Is physical activity or physical fitness more important in defining health benefits?

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ABSTRACT

BLAIR, S. N., Y. CHENG, and J. S. HOLDER. Is physical activity or physical fitness more important in defining health benefits? *Med. Sci. Sports Exerc.*, Vol. 33, No. 6, Suppl., 2001, pp. S379–S399. **Purpose:** We addressed three questions: 1) Is there a dose-response relation between physical activity and health? 2) Is there a dose-response relation between cardiorespiratory fitness and health? 3) If both activity and fitness have a dose-response relation to health, is it possible to determine which exposure is more important? **Methods:** We identified articles by PubMed search (restricted from 1/1/90 to 8/25/00) using keywords related to physical activity, physical fitness, and health. An author scanned titles and abstracts of 9831 identified articles. We included for thorough review articles that included three or more categories of activity or fitness and a health outcome and excluded articles on clinical trials, review papers, comments, letters, case reports, and nonhuman studies. We used an evidence-based approach to evaluate the quality of the published data. **Results:** We summarized results from 67 articles meeting final selection criteria. There is good consensus across studies with most showing an inverse dose-response gradient across both activity and fitness categories for morbidity from coronary heart disease (CHD), stroke, cardiovascular disease (CVD), or cancer; and for CVD, cancer, or all-cause mortality. **Conclusions:** All studies reviewed were prospective observational investigations; thus, conclusions are based on Evidence Category C. 1) There is a consistent gradient across activity groups indicating greater longevity and reduced risk of CHD, CVD, stroke, and colon cancer in more active individuals. 2) Studies are compelling in the consistency and steepness of the gradient across fitness groups. Most show a curvilinear gradient, with a steep slope at low levels of fitness and an asymptote in the upper part of the fitness distribution. 3) It is not possible to conclude whether activity or fitness is more important for health. Future studies should define more precisely the shape of the dose-response gradient across activity or fitness groups, evaluate the role of musculoskeletal fitness, and investigate additional health outcomes. **Key Words:** EPIDEMIOLOGY, MORTALITY, CARDIOVASCULAR DISEASE, CANCER, DIABETES, LONGITUDINAL STUDY

Physical activity and physical fitness are closely related in that physical fitness is mainly, although not entirely, determined by physical activity patterns over recent weeks or months. Genetic contributions to fitness are important but probably account for less of the variation observed in fitness than is due to environmental factors, principally physical activity (14). For most individuals, increases in physical activity produce increases in physical fitness, although the amount of adaptation in fitness to a standard exercise dose varies widely and is under genetic control. Thus, at one level the topic of this report reverts to the oft-considered question of the relative importance of nature versus nurture. Consensus has perhaps never been achieved in response to this nature-nurture issue in other contexts, but we will attempt to delimit and define the question addressed in this report so that many, if not most, can find some concepts or issues with which they can agree.

We considered the general case of health-related behaviors and health-related fitness as they relate to health outcomes (Fig. 1). Several examples, but not an exhaustive list, of health-related behaviors are shown on the left side of the figure. These behaviors, singly or in concert, are important determinants of the several components of health-related fitness listed in the middle of the figure. The fitness variables are important determinants of various health outcomes, and several specific biological mechanisms have been elucidated to confirm the causal relation of fitness variables to health. Just as for cardiorespiratory fitness, all of the fitness variables have genetic components but also are strongly influenced by environmental factors. For example, the blood lipid profile has a genetic component, but diet is of great importance. For most of these associations a critical issue is the genetic-environmental interactions that determine specific fitness levels. That is, a diet high in sodium may be especially important in hypertension risk in those with a genetic proclivity for salt sensitivity. Note also that for nonfatal health outcomes, there often may be a feedback loop whereby an outcome may influence one or more health behaviors.

The material presented in this review is used to address three specific questions:

1) Is there a dose-response relation between physical activity and health outcomes?

2) Is there a dose-response relation between cardiorespiratory fitness and health outcomes?

3) If both physical activity and cardiorespiratory fitness have a dose-response relation to health outcomes, is there a difference in the outcome gradient across categories for the

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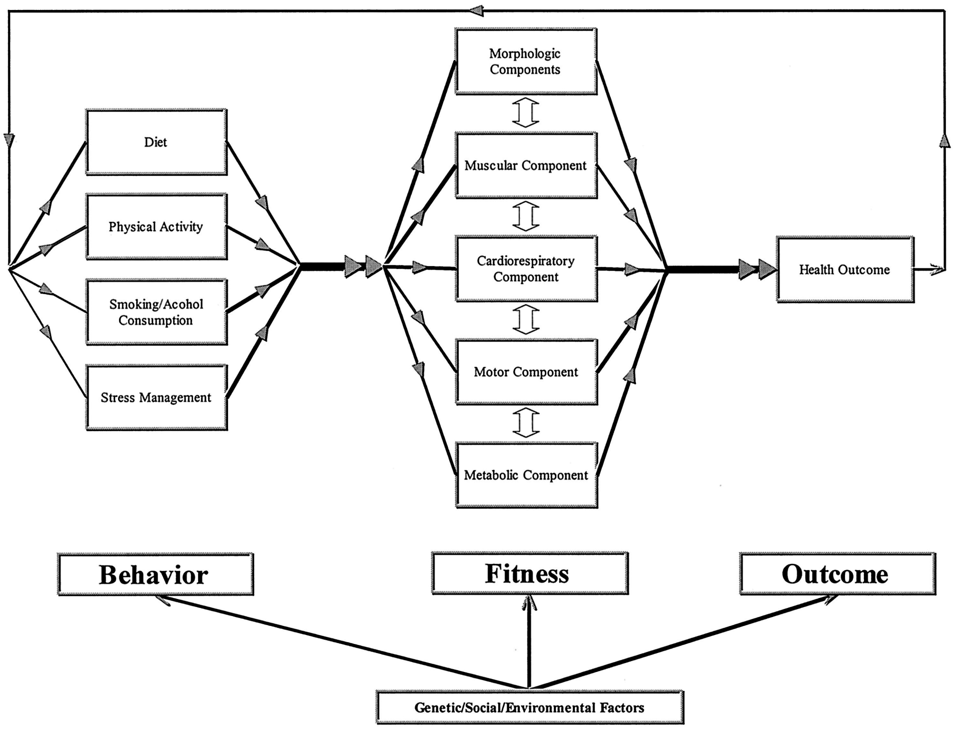

FIGURE 1—Interrelationships between health behaviors, various types of fitness, and health outcomes. Numerous health behaviors influence, singly or in concert, several different components of fitness—which in turn affect various health outcomes. Genetic, social, and environmental factors influence behaviors, fitness, and outcomes. Health outcomes can also influence behaviors.

two exposures, and is it possible to determine from the available data which exposure is more important for health?

METHODS

We first defined the exposure and outcome variables and delimited the scope of our review. We use the basic terminology presented by Howley in the introductory paper in this supplement, with some additional, more detailed specifications of some of the terms.

Exposure variables. Exposure variables for this report are physical activity and physical fitness. Physical activity in this report refers to either leisure-time physical activity or occupational activity, and we will not attempt to distinguish between these subtypes of activity. The physical fitness component addressed here is cardiorespiratory fitness, which was determined in the studies reviewed for this report by submaximal or maximal exercise tests of work performance rather than measured maximal oxygen uptake. These work performance tests, at least the maximal tests, correlate highly with measured maximal oxygen uptake (55,56).

Outcome variables. Health variables constitute the outcome variables for this report. We agree with the general definitions of health summarized by Howley, and that health is a multidimensional characteristic. Health is a diffuse and perhaps even an elusive concept and often presents a challenge to health researchers. We chose not to select various clinical measures, such as lipids, blood pressure, or body composition as outcomes, because these variables will be topics of other reports in this supplement. We also did not select one of the global definitions of health that includes physical, social, and psychological dimensions, such as those presented by Howley. These broad definitions are useful in philosophical considerations of health in broad terms, but they typically have not been used as outcome measures in research on physical activity or fitness. Therefore, we chose to examine the dose-response association of activity and fitness on major physical health outcomes, which is where there are sufficient studies. Specifically, we selected two types of health measures as the outcome variables for this report:

1) morbidity from major chronic diseases such as coronary heart disease (CHD), stroke, combined cardiovascular disease, or cancer, and

2) cardiovascular disease (CVD), cancer, or all-cause mortality.

We did not include diabetes, hypertension, or other chronic diseases as outcomes for this report. The tables,

TABLE 1. Process for identifying material included in review.

Performed PubMed computer search using keywords related to physical activity (physical activity, exercise, exertion), physical fitness (fitness, exercise tolerance, exercise test), and health outcomes (morbidity, mortality). Restricted the search from 1990 to August 25, 2000. (Because of the limited numbers of papers, search for physical fitness includes papers from the 1980s.) Computer search identified papers with at least one of the exposures (activity or fitness) and at least one of the health outcomes, and the initial search results were:

Physical activity and health	Physical fitness and health	Activity, fitness, and health
7335 papers	2706 papers	2213 papers

An author reviewed each of the papers identified above and applied selection criteria:
- Included papers with three or more levels of activity or fitness
- Excluded clinical trials, review papers, comments, letters, case reports, and non-human studies
- Selection process yielded final group of papers for thorough review

Activity and health	Fitness and health	Activity, fitness, and health
49 papers	9 papers	9 papers

TABLE 2. Physical activity and morbidity and mortality.

Study	Population/Design	Physical Activity Assessment	Adjusted for	Outcome	Summary of Results
Lee et al., 2000 (40)	N = 13,485 men Observational cohort study	Physical activity questionnaire: assessed number of blocks walked, flights of stairs climbed, and sports/recreation participation Categories in kJ·wk^{-1} for summed energy expenditure (1) $<$4200 (2) 4200–$<$8400 (3) 8400–$<$12,600 (4) 12,600–$<$16,800 (5) $\geq$16,800 **Categories in kJ·wk^{-1} for light, moderate, or vigorous energy activities (I) $<$630 (II) 630–$<$1680 (III) 1680–$<$3150 (IV) 3150–$<$6300 (V) $\geq$6300	Age, Quetelet's index, smoking, alcohol, and early parental death	All-cause mortality 2539 deaths	Adjusted RR (95% CI) Total energy expenditure (1) 1.0 (referent) (2) 0.80 (0.72–0.88) (3) 0.74 (0.65–0.83) (4) 0.80 (0.69–0.93) (5) 0.73 (0.64–0.84) Trend $P < 0.001$ Light activities ($<$4 METs) (**kJ·wk^{-1}) (I) 1.0 (referent) (II) 0.91 (0.74–1.12) (III) 0.93 (0.71–1.22) (IV) 1.07 (0.79–1.46) (V) 1.17 (0.83–1.64) Trend $P = 0.72$ Moderate activities (4–$<$6 METs) (**kJ·wk^{-1}) (I) 1.0 (referent) (II) 1.05 (0.90–1.23) (III) 0.89 (0.75–1.05) (IV) 0.82 (0.70–0.96) (V) 0.97 (0.85–1.10) Trend $P = 0.07$ Vigorous activities ($\geq$6 METs) (**kJ·wk^{-1}) (I) 1.0 (referent) (II) 0.89 (0.77–1.02) (III) 0.82 (0.70–0.96) (IV) 0.82 (0.71–0.96) (V) 0.77 (0.67–0.89) Trend $P = <0.001$
Andersen et al., 2000 (3)	N = 11,947 women and 10,650 men (20–93 yr) Observational cohort study	Self-reported physical activity Categories of leisure-time physical activity: 1 (sedentary) to 3 + 4 (most active) Levels 3 + 4 were analyzed together since the number of subjects and deaths in the most physically active in leisure time was limited	Age, systolic blood pressure, smoking, and other risk factors	All-cause mortality Men: 3259 deaths Women: 2458 deaths	Adjusted RR (95% CI) Men (1) 1.0 (referent) (2) 0.72 (0.66–0.78) (3 + 4) 0.71 (0.65–0.78) Women (1) 1.0 (referent) (2) 0.65 (0.60–0.71) (3 + 4) 0.59 (0.52–0.67)
Bijnen et al., 1999 (8)	N = 472 elderly Dutch men Observational cohort study Surveys taken in 1985 and 1990	Self-reported physical activity Categories based on tertiles of time spent on physical activity: (1) Low (2) Middle (3) High	Age, disease, functional status, and lifestyle factors adjusted in 1990	All-cause mortality 118 deaths	Adjusted RR (95% CI) All-cause (based on 1985 survey) (1) 1.0 (referent) (2) 1.25 (0.79–1.99) (3) 1.25 (0.73–2.12) Trend $P = 0.39$ All-cause (based on 1990 survey) (1) 1.0 (referent) (2) 0.56 (0.35–0.89) (3) 0.44 (0.25–0.80) Trend $P < 0.01$
Wannamethee et al., 1998 (72)	N = 4311 men Observational cohort study	Self-reported physical activity questionnaires in 1978–80 or 1992 measuring regular walking or cycling, recreational activity, or vigorous sports activity Categories of physical activity: (1) Inactive or occasionally active (2) Light (3) Moderate (4) Moderately vigorous/vigorous	Age, smoking, social class, body-mass index, and self-perception of health	All-cause and CVD mortality 219 deaths 93 CVD deaths	Adjusted RR (95% CI) All-cause (1) 1.0 (referent) (2) 0.61 (0.43–0.86) (3) 0.50 (0.31–0.79) (4) 0.65 (0.45–0.94) CVD (1) 1.0 (referent) (2) 0.61 (0.36–1.04) (3) 0.36 (0.16–0.80) (4) 0.65 (0.37–1.14)
Weller and Corey, 1998 (73)	N = 6620 Canadian women $>$ 30 yr of age Observational cohort study	Self-reported leisure and nonleisure time physical activities Categories of physical activity 1 (lowest) to 4 (highest)	Age	CVD and all-cause mortality 449 deaths 159 CVD deaths	Adjusted RR (95% CI) All-cause (1) RR = 1.0 (2) 0.86 (0.66–1.13) (3) 0.68 (0.51–0.91) (4) 0.73 (0.54–1.00) Trend $P = 0.03$ CVD (1) 1.0 (referent) (2) 1.01 (0.68–1.51) (3) 0.70 (0.44–1.11) (4) 0.51 (0.28–0.91) Trend $P = 0.01$

TABLE 2. *Continued*

Study	Population/Design	Physical Activity Assessment	Adjusted for	Outcome	Summary of Results
Bijnen et al., 1998 (7)	N = 802 Dutch men (64 to 84 yr at baseline) Observational cohort study	Self-reported physical activity Categories based on tertiles of time spent on physical activity (1) Low (2) Middle (3) High	Age, disease, and lifestyle factors	CVD, stroke, and all-cause mortality 373 deaths 199 CVD deaths 47 stroke deaths	Adjusted RR (95% CI) All-cause (1) 1.0 (referent) (2) 0.80 (0.63–1.02) (3) 0.77 (0.59–1.00) Trend P = 0.04 CVD (1) 1.0 (referent) (2) 0.75 (0.54–1.04) (3) 0.70 (0.48–1.01) Trend P = 0.04 Stroke (1) 1.0 (referent) (2) 0.65 (0.33–1.25) (3) 0.55 (0.24–1.26) Trend P = 0.12
Kujala et al., 1998 (34)	N = 7925 healthy men, and 7977 healthy women (25–64 yr) Observational twin cohort study	Self-reported leisure time physical activity Categories of leisure time physical activity (1) Sedentary (2) Occasional exercisers (3) Conditioned exercisers	Age and sex	All-cause mortality 1253 deaths Men: 829 Women: 424	Adjusted RR (95% CI) Overall all-cause mortality (1) 1.0 (referent) (2) 0.71 (0.62–0.81) (3) 0.57 (0.45–0.74) Trend $P < 0.001$ Twins healthy at baseline and discordant for death (1) 1.0 (referent) (2) 0.66 (0.46–0.94) (3) 0.44 (0.23–0.83) Trend P = 0.005
Kushi et al., 1997 (35)	N = 40,417 postmenopausal Iowa women (55–69 yr at baseline) Observational cohort study with 7 yr of follow-up	Self-reported physical activity Categories of physical activity include (1) Low (2) Medium (3) High	Age and other risk factors	All-cause mortality 2260 deaths	Adjusted RR (95% CI) Age-adjusted (1) 1.0 (referent) (2) 0.66 (0.60–0.73) (3) 0.58 (0.52–0.65) Trend $P < 0.001$ Multivariate-adjusted (1) 1.0 (referent) (2) 0.77 (0.69–0.86) (3) 0.68 (0.60–0.77) Trend $P < 0.001$
Morgan and Clark, 1997 (49)	N = 635 women and 406 men $\geq$65 yr Observational cohort study	Self-reported customary physical activity: outdoor productive activities, indoor productive activities, walking, shopping, and leisure time activities Categories of physical activity (1) Low (2) Middle (3) High		All-cause mortality Men: 247 deaths Women: 321 deaths	Adjusted RR (95% CI) Men (1) 1.59 (1.12–2.29) (2) 1.35 (0.96–1.89) (3) 1.0 (referent) Women (1) 2.07 (1.53–2.79) (2) 1.53 (1.12–2.09) (3) 1.0 (referent)
Folsom et al., 1997 (21)	N = 7852 biracial women and 6188 biracial men 45–64 yr Multicenter observational cohort study	Physical activity questionnaire Categories of physical activity are represented as quartiles (Q1 = low to Q4 = high) determined by index score on the questionnaire	Age, race, smoking, systolic blood pressure, education level, field center, and other risk factors	CHD incidence and all-cause mortality Men: 260 deaths and 223 CHD cases Women: 181 deaths and 97 CHD cases	Adjusted RR (95% CI) All-cause mortality Men Q1 1.0 (referent) Q2 0.81 (0.59–1.11) Q3 0.85 (0.57–1.26) Q4 0.63 (0.44–0.91) Trend P = 0.02 Women Q1 1.0 (referent) Q2 0.79 (0.54–1.17) Q3 1.05 (0.68–1.64) Q4 0.55 (0.35–0.86) Trend P = 0.04 CHD Incidence Men Q1 1.0 (referent) Q2 0.96 (0.67–1.37) Q3 0.70 (0.44–1.13) Q4 0.76 (0.51–1.13) Trend P = 0.08 Women Q1 1.0 (referent) Q2 0.74 (0.43–1.27) Q3 0.85 (0.44–1.64) Q4 0.56 (0.30–1.06) Trend P = 0.12

TABLE 2. *Continued*

Study	Population/Design	Physical Activity Assessment	Adjusted for	Outcome	Summary of Results
Haapanen et al., 1997 (25)	$N = 842$ men and 953 women 35–63 yr Observational cohort study	Self-reported leisure time physical activity Categories of physical activity based on index score from physical activity questionnaire (1) Low (2) Moderate (3) High	Age, smoking	CHD incidence Men: 108 cases Women: 75 cases	Adjusted RR (95% CI) CHD incidence Men (1) 1.98 (1.22–3.23) (2) 1.33 (0.78–2.27) (3) 1.0 (referent) Trend $P = 0.014$ Women (1) 1.25 (0.72–2.15) (2) 0.73 (0.38–1.39) (3) 1.0 (referent) Trend $P = 0.178$
Mensink et al., 1996 (48)	$N = 7689$ men and 7747 women 25–69 yr Observational cohort study	Self-reported leisure time physical activity Categories of physical activity (1) Low (2) Moderate (3) High	Age, BMI, smoking, systolic blood pressure, and other risk factors	All-cause and CVD mortality Men: 67 deaths 34 CVD deaths Women: 48 deaths 17 CVD deaths	Adjusted RR (95% CI) All-cause Men (1) 1.0 (referent) (2) 0.56 (0.30–1.04) (3) 0.78 (0.42–1.44) Women (1) 1.0 (referent) (2) 1.24 (0.60–258) (3) 1.29 (0.58–2.85) CVD Men (1) 1.0 (referent) (2) 0.38 (0.15–0.97) (3) 0.80 (0.34–1.85) Women (1) 1.0 (referent) (2) 3.20 (0.68–15.07) (3) 2.83 (0.54–14.80)
Kaplan et al., 1996 (32)	$N = 6131$ men and women Observational cohort study	Self-reported leisure time physical activity Physical activity categories divided into tertiles 1-Low activity 2-Moderate activity 3-High activity		All-cause and CVD mortality Men: 639 deaths 321 CVD deaths Women: 587 deaths 388 CVD deaths	All-cause Men Crude death rate/1000 py Tertile 1 24.68 Tertile 2 11.37 Tertile 3 7.59 Women Crude death rate/1000 py Tertile 1 18.03 Tertile 2 7.66 Tertile 3 3.88 CVD Men Crude death rate/1000 py Tertile 1 13.13 Tertile 2 5.87 Tertile 3 2.98 Women Crude death rate/1000 py Tertile 1 15.11 Tertile 2 3.46 Tertile 3 1.14
Haapanen et al., 1996 (24)	$N = 1072$ men Observational cohort study	Self-reported leisure time physical activity Categories of physical activity based on estimated energy expenditure ($kcal \cdot wk^{-1}$) (1) 0–800 (2) 800.1–1500 (3) 1500.1–2100 (4) >2100	Age, disease, and other risk factors	All-cause and CVD mortality 168 deaths 93 CVD deaths	Adjusted RR (95% CI) All-cause (1) 2.74 (1.46–5.14) (2) 1.10 (0.55–2.21) (3) 1.74 (0.87–3.50) (4) 1.0 (referent) Trend $P < 0.001$ CVD (1) 3.58 (1.45–8.85) (2) 0.99 (0.34–2.87) (3) 1.59 (0.56–4.49) (4) 1.0 (referent) Trend $P < 0.001$
Lee et al., 1995 (38)	$N = 17{,}321$ men Observational cohort study from 1962 to 1988	Self-reported physical activity on a mail-back questionnaire Physical activity divided into vigorous (requiring ≥ 6 METs) or nonvigorous (requiring < 6 METs) Physical activity levels further divided based on estimated energy expenditure ($kJ \cdot wk^{-1}$) (1) <630 (2) $630 < 1680$ (3) $1680 < 3150$ (4) $3150 < 6300$ (5) ≥ 6300	Age, smoking, and other risk factors	All-cause mortality 3728 deaths	Adjusted RR (95% CI) Vigorous activities (1) 1.0 (referent) (2) 0.88 (0.82–0.96) (3) 0.92 (0.82–1.02) (4) 0.87 (0.77–0.99) (5) 0.87 (0.78–0.97) Trend $P = 0.007$ Nonvigorous activities (1) 1.0 (referent) (2) 0.89 (0.79–1.01) (3) 1.00 (0.89–1.12) (4) 0.98 (0.88–1.12) (5) 0.92 (0.82–1.02) Trend $P = 0.36$

TABLE 2. *Continued*

Study	Population/Design	Physical Activity Assessment	Adjusted for	Outcome	Summary of Results
Rodriguez et al., 1994 (58)	N = 7074 Japanese-American men Observational cohort study	Self-reported physical activity Physical activity levels in tertiles (1) Low (2) Middle (3) High	Age, smoking, and other risk factors	CHD incidence and mortality 340 CHD deaths 789 CHD cases	Adjusted RR (95% CI) CHD mortality (1) 1.0 (referent) (2) 1.19 (0.93–1.53) (3) 0.85 (0.65–1.13) CHD incidence (1) 1.0 (referent) (2) 1.07 (0.90–1.26) (3) 0.95 (0.80–1.14)
Shaper and Wannamethee, 1991 (61)	N = 5714 men 40–59 yr without prior IHD Observational cohort study	Self-reported physical activity Scores based on frequency, type, and intensity of physical activity divided in the following categories (1) Inactive (2) Occasional (3) Light (4) Moderate (5) Moderately vigorous (6) Vigorous	Age, body mass index, social class, and smoking status **adjusted for additional risk factors (SBP, total cholesterol, HDL cholesterol, breathlessness, FEV, and heart rate)	Ischemic heart disease 488 cases of ischemic heart disease	Adjusted RR (95% CI) (1) 1.0 (referent) (2) 0.80 (0.50–1.20) (3) 0.80 (0.50–1.20) (4) 0.40 (0.20–0.80) (5) 0.40 (0.20–0.80) (6) 0.80 (0.40–1.40) **Adjusted for additional risk factors (1) 1.0 (referent) (2) 0.90 (0.50–1.30) (3) 0.90 (0.60–1.40) (4) 0.50 (0.20–0.80) (5) 0.50 (0.30–0.90) (6) 0.90 (0.50–1.80)
Lindsted et al., 1991 (46)	N = 9484 Seventh-day Adventist men Observational cohort study from 1960 to 1985	Self-reported physical activity Physical activity levels (1) Low (2) Moderate (3) High	Race, smoking, education, BMI, medical illness, marital status, and dietary pattern	All-cause CVD, and cancer mortality 3799 deaths 2137 CVD deaths 655 cancer deaths	Adjusted RR (95% CI) All-cause Age 50 (1) 1.0 (referent) (2) 0.61 (0.50–0.74) (3) 0.66 (0.50–0.87) 60 (1) 1.0 (referent) (2) 0.68 (0.59–0.78) (3) 0.76 (0.63–0.92) 70 (1) 1.0 (referent) (2) 0.76 (0.69–0.83) (3) 0.89 (0.78–1.01) 80 (1) 1.0 (referent) (2) 0.85 (0.78–0.92) (3) 1.03 (0.91–1.16) 90 (1) 1.0 (referent) (2) 0.94 (0.84–1.06) (3) 1.19 (0.99–1.43) CVD Age 50 (1) 1.0 (referent) (2) 0.57 (0.42–0.77) (3) 0.68 (0.45–1.02) 60 (1) 1.0 (referent) (2) 0.65 (0.53–0.81) (3) 0.78 (0.59–1.04) 70 (1) 1.0 (referent) (2) 0.75 (0.65–0.86) (3) 0.90 (0.75–1.07) 80 (1) 1.0 (referent) (2) 0.86 (0.77–0.96) (3) 1.03 (0.88–1.21) 90 (1) 1.0 (referent) (2) 0.98 (0.84–1.15) (3) 1.18 (0.93–1.51) Cancer Age 50 (1) 1.0 (referent) (2) 0.65 (0.42–1.01) (3) 0.75 (0.42–1.30) 60 (1) 1.0 (referent) (2) 0.78 (0.58–1.06) (3) 0.93 (0.63–1.35) 70 (1) 1.0 (referent) (2) 0.94 (0.76–1.17) (3) 1.15 (0.88–1.52) 80 (1) 1.0 (referent) (2) 1.13 (0.89–1.44) (3) 1.43 (1.02–2.00) 90 (1) 1.0 (referent) (2) 1.36 (0.95–1.95) (3) 1.78 (1.08–2.95)

TABLE 2. *Continued*

Study	Population/Design	Physical Activity Assessment	Adjusted for	Outcome	Summary of Results
Morris et al., 1990 (50)	N = 9376 male civil servants Observational cohort study	Self-reported leisure time physical activity Group 4 (no vigorous aerobic activity) to Group 1 (much vigorous aerobic activity)	Age, smoking, family history, stature, BMI, and "subclinical" CVD	CHD mortality 109 CHD deaths in ages 45–54 178 CHD deaths in ages 55–64	Adjusted RR (95% CI) Ages 45–54 Group 4 1.0 (referent) Group 3 1.41 (0.83–2.40) Group 2 1.98 (1.03–3.78) Group 1 0.25 (0.07–0.93) Ages 55–64 Group 4 1.0 (referent) Group 3 0.90 (0.57–1.44) Group 2 0.59 (0.34–1.05) Group 1 0.53 (0.21–1.32)
Physical activity and cancer					
Verloop et al., 2000 (70)	N = 1836 women Case-control study	Self-reported activities at age 10–12 yr and 13–15 yr, lifetime recreational activity, and title of longest held job Compare total physical activity at ages 10–12 yr and 13–15 yr with activity of their peers (1) less active (2) equally active (3) more active Lifetime physical activities (I) not active (II) moderate active: all recreational activity other than extreme activities (III) extreme active: more than 2 times/wk, duration > 11 yr, intensity > 5.5 MET score	Age, region, education, family history, benign breast disease, smoking habit, parity, parous, alcohol consumption, age at menarche, menstrual complaints, premenstrual complaints, BMI	Breast cancer morbidity 918 cases	Adjusted OR (95% CI) Activity compared with that of peer group at age 10–12 yr (1) 1.0 (referent) (2) 0.82 (0.61–1.09) (3) 0.68 (0.49–0.94) Activity compared with that of peer group at age 13–15 yr (1) 1.0 (referent) (2) 0.81 (0.61–1.07) (3) 0.77 (0.57–1.05) Lifetime recreational activities (I) 1.0 (referent) (II) 0.70 (0.56–0.89) (III) 0.60 (0.38–0.93)
Srivastava et al., 2000 (64)	N = 463 men Case-control study	Self-reported recreational and occupational physical activity. Moderate and strenuous levels not explicitly defined, but examples of activities such as "gardening" or "brisk walking" given for moderate activity; for strenuous activity, a minimum period of 20 min was specified Levels of recreational physical activity (1) < once/month (2) 1–3 times/month (3) 1–2 times/week (4) 3–5 times/week (5) >5 times/week Levels of occupational activity (1) Sitting (2) Light (3) Moderate (4) Strenuous	Age, BMI, marital status, education, smoking, vegetable consumption, fruit consumption	Testicular cancer morbidity 212 cases	Adjusted OR (95% CI) Recreational physical activity 2 previous yr Moderate / Strenuous (1) 1.0 (referent) / 1.0 (referent) (2) 1.68 (0.70–4.04) / 1.50 (0.77–2.90) (3) 1.06 (0.48–2.34) / 1.19 (0.64–2.23) (4) 1.42 (0.64–3.17) / 1.09 (0.57–2.09) (5) 1.41 (0.61–3.29) / 1.18 (0.52–2.65) Activity in teenage years Moderate / Strenuous (1) 1.0 (referent) / 1.0 (referent) (2) combine (3) / 1.94 (0.66–5.74) (3) 1.15 (0.54–2.44) / 2.04 (0.83–5.04) (4) 1.77 (0.88–3.53) / 2.07 (0.91–4.72) (5) 2.36 (1.20–4.64) / 2.58 (1.14–5.85) Activity in early 30s Moderate / Strenuous (1) 1.0 (referent) / 1.0 (referent) (2) 1.13 (0.44–2.89) / 1.37 (0.67–2.79) (3) 1.22 (0.51–2.91) / 1.20 (0.60–2.37) (4) 1.34 (0.56–3.22) / 1.21 (0.58–2.53) (5) 1.74 (0.68–4.42) / 1.27 (0.52–3.10) Occupational physical activity 2 previous yr (1) 1.0 (referent) (2) 1.32 (0.73–2.37) (3) 0.98 (0.55–1.75) (4) 0.94 (0.46–1.90) Activity in early 20s (1) 1.0 (referent) (2) 1.30 (0.71–2.39) (3) 1.85 (1.05–3.26) (4) 1.67 (0.92–3.00) Activity in early 30s (1) 1.0 (referent) (2) 0.99 (0.51–1.94) (3) 1.46 (0.77–2.78) (4) 1.30 (0.60–2.78)

TABLE 2. *Continued*

Study	Population/Design	Physical Activity Assessment	Adjusted for	Outcome	Summary of Results
Rockhill et al., 1999 (57)	N = 121,701 women Observational cohort study	Self-reported recreational physical activity Activity level (h·wk^{-1}) (1) <1 (2) 1.0–1.9 (3) 2.0–3.9 (4) 4.0–6.9 (5) ≥7	Age, BMI, age at menarche, benign breast disease, family history, parity, age at first birth, menopausal status, postmenopausal hormone use	Breast cancer morbidity and mortality 3137 cases	Adjusted RR (95% CI) Cumulative measurement averages / Baseline (1980 only) (one-time) (1) 1.0 (referent) / 1.0 (referent) (2) 0.88 (0.79–0.98) / 1.03 (0.90–1.17) (3) 0.89 (0.81–0.99) / 0.97 (0.88–1.07) (4) 0.85 (0.77–0.94) / 0.90 (0.80–1.01) (5) 0.82 (0.70–0.97) / 0.89 (0.80–0.98) Trend P = 0.004 / P = 0.004
Bergstrom et al., 1999 (5)	N = 674,025 men and 253,336 women Observational cohort study	Self-reported occupational physical activity Physical activities divided into 4 groups according to occupational code (1) Sedentary (2) Light (3) Medium (4) Very high/high	Age, socioeconomic status, place of residence, calendar year of follow-up	Renal cell cancer morbidity Men: 2704 cases Women: 587 cases	Adjusted RR (95% CI) Men / Women (1) 1.25 (1.02–1.53) / 0.80 (0.51–1.27) (2) 1.16 (0.99–1.36) / 1.01 (0.76–1.35) (3) 1.11 (0.97–1.27) / 0.99 (0.77–1.29) (4) 1.0 (referent) / 1.0 (referent) Trend P = 0.03 / P > 0.50
Lee et al., 1999 (43)	N = 13,905 men Observational cohort study	Self-reported physical activity Total energy expenditure at baseline physical activity levels (kJ·wk^{-1}): (1) <4200 (2) 4200–8399 (3) 8400–12,599 (4) ≥12,600 For sports or recreational activities, energy expenditure from light (<4.5 METs) and at least moderate intensity (≥4.5 METs) activities physical activity levels (kJ·wk^{-1}) (I) none (II) 1–1049 (III) 1050–2519 (IV) 2520–5879 (V) ≥5880	Age, smoking habit, BMI	Lung cancer morbidity and mortality 245 cases	Adjusted RR (95% CI) Total physical activities (1) 1.0 (referent) (2) 0.87 (0.64–1.18) (3) 0.76 (0.52–1.11) (4) 0.61 (0.41–0.89) Trend test: P = 0.008 <4.5 METs / ≥4.5 METs (I) 1.0 (referent) / 1.0 (referent) (II) 1.20 (0.79–1.83) / 0.84 (0.58–1.22) (III) 0.92 (0.57–1.48) / 0.64 (0.39–1.04) (IV) 0.81 (0.50–1.32) / 0.93 (0.62–1.39) (V) 0.99 (0.66–1.48) / 0.60 (0.38–0.96) Trend P = 0.62 / P = 0.046
Tang et al., 1999 (66)	N = 179 men and 137 women Case-control study	Self-reported leisure time physical activity The MET scoring system for physical activity level (1) Sedentary, 0 MET h·wk^{-1} (2) Moderate, 1–<20 MET h·wk^{-1} (3) Active, ≥20 MET h·wk^{-1}	Age, smoking habits, water intake, alcohol consumption, dietary habit	Colon or rectal cancer morbidity Men: 92 cases Women: 71 cases	Adjusted OR (95% CI) Colon cancer Men / Women (1) 1.0 (referent) / 1.0 (referent) (2) 2.22 (0.68–7.21) / 0.52 (0.13–2.03) (3) 0.19 (0.05–0.77) / 0.63 (0.18–2.18) Trend P = 0.03 / P = 0.48 Rectal cancer Men / Women (1) 1.0 (referent) / 1.0 (referent) (2) 1.48 (0.43–5.09) / 1.21 (0.42–3.46) (3) 0.44 (0.13–1.49) / 0.84 (0.28–2.46) Trend P = 0.24 / P = 0.74
Martinez et al., 1997 (47)	N = 89,448 women Observational cohort study	Self-reported recreational physical activity MET-h·wk^{-1} score (1) <2 (2) 2–4 (3) 4–10 (4) 11–21 (5) >21	Age, smoking history, family history, BMI, postmenopausal hormone use, aspirin use, intake of red meat, alcohol consumption	Colon cancer morbidity and mortality 396 cases	Adjusted RR (95% CI) (1) 1.0 (referent) (2) 0.71 (0.44–1.15) (3) 0.78 (0.50–1.20) (4) 0.67 (0.42–1.07) (5) 0.54 (0.33–0.90) Trend P = 0.03
Thune et al., 1997 (68)	N = 53,242 men and 28,274 women Observational cohort study	Self-reported occupational and recreational physical activity Occupational physical activities were categorized as (1) Mostly sedentary work (2) Work with much walking (3) Work with much lifting and walking (4) Heavy manual work Recreational activities categorized as (I) Reading, watching TV, or other sedentary activities (II) Walking, bicycling, or physical activities for at least 4 h·wk^{-1} (III) Exercise to keep fit, participating in recreational athletics, etc., for at least 4 h·wk^{-1}, regular hard training, or participation in competitive sports several times a week	Age, geographical region, smoking habits, BMI	Lung cancer morbidity Men: 402 cases Women: 51 cases	Adjusted RR (95% CI) Occupational physical activity Men / Women (1) 1.0 (referent) / 1.0 (referent) (2) 1.15 (0.90–1.47) / 0.81 (0.37–1.76) (3) 1.13 (0.87–1.47) / 0.79 (0.30–2.12) (4) 0.99 (0.70–1.41) / — Trend P = 0.71 / P = 0.30 Recreational physical activity Men / Women (I) 1.0 (referent) / 1.0 (referent) (II) 0.75 (0.60–0.94) / 0.91 (0.48–1.71) (III) 0.71 (0.52–0.97) / 0.99 (0.35–2.78) Trend P = 0.01 / P = 0.88

TABLE 2. *Continued*

Study	Population/Design	Physical Activity Assessment	Adjusted for	Outcome	Summary of Results
Thune et al., 1996 (67)	N = 53,242 men and 28,274 women Observational cohort study	Self-reported occupational and recreational physical activity Same scales for recreational and occupational activities as above reference Total physical activity levels (combined recreational and occupational) (1) Sedentary: R1+O1–2 (2) Moderate: R1+O3–4, O1+R3–4 (3) Active: O2–4+R2–4.	Age, BMI, serum cholesterol, and geographic region	Colon or rectal cancer morbidity Men: 496 cases Women: 153 cases	Adjusted RR (95% CI) Colon cancer and total physical activity Men / Women (1) 1.0 (referent) / 1.0 (referent) (2) 1.18 (0.76–1.82) / 0.97 (0.33–2.77) (3) 0.97 (0.63–1.50) / 0.63 (0.39–1.04) Trend P = 0.49 / P = 0.04 Rectal cancer and total physical activity Men / Women (1) 1.0 (referent) / 1.0 (referent) (2) 1.24 (0.73–2.08) / 0.96 (0.33–2.77) (3) 1.20 (0.72–2.02) / 1.27 (0.59–2.72) Trend P = 0.63 / P = 0.45
White et al., 1996 (74)	N = 484 men and 387 women Case-control study	Self-reported recreational and occupational activities Total recreational physical activity (episodes/week) (1) 0 (2) <1 (3) 1–<2 (4) 2–<4 (5) ≥4 Total occupational physical activity (h·wk^{-1}) Men / Women (I) <10 / 0 (II) 10.0-<20.0 / <13.5 (III) 20-<35.0 / ≥13.5 (IV) ≥35	Age	Colon cancer morbidity Men: 251 cases Women: 193 cases	Adjusted RR (95% CI) Total recreational physical activity Men / Women (1) 1.0 (referent) / 1.0 (referent) (2) 0.81 (0.45–1.44) / 0.94 (0.60–1.47) (3) 0.53 (0.30–0.94) / 0.77 (0.50–1.19) (4) 0.57 (0.33–1.00) / 0.57 (0.39–0.85) (5) 0.67 (0.40–1.11) / 0.83 (0.57–1.22) Trend P = 0.03 / P = 0.04 Total occupational physical activity Men / Women (I) 1.0 (referent) / 1.0 (referent) (II) 1.03 (0.61–1.75) / 1.26 (0.76–2.07) (III) 1.04 (0.63–1.71) / 1.00 (0.60–1.65) (IV) 0.86 (0.52–1.42) / — Trend P = 0.57 / P = 0.97
Bernstein et al., 1994 (6)	N = 1090 women Case-control study	Self-reported physical activities Physical activity levels (h·wk^{-1}) (1) none (2) 0.1–0.7 (3) 0.8–1.6 (4) 1.7–3.7 (5) ≥3.8	Age at menarche, age at first full-term pregnancy, number of full-term pregnancies, months of lactation, family history, Quetelet's index at reference date, total months of oral contraceptive use up to the reference date	Breast cancer morbidity 545 cases	Adjusted OR (95% CI) Overall activity (1) 1.0 (referent) (2) 0.95 (0.64–1.41) (3) 0.65 (0.45–0.96) (4) 0.80 (0.54–1.17) (5) 0.42 (0.27–0.64) Trend P = 0.0001 Activity within 10 years after menarche (1) 1.0 (referent) (2) 0.93 (0.63–1.38) (3) 0.78 (0.52–1.19) (4) 0.69 (0.45–1.05) (5) 0.70 (0.47–1.06) Trend P = 0.027
Dorgan et al., 1994 (15)	N = 2307 women Observational cohort study	Self-reported physical activity Physical activity index Sleep and rest = 1.0 Sedentary = 1.1 Slight = 1.5 Moderate = 2.4 Heavy = 5.0 Physical activity levels: 1–4 quartiles from lowest to highest	Age, age at first pregnancy, education, occupation, alcohol consumption	Breast cancer morbidity 117 cases	Adjusted RR (95% CI) Physical activity index by quartile (1) 1.0 (referent) (2) 1.2 (0.7–2.1) (3) 1.3 (0.7–2.4) (4) 1.6 (0.9–2.9)
Sturgeon et al., 1993 (65)	N = 702 women Case-control study	Self-reported physical activity (1) Inactive (2) Average (3) Active	Age, study area, education, parity, years use of oral contraceptives, years use of menopausal estrogens, smoking habits, BMI	Endometrial cancer morbidity 405 cases	Adjusted OR (95% CI) Recreational / Nonrecreational (1) 1.2 (0.7–2.0) / 2.0 (1.2–3.1) (2) 1.0 (0.6–1.5) / 1.2 (0.8–2.0) (3) 1.0 (referent) / 1.0 (referent)
Levi et al., 1993 (44)	N = 846 women Case-control study	Self-reported physical activity (1) Very low (2) Moderately low (3) Moderately high (4) High	Age, study center, education, parity, menopausal status, use of oral contraceptives and estrogen replacement treatment, BMI, estimated total calorie intake	Endometrial cancer morbidity 274 cases	Adjusted OR (95% CI) Sports and leisure activity (1) 1.9 (0.9–4.0) (2) 1.0 (0.5–2.3) (3) 1.0 (0.5–2.4) (4) 1.0 (referent) Trend P < 0.01 Occupational activity (1) 1.5 (1.0–2.2) (2) 1.0 (0.5–2.2) (3) 1.1 (0.5–2.3) (4) 1.0 (referent) Trend P < 0.05

TABLE 2. *Continued*

Study	Population/Design	Physical Activity Assessment	Adjusted for	Outcome	Summary of Results
Shu et al., 1993 (62)	N = 536 women Case-control study	Self-reported occupational and recreational physical activities Physical activity levels (kcal·d^{-1}) (1) ≤1833 (2) 1833–2126 (3) 2126–2463 (4) ≥2463	Age	Endometrial cancer morbidity 268 cases	Adjusted RR (95% CI) (1) 1.0 (referent) (2) 1.2 (0.7–2.1) (3) 1.2 (0.7–2.0) (4) 2.3 (1.4–3.7)
Lee et al., 1992 (42)	N = 17,719 men Observational cohort study	Self-reported physical activity Tertiles of energy expenditure (kcal·wk^{-1}) (1) Inactive (<1000) (2) Moderately active (1000–2500) (3) Highly active (>2500)	Age	Prostatic cancer morbidity and mortality 221 cases	Adjusted RR (95% CI) (1) 1.0 (referent) (2) 0.97 (0.77–1.21) (3) 0.99 (0.78–1.26) Trend P = 0.94
Lee et al., 1991 (41)	N = 17,148 men Observational cohort study	Self-reported physical activity Physical activity levels (kcal·wk^{-1}) (1) Inactive (<1000) (2) Moderately active (1000–2500) (3) Highly active (>2500)	Age	Colorectal cancer morbidity and mortality 269 cases	Adjusted RR (95% CI) Colon cancer / Rectal cancer (1) 1.0 (referent) / 1.0 (referent) (2) 0.88 (0.68–1.14) / 1.01 (0.54–1.89) (3) 0.85 (0.64–1.12) / 1.43 (0.78–2.60) Trend P = 0.31 / P = 0.34
De Verdier et al., 1990 (22)	N = 720 men and women Case-control study	Self-reported physical activity Physical activity levels (1) Sedentary during both working and recreational hours (2) All others than 1 and 3 (3) Very active during working and/or recreational hours	Year of birth, gender, BMI, intake of total energy, total fat, fiber, browned meat surface	Colon and rectal cancer morbidity Men: 270 cases Women: 299 cases	Adjusted OR (95% CI) Colon cancer / Right colon cancer (1) 1.8 (1.0–3.4) / 1.0 (0.4–2.4) (2) 1.4 (0.9–2.2) / 1.3 (0.7–2.2) (3) 1.0 (referent) / 1.0 (referent) Left colon cancer / Rectal cancer (1) 3.1 (1.4–7.0) / 0.9 (0.4–1.8) (2) 1.4 (0.7–2.7) / 0.8 (0.5–1.2) (3) 1.0 (referent) / 1.0 (referent)
Physical activity and stroke					
Hu et al., 2000 (29)	N = 72,488 women Observational cohort study	Self-reported recreational physical activity Physical activity levels (h·wk^{-1}) (1) 0–2.0 (2) 2.1–4.6 (3) 4.7–10.4 (4) 10.5–21.7 (5) >21.7	Age, follow-up time, smoking habit, BMI, menopausal status, postmenopausal and hormone replacement therapy history, family history, aspirin use, history of hypertension, diabetes, hypercholesterolemia	Ischemic stroke, hemorrhagic stroke morbidity and mortality 407 cases	Adjusted RR (95% CI) Ischemic stroke / Hemorrhagic stroke (1) 1.0 (referent) / 1.0 (referent) (2) 0.87 (0.62–1.23) / 0.92 (0.53–1.61) (3) 0.83 (0.58–1.19) / 0.89 (0.50–1.59) (4) 0.76 (0.52–1.11) / 0.69 (0.36–1.32) (5) 0.52 (0.33–0.80) / 1.02 (0.58–1.82) Trend P = 0.003 / P = 0.88
Ellekjaer et al., 2000 (17)	N = 14,101 women Observational cohort study	Self-reported recreational physical activity (1) Low (2) Medium (3) High	Age, smoking status, diabetes, BMI, antihypertensive medication, systolic blood pressure, angina pectoris, myocardial infarction, illness that impairs function, education	Stroke mortality 457 deaths	Adjusted RR (95% CI) (1) 1.0 (referent) (2) 0.77 (0.61–0.98) (3) 0.52 (0.38–0.72) Trend P < 0.0001
Lee et al., 1999 (37)	N = 21,823 men Observational cohort study	Self-reported recreational physical activities Physical activity levels (times/wk) (1) <1 (2) 1 (3) 2–4 (4) ≥5	Age, smoking habit, alcohol consumption, angina, family history, BMI, hypertension, high cholesterol, diabetes	Ischemic stroke, hemorrhagic stroke morbidity and mortality 533 cases	Adjusted RR (95% CI) Ischemic stroke / Hemorrhagic stroke (1) 1.0 (referent) / 1.0 (referent) (2) 0.90 (0.66–1.22) / 0.54 (0.25–1.13) (3) 0.95 (0.74–1.22) / 0.71 (0.41–1.23) (4) 0.97 (0.71–1.32) / 0.54 (0.26–1.15) Trend P = 0.81 / P = 0.10
Evenson et al., 1999 (19)	N = 6279 men and 8296 women Observational cohort study	Self-reported sport, leisure, and work physical activity Baecke score	Age, race-center, sex, education, smoking, hypertension, fibrinogen, BMI, diabetes	Ischemic stroke morbidity and mortality Men: 93 cases Women: 86 cases	Adjusted RR (95% CI) of incident ischemic stroke per 1-unit increase in Baecke score Sport: 1.03 (0.83–1.26) Leisure: 0.99 (0.75–1.29) Work: 0.94 (0.81–1.10)
Lee et al., 1998 (39)	N = 11,130 men Observational cohort study	Self-reported physical activity Physical activity levels (kcal/week) (1) <1000 (2) 1000–1999 (3) 2000–2999 (4) 3000–3999 (5) >3999	Age, smoking, alcohol consumption, family history	Stroke morbidity and mortality 378 cases	Adjusted RR (95% CI) (1) 1.0 (referent) (2) 0.76 (0.59–0.98) (3) 0.54 (0.38–0.76) (4) 0.78 (0.53–1.15) (5) 0.82 (0.58–1.14) Trend P = 0.05
Sacco et al., 1998 (59)	N = 489 men and 618 women Matched case-control study	Self-reported recreational physical activities Intensity (1) None (2) Light/moderate (3) Heavy Duration (h·wk^{-1}): (1) None (2) <2 (3) 2–5 (4) ≥5	Age, sex, race, hypertension, diabetes, cardiac disease, smoking, alcohol consumption	Cerebral infarction morbidity Men 163 cases Women 369 cases	Adjusted OR (95% CI or P-value) Physical activity intensity (1) 1.0 (referent) (2) 0.39 (0.26–0.58) (3) 0.23 (0.10–0.54) Physical activity duration (1) 1.0 (referent) (2) 0.42 (P < 0.05) (3) 0.35 (P < 0.05) (4) 0.31 (P < 0.05) Trend P = 0.006

TABLE 2. *Continued*

Study	Population/Design	Physical Activity Assessment	Adjusted for	Outcome	Summary of Results
Gillum et al., 1996 (23)	N = 5852 men and women Observational cohort study	Self-reported recreational and nonrecreational physical activity (1) Low (2) Moderate (3) High	Age, smoking, diabetes, heart disease, education, systolic blood pressure, cholesterol, BMI, hemoglobin	Stroke morbidity and mortality 623 cases	Adjusted RR (95% CI) (high level physical activity as a reference level) Recreational physical activity Men / Women 45–64 yr (1) 1.24 (0.63–2.41) / 3.13 (0.95–10.32) (2) 1.17 (0.61–2.27) / 1.80 (0.52–6.22) Trend $P > 0.05$ / $P = 0.008$ 65–74 yr (1) 1.29 (0.88–1.88) / 1.55 (0.95–2.53) (2) 0.86 (0.58–1.28) / 1.27 (0.76–2.12) Trend $P > 0.05$ / $P = 0.02$ Nonrecreational physical activity Men / Women 45–64 yr (1) 1.07 (0.40–2.86) / 3.51 (1.66–7.46) (2) 1.75 (1.04–2.96) / 1.07 (0.57–1.99) Trend $P > 0.05$ / $P = 0.01$ 65–74 yr (1) 1.82 (1.15–2.88) / 1.82 (1.10–3.02) (2) 1.20 (0.88–1.64) / 1.42 (1.01–2.00) Trend $P = 0.02$ / $P = 0.01$
Abbott et al., 1994 (1)	N = 7530 men Observational cohort study	Self-reported physical activity Physical activity levels (index) (1) Inactive (2) Partially active (3) Active	Systolic blood pressure, cholesterol, smoking, alcohol consumption, serum glucose, serum uric acid, hematocrit	Stroke morbidity and mortality 60 cases	Adjusted RR (95% CI) Thromboembolic stroke (age 55–68 yr) Nonsmoker / Smoker (1) 2.8 (1.2–6.7) / 1.2 (0.7–2.1) (2) 2.4 (1.0–5.7) / 0.7 (0.4–1.3) (3) 1.0 (referent) / 1.0 (referent) Hemorrhagic stroke 45–54 yr / 55–68 yr (1) 2.0 (0.8–5.1) / 3.7 (1.3–10.4) (2) 1.1 (0.4–3.3) / 2.2 (0.8–6.4) (3) 1.0 (referent) / 1.0 (referent)
Kiely et al., 1994 (33)	N = 2336 men and 2873 women Observational cohort study	Self-reported leisure or work physical activity Physical activity index tertiles (1) Tertile 1 (lowest) (2) Tertile 2 (3) Tertile 3 (highest)	Age, systolic blood pressure, cholesterol, smoking habit, glucose intolerance, total vital capacity, BMI, left ventricular hypertrophy, fibrillation, valvular disease, heart failure, heart disease, occupation	Stroke morbidity 1954–55 Men: 188 cases Women: 214 cases 1968–72 Men: 107 cases Women: 127 cases	Adjusted RR (95% CI) Men / Women Physical activity at exam 1954–55 (1) 1.0 (referent) / 1.0 (referent) (2) 0.90 (0.62–1.31) / 1.21 (0.89–1.63) (3) 0.84 (0.59–1.18) / 0.89 (0.60–1.31) Physical activity at exam 1968–1972 (1) 1.0 (referent) / 1.0 (referent) (2) 0.41 (0.24–0.69) / 0.97 (0.64–1.47) (3) 0.53 (0.34–0.84) / 1.21 (0.75–1.96)
Haheim et al., 1993 (26)	N = 14,403 men Observational cohort study	Self-reported physical activity (1) Sedentary (2) Moderate (3) Intermediate+great	None	Stroke morbidity and mortality 26 deaths 81 cases	RR (95% CI) Incidence / Mortality Physical activity at work (1) 1.0 (referent) / 1.0 (referent) (2) 0.66 (0.34–1.23) / 0.98 (0.33–2.69) (3) 1.62 (0.95–2.75) / 1.38 (0.46–3.81) Trend $P > 0.05$ / $P > 0.05$ Physical activity at leisure (1) 1.0 (referent) / 1.0 (referent) (2) 0.64 (0.38–1.08) / 0.82 (0.33–2.35) (3) 0.36 (0.15–0.80) / 0.29 (0.03–1.51) Trend $P > 0.10$ / $P > 0.09$
Herman et al., 1983 (28)	N = 235 men and 136 women Case-control study	Self-reported leisure physical activity (1) Little (2) Regular light (3) Regular heavy	Education, acute myocardial infarction, cardiac arrhythmia, high blood pressure, diabetes, obesity, transient cerebral ischemic attack, rhesus factor	Stroke morbidity Men: 83 cases Women: 49 cases	Adjusted OR (95% CI) (1) 1.0 (referent) (2) 0.49 (0.31–0.77) (3) 0.24 (0.10–0.59)
Change in physical activity					
Paffenbarger et al., 1998 (53)	N = 17,815 men Observational cohort study	1962/66 to 1977 (kcal·wk^{-1}) (1) increase ≥1250 (2) increase 750–1249 (3) increase 250–749 (4) unchanged (±249) (5) decrease 250–749 (6) decrease 750–1249 (7) decrease ≥1250)	Age, smoking habit, blood pressure status, body mass index, alcohol intake, parents dead before age 65 years, and chronic disease	All-cause mortality N = 4399	Adjusted RR (P-value) (1) 0.80 (<0.001) (2) 0.80 (0.003) (3) 0.93 (0.247) (4) 1.0 (referent) (5) 1.0 (0.934) (6) 1.15 (0.058) (7) 1.26 (0.001)

TABLE 3. Summary of studies on the dose-response relation of cardiorespiratory fitness to morbidity and mortality.

Study	Population/Design	Physical Fitness	Adjusted for	Outcome	Results
Farrell et al., 1998 (20)	N = 25,341 adult men Observational cohort study from 1970 to 1989 Average follow-up of 8.4 yr	Maximal exercise test on treadmill using a modified Balke protocol Cardiorespiratory fitness categories based on total treadmill time at baseline (1) Low fitness—least-fit 20% of each age group (2) Moderate fitness—next 40% of each age group (3) High fitness—remaining 40% of each age group	CVD mortality predictors included smoking, elevated systolic blood pressure, and elevated blood cholesterol	CVD mortality 226 deaths	Fitness category — CVD deaths/10,000 py 0 Mortality predictors (1) 14.1 (2) 4.2 (3) 4.5 1 Mortality predictor (1) 19.4 (2) 11.6 (3) 9.3 2–3 Mortality predictors (1) 21.7 (2) 20.5 (3) 10.2 Low fitness trend test $P = 0.001$ Moderate fitness trend test $P = 0.004$ High fitness trend test $P = 0.325$
Blair et al., 1996 (9)	N = 25,341 men Observational cohort study from 1970 to 1989	Maximal exercise test on treadmill using a modified Balke protocol Cardiorespiratory fitness categories based on total treadmill time at baseline (1) Low fitness—least-fit 20% of each age group (2) Moderate fitness—next 40% of each age group (3) High fitness—remaining 40% of each age group	Age, examination year, and other risk predictors	All-cause mortality 601 deaths	All-cause mortality **Deaths/10,000 py are estimated from Figure 3 in the paper Men Fitness category — Deaths/10,000 py 0 Mortality predictor (1) 28 (2) 18 (3) 17 1 Mortality predictor (1) 43 (2) 27 (3) 26 2–3 Mortality predictor (1) 57 (2) 42 (3) 25
Blair et al., 1991 (10)	N = 12,056 men 10,224 healthy normotensive men 1832 men with history of hypertension Observational cohort study from 1970–1985 Average follow-up 8 yr	Maximal exercise test on treadmill using a modified Balke protocol Cardiorespiratory fitness categories: treadmill time used to assign men to physical fitness quintiles (Q1 = least fit to Q5 = fittest)	Age	All-cause mortality Normotensive: 240 deaths Hypertensive: 78 deaths	Adjusted RR (95% CI) Normotensive men Quintiles Q1 3.4 (2.1–5.8) Q2 1.4 (0.8–2.5) Q3 1.5 (0.8–2.6) Q4 1.1 (0.6–2.2) Q5 1.0 (referent) Hypertensive men Q1 4.5 (2.9–6.9) Q2 1.2 (0.7–2.0) Q3 1.6 (1.0–2.7) Q4 2.4 (1.5–3.8) Q5 1.0 (referent)
Blair et al., 1989 (13)	N = 10,224 men and 3120 women Observational cohort study from 1970 to 1981 Average follow-up 8 yr	Maximal exercise test on treadmill using a modified Balke protocol Cardiorespiratory fitness categories: treadmill time used to assign men to physical fitness quintiles (Q1 = least fit to Q5 = fittest)	Age	All-cause mortality Men: 240 deaths Women: 43 deaths	Adjusted RR (95% CI) Men Q1 3.44 (2.05–5.77) Q2 1.37 (0.76–2.50) Q3 1.46 (0.81–2.63) Q4 1.17 (0.63–2.17) Q5 1.0 (referent) Women Q1 4.65 (2.22–9.75) Q2 2.42 (1.09–5.37) Q3 1.43 (0.60–3.44) Q4 0.76 (0.27–2.11) Q5 1.0 (referent)
Ekelund et al., 1988 (16)	N = 3106 healthy men (30–69 yr) Follow-up study	Submaximal treadmill exercise test using a modified Bruce protocol Fitness categories in quartiles based on heart rate taken during stage 2 of the exercise test: Q1-least fit to Q4-most fit		CHD and CVD mortality 45 deaths	CHD mortality Unadjusted Cumulative Mortality — 95% CI Q1 1.69 (0.77–2.61) Q2 0.91 (0.24–1.58) Q3 0.91 (0.24–1.58) Q4 0.26 (0.00–0.62) CVD mortality Unadjusted Cumulative Mortality — (95% CI) Q1 2.21 (1.16–3.25) Q2 1.56 (0.68–2.44) Q3 1.30 (0.49–2.11) Q4 0.26 (0.00–0.62)

TABLE 3. *Continued*

Study	Population/Design	Physical Fitness	Adjusted for	Outcome	Results
Lie et al., 1985 (45)	N = 2014 healthy men (40–59 yr of age) 7-yr follow-up study	Cycle ergometer test symptom-limited Fitness categories were determined by quartiles of cumulative work on the exercise test Q1-least fit to Q4-fittest		CHD mortality 58 deaths	Death rates Q1 5.74 Q2 2.38 Q3 2.20 Q4 1.19
Sandvik et al., 1993 (60)	N = 1960 healthy men Observational cohort study from 1972 to 1989 Average follow-up time 16 yr	Maximal exercise test on an electrically braked bicycle ergometer Cardiorespiratory fitness categories: change in fitness scores between the exams divided into quartiles (Q1 = least change, Q4 = most change)	Age and other risk factors	All-cause and CVD mortality 271 deaths 143 CVD deaths	Adjusted RR (95% CI) All-cause Q1 1.0 (referent) Q2 0.92 (0.66–1.28) P = 0.58 Q3 1.00 (0.71–1.41) P = 0.92 Q4 0.54 (0.32–0.89) P = 0.015 CVD Q1 1.0 (referent) Q2 0.59 (0.28–1.22) P = 0.15 Q3 0.45 (0.22–0.92) P = 0.026 Q4 0.41 (0.20–0.84) P = 0.013
Effects of change in fitness on morbidity and mortality					
Erikssen et al., 1998 (18)	N = 2014 healthy men (1st exam) 1756 participated in the 2nd exam Observational cohort study from 1972 to 1994 Interval between 1st and 2nd exam 7 yr Total follow-up time 22 yr	Maximal exercise test on an electrically braked cycle ergometer Cardiorespiratory fitness categories: Baseline fitness categories based on quartiles of fitness at 1st exam: Q1 (PF1) to Q4 (PF1) Change in fitness scores between 1st and 2nd exams divided into quartiles Q1-least change to Q4-most change	Age and other risk factors	All-cause mortality 1428 deaths	Standard Mortality Ratios All-cause Baseline Q1 (PF1) Q2 (PF1) Q3 (PF1) Q4 (PF1) Change in fitness scores Q1 1.22 1.19 0.87 0.73 Q2 0.80 0.77 0.62 0.46 Q3 0.72 0.33 0.60 0.17 Q4 0.47 0.43 0.40 0.17
Blair et al., 1995 (12)	N = 9777 men Observational cohort prospective study from 1970 to 1989 Average follow-up of 4.9 yr between 1st and 2nd examination Average follow-up for mortality was 5.1 yr after 2nd examination	Maximal exercise test on treadmill using a modified Balke protocol Cardiorespiratory fitness categories of quintile classifications at each exam and for some analyses Unfit = least-fit 20% of each age group Fit = all others Fitness categories after both examinations (1) Unfit-unfit (2) Unfit-fit (3) Fit-unfit (4) Fit-fit	Age	All-cause and CVD mortality 223 deaths 87 CVD deaths	Adjusted RR (95% CI) All-cause mortality (1) 1.0 (referent) (2) 0.56 (0.41–0.75) (3) 0.52 (0.38–0.70) (4) 0.33 (0.23–0.47) Quintiles Visits 1st 2nd RRs (95% CI) 2–3 2–3 1.0 (referent) 2–3 4–5 0.85 (0.56–1.29) 4–5 4–5 0.71 (0.46–1.09) CVD mortality (1) 1.0 (referent) (2) 0.48 (0.31–0.74) (3) 0.43 (0.28–0.67) (4) 0.22 (0.12–0.39) Visits 1st 2nd RRs (95% CI) 2–3 2–3 1.0 (referent) 2–3 4–5 0.72 (0.37–1.38) 4–5 4–5 0.48 (0.23–1.01)

especially Table 2, are already large, and we thought that we had enough data to address our questions without including nonfatal disease outcomes. We made one exception to this delimitation. We included one study in Table 4 on functional limitation as the outcome because we otherwise had only eight articles for this table, and several of them were relatively small.

Identifying source material. Our objective was to identify articles in the peer-reviewed literature that included data on at least one of the outcomes and on three or more levels of one or both of the exposure variables. To address questions 1 and 2, we reviewed studies that included assessments of either physical activity or cardiorespiratory fitness. Studies used to address question 3 were required to have data on both activity and fitness. Because there are many studies with physical activity and because these studies have been thoroughly reviewed recently (51,54,69), we restricted our review of studies to articles published in 1990 or later. Table 1 includes a summary of how material was selected for review.

Critical analysis of articles. At least two, and often all three, authors read each of the 67 articles on the final list. We summarized results in tabular form, with one table for each of the questions addressed in this report. Each table includes information on characteristics of the study population, method of assessing physical activity or fitness, information on confounding variables, and summary of study outcomes with an emphasis on the dose-response gradient. We used the evidence-based approach for rating the quality of the evidence

TABLE 4. Summary of 9 studies with assessments of both physical activity and fitness on the does-response relation to health outcomes.

Study	Population	Physical Activity or Fitness	Adjusted for	Outcome	Results
Huang et al., 1998 (30)	N = 3495 men and 1175 women Observational cohort study	Cardiorespiratory fitness Maximal exercise treadmill test (1) Low fit = least fit 20% (2) Moderate = 21–60% (3) High fit = 61–100% Self-reported leisure physical activity (I) Sedentary (none) (II) Moderate activity (walking or jogging <10 miles·wk^{-1} or other activity) (III) High active (walking or jogging $\geq$10 miles·wk^{-1})	Age, BMI, smoking, alcohol consumption, health status	Functional limitation	Adjusted OR (95% CI) Cardiorespiratory fitness Men / Women (1) 1.0 (referent) / 1.0 (referent) (2) 0.4 (0.2–0.6) / 0.5 (0.3–0.7) (3) 0.3 (0.2–0.4) / 0.3 (0.2–0.5) Physical activity Men / Women (I) 1.0 (referent) / 1.0 (referent) (II) 0.7 (0.5–0.9) / 0.7 (0.5–1.1) (III) 0.5 (0.3–0.8) / 0.7 (0.4–1.2)
Villeneuve et al., 1998 (71)	N = 6246 men and 8196 women Observational cohort study	Cardiorespiratory fitness Maximum of 3 stages of climbing steps for 3 min per stage (1) Undesirable (2) Minimum (3) Recommended Self-reported leisure activities kcal·kg^{-1}·d^{-1} (I) 0–0.5; (II) 0.5–1.5; (III) 1.5–3.0; (IV) $\geq$3.0	Age, sex, smoking habit	All-cause mortality Men 614 deaths Women 502 deaths	Adjusted RR (95% CI) Cardiorespiratory fitness Men and Women (1) 1.52 (0.72–3.18) (2) 1.02 (0.69–1.51) (3) 1.0 (referent) Physical activity Men / Women (I) 1.0 (referent) / 1.0 (referent) (II) 0.81 (0.59–1.11) / 0.94 (0.69–1.30) (III) 0.79 (0.54–1.13) / 0.92 (0.64–1.34) (IV) 0.86 (0.61–1.22) / 0.71 (0.45–1.11)
Kampert et al., 1996 (31)	N = 25,341 men and 7080 women Observational cohort study	Cardiorespiratory fitness Maximal exercise treadmill test (1) Quintile 1 (lowest) (2) Quintile 2 (3) Quintile 3 (4) Quintile 4 (5) Quintile 5 (highest) Self-reported leisure physical activity (miles·wk^{-1}) (I) Sedentary (II) 1–10 (III) 11–20 (IV) 21–40 (V) >40	Age, examination year, smoking, chronic illnesses, ECG abnormalities	All-cause and cancer mortality Men 601 deaths; 179 cancer Women 89 deaths; 44 cancer	Adjusted RR (95% CI) Cardiorespiratory fitness Men All-cause deaths / Cancer deaths (1) 1.0 (referent) / 1.0 (referent) (2) 0.55 (0.44–0.70) / 0.54 (0.35–0.84) (3) 0.61 (0.48–0.78) / 0.56 (0.36–0.87) (4) 0.52 (0.41–0.66) / 0.59 (0.38–0.90) (5) 0.49 (0.37–0.64) / 0.36 (0.21–0.61) Trend P = 0.001 / P = 0.001 Women All-cause deaths / Cancer deaths (1) 1.0 (referent) / 1.0 (referent) (2) 0.53 (0.30–0.95) / 0.63 (0.26–1.54) (3) 0.56 (0.31–1.01) / 0.76 (0.32–1.80) (4) 0.22 (0.10–0.49) / 0.38 (0.14–1.03) (5) 0.37 (0.19–0.72) / 0.47 (0.18–1.22) Trend P = 0.001 / P = 0.073 Physical activity Men All-cause deaths / Cancer deaths (I) 1.0 (referent) / 1.0 (referent) (II) 0.71 (0.58–0.87) / 0.71 (0.49–1.03) (III) 0.83 (0.59–1.16) / 0.42 (0.18–0.97) (IV) 0.57 (0.30–1.08) / 0.15 (0.02–1.12) (V) 0.92 (0.29–2.88) / (IV & V) Trend P = 0.011 / P = 0.002 Women All-cause deaths / Cancer deaths (I) 1.0 (referent) / 1.0 (referent) (II) 0.68 (0.39–1.17) / 0.84 (0.38–1.88) (III) 0.39 (0.09–1.65) / 0.95 (0.21–4.37) (IV & V) 1.14 (0.27–4.80) / 2.85 (0.62–13.16) Trend P = 0.217 / P = 0.557
Oliveria et al., 1996 (52)	N = 12,975 men Observational cohort study	Cardiorespiratory fitness Maximal exercise treadmill test (min) (1) <13.7 (2) 13.7–17 (3) 17.0–21.0 (4) $\geq$21.0 Self-reported leisure physical activity (kcal·wk^{-1}) (I) <1000 (II) 1000–2000 (III) 2000–3000 (IV) $\geq$3000	Age, BMI, smoking	Prostate cancer 94 cases	Adjusted RR (95% CI) Cardiorespiratory fitness (1) 1.0 (referent) (2) 1.10 (0.63–1.77) (3) 0.73 (0.41–1.29) (4) 0.26 (0.10–0.63) Trend P = 0.0036 Physical activity (I) 1.0 (referent) (II) 0.37 (0.17–0.79) (III) 0.62 (0.27–1.41) (IV) 0.37 (0.14–0.98) Trend P = 0.8263
Lakka et al., 1994 (36)	N = 1453 men Observational cohort study	Cardiorespiratory fitness Maximal oxygen uptake (L·min^{-1}) (1) <2.2 (2) 2.2–2.7 (3) >2.7 Self-reported leisure physical activity (h·wk^{-1}) (I) <0.7 (II) 0.7–2.2 (III) >2.2	Age, year of examination, height, weight, season of examination, type of respiratory-gas analyzer used	Acute myocardial infarction morbidity and mortality 57 cases	Adjusted RR (95% CI) Cardiorespiratory fitness (1) 1.0 (referent) (2) 0.76 (0.38–1.50) (3) 0.26 (0.10–0.68) Trend P = 0.006 Physical activity (I) 1.0 (referent) (II) 1.11 (0.58–2.12) (III) 0.31 (0.12–0.85) Trend P = 0.04

TABLE 4. *Continued*

Study	Population	Physical Activity or Fitness	Adjusted for	Outcome	Results
Blair et al., 1993 (11)	$N = 10{,}224$ men and 3120 women Observational cohort study	Cardiorespiratory fitness Maximal exercise treadmill test (1) Low fit, least fit 20% (2) Moderate, 21–60% (3) High fit, 61–100% Self-reported leisure physical activity (I) Sedentary (II) Moderate (III) Active	Age	All-cause mortality Men: 240 deaths Women: 43 deaths	Age adjusted RR (95% CI) Cardiorespiratory fitness Men / Women (1) 3.16 (1.92–5.20) / 5.35 (2.44–11.73) (2) 1.30 (0.73–2.32) / 2.22 (0.93–5.30) (3) 1.0 (referent) / 1.0 (referent) Trend $P = 0.001$ Physical activity Men / Women (I) 1.70 (1.06–2.74) / 0.95 (0.54–1.70) (II) 1.48 (0.9–2.42) / 0.75 (0.41–1.39) (III) 1.0 (referent) / 1.0 (referent) Trend $P = 0.305$
Hein et al., 1992 (27)	$N = 4999$ men Observational cohort study	Cardiorespiratory fitness Maximal cycle ergometer test (1) I (lowest quintile) (2) II (3) III (4) IV (5) V (highest quintile) Self-reported leisure physical activity (I) Low (rare or none) (II) Medium and high	Age	All-cause mortality 266 deaths	Age adjusted mortality for fitness In medium and high activity population (1) 17.0 (2) 15.9 (3) 16.5 (4) 18.5 (5) 12.5 Trend $P < 0.05$ In low activity population (1) 26.9 (2) 25.7 (3) 25.3 (4) 24.7 (5) 25.4 Trend $P > 0.05$
Arraiz et al., 1992 (4)	$N = 13{,}379$ men and women Observational cohort study	Cardiorespiratory fitness Using the observed and age, sex-specific reference pulse rates (1) Unacceptable (2) Acceptable (3) Recommended Self-reported physical activity Minutes in 2 wk (I) Inactive (0–1749) (II) Moderate (1750–2999) (III) Active (3000–5499) (IV) Very active (5500+)	Age, sex, smoking, alcohol consumption	All-cause, CVD, and cancer mortality 691 deaths men and women CVD: 256 men and women Cancer: 229 men and women	Adjusted RR (95% CI) Cardiorespiratory fitness All-cause deaths (1) 2.7 (1.4–5.5) (2) 1.6 (0.6–4.2) (3) 1.0 (referent) CVD deaths (1) 5.4 (1.9–15.9) (2) 0.8 (0.1–7.6) (3) 1.0 (referent) Cancer deaths (1) 1.9 (0.8–4.5) (2) 1.6 (0.4–5.4) (3) 1.0 (referent) Physical activity All-cause deaths (I) 1.5 (0.7–3.6) (II) 1.0 (0.4–2.8) (III) 1.5 (0.6–3.7) (IV) 1.0 (referent) CVD deaths (I) 0.9 (0.4–2.2) (II) 0.4 (0.01–1.0) (III) 1.0 (0.4–2.7) (IV) 1.0 (referent) Cancer deaths (I) 1.2 (0.7–1.9) (II) 0.8 (0.4–1.4) (III) 1.4 (0.8–2.3) (IV) 1.0 (referent)
Sobolski et al., 1987 (63)	$N = 2363$ men Observational cohort study	Cardiorespiratory fitness Defined as the work load at heart rate 150 beats·min^{-1} divided by body weight (kg) Quintiles (1) lowest to (4) highest Self-reported occupational and leisure physical activity metabolic index (I) lowest to (IV) highest	Age, HDL cholesterol, smoking, physical activity, systolic blood pressure, BMI	Ischemic heart disease incidences 31 cases	Incidence (%) cardiorespiratory fitness (1) 2.2 (2) 1.7 (3) 1.1 (4) 0.3 Trend $P < 0.05$ Incidence (%) physical activity Occupational / Leisure time (I) 1.6 / 1.2 (II) 1.0 / 1.7 (III) 1.5 / 1.3 (IV) 1.8 / 1.7 Trend $P > 0.05$ / $P > 0.05$ After controlling for other variables, physical fitness remained associated with incidence ($P < 0.05$)

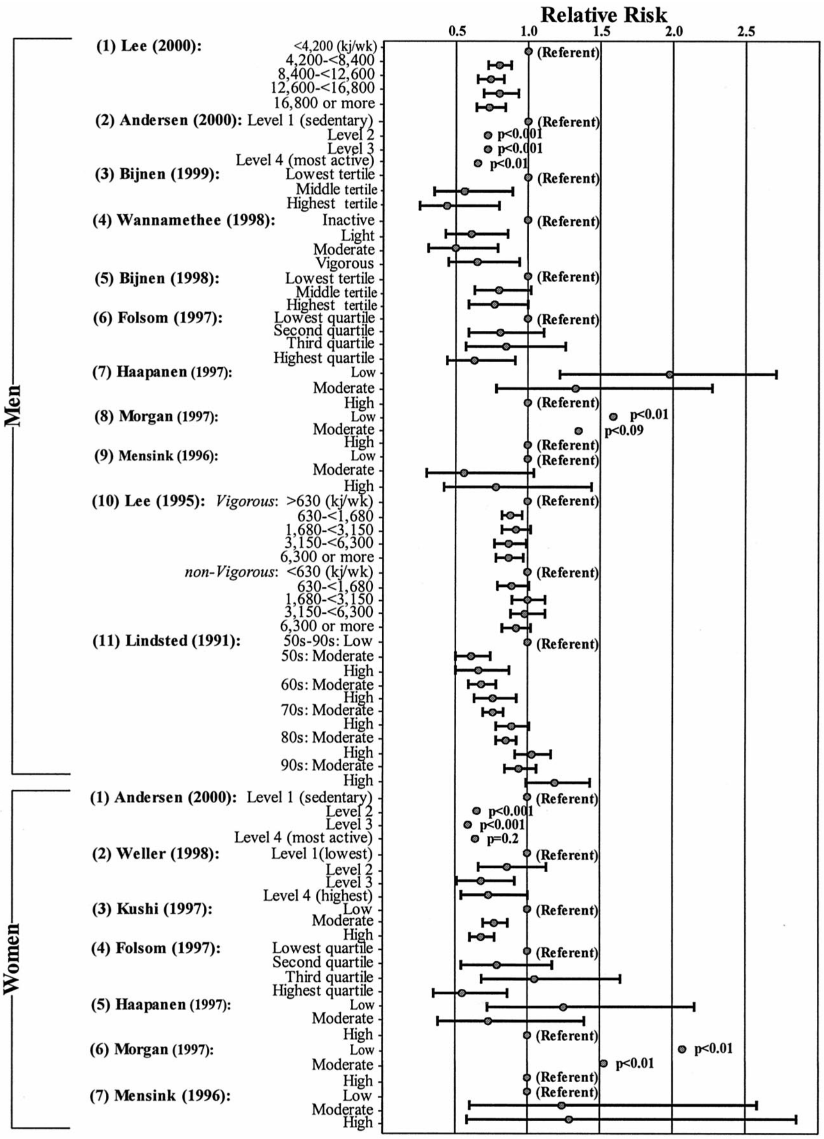

FIGURE 2—Dose-response for all-cause mortality across categories of physical activity in men (11 studies) and women (7 studies). Relative risks are shown for categories of physical activity. Note that the referent category in some studies is the least active group and for other studies is the most active group; 95% confidence intervals are included if they were available, otherwise only the point estimates (with *P*-values) are given. For some studies, point estimates are given for categories of physical activity within other strata (Lee et al. (38), by strata of vigorous and nonvigorous activity; Linsted et al. (46), by age groups).

discovered and summarized in the review. There are no randomized controlled clinical trials of either physical activity or fitness and the outcomes considered here, and thus the quality of evidence is Category C for each question we addressed.

RESULTS

Separate tables are presented for the dose-response associations of physical activity, fitness, or both exposures to the outcomes of morbidity and mortality.

Physical activity dose-response. Table 2 includes a summary of the evidence from 49 studies on the dose-response relation of physical activity to health outcomes. A majority of these papers have mortality as an outcome (CHD, CVD, stroke, site-specific cancer, or all-cause mortality); however, some studies include data on nonfatal chronic disease outcomes. Due to the large number of studies reviewed here with various health outcomes, vastly different approaches to assessing physical activity, and other methodological differences, it is not possible to accurately quantify a general dose-response gradient for physical activity. Nonetheless, and although there are exceptions (15,46,64), most studies show a general inverse dose-response gradient across physical activity categories for most health outcomes. The shape of the dose-response curves differ, but many of them show an asymptote, which suggests a threshold for benefits. Figure 2 shows point estimates for all-cause mortality by categories of activity for women (7 studies) and men (11 studies), respectively. In general, the point estimates for activity categories are more variable in women than in men, with one study in women (48) even showing nonsignificantly higher mortality in the more active women.

Cardiorespiratory fitness dose-response. Table 3 includes a summary of the evidence from nine studies on cardiorespiratory fitness and mortality (CHD, CVD, or all-cause mortality). There is remarkable consistency across studies, with all showing a strong inverse gradient of mortality across fitness groups. It should be noted that five of the nine studies are from the Aerobics Center Longitudinal Study (ACLS) data; and although these are from different

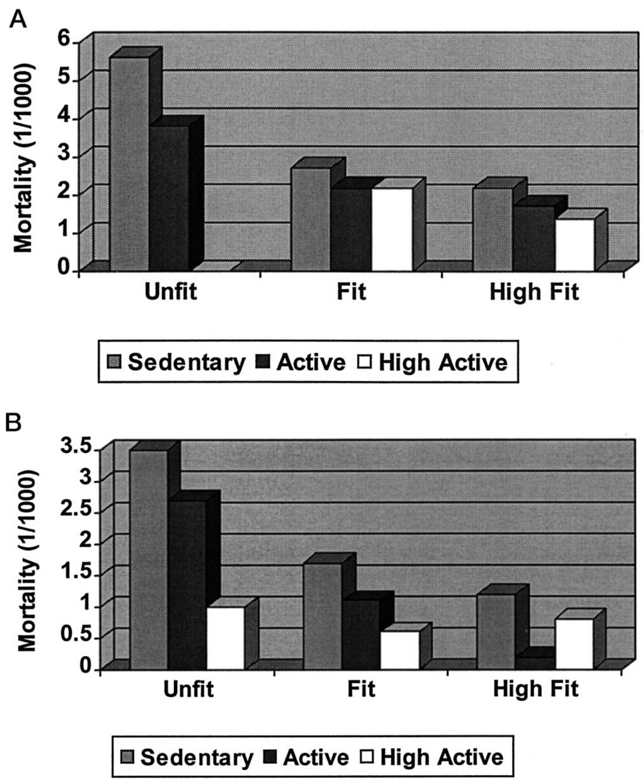

FIGURE 3—All-cause mortality rates by cardiorespiratory fitness and physical activity categories in 26,764 men (A) and 8755 women (B) participating in the Aerobics Center Longitudinal Study. Height of the bars represents the death rate per 1000 person-yr of observation. Death rates are based on 307,594 man-yr and 96,608 woman-yr of observation, and on 805 deaths in men and 146 deaths in women. Unfit participants are the least fit 20% in each age-sex group, fit are the next 40% of the fitness distribution, and high fit are the most fit 40%. Sedentary persons reported no physical activity, active individuals reported up to 19.9 MET·h^{-1} of physical activity per week, and high active individuals reported 20 or more MET·h^{-1}.

subgroups of the ACLS, one would expect to find similar results in these different analyses. The reports from the ACLS are the only ones to include women, and it appears that the association between fitness and mortality is similar in women and in men. Data are somewhat sparse, but the pattern of results is similar in normotensive and hypertensive men, and within different age groups.

Three of the studies included data on change in fitness from one examination to a second examination, with subsequent follow-up for mortality. Results from these studies are consistent with those from studies in which fitness was assessed only at baseline and study participants followed for mortality. Men who made greater improvements in fitness had greater reductions in mortality than was observed in men with little or no change in fitness.

The magnitude of reduction in mortality across fitness groups is substantial. Essentially all analyses show at least a 50% lower mortality rate in the high fit as compared with the low fit individuals. In some studies, the difference in mortality rates between the most and least fit individuals was on the order of three- to four-fold (10,13), and the difference was even greater in the report by Ekelund et al. (16).

Activity and fitness dose-response. Table 4 includes a summary of the evidence from nine studies that include both exposures of cardiorespiratory fitness and physical activity in relation to health outcomes. All studies show an inverse gradient across fitness categories for the various health outcomes, and most show an inverse gradient across physical activity categories. In general, the gradients are steeper for fitness than for activity. For example, the report by Arraiz et al. (4) shows RRs for all-cause mortality across three fitness groups of 2.7, 1.6, and 1.0 for the most fit; and RRs for all-cause mortality across activity groups in this study were 1.5, 1.0, 1.5, and 1.0 for the most active. A similar pattern was noted in the ACLS for women (11). None of the reports summarized in Table 4 include data from a multivariable model in which activity and fitness were both included. We included one report in Table 4 that had an outcome measure different from other studies in this review. Huang et al. (30) evaluated the relation of activity and fitness to the prevalence of functional limitations. These data show an inverse gradient across both activity and fitness groups in both men and women, and the gradients are steeper for fitness than for activity.

Aerobics Center Longitudinal Study. As shown in Table 4, there are only nine published reports from prospective studies meeting our inclusion criteria in which both physical activity and cardiorespiratory fitness have been assessed. Four of the studies summarized in Table 4 are from our ACLS database. We have recently extended mortality surveillance in our cohort and therefore decided to perform some preliminary analyses with our data specifically in relation to addressing question 3 established for this report.

From 1970 to 1994, there were 40,391 patients aged 20—90 yr who were examined at least once at the Cooper Clinic. We selected participants for these preliminary analysis who were healthy (no history of CVD, diabetes, or cancer and had a normal ECG) and achieved at least 85% of age-predicted maximal heart rate on the treadmill test. The 8755 women and 26,764 men who met these criteria were followed from the date of their baseline examination to date of death or to December 31, 1994, for survivors. These participants contributed 96,608 woman-yr and 307,594 man-yr of follow-up, during which 146 women and 805 men died. We assigned participants to three categories of physical activity based on their responses to their activity habits during the 3 months before their baseline examination. We calculated MET hours per week using Ainsworth et al.'s physical activity compendium (2) and assigned each participant to one of three activity categories: no reported activity = sedentary; up to 19.9 MET hours per week = active, and 20 or more MET hours per week = highly active. Study participants also were assigned to fitness categories based on age-sex treadmill time distributions: low fitness = least fit 20%, moderate fitness = next 40%, and high fitness = most fit 40%, as in our published studies referenced here.

We cross-tabulated the three activity and three fitness categories and calculated all-cause death rates per 1000 person-yr of observation (Fig. 3). There was an inverse mortality gradient across both activity and fitness categories in both men and women. The highest death rates for both men and women were in the unfit-sedentary group and the lowest death rates were in the high fit-highly active group. We then submitted these data to a proportional hazards analysis, with physical activity, cardiorespiratory fitness, BMI, smoking habit, alcohol intake, and parental history of CVD included in the model. Physical activity was not associated with mortality in these analyses, but the inverse gradient across fitness groups remained, with a 50% reduction in mortality in the moderately fit women and men and a 70% reduction in the high fit individuals, when compared with those in the low fit category.

CONCLUSIONS

The review performed for this report focused on three specific questions. Evidence statements and a rationale are provided below for each of the questions. All statements are based on Category C Evidence.

1. Is there a dose-response relation between physical activity and health outcomes?

Evidence statement. Individuals who are regularly physically active are less likely than sedentary individuals to develop health problems. The inverse gradient of risk across activity groups is seen in different population groups and for fatal and nonfatal outcomes.

Rationale. Some health outcomes are probably not associated with physical activity habits, for example, rectal cancer. There is compelling evidence that regular physical activity extends longevity and reduces risk for CHD, CVD, stroke, and colon cancer. For these outcomes, there is consistent evidence for an inverse dose-response effect across physical activity groups. Data are not sufficient to determine whether the slope of the gradient is different for different health outcomes or whether the shape of the dose-response curve is linear or curvilinear.

2. Is there a dose-response relation between cardiorespiratory fitness and health outcomes?

Evidence statement. There is an inverse gradient across categories of cardiorespiratory fitness for risk of fatal and nonfatal health outcomes. The pattern of association between fitness and outcomes is highly consistent across studies.

Rationale. There are fewer studies on cardiorespiratory fitness and health than are available on physical activity and health; however, the fitness studies are compelling in their consistency and in the steepness of the dose-response gradient across fitness groups. Studies including measures of fitness are of necessity laboratory- or clinic-based and, thus, also usually have extensive and objective data on health status and potential confounding variables, such as data from clinical chemistry analyses, blood pressure, and body composition. Most of the studies show a curvilinear dose-response association for most outcomes, with an asymptote occurring in the upper part of the fitness distribution.

3. If both physical activity and cardiorespiratory fitness have a dose-response relation to health outcomes, is there a difference in the outcome gradient across categories for the two exposures, and is it possible to determine from the available data which exposure is more important for health?

Evidence statement. The dose-response gradient for various health outcomes is steeper across categories of cardiorespiratory fitness than across physical activity groups. In preliminary analyses from the ACLS, when activity, fitness, and possible confounding variables are included in a multivariate model, fitness remains strongly associated with mortality, and the association for activity and health is no longer significant.

Rationale. As indicated in the evidence statements for questions 1 and 2, data from existing studies indicate dose-response gradients across categories of activity and fitness for multiple health outcomes. It is not possible to determine from these studies whether one of the exposure variables is more important than the other as a predictor of health. Data in Table 4 suggest that fitness is more important than activity in relation to health outcomes; however, we do not think this is a valid conclusion. Physical activity is the principal determinant of cardiorespiratory fitness, although there is a genetic component. We think that the most likely explanation for the stronger dose-response gradient for fitness shown in Table 4 is that fitness is measured objectively and physical activity is assessed in the studies reviewed here by self-report, which inevitably leads to misclassification—often substantial misclassification. With activity usually producing greater misclassification rates than are seen for fitness, it follows that data from observational studies will typically show a stronger association between fitness and health outcomes than for activity and health outcomes.

ISSUES AND LIMITATIONS

The question posed in the title of this report is the major issue. This question has received attention over the past several years, which escalated after publication of the CDC/ACSM public health recommendation for physical activity (54). The focus of that recommendation was on *accumulating* activity of *moderate* intensity, and this approach was difficult for some to reconcile with prior exercise recommendations that emphasized continuous bouts of relatively vigorous exercise. Some individuals began to talk about two principal types of physical activity—activity for health benefits and activity for improving fitness. The underlying notion for this concept was apparently that low amounts and intensities of activity might improve health (reduce risk of morbidity or mortality) but not produce any improvements in fitness. Our view is that activity cannot be designated as either for health or for fitness. We submit that any physical activity that has the capacity to change either health or fitness will change both. It may well be that there are minimum amounts and intensities that are required for any physiological or psychological adaptations to occur, that specific adaptations may be produced by specific amounts and types of activity, and that it might require a large sample size to confirm that small changes in activity are associated with small changes in both health and fitness. Nonetheless, we interpret a demonstrated dose-response relationship to mean that any change in dose will produce a known response. This leads to the conclusion that given a sufficiently large sample size, an increase in physical activity of 10 $kcal \cdot d^{-1}$ would lead to detectable increments of change in physiological and psychological variables that are affected by activity. Thus, we think that the focus should be on learning more about exercise dose-response relationships in general, rather than trying to determine whether physical activity or physical fitness is more important to health benefits.

From a public health policy perspective, it is clear that recommendations and programs should be designed to promote physical activity and not fitness. It would not make sense to encourage individuals to "become fit," but instead we can, and should, recommend that individuals "increase activity." We think it is likely that if sedentary persons do the latter, they will achieve the former.

Our review has limitations. We imposed the limitations of the selection criteria described earlier. These criteria limited the diseases, health conditions, and clinical outcomes considered and restricted the review to human studies. In addition, there were limitations resulting from the available literature. Current studies are limited by relatively few women and by severe limitations of racial/ethnic, socioeconomic, geographic, and other diversity characteristics.

RESEARCH RECOMMENDATIONS

Additional research is needed to address the issues discussed here. We do not think that it is important, or even desirable, to try to determine whether physical activity or cardiorespiratory fitness is more important for health. Fitness is developed by activity, although the magnitude of response to the exercise stimulus is genetically determined. Nonetheless, it seems likely that activity will be required to develop and maintain levels of fitness that are consistent with good health. Although we do not recommend additional research to pursue the elusive question posed in the title of this report, there are important studies that should be conducted.

1) Studies of both activity and fitness should focus on defining more precisely the shape of the dose-response curve. It is established that 30 min of moderate intensity activity on most days of the week will produce important health benefits. However, suppose that a person only participates in 15 min of moderate intensity activity per day. Will he or she receive any health benefits? Conversely, are additional health benefits expected if a person obtains 60 min of activity per day? These and other issues need further exploration in randomized controlled clinical trials.

2) It is clear that cardiorespiratory fitness, which is produced by aerobic exercise, has substantial health benefits. Musculoskeletal fitness, as developed by resistance exercise, clearly has benefits for preservation or regaining function. It is unclear whether resistance exercise training would reduce the risk of chronic diseases such as hypertension, CHD, or type 2 diabetes. Furthermore, if resistance training does affect risk of chronic disease, what is the shape of the dose-response curve? These issues need to be addressed in future research studies.

3) Although it is clear there is a dose-response relationship between both activity and fitness and several health outcomes, other outcomes need further research. Are activity and fitness inversely related to the risk of breast, prostate, and lung cancer; depression and anxiety disorders; psychotic episodes; gall bladder disease; or other health conditions that have not been studied?

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