Ann. Rev. Public Health. 1987. 8:253–87

PHYSICAL ACTIVITY AND THE INCIDENCE OF CORONARY HEART DISEASE[1]

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INTRODUCTION

The role of habitual physical activity in the primary prevention of coronary heart disease (CHD) has been reviewed by a number of qualified authors. Most recent reviews conclude that physically active individuals are at lower risk for CHD than less active persons (4, 19, 30, 63, 65, 83, 86). Reviews of this topic generally have adopted one of two approaches: a tally of "positive" and "negative" studies or a selection of the "best" studies. The tally approach fails to account for the varying quality of the reported studies, whereas the selective approach depends heavily on the reader's willingness to accept the judgment of the author. In this review, we combine the two approaches. We systematically review the literature, include all articles that meet pre-determined minimal requirements, and present a summary of the results of the studies. We also examine the methods used in the studies and provide our assessment of the quality of each study.

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Methods

We compiled a list of articles from a computerized search of the literature, the files of one of the authors (C. J. C.), and a manual review of the *Journal of Chronic Diseases* and the *American Journal of Epidemiology* from 1983 to 1985. Articles about the same study were grouped. The initial list included 121 articles representing at least 54 studies. Each study was randomly assigned to two of the authors for detailed review.

Studies were accepted for inclusion in this review only if (*a*) incident cases could be separated from prevalent cases, and (*b*) it was possible to estimate incidence rates, relative risks, odds ratios, or mortality ratios, or if a regression analysis had been done. Forty-three studies met the selection criteria. We were particularly interested in data comparing the risk of CHD between inactive and active persons. Some reports did not present the risk estimate but did present sufficient data to calculate the risk. For 18 studies we performed the calculations and present the relative risk estimates with 95% test-based confidence intervals (1, 2, 8–10, 14, 24, 25, 27, 29, 32, 58, 59, 68, 75, 78, 80, 90, 92, 93, 98, 107). In each comparison, the highest activity group is the reference category.

An abstract form was prepared, tested on a few articles, and revised. The form was designed to capture the essential elements of the definition and measurement of physical activity and CHD, to provide a summary of the results, and to allow an assessment of how well the study satisfied recommended standards for epidemiologic studies (21, 22, 36). The standards were adapted to the specific needs of studies of exercise and CHD. In addition, we provided our assessment of the quality of the definition and measurement of physical activity and CHD, and of other epidemiologic aspects of the study.

RESULTS

General Information

Tables 1–4 summarize the characteristics of the 43 studies, including their measures of physical activity, CHD, and epidemiologic methods. Of the 43 studies summarized, 36 followed specific groups of individuals with different activity levels to determine their subsequent incidence of CHD (cohort studies) (Tables 1 and 2); three compared the previous physical activity of all persons in a specified population who had died from CHD (mortality studies) (Table 3); and four compared the activity levels of persons with incident CHD to the activity levels of persons without CHD (case-control studies) (Table 4). All but six (7, 14, 56, 58, 59) were concluded after 1955. Twenty-three of the studies, including a study of Japanese-Americans in Hawaii and a study in Puerto Rico, were done in the United States; six were conducted in Great Britain, 13 elsewhere in Europe, and one in Israel. Thirty-two studies were limited to persons 65 years of age or less. Thirty-six studies included only men. Only five (8, 41, 48, 51, 80) analyzed and presented the data on women separately. Therefore, the 43 studies provide information primarily about North American and European working-aged men.

Measurement of Activity

The concept and operational definition of physical activity is vital to the value of these studies. Physical activity is a complex behavior for which there is no standard measurement (11, 49, 101). It is not readily dichotomized, such as smoking versus nonsmoking, nor does it conform to a readily measured continuum, such as cholesterol or blood pressure. The methods of measurement used in these studies varied considerably, ranging from an estimated 24-hour energy expenditure in Framingham to a separation of British civil servants into those who had spent five or more minutes in a very vigorous activity on a specific weekend and those who had not (41, 56). Only a few measurement instruments were used in more than one study: occupation as listed on the death certificate, three times (7, 58, 69); the Framingham Index of Physical Activity, three times (28, 41, 105); and the instrument developed for the Health Insurance Program (HIP) of New York Study, twice (33, 82). We assume that participants in the Seven Countries Study used essentially the same instrument (1, 10, 25, 54).

Early researchers focused on occupational activity. Twenty of the 24 studies conducted before 1970 examined only occupational activity. In contrast, only 3 of the 19 analyses done after 1969 examined only occupational activity. This shift in emphasis appears justified because of the decline in occupational physical activity. The study of San Francisco longshoremen, for example, would not now be possible because the proportion of men in the highest energy category has fallen from 40% to 5% (6). Further, in terms of preventing CHD, altering leisure-time activity is probably more easily done than changing occupational activity.

Evaluation Criteria for the Measurement of Physical Activity (Tables 1–4)

CLEAR The operational definition of physical activity should be stated and understandable. For 33 studies (77%), we found a clear definition of how the level or category of physical activity was determined.

ACCURATE (ACCUR) The reliability and validity of the measurement instrument should be determined. The accuracy of no physical activity measure is well established (49, 101). In 11 studies (26%), the researchers used an instrument for which some degree of reliability or validity has been established. If the reliability and/or validity of the instrument was established

Table 1 *Cohort studies of occupational physical activity and CHD: Characteristics of the study and quality of the measure of physical activity, the measure of CHD,* and the epidemiologic methods; 20 studies

					Physical activity measure[b]									CHD measure[b]					Epidemiologic methods[b]					
Location	Years	Number	Sex	Ages	FOCUS[a]	CLEAR	ACCUR	INDIV	DOSE	PAST	ADHERE	COLL	EVAL[c]	SPEC	COLL	OBJ	EQUAL	EVAL[c]	SEQ	ADJUST	REP	LOST	RANDOM	EVAL[c]
London postal workers and civil servants (58)	1949–1950	110,000	M	35–59	W	++	·	·	·	·	·	++	U	·	++	++	++	S	+	+	++	·	·	U
London Transport busmen (58)	1949–1950	31,000	M	35–64	W	++	·	·	·	·	·	++	S	·	++	++	++	S	+	+	++	·	·	U
London Transport busmen (32)	1949–1958	92,000	M	35–64	W	++	·	·	·	·	·	++	S	·	++	++	++	S	+	·	++	·	·	U
London Transport busmen (57)	1956–1965	667	M	30–69	W	++	·	·	·	·	·	++	S	++	++	++	++	G	++	+	+	++	·	S
Los Angeles civil servants (14)	1949–1954	955	M	40–70	W	++	·	·	·	·	·	++	U	++	++	·	++	S	++	·	++	++	·	S
Bell Telephone employees (59)	1951–1955	75,000	M	40–64	W	++	·	·	·	·	·	++	U	·	++	++	++	S	·	·	++	·	·	U
US railroad workers (93)	1954–1956	191,609	M	40–64	W	++	·	·	·	·	·	++	U	++	++	++	++	G	+	+	++	++	·	S
US railroad workers (92)	1957–1962	2085	M	40–59	W	++	++	·	·	·	·	++	S	++	++	++	++	G	++	+	++	++	·	G

North Dakota residents (107)	1956–1957	20,000	M	≥35	W	++	+	·	·	·	+	++	U	·	·	+	++	S	+	+	++	++	·	S
Chicago utility company employees (90)	1954–1957	784	M	50–59	W	·	·	·	·	·	·	++	U	++	++	·	++	S	++	+	++	++	·	S
Washington DC postal workers (39)	1906–1962	1664	M	<65	W	++	·	·	·	·	++	++	S	·	++	++	++	S	++	+	++	++	·	G
Yugoslavia residents (9, 10)	1958–1963	1371	M	40–59	W	·	·	·	·	·	·	++	U	++	++	·	++	S	++	·	++	++	·	G
Rural Italy residents (24, 25)	1960–1965	1712	M	40–59	W	·	·	·	·	·	·	++	U	++	++	++	++	G	++	·	++	++	·	G
Greek islands residents (1, 2)	1960–1965	1215	M	40–59	W	·	·	·	·	·	·	++	U	++	++	·	++	S	++	·	++	++	·	G
Italian railroad employees (54)	1963–1973	172,459	M	20–65	W	++	·	·	·	·	·	++	U	++	++	++	++	G	++	+	++	·	·	S
Israeli kibbutzim residents (8)	1949–1964	5288 5229	M F	40–64	W	++	·	·	·	·	++	++	S	++	·	++	++	S	++	+	++	++	·	G
Evans County, Georgia residents (12, 53)	1960–1969	934	M	≥40	W	+	·	·	·	·	·	++	U	++	++	·	++	S	++	+	++	++	·	G
East Finland residents (73)	1959–1969	671	M	40–59	W	++	·	·	·	·	·	++	U	·	++	++	++	S	++	·	++	·	·	S
West Finland residents (73)	1959–1969	721	M	40–59	W	++	·	·	·	·	·	++	U	·	++	++	++	S	++	·	++	·	·	S
San Francisco longshoremen (6, 64)	1951–1972	3686–3975	M	35–74	W	++	++	·	++	·	++	++	G	·	++	++	++	S	++	+	++	++	·	G

[a] W = work.
[b] ++ = yes, + = in part, · = no or uncertain. See text for explanation of columns.
[c] G = good, S = satisfactory, U = unsatisfactory.

Table 2 Cohort studies of various measures of physical activity and CHD: Characteristics of the study and quality of the measure of physical activity, the measure of CHD, and the epidemiologic methods; 16 studies

					Physical activity measure[b]									CHD measure[b]					Epidemiologic methods[b]					
Location	Years	Number	Sex	Ages	FOCUS[a]	CLEAR	ACCUR	INDIV	DOSE	PAST	ADHERE	COLL	EVAL[c]	SPEC	COLL	OBJ	EQUAL	EVAL[c]	SEQ	ADJUST	REP	LOST	RANDOM	EVAL[c]
Chicago Western Electric employees (68)	1957–1962	1989	M	40–55	L	++	·	++	·	·	·	++	S	++	++	·	++	G	++	·	·	·	·	U
Harvard alumni (66, 67)	1962–1978	16,936	M	35–74	L	++	++	++	++	+	·	++	G	·	++	++	++	S	+	+	·	++	·	S
British civil servants (15, 56)	1968–1978	17,944	M	40–65	L	++	++	++	++	·	·	++	G	·	++	++	++	S	++	+	++	++	·	G
Framingham residents (40, 41)	1956–1970	1909 2311	M F	35–64	T	++	++	++	++	·	·	++	G	++	++	++	++	G	++	++	++	++	·	G
Puerto Rico residents (28)	1965–1973	8155	M	45–64	T	++	++	++	++	·	·	++	G	++	++	++	++	G	++	++	++	++	·	G
Honolulu Heart Program, Japanese (105)	1965–1978	7705	M	45–68	T	++	++	++	++	·	·	++	G	++	++	++	++	G	++	++	·	·	·	S
Los Angeles firemen and policemen (69)	1971–1978	2779	M	35–54	F	++	++	++	·	·	·	++	S	++	++	+	++	G	++	++	++	++	·	G

Gothenberg, Sweden residents (99)	1963–1973	703	M	54	F	++	++	++	·	·	·	++	S	++	++	++	++	G	·	++	++	++	·	U
Gothenberg, Sweden residents (98)	1963–1967	803	M	54	L	+	·	++	·	·	·	++	U	++	++	++	++	G	·	++	++	++	·	U
Gothenberg, Sweden residents (99)	1970–1975	8125	M	47–54	L	+	·	++	·	·	·	++	U	++	++	+	++	G	·	++	·	++	·	U
Gothenberg, Sweden residents (48)	1968–1981	1462	F	38–60	W,L	++	·	++	·	·	·	++	S	++	++	++	++	G	++	++	++	++	·	G
New York health insurance subscribers (82)	1961–1963	61,000	M	35–64	W,L, B	++	·	++	·	·	·	++	S	++	++	+	++	G	·	+	++	++	·	S
San Francisco corporate employees (75)	1960–1969	3154	M	39–59	W	·	·	++	·	·	·	++	U	+	++	·	++	S	++	+	++	++	·	S
					L	++	·	++	·	·	·	++	S											
San Francisco federal employees (74)	1971–1974	1741	M	35–59	B	++	·	++	++	·	·	++	G	·	++	·	++	S	++	++	++	·	·	S
Oslo, Norway residents (35)	1972–1977	17,965	M	40–59	W,L	+	·	++	·	·	·	++	S	·	++	++	++	S	++	·	·	+	·	U
North Karelia, Finland residents (29, 80)	1972–1978	3978	M	30–59	W,L, B	++	++	++	·	·	·	++	S	·	++	++	++	G	++	++	++	·	·	G
		3688	F	35–59																				

[a] W = work, L = leisure, B = both, T = total 24 hour day, F = fitness measured rather than physical activity.
[b] ++ = yes, + = in part, · = no or uncertain. See text for explanation of columns.
[c] G = good, S = satisfactory, U = unsatisfactory.

Table 3 Mortality studies of occupational physical activity and CHD: Characteristics of the study and quality of the measure of physical activity, the measure of CHD, and the epidemiologic methods; 3 studies

					Physical activity measure[b]									CHD measure[b]					Epidemiologic methods[b]					
Location	Years	Number	Sex	Ages	FOCUS[a]	CLEAR	ACCUR	INDIV	DOSE	PAST	ADHERE	COLL	EVAL[c]	SPEC	COLL	OBJ	EQUAL	EVAL[c]	SEQ	ADJUST	REP	LOST	RANDOM	EVAL[c]
Great Britain residents (58)	1930–1932	2,617,000	M	45–74	W	++	·	·	·	+	NA	++	S	·	++	++	++	S	·	·	++	NA	NA	U
California residents (7)	1949–1951	3,200,000	M	20–64	W	++	·	·	·	+	NA	++	S	·	++	++	++	S	·	+	++	NA	NA	U
Iowa residents (70)	1964–1978	710,000	M	20–64	W	++	·	·	·	+	NA	++	S	·	++	++	++	S	·	+	++	NA	NA	U

[a] W = work.
[b] ++ = yes, + = in part, · = no or uncertain, NA = not applicable. See text for explanation of columns.
[c] G = good, S = satisfactory, U = unsatisfactory.

Table 4 Case control studies of occupational and leisure physical activity and CHD: Characteristics of the study and quality of the measure of physical activity, the measure of CHD, and the epidemiologic methods; 4 studies

					Physical activity measure[b]									CHD measure[b]					Epidemiologic methods[b]						
Location	Years	Number	Sex	Ages	FOCUS[a]	CLEAR	ACCUR	INDIV	DOSE	PAST	ADHERE	COLL	EVAL[c]	SPEC	COLL	OBJ	EQUAL	EVAL[c]	SEQ	ADJUST	REP	PREDET	BLIND	EXCLU	EVAL[c]
San Francisco coroner's cases (27)	before 1973	80	?	≤65	W,L	·	·	·	·	·	NA	++	U	·	++	++	++	S	·	+	·	·	·	·	U
Netherlands residents (51)	1970–1974	1348	M	35–69	L	·	·	++	·	·	NA	++	U	·	·	·	·	U	++	+	++	++	·	·	S
			F	45–69																					
Florida residents (33)	before 1977	1136	M	30–70	W,L	++	·	++	·	·	NA	++	S	·	++	++	++	S	·	+	++	++	·	·	S
Seattle residents (87, 88)	1979–1981	266	M	25–75	L	++	++	++	++	·	NA	++	G	++	++	++	++	G	++	+	++	++	·	++	G
		60	F	25–75																					

[a] W = work, L = leisure.
[b] ++ = yes, + = in part, · = no or uncertain, NA = not applicable. See text for explanation of columns.
[c] G = good, S = satisfactory, U = unsatisfactory.

for one population, we assumed that it would also be reliable or valid in another population, even though not specifically tested.

INDIVIDUAL (INDIV) The activity measure should be based on the activities reported specifically for each participant rather than on presumed activities based on membership in a group. Group assignments are more likely to result in misclassification and a blunted assessment of the strength of an association. Taylor et al (92), for example, classified railroad switchmen as more active than clerks, but noted that this generalization misclassified some members of both groups. Overall, 19 (44%) of the studies measured activity for each participant as an individual. Of the 34 studies that used occupational activity as the sole or component measure of activity, only ten (29%) categorized participants by individually reported actions on the job. In contrast, 13 of 14 studies that examined leisure-time activities used an individual measure.

DOSE The measure should include information about the frequency, duration, and intensity of the activities encompassed. Only eight studies (19%) specifically included all of this information in their measurement of physical activity.

PAST ACTIVITY (PAST) The level of physical activity during earlier periods of life should be determined. Only four studies (9%), including three mortality studies that determined activity class by the usual lifetime occupation as listed on the death certificate, provided any information about activity habits more than a few months before the start of the study. However, these only received partial credit because they did not fully characterize lifetime physical activity.

ADHERENCE (ADHER) For cohort studies, adherence to the original physical activity classification should be determined. Only three (8%) (6, 8, 39) of the 36 cohort studies obtained this information or even considered this issue in their analysis.

COLLECTION (COLL) The information about the physical activity measure should be systematically collected with specified standard methods. All studies satisfied this criterion.

In addition, we provide our overall evaluation (EVAL) of the physical activity measure. This summarization is more than a tally of the preceding criteria; it also includes our subjective impressions from carefully reading the papers. Overall, we conclude that eight (19%) of the studies had used good measures of physical activity, 17 (40%) were satisfactory, 17 (40%) were unsatisfactory, and one had a satisfactory measure of leisure-time activity but an unsatisfactory measure of occupational activity.

MEASUREMENT OF CHD CHD may present as myocardial infarction (MI), sudden death (SD), angina pectoris (AP), and less frequently as congestive heart failure (CHF) or cardiac arrhythmias. We considered CHD, as have most researchers, to encompass MI, SD, and AP. If CHF or cardiac arrythmias are included, they are specifically mentioned.

Evaluation Criteria for the Measurement of CHD (Tables 1–4)

SPECIFIC CRITERIA (SPEC) The criteria for the diagnosis of CHD should be clearly specified and applied consistently throughout the study. Physician judgment alone does not meet this standard. Diagnoses based on death certificates also do not meet this standard because they represent physician judgment without reference to a constant set of specific criteria. Twenty-two studies (51%) had specific criteria for the diagnosis of CHD.

COLLECTION (COLL) The information about the diagnosis of CHD should be systematically collected by using specified, standard sources and methods. Forty studies (93%) used a systematic review of records to identify persons with CHD.

OBJECTIVE (OBJ) The diagnoses included should be as objective as possible. The 30 (70%) studies that presented information separately about CHD death or that performed periodic or final screening examinations to detect asymptomatic MIs are considered superior. Angina is an inherently subjective diagnosis. Furthermore, active individuals may be more likely to induce exertional angina and to receive the diagnosis of CHD. Therefore, the nine studies (21%) that included angina as an inseparable component of CHD are considered inferior. Four studies (9%) that included MI but had no final screening evaluation to identify persons with asymptomatic MI are given partial credit.

EQUAL OPPORTUNITY FOR DIAGNOSIS (EQUAL) The identification of persons with CHD should be independent of their activity status. Studies that include nonfatal outcomes should make special provisions to ensure that all participants with CHD have an equal likelihood of diagnosis. Cohort studies that include periodic or final examinations and case-control studies in which cases and controls are subject to the same diagnostic evaluation are preferred. We did not automatically penalize studies that included angina because angina had been considered earlier. Forty-two of the studies (98%) satisfied this criterion.

As with the definition and measurement of physical activity, we provide our summary assessment (EVAL) of the definition and measurement of CHD.

Overall, the 43 studies had better evaluations for CHD than for physical activity or epidemiologic methods. Seventeen (40%) were considered to have good measures of CHD, 25 (58%) were satisfactory, and only 1 (2%) was considered unsatisfactory.

Evaluation Criteria for Epidemiologic Methods

SEQUENCE (SEQ) The physical activity status should be determined for a period that precedes the onset of CHD. Cohort studies that medically examine all participants prior to the observation period, and case-control studies that exclude persons with early manifestations of CHD from both cases and controls, satisfy this criterion. Twenty-seven (63%) studies provided good evidence that the measured activity pattern predated the manifestation of CHD.

ADJUSTED (ADJUST) Sex, age, blood pressure, smoking status, and serum cholesterol are known to be related to the risk of CHD and may confound an observed relationship between physical activity and CHD. These variables should be adjusted for in the analysis or by the study design. All but one report indicated either that the study was limited to men or the analysis was adjusted for gender (27). Ten studies (23%) controlled for all four of the other major risk factors: age, blood pressure, smoking status, and cholesterol; 11 studies (26%) did not control for any of these four risk factors. The specific variables accounted for in the design or analysis are shown for each study in Tables 5–8.

REPRESENTATIVE (REP) For cohort studies, the original group of participants should be typical of the population from which they are drawn. They should be either the entire population or a random sample of the entire population. Thirty (83%) of the 36 cohort studies began with a representative sample of the population being studied. For case-control studies, both cases and controls should come from the same population. Three of the four satisfied this criterion.

LOST TO FOLLOW-UP (LOST) For cohort studies, few participants should be lost to follow-up, or it should be established that the original activity status is similar for those who are lost and those who remain. We considered attrition rates up to 20% acceptable. Twenty-four (67%) of the 36 cohort studies fully satisfied this criterion; for 11 (31%), the information was not available.

RANDOM Cohort studies are less likely to be biased by unrecognized confounding variables if participants are randomly assigned to activity groups. All of these studies were observational studies, so in none were participants randomly assigned to active and inactive groups.

PREDETERMINED SELECTION (PREDET) For case-control studies, cases and controls should be chosen and the data collected according to a predetermined protocol. Three of the four case-control studies described a predetermined protocol for the selection of cases and controls.

BLINDED COLLECTION (BLIND) For case-control studies, both data collectors and respondents should be unaware of the hypothesis under consideration. The potential protective effect of activity on CHD and the risk of cardiac complications during exercise are so well known that it would be difficult to obtain self-reported information that is immune to recall bias. None of the four case-control studies provided information about this subject.

EQUAL EXCLUSIONS (EXCLU) For case-control studies, any constraint should apply equally to cases and controls. Only one of the four studies provided evidence that exclusionary criteria applied equally to cases and controls.

In terms of epidemiologic methods, we considered 15 studies (35%) to be good, 15 (35%) to be satisfactory, and 13 (30%) to be unsatisfactory.

Relative Risk

Tables 5–8 show the relative risk of CHD for less active persons compared with the most active persons for each study, either as reported in the study or as calculated by us. Also presented are the CHD outcome variables included in the comparison, a brief description of the physical activity exposure variables, the adjustments made in the analysis, and our evaluation of the activity measure, CHD measure, and epidemiologic methods. The varying definitions of exercise and CHD, the varying quality of the different studies, and the multiple and varying comparisons presented by several studies make it difficult to summarize the findings. Nevertheless, patterns do exist. For example, no study reported a significantly greater risk of CHD for more active persons.

To facilitate the rapid categorization of the study results, we have provided a summary *score* for each set of risk determinations. Each set of determinations was scored a "0" if no statistically significant association was found, "+" if the association was significant but the relative risk was <1.5, and "++" if the association was significant and the relative risk was ≥ 1.5. In addition, a "+" was added to the score if the relative risk exhibited a graded or dose response, regardless of statistical significance. Studies that used regression techniques and reported an inverse association were considered to have reported a graded response. The comparison was not scored if the statistical significance or confidence interval for the relative risk was not available. Of the 96 sets of risk determinations in these 43 studies, 38 (40%)

Table 5 Cohort studies of occupational physical activity and CHD: Relative risk of CHD by CHD outcome, activity group, adjustments, and methodologic quality; 20 studies

Study location	Outcome[a]	High-activity group	Low-activity group	Relative risk	Score[b]	Adjustments[c]	Evaluation[d] act	CHD	epi
London postal workers and civil servants (58)	CHD death	postmen	intermediate	1.4(1.0–2.0)	+++	none	U	S	U
			sedentary	2.0(1.4–2.8)					
	MI	postmen	intermediate	1.3(0.9–1.9)	+	none			
			sedentary	1.4(0.9–2.1)					
	AP	postmen	intermediate	0.6(0.4–0.9)	O	none			
			sedentary	0.8(0.5–1.2)					
	CHD	postmen	intermediate	1.1(0.9–1.4)	++	A			
			sedentary	1.3(1.0–1.6)					
London Transport busmen (58)	SD (72 hr)	conductors	drivers	2.3(1.4–3.8)	++	none	S	S	U
	MI	conductors	drivers	2.3(1.3–4.2)	++	none			
	AP	conductors	drivers	0.5(0.2–1.2)	O	none			
	CHD	conductors	drivers	1.5(1.0–2.2)	++	A			
London Transport busmen (32)	SD	conductors	drivers	1.9(1.3–2.6)	++	A	S	S	U
London Transport busmen (57)	CHD	conductors	drivers	1.8(0.9–3.3)	O	A	S	G	S
Los Angeles civil servants (14)	CHD	work, heavy	medium	0.5(0.2–1.4)	O	none	U	S	S
			light	0.7(0.3–1.5)					
			sedentary	0.5(0.1–1.6)					
Bell Telephone employees (59)	CHD death	work, nonmanagement	management	1.1(0.9–1.2)	O	none	U	S	U

US railroad workers (93)	CHD death	section men	switchmen clerks	1.4(1.1–1.7) 2.0(1.7–2.5)	+++	A	U	G	S
US railroad workers (92)	CHD death MI, SD AP	switchmen switchmen switchmen	sedentary clerks sedentary clerks sedentary clerks	1.2(0.6–2.4) 1.1(0.5–2.4) 1.2(0.7–1.9)	O O O	A A A	S	G	G
North Dakota residents (107)	MI, SD	farmers	nonfarmers	1.8(1.2–2.7)	++	A	U	S	S
	AP, coronary insufficiency	farmers	nonfarmers	1.3(0.8–2.1)	O	A			
Chicago utility company employees (90)	CHD, CHF	work, medium and light	sedentary	1.1(0.6–2.2)	O	A	U	S	S
Washington DC postal workers (39)	CHD death	letter carriers, ≥5 yr on job	postal clerks, ≥5 yrs on job	2.8($p < .05$)	++	A	S	S	G
Yugoslavia residents (9, 10)	CHD	work, heavy	moderate sedentary	1.4(0.6–3.6) 1.9(0.9–4.0)	+	none	U	S	G
Italy residents (24, 25)	MI, SD	work, heavy	moderate sedentary	1.8(0.8–4.1) 3.1(1.2–7.5)	+++	none	U	G	G
Greek islands residents (1; 2)	CHD	work, heavy	moderate sedentary	1.2(0.4–3.6) 2.0(0.6–6.0)	+	none	U	S	G

Table 5 *(Continued)*

Study location	Outcome[a]	High-activity group	Low-activity group	Relative risk	Score[b]	Adjustments[c]	Evaluation[d] act	Evaluation[d] CHD	Evaluation[d] epi
Italian railroad employees (54)	CHD death	work, heavy	moderate sedentary	1.9($p < .001$) 1.6($p < .001$)	++	A	U	G	S
Israeli kibbutzim, male residents (8)	AP	work, less than 80% seated	at least 80% seated	2.6(1.8–3.6)	++	A	S	S	G
	MI	work, less than 80% seated	at least 80% seated	2.5(1.8–3.4)	++	A			
	CHD death	work, less than 80% seated	at least 80% seated	2.0(1.2–3.3)	++	A			
Israeli kibbutzim, female residents (8)	AP	work, less than 80% seated	at least 80% seated	3.5(2.1–6.0)	++	A			
	MI	work, less than 80% seated	at least 80% seated	1.8(0.6–5.1)	O	A			
	CHD death	work, less than 80% seated	at least 80% seated	3.0(0.3–29.4)	O	none			
Evans County, Georgia residents (12, 53)	CHD	sharecroppers and farm laborers	professionals tradesmen clerks laborers (nonfarm) farm owners	3.0(NA) 4.6(NA) 5.8(NA) 6.1(NA) 3.2(NA)	?	A	U	S	G

East Finland residents (73)	CHD death	work, category 4 (most active)	category 3 category 2 category 1	0.7(0.3–1.6) 1.6(0.7–3.3) 1.1(0.4–3.1)	O	none	U	S	S
West Finland residents (73)	CHD death	work, category 4 (most active)	category 3 category 2 category 1	1.1(0.2–8.4) 2.4(0.3–18.5) zero cell	+	none	U	S	S
San Francisco longshoremen (6, 64)	CHD death	work, heavy tasks require >5.0 kcal/min	moderate and light tasks (≤5.0 kcal/min)	1.6(p < .005)	++	A	G	S	G
	CHD death, includes prevalent cases	multiple regression on kcal/min		risk increases as activity decreases	+++	A,BP,SM,O,GI, EKG status, race			
		7 kcal/min	1 kcal/min	2.2(p < .05)					

[a] AP = angina, CHD = coronary heart disease, CVD = cardiovascular disease, CHF = congestive heart failure, MI = myocardial infarction, SD = sudden death. CHD includes AP, MI, and SD; CHD death includes fatal MI and SD.

[b] ++ = RR of ≥1.5 and p < .05, + = 1.0 <RR <1.5 and p < .05, trend adds + to every value.

[c] A = age, BP = blood pressure, CH = cholesterol, SM = smoking, O = obesity, GI = glucose intolerance or diabetes, LVH = left ventricular hypertrophy.

[d] G = good, S = satisfactory, U = unsatisfactory.

had a score of "0," 9 (9%) had a score of "+," 34 (38%) of "++," 10 (11%) of "+++," and 3 (3%) could not be scored because a dose-response trend was not apparent and statistical significance was not reported. For the remainder of this review, any set of risk determinations that has a summary score of "+" or more is considered to have found an inverse association between level of physical activity and the incidence of CHD.

Comparisons that included women as subjects or angina as an outcome measure were distinctly different from the overall pattern. Five studies presented separate results for women. Of the 14 sets of risk determinations in these five studies of women, 10 (71%) were scored "0;" six of the 10 were from a single study (48). Of the five studies, two found no association between physical activity and CHD, two found an inverse association (51, 80), and one found an inverse association for angina but not for MI or CHD death (8). Nine studies presented separate comparisons for angina (8, 48, 56, 58, 67, 82, 105, 107). Of the 13 sets of risk determination in which angina was the only outcome variable, only three (23%) scored "+" or more. In contrast, 64% of the other comparisons scored "+" or more. Therefore, for subsequent summarizations, comparisons that included only women or only angina have been excluded.

Eight studies presented data for more than one component of the CHD measure (8, 56, 58, 66, 67, 80, 92, 105). In four of the eight studies, the score was "+" or more for each outcome measure (8, 56, 58), while one study scored "0" for each outcome measure (92). In one study the association between activity and SD was not statistically significant but the associations among activity and nonfatal MI, fatal MI, MI and SD combined, and fatal MI and SD combined all were (66, 67). Another study revealed an inverse association between activity and CHD, but no association between activity and CHD components; it was considered to have shown an association (105). To prevent these eight studies from carrying disproportionate weight because they presented data for more than one outcome, each is counted only once in subsequent summarizations, except for the one study that revealed an inverse association for CHD death and MI with work activity but not with leisure (80). This last set of results is counted separately in subsequent sections.

Whether the study focused on leisure or occupational physical activity did not appreciably affect the frequency of observed association. An inverse association between level of physical activity and incidence of CHD was noted for 18 of 29 (62%) of occupational studies, 9 of 14 (64%) leisure-time, 5 of 6 (83%) that combined work and leisure, and 2 of 2 that objectively assessed level of fitness. Six studies presented data for work and leisure activity separately. One scored "+" or more for both work and leisure activity (82), three scored "0" for work but "+" or more for leisure activity (33, 35, 75), one scored "+" or more for work and "0" for leisure activity (80), and

Table 6 Cohort studies of various measures of physical activity and CHD; Relative risk of CHD by CHD outcome, activity group, adjustments, and methodologic quality; 16 studies

Study location	Outcome[a]	High-activity group	Low-activity group	Relative risk	Score[b]	Adjustments[c]	Evaluation[d] act	CHD	epi
Chicago Western Electric employees (68)	CHD	leisure, sport participant	nonparticipant	2.0(1.3–3.0)	++	none	S	G	U
Harvard alumni (67)	CHD	≥2000 kcal/wk in leisure activity	<2000 kcal/wk	1.6($p < .001$)	++	A	G	S	S
	CHD death	≥2000 kcal/wk in leisure activity	<2000 kcal/wk	2.0($p = .001$)	++	A			
	SD	≥2000 kcal/wk in leisure activity	<2000 kcal/wk	1.2($p = .594$)	O	A			
	nonfatal MI	≥2000 kcal/wk in leisure activity	<2000 kcal/wk	1.3($p = .05$)	+	A			
	AP	≥2000 kcal/wk in leisure activity	<2000 kcal/wk	1.9($p = .005$)	++	A			
Harvard alumni (66)	CHD death	≥2000 kcal/wk in leisure activity	500–1999 kcal/wk <500 kcal/wk	1.3 1.6 ($p = .002$)	+++	A,BP,SM			
British civil servants (15, 56)	CHD	vigorous exercise (VE) in sports (≥5 min at ≥7.5 kcal/min	no VE in sports or around the house	2.2(NA)	?	A	G	S	G
	CHD nonfatal	VE sports	no VE	2.0($p < .001$)	++	A			
	CHD death	VE sports	no VE	2.6($p < .001$)	++	A			
	AP	VE sports	no VE	2.5(NA)	?	A			
Framingham male residents (40)	CHD death	physical activity index scores of 38–83	scores 34–37 scores 30–33 scores 24–29	1.2(NA) 1.6(NA) 1.9(NA)	+	A	G	G	G

Table 6 *(Continued)*

Study location	Outcome[a]	High-activity group	Low-activity group	Relative risk	Score[b]	Adjustments[c]	Evaluation[d] act	Evaluation[d] CHD	Evaluation[d] epi
Framingham male residents (41)	CHD death	multiple regression on physical activity index		risk increases as activity decreases ($p < .05$)	++	A,BP,CH, SM,GI,LVH	G	G	G
Framingham female residents (41)	CHD death	multiple regression on physical activity index		no significant relationship	O	A,BP,CH, SM,GI,LVH			
Puerto Rico rural residents (28)	MI, SD	multiple regression on Framingham physical activity index		risk increases as activity decreases ($p < .05$)	++	A,BP,CH,SM,O heart rate	G	G	G
Puerto Rico urban residents (28)	MI, SD	multiple regression on Framingham physical activity index		risk increases as activity decreases ($p < .05$)	++	A,BP,CH,SM,O heart rate			
Honolulu Heart Program, Japanese (105)	CHD	multiple regression on Framingham physical activity index		risk increases as activity decreases ($p < .05$)	++	A,BP,CH,SM,O	G	G	S
	CHD death	multiple regression on Framingham physical activity index		no significant relationship	O				
	MI	multiple regression on Framingham physical activity index		no significant relationship	O				
	AP	multiple regression on Framingham physical activity index		no significant relationship	O				

Los Angeles firemen and policemen (69)	MI, SD	above median cardiovascular fitness	below median cardiovascular fitness	2.4(1.1–5.9)	++	A,BP,CH,SM,O	S	G	G
Gothenberg, Sweden residents (99)	MI, SD	above median cardiovascular fitness	below median cardiovascular fitness	2.3(1.4–4.0)	++	A,BP,CH,SM	S	G	U
Gothenberg, Sweden residents (98)	MI, SD	multiple regression on leisure time physical activity index		no significant relationship	O	A,BP,CH,SM EKG changes.	U	G	U
Gothenberg, Sweden residents (99)	MI, SD	multiple regression on leisure time physical activity		no significant relationship	O	A,BP,CH,SM	U	G	U
Gothenberg, Sweden female residents (48)	MI, SD	multiple regression on occupational activity		no significant relationship	O	A,BP,CH,SM,O SES, Educ, TG	S	G	G
	AP	multiple regression on occupational activity		no significant relationship	O				
	EKG changes	multiple regression on occupational activity		no significant relationship	O				
	MI, SD	multiple regression on leisure activity		no significant relationship	O	A,BP,CH,SM,O SES, Educ, TG			
	AP	multiple regression on leisure activity		no significant relationship	O				
	EKG changes	multiple regression on leisure activity		no significant relationship	O				

Table 6 *(Continued)*

Study location	Outcome[a]	High-activity group	Low-activity group	Relative risk	Score[b]	Adjustments[c]	Evaluation[d] act	Evaluation[d] CHD	Evaluation[d] epi
New York health insurance subscribers (82)	CHD, CHF, conduction defects	work 11–28 points on 28 point scale	1–10 points	1.6(1.2–2.1)	++	A	S	G	S
	CHD, CHF, conduction defects	leisure, 2–10 points on 10 point scale	0–1 points	1.5(1.1–2.0)	++	A			
	CHD, CHF, conduction defects	work and leisure, 13 most active categories	3 least active categories	1.7(1.3–2.2)	++	A			
	AP	work, 19–28 points	1–18 points	0.7(0.5–1.0)[d]	O	A			
	AP	leisure, 6–10 points	0–5 points	0.8(0.5–1.1)[d]	O	A			
	AP	work and leisure, 7 most active categories	9 least active categories	0.7(0.5–1.0)[d]	O	A			
San Francisco corporate employees (75)	CHD	work, moderate and heavy	sedentary and light	0.9(0.6–1.4)	O	A	U	S	S
	CHD	leisure, regular activities	occasional or no activities	1.5(1.1–2.1)	++	A	S	S	S
San Francisco federal employees (74)	CHD	multiple regression on total daily calories from work and leisure		1.2(p = 0.23)	O	A,BP,CH,SM	G	S	S

Oslo, Norway residents (35)	CHD death	work activity, great	intermediate	0.9(NA)	O		S	S	U
			moderate	0.7(NA)					
			sedentary	0.5(NA)					
	CHD death	leisure activity, intermediate	moderate	1.3(NA)	+				
			sedentary	2.5(NA)					
North Karelia, Finland male residents (80)	MI	high work	low work	1.5(1.2–2.0)[e]	++	A,BP,CH,SM,O	S	G	G
	CHD death	high work	low work	1.6(1.1–2.3)[e]	++	A,BP,CH,SM,O			
	MI	high leisure	low leisure	1.2(0.9–1.5)[e]	O	A,BP,CH,SM,O			
	CHD death	high leisure	low leisure	1.4(1.0–2.1)[e]	O	A,BP,CH,SM,O			
	MI	high work and high leisure	high/low or low/high	1.3(1.0–1.7)	+++	A			
			low/low	2.5(1.8–3.7)					
North Karelia, Finland female residents (80)	MI	high work	low work	2.4(1.5–3.7)[e]	++	A,BP,CH,SM,O	S	G	G
	MI	high leisure	low leisure	1.5(0.9–2.5)[e]	O	A,BP,CH,SM,O			
	MI	high work and high leisure	high/low or low/high	1.8(0.9–3.5)	+++	A			
			low/low	4.0(2.1–7.8)					

[a] AP = angina, CHD = coronary heart disease, CVD = cardiovascular disease, CHF = congestive heart failure, MI = myocardial infarction, SD = sudden death. CHD includes AP, MI, and SD; CHD death includes fatal MI and SD. SES = socioeconomic status, Educ = education, TG = triglyerides.

[b] ++ = RR of ≥ 1.5 and $p < .05$, + = $1.0 < RR < 1.5$ and $p < .05$, trend adds + to every value in the series.

[c] A = age, BP = blood pressure, CH = cholesterol, SM = smoking, O = obesity, GI = glucose intolerance or diabetes.

[d] G = good, S = satisfactory, U = unsatisfactory.

[e] 90% confidence intervals.

Table 7 Mortality studies of occupational physical activity and coronary heart disease: Relative risk of CHD by CHD outcome, activity group, adjustments, and methodologic quality; 3 studies

Study location	Outcome[a]	High-activity group	Low-activity group	Relative risk	Score[b]	Adjustments[c]	Evaluation[d] act	Evaluation[d] CHD	Evaluation[d] epi
Great Britain residents (58)	CHD death	work, heavy	intermediate light	1.4(1.3–1.6) 2.2(2.0–2.4)	+++	none	S	S	U
California residents (7)	CHD death	farmers and farm laborers	nonfarm heavy nonfarm medium nonfarm light sedentary	1.3(NA) 1.4(NA) 1.5(NA) 1.5(NA)	+	A, general risk of mortality	S	S	U
Iowa residents (70)	CHD death	farmers	nonfarmers	1.1($p < .05$)	+	A	S	S	U

[a] CHD = coronary heart disease.
[b] ++ = RR of $\geq$1.5 and $p < .05$, + = 1.0 <RR <1.5 and $p < .05$, trend adds + to every value in the series.
[c] A = age.
[d] G = good, S = satisfactory, U = unsatisfactory.

Table 8 Case-control studies of occupational and leisure physical activity and coronary heart disease: Relative risk of CHD by CHD outcome, activity group, adjustments, and methodologic quality; 4 studies

Study location	Outcome[a]	High-activity group	Low-activity group	Relative risk	Score[b]	Adjustments[c]	Evaluation[d] act	CHD	epi
San Francisco coroner's cases (27)	SD	work, heavy and moderate	no activity	1.5(0.5–4.4)	O	A	U	S	U
	SD	leisure, heavy and moderate	no activity	1.1(0.6–1.9)	O	A			
Netherlands, male residents (51)	CHD	habitual walk, cycle or garden	occasional	1.6(1.1–2.1)	++	A,BP,SM,O	U	U	S
	CHD	vigorous exercise	no vigorous exercise	1.7(1.2–2.3)	++	A,BP,SM,O			
Netherlands, female residents (51)	CHD	habitual walk, cycle or garden	occasional	5.3(2.6–10.0)	++	A,BP,SM,O			
	CHD	vigorous exercise	no vigorous exercise	4.0(1.6–10.0)	++	A,BP,SM,O			
Florida residents (33)	CHD death	HIP[e] questionnaire, regression on within pair difference for work activity		no significant relationship	O	A,BP,SM,O	S	S	S
	CHD death	regression on within pair difference for leisure activity		risk increases as activity decreases ($p < .001$)	+++	A,BP,SM,O			
Seattle residents (87, 88)	Primary cardiac arrest	≥124 kcal/day in high intensity leisure activity	17–123 kcal/day 1–16 kcal/day 0 kcal/day	1.3(0.7–2.4) 2.2(1.1–4.1) 2.5(1.3–5.1)	+++	A,BP,SM	G	G	G

[a] SD = sudden death, CHD = coronary heart disease. CHD includes angina, myocardial infarction (MI) and sudden death; CHD death includes fatal MI and sudden death.
[b] ++ = RR of ≥1.5 and $p < .05$, + = 1.0 <RR <1.5 and $p < .05$, trend adds + to every value in the series.
[c] A = age, BP = blood pressure, SM = smoking, O = obesity.
[d] G = good, S = satisfactory, U = unsatisfactory.
[e] Health Insurance Program of New York.

one scored "0" for both (27). In subsequent tabulations, these six studies are included twice, once for their assessment of occupational activity and once for their assessment of leisure activity.

Of the original 96 comparisons in these 43 studies, 47 are left after excluding the studies of only women, excluding the study that could not be scored, and counting only once the studies that presented results for more than one CHD measure. Among these 47, 32 (68%) found an inverse association between level of physical activity and incidence of CHD (i.e. score of "+" or more). Better studies were more likely to report an association. Of those studies whose activity measure, CHD measure, and epidemiologic method were not considered to be good, only 57% (12 of 21) reported an inverse association. In contrast, 73% (11 of 15) of the comparisons that received one good evaluation and 82% (9 of 11) that received two or three good evaluations reported an inverse association. When each of the three areas of evaluation were considered separately, similar observations were made. An inverse association was reported by 50% (9 of 18) of the studies with an unsatisfactory measure of physical activity and 88% (7 of 8) of the studies with a good measure. Similarly, an inverse association was reported by 60% (9 of 15) of those with unsatisfactory epidemiologic methods and 86% (12 of 14) of those with good methods. The trend was less apparent for the measure of CHD. The only study considered to have an unsatisfactory measure of CHD reported an inverse association; 64% (18 of 28) of those considered satisfactory and 72% (13 of 18) of those considered good also reported an inverse association.

DISCUSSION

We conducted this review to evaluate existing data concerning the hypothesis that physical activity reduces the risk of CHD and to make our best inference regarding causation. In the most fundamental sense, empirical data, whether from experimental (randomized) or nonexperimental (observational) designs, never prove causation. Criteria have been recommended for evaluating scientific literature and making practical decisions for public health policy and medical practice (34, 77). We have been guided by these criteria. Associations that are consistent, strong, appropriately sequenced, graded, plausible, coherent, and supported by experimental evidence are firmly enough established to be acted upon. Not all seven of these must be satisfied, and only an appropriate sequence is absolutely essential; taken as a group, however, they provide a framework for evaluating the overall persuasiveness of scientific observations.

CONSISTENCY Approximately two thirds of the studies reported a statistically significant association, a graded response, or both. The repeated observation in many settings and populations is evidence that physical inactivity is a component cause of CHD. Methodologically superior studies were more likely to report an inverse association. This suggests that misclassification and other errors have obscured the association in less carefully conducted investigations.

STRENGTH The relative risk of CHD associated with inactivity varies among studies but generally ranges from 1.5 to 2.4, with a median of about 1.9 for all 47 determinations. The median for the 32 determinations that show an inverse association is also 1.9. Better studies tended to report higher relative risks. When only studies with inverse associations (score of "+" or more) were included, the medians for studies with zero, one, or ≥ two good evaluations, respectively, were 1.9, 2.0, and 2.4. The strength of an association depends upon the prevalence of other causes. Therefore, the modest size of the inverse association between physical activity and CHD probably reflects the fact that CHD has multiple component causes. Even the more well-accepted risk factors such as hypertension, cholesterol, and smoking have relative risks only slightly greater than inactivity. For example, the final report of the Pooling Project indicates that the age-standardized risk ratio for MI and SD among men with a systolic pressure >150 mmHg compared with those with a systolic pressure ≤120 mmHg is 2.1; 2.4 for men with a serum cholesterol >268 mg/dl compared with those with a cholesterol ≤218 mg/dl; and 2.5 for those who smoke ≥ 1 pack of cigarettes per day compared with those who don't smoke (71).

APPROPRIATELY SEQUENCED The data in Tables 1–4 indicate that nearly two thirds of the studies adequately demonstrated that the activity level predated the onset of CHD. Studies that did so were more likely to identify an association than those that failed to do so.

BIOLOGIC GRADIENT Twenty-five sets of risk determinations allowed an assessment of a graded response because they utilized either a regression analysis or more than two levels of physical activity. Of these, 17 (68%) demonstrated increasing risk with decreasing activity. All seven with more than one good evaluation reported a graded response.

PLAUSIBILITY AND COHERENCE Physical activity could reduce the incidence of CHD by retarding the atherosclerotic process, modifying the structure of the coronary arteries, reducing vasospasm, enhancing myocardial electrical stability, or increasing fibrinolysis. Exercise improves glucose tolerance and insulin sensitivity (42), assists in weight control, and may reduce blood pressure (81). Several studies controlled for glucose intolerance, obesity, hypertension, and total cholesterol (Tables 5–8). None, however, controlled for high-density lipoprotein (HDL) cholesterol. Reduced HDL cholesterol is a powerful CHD risk factor (13, 104). HDL levels are increased in endurance athletes (96, 102), in sedentary men after exercise training (38, 46, 50), and even in men who simply report some regular strenuous activity (31). Vigorous activity also reduces fasting triglyceride concentrations (17) and augments intravenous fat clearance (79). Fasting triglycerides are not presently considered an independent risk factor for CHD (37), but triglyceride-rich lipoproteins may be atherogenic (106), and their reduced concentration and enhanced clearance in active people may be beneficial. Exercise training in subhuman primates results in higher HDL and lower triglyceride levels and apparently less coronary atherosclerosis (47). Few comparisons have been made of coronary atherosclerosis in active and sedentary men, however, and available studies in humans are not convincing (89).

Physical activity also increases the caliber of epicardial coronary arteries (5, 47, 103) and enhances coronary collateral development (60) in animal models of CHD. Similar evidence is difficult to obtain in humans. Only anecdotal reports (18) suggest the presence of larger coronary arteries in active subjects, and angiographic studies have failed to demonstrate collateral vessel development in CHD patients after 3 to 13 months of exercise training (16, 23, 43, 62, 84).

Nevertheless, a reduction in CHD incidence could occur without alterations in the atherosclerotic process or increases in coronary artery diameter. Even brief exercise acutely increases fibrinolysis (20, 76) and exercise training augments the fibrinolytic response to venous occlusion (100) and might reduce the incidence of coronary thrombosis. Moreover, physical training in dogs reduces coronary vasospasm during adrenergic stimulation (5), an important effect given the possible role of coronary vasospasm in acute MI (52). Alternatively, exercise could prevent sudden cardiac death by enhancing myocardial electrical stability. Physical training in humans increases cardiac parasympathetic tone (44). Parasympathetic stimulation reduces ventricular fibrillation during cardiac ischemia (45), and animal models of sudden cardiac death document a heightened resistance to ventricular fibrillation after exercise training (3, 61).

Animal models, therefore, demonstrate that physical activity may reduce CHD by retarding its development, enlarging the coronary bed, or preventing acute cardiac events. All are biologically plausible and coherent mediators for a beneficial effect of physical activity and may contribute to an exercise effect.

EXPERIMENTAL EVIDENCE No experimental study of the effect of physical activity on the primary prevention of CHD in humans has been done. The size, cost, and adherence problems attendant to such a study make the conducting of a randomized, controlled trial unlikely (26, 94, 95). Randomized, controlled trials may be useful in solving some of the important questions that remain, but sufficient data exist to conclude that physical activity is inversely associated with the incidence of CHD.

Biases

CONFOUNDING VARIABLES Confounding is unlikely to account for the observed association. Age, sex, blood pressure, smoking status, total serum cholesterol, and other factors were considered by many of the studies (Tables 5–8). Studies that made adjustments were just as likely to find an association as those that made no adjustments. The strength of the crude association was generally diminished only slightly by these adjustments. These observations suggest that physical activity exerts an effect on CHD that is independent of these other risk factors. Because some of the effect of activity may be mediated through blood pressure or serum lipids, one could argue that these other risk factors should not be controlled for in the analysis. By using a large data set, the extent of the direct and indirect contributions of these variables could be measured.

POSITIVE PAPER BIAS Studies that show a statistically significant direct or inverse association may be more likely to be published than those that do not. This bias is unlikely to explain our findings, however. If there were no association between physical activity and CHD, the number of studies that report an inverse association should equal the number that report a direct association. In fact, no study reported a significant direct association between physical activity and the incidence of CHD.

It is possible, however, that some comparisons were made but not reported. The unreported comparisons were likely the ones that were not "significant." Of particular help would be for studies to report their findings according to the relatively standard categories of SD, MI, AP, CHD-death, SD and MI combined, and all CHD combined. Results of all comparisons made should be reported.

SELECTION BIAS Self-selection is unavoidable in observational studies. It may affect the analyses in several ways. First, if adequate attention has not been given to assuring that the measured activity level preceded the onset of CHD, individuals with preexisting CHD could constitute a disproportionate number of the inactive group. If this were an important problem with the published papers, cohort studies with medical screening before the observation period should show smaller and less consistent associations than those without prior screening. This was not observed. Similarly, if persons with subclinical CHD are over-represented in the inactive group, the strength of the inverse relationship should weaken over time. A few cohort studies have examined data among only those who have survived a certain length of time and found that the inverse association persists (6, 55, 80). This result indicates that inactivity is not due to prodromal symptoms of CHD. Furthermore, Morris et al (55) have pointed out that the misclassification produced by minimally ill persons shifting to the inactive group is not large enough to produce the observed results.

Second, selection bias may alter the results via an association between activity and other risk factors. However, as noted above, the association persists after adjustment for age, blood pressure, smoking, total cholesterol, and other factors.

Finally, reduced physical activity could reflect a "constitutional" factor that truly causes CHD. College athletic participation does not predict future risk of CHD but current physical activity does (66). Such results suggest that physical activity is more likely responsible for the lower risk of CHD than an unmeasured constitutional factor (86).

FUTURE DIRECTIONS The existing literature supports the conclusion that an inverse association exists between physical activity and CHD. Some important details remain to be elucidated. Since few studies provide information about women or older men, it is important to determine whether the association holds for them as well as middle-aged men. Currently available data indicate that persons with other risk factors, such as hypertension, obesity, or smoking, may benefit from regular physical activity as much as or more than persons without those factors (86, 87). However, Siscovick et al reported that the level of physical activity does not influence mortality among men with extreme hypercholesterolemia (85). These reports need to be evaluated in other populations. What biochemical or metabolic mechanisms mediate the effect? What is the role, if any, of cardiorespiratory fitness? How rapidly after the onset of an exercise regimen do the benefits accrue or how quickly after cessation are they lost? How important is the intensity of the activity and what is the value of low-intensity activities? These and other facets of the relationship between exercise and CHD deserve attention.

Future studies can benefit by recognizing and correcting the weaknesses of past investigations. Careful attention must be given to the operational definitions of physical activity and CHD. The measure of activity should be based on the individual rather than the group and should include an estimate of the dose based on the intensity, frequency, and duration of activity. The standard estimates of the intensity of an activity may be improved by taking into account the perceived level of effort in that activity. Information about the lifetime pattern of activity has rarely been obtained; it could provide data about how long one needs to be active to benefit and how long the benefit persists after regular activity ceases.

Research to identify reliable and valid activity measures is needed. Because leisure-time physical activity appears to constitute an increasing portion of total physical activity, creative approaches will be needed to obtain information that is free from the inherent bias of recall data.

SUMMARY AND CONCLUSIONS

Our review focuses on all articles in the English language that provide sufficient data to calculate a relative risk or odds ratio for CHD at different levels of physical activity. The inverse association between physical activity and incidence of CHD is consistently observed, especially in the better designed studies; this association is appropriately sequenced, biologically graded, plausible, and coherent with existing knowledge. Therefore, the observations reported in the literature support the inference that physical activity is inversely and causally related to the incidence of CHD.

The two most important observations in this review are, first, better studies have been more likely than poorer studies to report an inverse association between physical activity and the incidence of CHD and, second, the relative risk of inactivity appears to be similar in magnitude to that of hypertension, hypercholesterolemia, and smoking. These observations suggest that in CHD prevention programs, regular physical activity should be promoted as vigorously as blood pressure control, dietary modification to lower serum cholesterol, and smoking cessation. Given the large proportion of sedentary persons in the United States (91), the incidence of CHD attributable to insufficient physical activity is likely to be surprisingly large. Therefore, public policy that encourages regular physical activity should be pursued.

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