Determining the incidence or prevalence of adverse effects of physical activity, or factors that influence the likelihood of their occurrence, is hampered by not knowing how many people have similar physical activity patterns and are thus similarly at risk of an adverse event, or how many inactive people sustain similar injuries. Nevertheless, a few studies have provided some insight into the occurrence of adverse events. Of the activities that are common in the United States, including jogging/running, walking, gardening, bicycling, swimming, aerobic dance, and softball, running has received the most attention by researchers.

Injuries among runners are common, ranging from 25 through 65 percent (Jones, Cowan, Knapik 1994). Most running-related injuries involve the leg and foot and are usually self-correcting in a relatively short time. Studies of such injuries have generally shown that occurrence of musculoskeletal injury is directly related to mileage run (Blair, Kohl, Goodyear 1987; Hoeberigs 1992; Koplan et al. 1982; Macera 1992; Macera et al. 1989; Marti 1988; Marti et al. 1988; Walter et al. 1989) or to frequency or duration of running (Pollock et al. 1977). Previous injury appears to be a risk factor for subsequent injury. In one small study of people aged 70–79 years, the injury rate was lower for walking than jogging (5 percent vs. 57 percent) (Pollock et al. 1991). Whether this finding is true only among the elderly or is characteristic of these activities at all ages remains to be determined.

Although few studies of aerobic dance have been conducted, the injury rate appears to be higher among those taking more than 4 classes per week (Richie, Kelso, Bellucci 1985).

Conclusions

A wide spectrum of adverse events can occur with physical activity, ranging from those that cause minor inconvenience to those that are life-threatening. At least some of the musculoskeletal injuries are likely to be preventable if people gradually work up to a physical activity goal and avoid excessive amounts of physical activity or excessively high levels of intensity. Although adverse cardiac events are more likely to occur with physical exertion, the net effect of regular physical activity is a lower CVD mortality rate among active than inactive people (see earlier sections of this chapter).

People should be advised not to undertake physical activities well beyond their normal level of exertion. Inactive people wishing to begin a new program of moderate activity should begin with short durations and gradually lengthen them toward their target. Men over age 40 and women over age 50 who wish to begin a new program involving vigorous-intensity activity, people who have preexisting health problems, and people who are at high risk of CVD should consult a physician before embarking on a program of physical activity to which they are unaccustomed (ACSM 1991).

Nature of the Activity/Health Relationship

Causality

The studies reviewed in this chapter indicate that physical activity is associated with a reduction in risk of all-cause mortality, all CVDs combined, CHD, hypertension, colon cancer, and NIDDM. To evaluate whether the information presented is sufficient to infer that these associations are causal in nature, it is useful to review the evidence according to Hill's classic criteria for causality (Hill 1965; Paffenbarger 1988).

Strength of Association. The numerous estimated measures of association for cardiovascular outcomes presented in this chapter generally fall within the range of a 1.5- to 2.0-fold increase in risk of adverse health outcomes associated with inactivity. This range represents a moderately strong association, similar in magnitude to the relationship between CHD and smoking, hypertension, or elevated cholesterol. The associations with NIDDM, hypertension, and colon cancer have been somewhat smaller in magnitude. The difficulty in measuring physical activity may lead to substantial misclassification, which in turn would bias studies toward finding less of an effect of activity than may actually exist. On the other hand, not controlling for all potential confounders could bias studies toward finding more of an effect than may actually exist. Efforts to stratify studies of physical activity and CHD by the quality of

measurement have found that the methodologically better studies showed larger associations than those with lower quality scores (Powell et al. 1987; Berlin and Colditz 1990). In addition, cardiorespiratory fitness, which is more objectively and precisely measured than the reported level of physical activity, often is also more strongly related to CVD and mortality. Measures of association between physical activity and health outcomes thus might be stronger if physical activity measurements were more accurate.

Consistency of Findings. Although the epidemiologic studies of physical activity have varied greatly in methodology, in ways of classifying physical activity, and in populations studied, the findings have been remarkably consistent in supporting a reduction in risk as a function of greater amounts of physical activity, or conversely, an increase in risk as a function of inactivity.

Temporality. For most of the health conditions included in this chapter (all-cause mortality, CVD, CHD, hypertension, NIDDM), longitudinal data from cohort studies have been available and have confirmed a temporal sequence in which physical activity patterns are determined prior to development of disease. For obesity and mental health, fewer longitudinal studies have been conducted, and findings have been more equivocal. Perhaps the strongest evidence for temporality comes from two studies of the effect of changes in activity or fitness level. Men who became more active or more fit had a lower mortality rate during follow-up than men who remained inactive or unfit (Paffenbarger et al. 1993; Blair et al. 1995).

Biological Gradient. Studies of all-cause mortality, CVD, CHD, and NIDDM have shown a gradient of greater benefit associated with higher amounts of physical activity. Most studies that included more than two categories of amount of physical activity and were therefore able to evaluate a dose-response relationship found a gradient of decreasing risk of disease with increasing amounts of physical activity (see Tables 4-1 through 4-8).

Biologic Plausibility. Evidence that physiologic effects of physical activity have beneficial consequences for CHD, NIDDM, and obesity is abundant (see Chapter 3, as well as the biologic plausibility sections of this chapter). Such evidence includes beneficial effects on physiologic risk factors for disease, such as high blood pressure and blood lipoproteins, as well as beneficial effects on circulatory system functioning, blood-clotting mechanisms, insulin production and glucose handling, and caloric balance.

Experimental Evidence. Controlled clinical trials have not been conducted for the outcomes of mortality, CVD, cancer, obesity, or NIDDM. However, randomized clinical trials have determined that physical activity improves these diseases' risk factors, such as blood pressure, lipoprotein profile, insulin sensitivity, and body fat.

The information reviewed in this chapter shows that the inverse association between physical activity and several diseases is moderate in magnitude, consistent across studies that differed substantially in methods and populations, and biologically plausible. A dose-response gradient has been observed in most studies that examined more than two levels of activity. For most of the diseases found to be inversely related to physical activity, the temporal sequence of exposure preceding disease has been demonstrated. Although controlled clinical trials have not been conducted (and are not likely to be conducted) for morbidity and mortality related to the diseases of interest, controlled trials have shown that activity can improve physiologic risk factors for these diseases. From this large body of consistent information, it is reasonable to conclude that physical activity is causally related to the health outcomes reported here.

Population Burden of Sedentary Living

Given that the relationship between activity and several diseases is likely to be causal, it follows that a large number of Americans unnecessarily become ill or die each year because of an inactive way of life. Published estimates of the number of lives lost in a year because of inactivity have ranged from 200,000 for inactivity alone to 300,000 for inactivity and poor diet combined (Hahn et al. 1990; Powell and Blair 1994; McGinnis and Foege 1993). Such estimates are generally derived by calculating the population attributable risk (PAR), which is based on both the relative mortality rate associated with inactivity and the prevalence of inactivity in the population. Such estimates are inherently uncertain because they do

not take into account the reality that some people have more than one risk factor for a disease; for these people, the elimination of a single risk factor (e.g., by becoming physically active) may not reduce mortality risk to the level attainable for people who initially have only that one risk factor. PAR methods thus overestimate the proportion of deaths avoidable by eliminating one modifiable risk factor, in this case physical inactivity. On the other hand, PAR estimates of avoidable mortality do not address other important aspects of the population burden of sedentary living. The benefits of reducing the occurrence of CHD, colon cancer, and diabetes greatly surpass the benefits of reducing premature mortality, yet the reductions in avoidable disease, disability, suffering, and health care costs have not been calculated. Similarly, the health benefits of improved mood, quality of life, and functional capacity have not been quantified. Although the total population burden of physical inactivity in the United States has not been quantified, sedentary living habits clearly constitute a major public health problem.

Dose

Using the epidemiologic literature to derive recommendations for how much and what kind of physical activity a person should obtain is problematic, in part because the methods for measuring and classifying physical activity in epidemiologic studies are not standardized. Measurement of physical activity generally relies on self-reported information in response to questionnaires, although some studies use occupation to categorize a person's presumed level of physical activity at work. Responses to questions or occupational activity categories are usually transformed, using a variety of methods, into estimates of calories expended per week, minutes of activity per week, categories of total activity, or other types of composite scores.

Numerous studies have used this type of information to estimate total amount of activity, and many have been able to explore dose-response relationships across categories of activity amount. For the most part, these studies demonstrate that amount of benefit is directly related to amount of physical activity (see Tables 4-1 through 4-8), rather than showing a threshold level of activity necessary before health benefits accrue. Such studies are less helpful, however, in assessing the relationship of health benefits to intensity of physical activity (i.e., how hard one must work during the activity itself) because few studies have separately measured or analyzed levels of intensity while taking into account the other dimensions of activity (e.g., frequency, duration, total caloric expenditure). As described earlier, however, for some health benefits (e.g., blood pressure lowering), clinical trials of exercise intensity suggest similar, if not greater, benefit from moderate- as from vigorous-intensity exercise.

It is often asked how little physical activity a person can obtain and still derive health benefit. Although the dose-response relationship appears not to have a lower threshold, thereby indicating that any activity is better than none, some quantitation of a target "dose" of activity is helpful for many people. It has been shown that total amount of physical activity (a combination of intensity, frequency, and duration) is related to health outcomes in a dose-response fashion, but the absolute difference in amount of physical activity in kilocalories of energy expended between exposure categories has not been estimated routinely. Several studies, however, have estimated average caloric expenditure for the activity categories studied and thus allow quantitation of amount of physical activity associated with improved health outcomes. Paffenbarger and colleagues (1986) found that compared with the least active group in the study, those who expended 71–143 kilocalories of energy per day had a 22 percent reduction in overall mortality, and those who expended 143–214 kilocalories per day had a 27 percent reduction. Leon and colleagues (1987) showed that a difference of about 30 minutes per day of activity (light, moderate, and vigorous activity combined), equivalent to an average difference of about 150 kilocalories of energy expended per day, was associated with a 36 percent lower risk of CHD mortality and a 27 percent lower risk of all-cause death, after the analysis adjusted for other factors that can effect CHD and total mortality. Slattery and colleagues (1989) found that a daily average of 73 more kilocalories of total activity than were expended among the least active group was associated with a 16 percent reduction in CHD mortality and a 14 percent reduction in all-cause mortality. Furthermore, in the majority (62 percent)

of that study population, no vigorous activity was reported. In that group, a daily average of 150 kilocalories greater expenditure in light-to-moderate activity was associated with a 27 percent lower CHD mortality and a 19 percent lower total mortality. The effects of light-to-moderate activity on CHD death remained significant after the analysis adjusted for potential confounders. Similarly, in a study of NIDDM (Helmrich et al. 1991) that showed a significant inverse trend between kilocalories expended in activity and development of NIDDM, total activity of 140–215 kilocalories per day was associated with a 21 percent reduction in NIDDM onset. In the group that obtained this level of energy expenditure without any vigorous sports participation, the reduction in NIDDM onset was 13 percent.

Based on these studies, it is reasonable to conclude that activity leading to an increase in daily expenditure of approximately 150 kilocalories/day (equivalent to about 1,000 kilocalories/week) is associated with substantial health benefits and that the activity does not need to be vigorous to achieve benefit. It should be emphasized that this is an estimate based on few studies, and that further research will be required to refine it. For example, it is not clear whether it is the total amount of caloric expenditure or the amount of caloric expenditure per unit of body weight that is important. Nonetheless, this amount of physical activity can be obtained in a variety of ways and can vary from day to day to meet the needs and interests of the individual. An average expenditure of 150 kilocalories/day (or 1,000 kilocalories/week) could be achieved by walking briskly for 30 minutes per day, or by a shorter duration of more vigorous activity (e.g., 15 minutes of running at 10 minutes per mile), or by a longer duration of more vigorous activity less frequently (e.g., running at 10 minutes per mile for about 35 minutes 3 times per week). Other sample activities are provided in Table 4-10.

In addition to the health effects associated with a moderate amount of physical activity, the dose-response relationships show that further increases in activity confer additional health benefits. Thus people who are already meeting the moderate activity recommendation can expect to derive additional benefit by increasing their activity. Since amount of activity is a function of intensity, frequency, and duration, increasing the amount of activity can be accomplished by increasing any, or all, of those dimensions.

There is evidence that increasing physical activity, even after years of inactivity, improves health. Studies of the health effects of increasing physical activity or fitness (Paffenbarger et al. 1993; Blair et al. 1995) have shown a reduced mortality rate in men who become more active or more fit compared with those who remain sedentary. This benefit was apparent even for men who became physically active after the age of 60.

Most importantly, a regular pattern of physical activity must be maintained to sustain the physiologic changes that are assumed responsible for the health benefits (see Chapter 3). Thus it is crucial for each person to select physical activities that are sustainable over the course of his or her life. For some people, a vigorous workout at a health club is the most sustainable choice; for others, activities integrated into daily life (e.g., walking to work, gardening and household chores, walking after dinner) may be a more sustainable option. Periodic reevaluation may be necessary to meet changing needs across the life span.

A related issue of pattern of physical activity (frequency and duration in the course of a day) has recently come under review. Three studies have held constant both total amount of activity and intensity of activity while daily pattern was varied (one long session versus shorter, more frequent sessions). Two studies showed equivalent increases in cardiorespiratory fitness (Jakicic et al. 1995; Ebisu 1985). One study showed gains in cardiorespiratory fitness for both the "short bout" and "long bout" groups, although on one of three measures (maximal oxygen uptake versus treadmill test duration and heart rate at submaximal exercise), the gain in fitness was significantly greater in the long bout group (DeBusk et al. 1990). These observations give rise to the notion that intermittent episodes of activity accumulated in the course of a day may have cardiorespiratory fitness benefits comparable to one longer continuous episode. Whether this assumption holds true for the outcomes of disease occurrence and death remains to be determined. Nevertheless, some previous observational studies have shown lower rates of CHD, CVD, and all-cause mortality among people with an active

Table 4-10. Duration of various activities to expend 150 kilocalories for an average 70 kg adult

Intensity	Activity	Metabolic equivalents METs*	Approximate duration in minutes†
Moderate	Volleyball, noncompetitive	3.0	43
Moderate	Walking, moderate pace (3 mph, 20 min/mile)	3.5	37
Moderate	Walking, brisk pace (4 mph, 15 min/mile)	4.0	32
Moderate	Table tennis	4.0	32
Moderate	Raking leaves	4.5	32
Moderate	Social dancing	4.5	29
Moderate	Lawn mowing (powered push mower)	4.5	29
Hard	Jogging (5 mph, 12 min/mile)	7.0	18
Hard	Field hockey	8.0	16
Very hard	Running (6 mph, 10 min/mile)	10.0	13

*Based on average METs in Ainsworth et al. 1993.

†Formula: $\frac{150 \text{ kcal} \times 60 \text{ min/hour}}{\text{METs (kcal/kg/hr)} \times \text{kg}} = \text{minutes}$

lifestyle that included activities such as walking, stair climbing, household or yard work, and gardening—activities that are often performed intermittently (Leon et al. 1987; Paffenbarger et al. 1986). This information, together with evidence that some people may adhere better to an exercise recommendation that allows for accumulating short episodes of activity as an alternative to one longer episode per day (Jakicic et al. 1995), supports the notion that accumulation of physical activity throughout the day is a reasonable alternative to setting aside an uninterrupted period of time for physical activity each day. Although more research is clearly needed to better define the differential effects of various patterns of activity, experts have agreed that intermittent episodes of activity are more beneficial than remaining sedentary. This consensus is reflected in recent physical activity recommendations from the CDC and the ACSM (Pate et al. 1995) and from the NIH Consensus Development Panel on Physical Activity and Cardiovascular Disease (see Chapter 2, Appendix B).

Conclusions

The findings reviewed in this chapter form the basis for concluding that moderate amounts of activity can protect against several diseases. A greater degree of protection can be achieved by increasing the amount of activity, which can be accomplished by increasing intensity, frequency, or duration. Nonetheless, modest increases in physical activity are likely to be more achievable and sustainable for sedentary people than are more drastic changes, and it is sedentary people who are at greatest risk for poor health related to inactivity. Thus the public health emphasis should be on encouraging those who are inactive to become moderately active. These conclusions are consistent with the recent CDC-ACSM recommendations for physical activity (Pate et al. 1995) and the NIH Consensus Development Conference Statement on Physical Activity and Cardiovascular Health (see Chapter 2, Appendix B), which emphasize the importance of obtaining physical activity of at least moderate amount on a regular basis. The recommendations also encourage those

who are already moderately active to become more active to achieve additional health benefits, by increasing the intensity, duration, or frequency of physical activity. Further study is needed to determine which combinations of these interrelated factors are most important for specific health benefits. Most important, however, is the recognition that physical activity recommendations should be tailored to an individual's needs and preferences. Encouraging sedentary people to become moderately active is likely to reduce the burden of unnecessary suffering and death only if the activity can be sustained on a daily basis for many years.

Chapter Summary

Despite the variety of methods used to measure and classify physical activity, the imprecision of these measures, and the considerable variation in study designs and analytic sophistication, several findings consistently emerge from the epidemiologic literature on physical activity and health. Physical activity of the type that improves cardiorespiratory endurance reduces the risk of developing or dying from CVD (CHD in particular), hypertension, colon cancer, and NIDDM and improves mental health. Findings are highly suggestive that endurance-type physical activity may reduce the risk of developing obesity, osteoporosis, and depression and may improve psychological well-being and quality of life. There is promising evidence that muscle strengthening (resistance) exercise reduces the risk of falling and fractures among the elderly. Furthermore, there appears to be a dose-response relationship between physical activity and disease prevention: higher levels of activity appear to have the most benefit, but lower levels have demonstrable benefits for some diseases as well. For the U.S. population, in which the majority of people are sedentary or only minimally active, achievable increases in physical activity of a moderate amount, including some resistance exercise to strengthen muscle, are likely to substantially improve the health and quality of life of many people.

Conclusions

Overall Mortality

1. Higher levels of regular physical activity are associated with lower mortality rates for both older and younger adults.
2. Even those who are moderately active on a regular basis have lower mortality rates than those who are least active.

Cardiovascular Diseases

1. Regular physical activity or cardiorespiratory fitness decreases the risk of cardiovascular disease mortality in general and of coronary heart disease (CHD) mortality in particular. Existing data are not conclusive regarding a relationship between physical activity and stroke.
2. The level of decreased risk of CHD attributable to regular physical activity is similar to that of other lifestyle factors, such as keeping free from cigarette smoking.
3. Regular physical activity prevents or delays the development of high blood pressure, and exercise reduces blood pressure in people with hypertension.

Cancer

1. Regular physical activity is associated with a decreased risk of colon cancer.
2. There is no association between physical activity and rectal cancer. Data are too sparse to draw conclusions regarding a relationship between physical activity and endometrial, ovarian, or testicular cancers.
3. Despite numerous studies on the subject, existing data are inconsistent regarding an association between physical activity and breast or prostate cancers.

Non–Insulin-Dependent Diabetes Mellitus

1. Regular physical activity lowers the risk of developing non–insulin-dependent diabetes mellitus.

Osteoarthritis

1. Regular physical activity is necessary for maintaining normal muscle strength, joint structure, and joint function. In the range recommended for health, physical activity is not associated with joint damage or development of osteoarthritis and may be beneficial for many people with arthritis.
2. Competitive athletics may be associated with the development of osteoarthritis later in life, but sports-related injuries are the likely cause.

Osteoporosis

1. Weight-bearing physical activity is essential for normal skeletal development during childhood and adolescence and for achieving and maintaining peak bone mass in young adults.
2. It is unclear whether resistance- or endurance-type physical activity can reduce the accelerated rate of bone loss in postmenopausal women in the absence of estrogen replacement therapy.

Falling

1. There is promising evidence that strength training and other forms of exercise in older adults preserve the ability to maintain independent living status and reduce the risk of falling.

Obesity

1. Low levels of activity, resulting in fewer kilocalories used than consumed, contribute to the high prevalence of obesity in the United States.
2. Physical activity may favorably affect body fat distribution.

Mental Health

1. Physical activity appears to relieve symptoms of depression and anxiety and improve mood.
2. Regular physical activity may reduce the risk of developing depression, although further research is required on this topic.

Health-Related Quality of Life

1. Physical activity appears to improve health-related quality of life by enhancing psychological well-being and by improving physical functioning in persons compromised by poor health.

Adverse Effects

1. Most musculoskeletal injuries related to physical activity are believed to be preventable by gradually working up to a desired level of activity and by avoiding excessive amounts of activity.
2. Serious cardiovascular events can occur with physical exertion, but the net effect of regular physical activity is a lower risk of mortality from cardiovascular disease.

Research Needs

1. Delineate the most important features or combinations of features of physical activity (total amount, intensity, duration, frequency, pattern, or type) that confer specific health benefits.
2. Determine specific health benefits of physical activity for women, racial and ethnic minority groups, and people with disabilities.
3. Examine the protective effects of physical activity in conjunction with other lifestyle characteristics and disease prevention behaviors.
4. Examine the types of physical activity that preserve muscle strength and functional capacity in the elderly.
5. Further study the relationship between physical activity in adolescence and early adulthood and the later development of breast cancer.
6. Clarify the role of physical activity in preventing or reducing bone loss after menopause.

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