Clinical Exercise Prescription: No Pain, No Gain?

Steven L. Leach, M.D.
Division of General Internal Medicine

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Biographical Information

Name: Steven L. Leach, M.D.

Rank: Assistant Professor of Internal Medicine

Division: General Internal Medicine

Interests: Preventive medicine, hypertension, liver disease

> All parts of the body which have a function, if used in moderation and exercised in labours in which each is accustomed, become thereby healthy, well-developed and age more slowly, but if unused and left idle they become liable to disease, defective in growth, and age quickly.
>
> Hippocrates[1]

Introduction

Data defining the effects of exercise on fitness have been accumulating since the 1920's. Based upon this wealth of information, health organizations have made numerous formal exercise recommendations. For instance, in 1972 the American Heart Association (AHA) recommended that otherwise healthy persons should perform continuous aerobic exercise 3-7 times per week for 15-20 minutes with an intensity level of 70-85% of their maximum predicted heart rate (MHR).[2] The American College of Sports Medicine (ACSM) offered similar standards in 1978, recommending continuous aerobic exercise 3-5 times per week for 15-60 minutes at an intensity of 60-90% of MHR (or 50-85% of VO_2max).[3] The purpose of these recommendations was to define the amount of exercise needed to develop and maintain cardiorespiratory fitness. The principles upon which they are founded are sound, and the specifics have been modified very little over time. In spite of this solid scientific foundation, the reality is that only a small fraction of Americans have ever followed them. In fact, in a society that is becoming increasingly sedentary, the more common question is not what one has to do to be fit, but rather, how one can acquire the maximum benefit with the smallest effort.

Data measuring the direct health benefits of varying levels of physical activity have only slowly accumulated since the 1950's. Nevertheless, this data has indeed provided a convincing link between physical inactivity and cardiovascular morbidity and mortality. To the surprise of many investigators, emerging data also indicates that the benefits of physical activity accrue at levels far below what was previously thought. This new appreciation is evident in a joint statement from the Centers for Disease Control and Prevention (CDC) and the ACSM issued in 1995. Acknowledging that physical activity need not be of vigorous intensity to improve health, this committee established a new minimum standard, recommending that every adult accumulate at least 30 minutes or more of moderate-intensity physical activity on most, preferably all, days of the week.[4] Although not intended to replace previous recommendations, this amendment was based upon practical considerations, such as safety, feasibility and anticipated health benefits, rather than the development of fitness.[5] In 1996, the National Institutes of Health, AHA and the Surgeon General all issued separate reports with similar conclusions.[6,7,8]

The practicality of these "user friendly" recommendations is easily deduced from epidemiological surveys. The CDC estimates that physical inactivity is a risk factor accounting for as many and 250,000 premature deaths per year.[4] Other data from the CDC indicate that as many as 29% of Americans get no leisure-time physical activity. Inactivity is more common in women (31.4%) and in certain racial and ethnic groups, such as Hispanics, where 41% get no leisure-time physical activity.[9] Physical inactivity is becoming more common among youth and children as well. From 1991 to 1995 the percentage of high school students participating in physical education classes decreased form 42% to 25%.[9] Inactivity has been blamed for the disturbing trends of increasing incidence of obesity and type 2 diabetes mellitus. Between 1980 and 1994, the prevalence of type 2 diabetes increased from 8.9% to 12.3% of the U.S.

population. Among Mexican-Americans, prevalence is now 20.3%.[10] Nearly 55% of Americans were overweight in 1998 (BMI≥25).[9] Data from NHANES III (1988-1994) indicate that nearly 20% of men and 25% of women in the U.S. are obese (BMI≥30).[11]

Certainly the changing demographics of the American economy have a lot to do with these trends. It is also clear that the medical community in general is not doing enough to encourage physical activity. Many physicians rarely provide specific exercise recommendations. Rather, patients are left to themselves to determine what type of exercise they should perform and how much they should do. The purpose of these grand rounds is to review pertinent data about the anticipated benefits of regular physical activity, the safety of exercise, and what specific recommendations can be provided to patients.

Physical Activity, Exercise and Fitness

The recent position statements emphasize increasing physical activity, even if it does not result in increased levels of fitness. Understanding these terms as they are used in epidemiological studies is important. *Physical activity* is defined as any bodily movement that is produced by the contraction of skeletal muscle and that substantially increases energy expenditure. For research purposes, physical activity is often categorized broadly as work-related or leisure-time. *Exercise* is a subclass of physical activity defined as planned, structured repetitive bodily movement done to improve or maintain one or more components of physical fitness. *Physical fitness* is a set of attributes that people have or achieve that relates to the ability to perform physical activity.[12] In physiologic terms, cardiovascular fitness is defined by the improvement in maximal oxygen uptake and lactate threshold.

Though voluminous, epidemiological studies of physical activity and exercise are unfortunately limited in their scope. Most studies have been limited to men, usually Caucasian and middle class. For instance, of 36 studies of physical activity and CHD reviewed in the Surgeon General's report, only 4 included women.[7] Consequently, the generalizability of the data is uncertain. The quality of research is also limited by the difficulty of measuring physical activity. Studies of physical activity typically use three different types of estimates: occupational classification, self-reported activity (work or leisure-time), or direct measures of physical fitness. The last of these is the most reliable, since fitness (a condition) is more objectively measured than physical activity (a behavior). Fitness is also not subject to recall bias. However, there is much of physical fitness that is genetically determined, making it difficult to measure the added effect of activity. Another limitation is that most studies have been cohort studies that assessed activity or fitness at one point in time and then followed the cohort longitudinally, without regard for changes in activity over time. Lack of information about cross-over potentially dilutes the data, making it more difficult to detect a difference. In spite of the limitations of these studies, there is general consistency in the data supporting the idea that physical activity improves health.

Cardiovascular and All-Cause Mortality Benefits of Physical Activity and Physical Fitness

The Effects of Work-related Physical Activity

The earliest measures of the effect of physical activity on health focused on work-related activity. The quality of the studies was variable and the results were not entirely consistent. However, most revealed reduced all-cause mortality and mortality from coronary heart disease (CHD), although not always statistically significant. Morris et. al., compared the incidence of cardiovascular events between conductors (high activity) vs. drivers (low activity) among 31,000 London busmen ranging in age from 35 to 64. Sedentary work activity was associated with a one-year relative risk (RR) of myocardial infarction (MI) of 2.3 (95% CI 1.3-4.2).[13] A similar study of 110,000 London civil servants by the same authors compared two-year event rates between postmen (high activity) and other civil servants categorized as having low or intermediate levels of work-related activity. Low activity was associated with a relative risk of death of 2.0 (95% CI 1.4-2.8), and intermediate activity was associated with a RR of 1.4 (95% CI 1.0-2.0).[13] Neither of these studies included adjustments for confounding factors. In the United States, a study of over 191,000 railroad workers comparing section men (high activity) to switchmen and clerks (low activity) found a five-year, age-adjusted relative risk of CHD-related death among switchmen of 1.4 (95% CI 1.1-1.7) and a relative risk of 2.0 (95% CI 1.7-2.5) for clerks.[14,15]

Paffenbarger followed 6351 San Francisco Bay Area longshoremen for 22 years (1951-1972).[16] Workers were categorized into 3 groups based on their estimated energy output per 8 hour shift above basal rates (heavy 1876 kcal, moderate 1473 kcal, and light 865 kcal). The age-adjusted coronary death rate for high-activity workers was 26.9 per 10,000 work-years, 46.3 for the moderate category and 49.0 for light. Age-adjusted relative risk of death from CHD for moderate and light activity compared to heavy was 1.6 (95% CI 1.2-2.2). Indicative of a changing economy, he also found that the proportion of longshoremen engaged in heavy work declined from 40% in the first decade, to 15% in the second, to 5% by the end of the study.

Salonen and colleagues in Finland looked at the effect for work-related activity on cardiovascular disease and all-cause mortality over seven years. After adjustment for age and other cardiovascular risk factors, low work activity was associated with increased risk of acute MI (RR 1.5; 90% CI 1.2-2.0), death from ischemic heart disease (RR 1.6; 90% CI 1.1-2.3), stroke (RR 1.6; 90% CI 1.1-2.5), and death from all causes (RR1.9; 90% CI 1.5-2.5).[17]

Table 1. Pooled Relative Risks from Studies of Occupational Activity and Risk of Heart Disease

Outcome*	**No. of studies**	**Relative risk (95%CI)**
Relative risks for sedentary groups vs. high activity		
CHD	4	1.4 (1.0-1.8)
CHD death	5	1.9 (1.6-2.2)
MI	1	1.4 (0.9-2.1)
MI + SD	1	3.1 (1.2-7.5)
AP	1	0.8 (0.5-1.2)

*Abbreviations: AP, angina pectoris; CHD, coronary heart disease; MI, myocardial infarction; SD, sudden death.
Source: Berlin & Colditz. Am J Epidemiol 1990;132:612-28.

A meta-analysis of available studies was performed by Berlin and Colditz in 1990. The pooled relative risk for death from CHD based on 17 studies was 1.4 (95% CI 1.2-1.8) for moderate activity compared to high activity, 1.9 (95% 1.6-2.2) for sedentary activity compared to high, and 1.5 (95% CI 1.1-2.0) for low + moderate activity compared to high activity.[18] The association was strongest among studies deemed to be of highest quality. Based upon this and other similar data, it appears that the physical activity of work has a modest beneficial effect on both CHD-related mortality and all-cause mortality.

Leisure-time Physical Activity and Total Activity

As work patterns have changed from an industrial economy to more sedentary types of work, more recent studies have focused on the benefits of leisure-time physical activity and total activity. Fortunately, there is much more data available on these measures. However, as with studies of work-related activity, those evaluating leisure-time activity have focused largely on white, middle-aged men. Consequently, the implications for other groups of people uncertain.

Table 2. Cardiovascular and Non-cardiovascular Mortality by Physical Activity Index in Men aged 45 to 64: 24-year Follow-up, Framingham Study

	Cumulative 24-year, age-adjusted rate per 1000			
Physical activity index	*Non C-V* mortality*	C-V‡ *mortality*	Overall* *mortality*	CHD^{t} *mortality*
<29	229	367	596	255
30-34	261	283	544	184
>34	300	226	526	152
All	264	285	549	189

C-V = cardiovascular; CHD = coronary heart disease
*$p < 0.05$, $^{t}p < 0.01$, $^{\ddagger}p < 0.001$
Source: Kannel et al. Arch Intern Med 1979:139;857-61.

The Framingham Heart Study began following a cohort of 5209 persons in 1948. Although it was not specifically designed for this purpose, a subset of this cohort (1166 men between the ages of 45 and 64) were evaluated for the effects of activity on cardiovascular disease. Total daily physical activity was estimated by summing weighted estimates of various types of activity (flights of stairs climbed, distance walked, sports and other activities) over 24 hours, and reported as a physical activity index. Participants were grouped into tertiles for comparison. Age-adjusted, cumulative mortality is shown in Table 2. The cumulative death rate over 24 years was 596 per 1000 participants for the least active group and 526 for the most active. More notable were the findings for CVD–related death, where the mortality rate for the least active group was 367/1000 vs. 226/1000 for the most active, representing a 60% excess mortality rate in inactive persons. This large contribution of cardiovascular mortality to overall mortality has been seen in numerous studies. Interestingly, the improvement in cardiovascular mortality was offset to some degree by increased non-cardiovascular mortality. It is also noteworthy, that when work activity alone was evaluated, there was a non-significant trend toward improvement, suggesting a complementary effect of work and leisure-time activity.[19]

The results of the Multiple Risk Factor Intervention Trial (MRFIT) were somewhat less impressive. MRFIT was designed to determine whether multifactorial intervention would result in a significant reduction in CHD mortality in middle-aged men ages 35 to 57 who at the time of entry were in the upper 10% to 15% of a cardiac risk score derived from the Framingham Heart Study. Results have been published for follow-up at 7 years and 10.5 years.[20,21] Formal exercise was not one of the interventions. However, patients completed a questionaire which measured leisure-time activity at baseline and at 2 year intervals thereafter. Participants were classified into tertiles ranging from the least active (tertile 1) to the most active (tertile 3). The results are presented in Table 3. Compared to the least active group, those who were most active had a relative risk of all-cause mortality of 0.87 (95% CI 0.74-1.01). This difference was not statistically significant, but the RR of 0.85 (95% CI 0.73-0.99) for those in the middle tertile was. When adjusted for other cardiovascular risks, the differences were statistically significant only for death from coronary heart disease. In this study, all of the benefit of activity occurred in comparison between those who were least active (average 15 minutes/day) vs. those who were moderately active (average 47 minutes/day). Although it was not statistically significant, there was once again a trend toward increased non-cardiovascular death (in this case only cancer death was reported).

Table 3. Risk Ratios and Major Endpoints (and 95% Confidence Limits) by Tertile of Leisure Time Physical Activity in Men in the Multiple Risk Factor Intervention Trial

Vital endpoints	*1*	*2*	*3*
		Age-adjusted risk ratios	
Cardiovascular disease	1.00	0.78* (0.63, 0.96)	0.79* (0.68, 1.04)
Coronary heart disease	1.00	0.73* (0.57, 0.92)	0.84 (0.62, 1.00)
Cancer	1.00	1.11 (0.85, 1.52)	1.00 (0.66, 1.21)
All causes	1.00	0.85* (0.73, 0.99)	0.87* (0.74, 1.01)
		Proportional hazards regression	
Cardiovascular disease	1.00	0.81* (0.66, 1.01)	0.89 (0.72, 1.09)
Coronary heart disease	1.00	0.75* (0.59, 0.96)	0.82 (0.65, 1.04)
Cancer	1.00	1.22 (0.91, 1.63)	1.06 (0.78, 1.44)
All causes	1.00	0.89 (0.77, 1.04)	0.92 (0.79, 1.07)

*P<0.05
Tertile 1=least fit; Tertile 3=most fit.
Source: Leon & Connett. Int J Epidemiol 1991;20:690-7.

The U.S. Railroad Study was conducted from 1957-1977. Over 3,000 white, middle-aged railroad workers were enrolled and followed for 17-20 years. Physical activity was ascertained by the same questionaire used in the MRFIT trial and participants were grouped into 4 levels of activity. Furthermore, participants were stratified according to level of activity at work. The results are shown in Table 4. In those who were sedentary at work, there was significantly improved mortality with increased activity which is most pronounced when one moves from sedentary to moderate activity. In fact, no additional improvement accrued above 1000 kcal of expended energy per week. However, when one was active at work, increasing leisure-time activity had no increased beneficial effect on all-cause mortality and had only a modest beneficial effect on the prevention of coronary heart disease, once again underscoring the interaction between the effects of work activity and leisure-time activity.[22]

Table 4. The 17-20-Year Death Rates by Occupational and Leisure-time Physical Activity Status—U.S. Railroad Study

Total leisure time Physical activity (kcal/wk)	*n*	Geometric mean (kcal/wk)	Age-adjusted, cause-specific death rate/100: Coronary heart disease	Cardiovascular disease	All cause
Sedentary at work					
≤ 250	350	41.3	13.0	18.8	30.3
251-1,000	545	548.0	10.8	15.7	24.7
1,001-1,999	234	1,378.0	9.2	13.2	23.8
≥ 2,000	186	3,524.0	9.2	11.0	24.4
Hazard rate ratio			1.41	1.71	1.24
Active at work					
≤ 250	284	39.0	12.3	16.0	26.7
251-1,000	470	559.5	10.8	15.0	26.7
1,001-1,999	243	1,366.0	9.8	12.6	25.6
≥ 2,000	248	3,725.0	10.8	14.6	27.1
Hazard rate ratio			1.14	1.10	1.07

Source: Slattery et al. Circulation 1989;79:304-311.

Finally, the Harvard Alumni Study has been the basis of numerous papers on the effects of physical activity on health.[23] All alumni who matriculated at Harvard between 1916 and 1950 were eligible to participate. Data on physical activity and health were obtained by questionaire between 1962 and 1966. Paffenbarger and colleagues published 12-year follow-up on a cohort of 16,936 of these men. Data is shown in Table 5. Participants were stratified according to kcal of energy expended in leisure-time activity. The age-adjusted relative risk of death from all causes reveals an inverse, graded relationship with physical activity up to 3500 kcal per week, a finding that was highly significant. As in the MRFIT trial, the greatest benefit seemed to occur as one increased from the lowest level of activity (<500 kcal) to the next highest (500-999 kcal). In another cohort of 10,269 men from the Harvard study followed from 1977-1985, the same dramatic improvement was seen between the two lowest activity categories. In this cohort, maximal improvement occurred at about 2500 kcal/week.[24]

Table 5. Age-Adjusted Rates and Relative Risks of Death from All Causes Among Harvard Alumni, 1962-1978, According to Measures of Physical Activity

Physical Activity (Weekly)	Prevalence (Man-Years, %)	No. of Deaths	Deaths Per 10,000 Man-Years	Relative Risk of Death
Physical-activity index (kcal) ‡				
<500	15.4	308	93.7	1.00
500-999	20.9	322	73.5	0.78
1000-1499	15.2	202	68.2	0.73
1500-1999	10.4	121	59.3	0.63
2000-2499	8.1	89	57.7	0.62
2500-2999	6.9	62	48.5	0.52
3000-3499	5.0	42	42.7	0.46
>3500	18.1	203	58.4	0.62

‡ With or without light sports play.
Source: Paffenbarger et al. N Engl J Med 1986;314:605-13.

An extension of the Harvard Alumni study looking at the development of CHD was published earlier this year. This study followed a cohort of 14,365 men between 1977 and 1993. Compared to those acquiring <500 kcal per week of leisure-time physical activity, those getting 500-999 had a statistically significant, age-adjusted RR of 0.85 (95% CI 0.74-0.97) and those getting 1000-1999 had a RR of 0.75 (95% CI 0.66-0.85). No additional benefit was obtained for levels of activity above this, again underscoring the significance of even small amounts of increased activity in sedentary persons.[25]

As noted, much of the overall mortality improvement with exercise is a result of reduced CHD-related mortality. The meta-analysis by Berlin and Colditz also looked at relative risks for non-occupational activity. In studies comparing low activity with high activity the relative risk of CHD-related death was 1.7 (95% CI 1.2-2.3). For moderate activity compared to high activity the RR was 1.1 (95% CI 1.0-1.3). Data comparing low with moderate activity was not calculated.[18]

In summary, leisure-time physical activity appears to be most important for those who are sedentary at work. Benefit may accrue up to 3500 kcal/week, although the most significant improvement occurs at low levels (about 1000 kcal/week). These benefits extend to both CHD-related mortality and all-cause mortality.

The Effect of Physical Fitness on Mortality

Numerous studies have evaluated the effects of physical fitness. Most of these have looked at the effects on cardiovascular disease, but a number have also looked at all-cause mortality as well. Peters measured physical work capacity by cycle ergometry in men under the age of 55 at baseline. Adjusted for conventional risk factors, the RR of MI over 5 years for those with below median physical work capacity was 2.2 (95 % CI 1.1-4.7). Among men with at least 2 cardiovascular risk factors, the relative risk for below average work capacity was 6.6 (95% CI 2.3-27.8).[26] Sandvik studied 1960 middle-aged Norwegian men for 16 years. Participants were grouped according to quartiles of fitness. Adjusting for age and other cardiovascular risk factors, the relative risk of cardiovascular mortality in the most fit group, when compared to the least fit, was 0.41 (95% CI 0.20-0.84). Adjusted for the same risk factors, the relative risk of death from all causes was 0.54 (95% CI 0.32-0.89). Fifty-three percent of the deaths in this study were from cardiovascular disease.[27]

Blair and colleagues from The Cooper Clinic published data on 10,224 men followed for an average of 8 years following a baseline health examination. Based upon a maximal treadmill test, participants were categorized into quintiles of fitness for comparison. Results of the study are shown in Table 6. As was seen with measures of physical activity, there was a graded, inverse relationship between level of fitness and all-cause mortality. Interestingly, however, this finding was only statistically significant for the least fit quintile. Although benefit occurs in a graded, inverse fashion, the greatest benefit accrues as one moves from the least fit quintile to the next quintile. In contrast to studies of physical activity, where non-cardiovascular mortality was sometimes increased, cause specific mortality rates showed graded inverse relations for both cardiovascular disease and cancer.[28]

Table 6. Age-Adjusted All-Cause Death Rates per 10,000 Person-Years of Follow-up (1970 to 1985) by Physical Fitness Groups in Men and Women in the Aerobics Center Longitudinal Study

Fitness Group	Person-Years of Follow-up	No. of Deaths	Age-adjusted Rates per 10,000 Person-Years	Relative Risk	95% Confidence Limits
Men					
1 (low)	14,515	75	64.0	3.44*	2.05, 5.77
2	16,898	40	25.5	1.37	0.76, 2.50
3	17,287	47	27.1	1.46	0.81, 2.63
4	18,792	43	21.7	1.17	0.63, 2.17
5 (high)	17,557	35	18.6	1.00	...
Women					
1 (low)	4,916	18	39.5	4.65†	2.22, 9.75
2	5,329	11	20.5	2.42	1.09, 5.37
3	5,053	6	12.2	1.43	0.60, 3.44
4	5,522	4	6.5	0.76	0.27, 2.11
5 (high)	4,613	4	8.5	1.00	...

*Test for linear trend, slope=-4.5; 95% confidence limits, -7.1, -1.9.
†Test for linear trend, slope=-5.5; 95% confidence limits, -9.2, -1.9.
Source: Blair et al. JAMA 1989;262:2395-401.

An arm of the U.S. Railroad study also looked at the effects of physical fitness on mortality. This included a cohort of 3043 white men ranging in age from 22 to 79 for an average follow-up of 20 years. Participants were grouped into quartiles based on HR at a given work load during exercise testing. The relative risk for all-cause mortality for the least fit group when compared to the most fit was a modest 1.23 (95% CI 1.17-1.56) and 1.20 (95% CI 1.10-1.26) for CVD mortality.[29]

In summary, physical fitness is associated with mortality in an inverse graded fashion with the greatest benefit acquired by those achieving very modest levels of fitness.

The Interaction Between Physical Activity and Physical Fitness

As compared to studies of physical activity, studies of the effects of physical fitness have generally shown greater improvement in measured endpoints. Consequently, it has been suggested that fitness is a better measure of risk and should be the focus of attention in public health matters. For instance, in the study by Sandvik in Norwegian men, only fitness had a statistically significant association with decreased mortality.[27] Physical activity did not. In the Cooper clinic study, activity had a weaker association with mortality than fitness.[28] However, it has been estimated that as much as 25-40% of physical fitness may be genetically determined, consequently, masking the added benefits of physical activity.[30]

Hein and coworkers looked at the effects of physical activity across quintiles of physical fitness. Nearly 5,000 men aged 40-59 were classified according to level of physical fitness and were followed for 17 years. As expected, the least fit quintile had the highest mortality. What was striking, however, was the finding that sedentary persons from the least fit and most fit quintiles had the same mortality rates. In short, fitness alone was not protective. Mortality differences were noted only for men who were moderately or highly active.[31]

The Effect of Changes in Physical Activity and Physical Fitness

The studies cited so far are all cohort studies that measured the association of levels of activity or fitness at one point in time with respect to the long-term development of CVD and mortality. A more meaningful measure is the effect of change in activity over time. In another analysis of the Harvard Alumni study, 10,269 men were evaluated at baseline (1962 or 1966) and again in 1977 for levels of activity and then followed until 1985. A value of 2000 kcal/week was arbitrarily chosen for comparison. Relative risks of death from all causes for the four possible interactions are shown in Table 7. Interestingly, those who were active at baseline, but became inactive at follow-up had higher mortality than those who were never active. Those who were inactive at baseline but then became active had essentially the same RR as those who were active at both evaluations. However, none of these was statistically significant. When moderately vigorous activity was used as the benchmark, those getting some vigorous activity at the second evaluation (regardless of baseline level) had a statistically significant decreased RR compared to those who did not.[24]

This same data was extended another 3 years and was published again, this time with a cutoff for physical activity of 1500 kcal per week. In this analysis, the RR risk of those becoming inactive was 1.13 (CI 1.01-1.26). The relative risk of those who were inactive at baseline but then became active was 0.72 (CI 0.64-0.82) and for those who were active at both evaluations it was 0.77 (CI 0.69-0.85). All of these were statistically significant.[32] Finally, in another evaluation, alumni who were ex-varsity athletes were compared to those who had been inactive as students with regard to the development of CHD. Ex-varsity athletes who were inactive as alumni equaled the highest risk. Inactive students who became active as alumni had a risk as low as that of active ex-varsity athletes.[33] Simply having been fit at one point in time provided no lasting benefit if one became inactive.

Table 7. Rates and Relative Risks of Death from All Causes among 10,269 Harvard Alumni from 1977 through 1985, According to Changes in Patterns of Physical Activity and Other Characteristics between 1962 or 1966 and 1977.

Characteristic†	*1962 or 1966*	*1977*	*Prevalence (% of Man-Years)*	*No. of Deaths*	*Deaths /10,000 Man-Years*	*Relative Risk of Death (95% CI)*	*P Value*
Physical-activity index ≥ 2000 kcal/wk‡	No	No	41.1	221	54.6	1.00	--
	Yes	No	15.5	85	60.3	1.10 (0.78-1.50)	0.543
	No	Yes	19.5	69	46.6	0.85 (0.65-1.13)	0.256
	Yes	Yes	23.9	83	44.8	0.82 (0.63-1.08)	0.124
Moderately vigorous sports activity (≥ 4.5 METS)	No	No	17.0	139	61.7	1.00	--
	Yes	No	3.1	26	70.7	1.15 (0.73-1.71)	0.608
	No	Yes	38.1	131	47.4	0.77 (0.58-0.96)	0.015
	Yes	Yes	41.9	116	43.8	0.71 (0.55-0.96)	0.011

Source: Paffenbarger et al. N Engl J Med 1993;328:538-45.

Blair and colleagues from the Cooper Clinic have also published data on the effects of changes in physical fitness on all-cause mortality. They studied 9777 men ages 20 to 82 who all completed two clinical examinations (mean interval between exams, 4.9 years) and followed them until death or to the end of the study period (mean follow-up from second exam, 5.1 years). Participants were categorized into quintiles and comparisons were made between the lowest quintile compared to quintiles 2-5 combined. Using those who were unfit at both exams as the referent group, the relative risk of death from all causes was 0.56 (95% CI 0.41-0.75) for those who were initially unfit but became fit, 0.52 (95% CI 0.38-0.70) for those who were fit at baseline but then became unfit, and 0.33 (95% CI 0.23-0.47) for those who were fit at both exams.[34] This trend was seen for all age groups. The findings were similar and in fact more pronounced for death from cardiovascular disease. In summary, the greatest benefit accrued in persons who maintained fitness over time.

Table 8. Changes in Physical Fitness and Age-Adjusted, All-Cause, and Cardiovascular Disease Mortality in 9777 Men--Aerobics Center Longitudinal Study, (1970 – 1989)

1st Exam	2nd Exam	Man-Years (MY) of Follow-up	No. of Men	No. of Deaths	Age-Adjusted Death Rate/10,000 MY	Relative Risk	95% Confidence Interval
			All Cause				
Unfit*	Unfit	2937	373	32	122.0	1.00	...
Unfit	Fit†	4054	650	25	67.7	0.56	0.41-0.75
Fit	Unfit	1624	221	9	63.3	0.52	0.38-0.70
Fit	Fit	38946	8533	157	39.6	0.33	0.23-0.47
Quintiles	Quintiles						
2-3	2-3	9759	1506	46	48.6	1.00	...
2-3	4-5	6748	1517	25	41.3	0.85	0.56-1.29
4-5	4-5	19713	5025	69	34.4	0.71	0.46-1.09
		Cardiovascular Disease					
Unfit	Unfit	2826	356	15	65.0	1.00	...
Unfit	Fit	4017	638	13	31.4	0.48	0.31-0.74
Fit	Unfit	1594	215	3	27.9	0.43	0.28-0.67
Fit	Fit	38572	8432	56	14.2	0.22	0.12-0.39
Quintiles	Quintiles						
2-3	2-3	9637	1480	20	21.6	1.00	...
2-3	4-5	6667	1501	9	15.5	0.72	0.37-1.38
4-5	4-5	19560	4977	21	10.5	0.48	0.23-1.01

*Quintile 1 of age-specific fitness distribution.
†Quintiles 2 through 5 of age-specific fitness distribution.
Source: Blair et al. JAMA 1995;273:1093-1099.

Vigorous vs. Non-vigorous Physical Activity

It is fairly clear that physical activity is good. Just how intense the activity has to be to provide benefit is still debated. The data cited so far indicate that perhaps the greatest health benefit of activity occurs at very modest levels, particularly in sedentary persons. However, this is not to say that additional benefit will not accrue with more vigorous exercise. In fact, the CDC report states that the current recommendations are not intended to supercede previous guidelines, and that, "people who already meet the recommendations are also likely to derive some additional health and fitness benefits from becoming more physically active."

The U.S. Railroad Study also looked at the effect of vigorous activity on cardiovascular and all-cause mortality. In this analysis, those who participated in at least some vigorous leisure-time activity were compared to those who got none. In both instances, increased total activity was inversely related to death from CHD, CVD, and all causes. However, the effects were most pronounced in those who got at least some vigorous activity.[22]

Table 9. The 17-20 Year Death Rates by Component Parts of Leisure-Time Physical Activity*--U.S. Railroad Study

Intense activity		Light-to-moderate activity		Age-adjusted cause-specific death rate/100		
Category	Geometric mean (kcal/wk)	Category	Geometric mean (kcal/wk)	Coronary heart disease	Cardio-vascular disease	All causes
None	0	≤160	15	13.2	18.8	34.0
	0	161-750	382	14.6	19.7	31.2
	0	751-1,700	1,074	9.6	14.5	27.5
	0	>1,700	3,204	10.1	13.2	27.0
Any	136	≤160	22	11.5	14.2	20.2
	96	161-750	400	6.0	8.9	16.2
	98	751-1,700	1,090	10.1	14.0	27.3
	110	>1,700	3,132	8.0	10.7	17.2

n=2,562 men free of pre-existing cardiovascular disease.
*Age-adjusted by analysis of covariance.
Source: Slattery et al. Circulation 1989;79:304-11.

Two reports of the Harvard Alumni Study have also addressed the issue of intensity. The same study that assessed the effects of change in activity also looked at the association with intensity. In this instance, moderate activity was defined as anything requiring greater than or equal to 4.5 METS and light activity was anything less than this. Only moderate activity was associated with statistically significant improvement in mortality rates.[24]

In another analysis, Lee and colleagues independently calculated total energy expenditure, energy expended on vigorous activity (regardless of amount of non-vigorous activity), and non-vigorous activity (regardless of amount of vigorous activity) in 17, 321 Harvard Alumni Study participants who were followed for up to 26 years. In this instance, vigorous activity was defined as ≥ 6 METS. Mortality rates declined with increasing energy expenditure for both total output and vigorous activity, but not for non-vigorous. These trends were confirmed with multivariate analysis. They also performed subset analysis on those with only vigorous activity and those with only non-vigorous activity, with beneficial effects only in those acquiring vigorous activity.[35] In a similar study, Lakka and colleagues found a strong graded inverse relationship between acute MI and vigorous leisure-time physical activity (> 6 METS) and physical fitness, but not for non-vigorous activity.[36]

In contrast, in a Dutch case-control study of 473 persons who had sustained acute coronary events, Mangus found that habitual moderate activity significantly decreased the rate of acute coronary events, with no additional benefit from more vigorous activity.[37] Since walking is the most common form of physical activity in older adults, the effects of walking have been studied in various ways. In a study of 1645 men and women 65 years of age and older who reported walking for exercise, walking 4 hours per week was associated with a reduced risk of death (RR 0.69; 95% CI 0.52-0.90), regardless of participation in vigorous activity.[38] Similarly, in the Honolulu Heart Study, of men aged 61-81 who were otherwise free from significant disease, the mortality rate among those who walked less than one mile per day was nearly twice that of those who walked more than 2 miles per day (40.5% vs. 23.8%; p=0.001).[39] In another report from the Honolulu Heart study, men who walked <0.25 miles per day had twice the risk of developing CHD over 2 to 4 years of follow-up (5.1% vs. 2.5%; p<0.01) when compared to those who walked > 1.5 miles/day.[40] These studies all showed significant beneficial effects at levels below 6 METS, the cutoff used by Lakka and in the Harvard study.

Although additional benefit may accrue from more vigorous exercise, there is good evidence that non-vigorous activity is in fact protective.

Special Groups

What About Women?

The data cited so far refer to men. It is not clear whether it can be generalized to other populations, such as women. For instance, only about 50% of studies of physical activity in women show a statistically significant beneficial effect. One explanation for this is that the questionaires used to measure activity were developed and validated in men.[28] In spite of the relative paucity of information pertaining to women, a number of studies have been published.

Brunner and colleagues studied the effects of work-related activity in over 5200 middle-aged women living in an Israeli Kibbutzim. Women were categorized as sedentary if more than 80% of work-related activity was sedentary, and non-sedentary if this number was less than 80%. After 15 years of follow-up, the relative risk of death from ischemic heart disease for sedentary work, when compared to non-sedentary, was 3.0 (95%CI 0.3-29.4), which was not statistically significant. Essentially the same study in nearly 5300 men yielded a statistically significant RR of 2.0 (95% CI 1.2-3.3).[41] A Finnish study looked at the effect of work-related activity on acute MI, death from ischemic heart disease, stroke and all-cause mortality over seven years. Low physical activity at work was associated with statistically significant increased risk of AMI, stroke and all-cause mortality. Low activity in leisure-time was likewise associated with increased risk of death from all causes, but was not statistically significant for AMI or stroke.[17]

Sherman et. al., published data on a cohort of women from the Framingham Heart Study. Over 1400 women ranging in age from 50-74, who were free from known cardiovascular disease at study entry, were stratified into quartiles of activity and followed for 16 years. With the least active group as the referent, the 2nd, 3rd and 4th quartiles had multivariate relative risks of death from all causes of 0.91 (95% CI 0.66-1.25), 0.63 (95% CI 0.44-0.90), and 0.66 (95% CI 0.46-0.95).[42] There was no reduction in the rate of CVD-related death.

Kushi et. al., studied 40,417 participants in the Iowa Women's Health Study. Postmenopausal women between the ages of 55 and 69 were followed for 7 years (Table 10). Stratified into tertiles according to physical activity index, the medium and highly active groups had multivariate relative risks of 0.77 (95% CI 0.69-0.86) and 0.68 (95% CI 0.60-0.77), both of which were statistically significant. Statistically significant, graded, inverse relations were found for both moderate and vigorous physical activity.[43]

Table 10. Relative Risks (RR) of Total Mortality According to Level of Physical Activity Among 40417 Postmenopausal Women in Iowa, 1986-1992.

			RR (95% Confidence Interval)	
Physical Activity Variables	**Deaths**	**Person-Years**	**Age-Adjusted**	**Multivariate-Adjusted***
Regular physical activity				
No	1,518	157,379	1.00	1.00
Yes	742	111,811	0.67 (0.61-0.73)	0.78 (0.71-0.86)
Frequency of moderate physical activity				
Rarely/never	722	55,404	1.00	1.00
1/wk to a few a month	621	76,318	0.63 (0.57-0.70)	0.71 (0.63-0.79)
2-4 times/wk	560	82,633	0.51 (0.46-0.57)	0.63 (0.56-0.71)
>4 times/wk	365	55,973	0.48 (0.42-0.54)	0.59 (0.51-0.67)
P value for trend			<.001	<.001
Frequency of vigorous physical activity				
Rarely/never	2,000	222,967	1.00	1.00
1/wk to a few a month	139	23,138	0.70 (0.59-0.83)	0.83 (0.69-0.99)
2-4 times/wk	85	16,423	0.61 (0.49-0.76)	0.74 (0.59-0.93)
>4 times/wk	30	6,242	0.55 (0.38-0.79)	0.62 (0.42-0.90)
P value for trend			<.001	.009
Physical Activity Index				
Low	1,309	126,545	1.00	1.00
Medium	519	74,170	0.66 (0.60-0.73)	0.77 (0.69-0.86)
High	415	67,138	0.58 (0.52-0.65)	0.68 (0.60-0.77)
P value for trend			<.001	>.001

*Adjusted for age at baseline, age at menarche, age at menopause, age at first live birth, parity, alcohol intake, total energy intake, cigarette smoking, estrogen use, body mass index at baseline, body mass index at age 18 years, waist-to-hip ratio, first-degree female relative with cancer, high blood pressure, diabetes, education level, and marital status.
Source: Kushi et al. JAMA 1997;277:1287-92.

In the Nurse's Health Study, over 72,400 women between the ages of 40 and 65 were divided into quintiles of activity and followed for eight years. Age-adjusted and multivariate analyses of coronary events and total activity revealed a graded, inverse relationship was highly statistically significant (p for trend 0.002). Both brisk walking and vigorous activity were found to be protective. Women who participated in both walking and vigorous activity derived greater benefit than either type of activity alone.[44]

Finally, the effect of physical fitness on all-cause mortality in women was studied in the Aerobics Center Longitudinal Study. In this study, women in the lowest quintile for fitness had an adjusted RR of 3.00 (95% CI 1.06-8.51), for those followed for more than 3 years (Table 6). The corresponding value in men was only 1.45 (95% CI 1.08-1.96), suggesting that physical fitness may have even greater benefit in women.[28]

Contrary to these positive findings, in a 1987 review of 14 studies of physical activity and cardiovascular disease in women, 10 showed no association.[45] Similarly, in the Cooper Clinic study of fitness in women which revealed a significant mortality benefit in those who were fit, analysis of the effect of physical activity revealed no benefit.[46] The results of studies of physical activity in women are conflicting. Measurement bias is a likely cause for much of this. In spite of the number of older studies that did not show statistically significant results, in general, they did show a trend to improvement. In light of the newer data, there is good reason to believe that women can derive the same benefits from physical activity as men.

The Elderly

Studies of the benefits of physical activity in the elderly have been mixed, but generally show significantly reduced mortality risk. The Zutphen Elderly Study followed 802 Dutch men aged 64-84 for 10 years. In comparing the most active group with the least active and adjusted for other risk factors, physical activity was associated with RR of 0.70 (95% CI 0.48-1.10) for CVD mortality, 0.85 (95% CI 0.51-1.44) for CHD-related mortality, 0.55 (95% CI 0.24-1.26) for stroke mortality, and 0.77 (95 % CI 0.59-1.00) for all-cause mortality.[47] The Alameda County Study evaluated the effects of multiple risk factors in a cohort of 60-94 year-olds for 17 years. Physical inactivity was associated with increased mortality in all age groups, including a relative hazard of 1.37 (95% CI 1.09-1.72) in those over 70.[48]

A cohort of men and women from the Framingham Heart Study, all of whom were at least 75 at baseline, were followed for 10 years. Women in the second most active quartile were found to have a RR of all-cause mortality of 0.26 (95% CI 0.12-0.55) when compared to those who were least active, whereas women in the most active quartile had a RR 0.39 (95% CI 0.20-0.77). Although both of these were significant, the slightly increased relative risk for the most active group suggested that there may be a level of activity above which no further benefit is attained. CVD-related death was also decreased with increasing activity, but did not reach statistical significance. In men, all-cause mortality and CVD-related mortality both decreased in a linear fashion, but did not reach statistical significance.[49]

Obesity and The Metabolic Syndrome

As noted previously, the incidence of overweight and obesity are increasing at an alarming rate in the United States. Related to this is the metabolic syndrome, consisting of obesity, hypertension, insulin resistance, glucose intolerance and dyslipidemia. The clinical importance of this is the clustering of cardiovascular risk factors in the same person. Another important feature is that all of these risk factors are influenced to some degree by physical activity. It has been estimated that 25-35% of westerners manifest the metabolic syndrome and that only about one third of persons are free of all manifestations of this condition.[50]

Exercise is an important component of weight loss programs. It is effective alone when caloric intake is held constant and increases weight loss during calorie restriction.[51,52] It is also associated with a number of other beneficial effects, including decreased visceral fat and insulin resistance. Exercise has favorable effects on total cholesterol, HDL and triglycerides.[53,54] Exercise has been shown to reduce both systolic and diastolic blood pressure.[55] Both vigorous and non-vigorous activity have been shown to favorably affect insulin sensitivity.[56]

Diabetics

The beneficial effects of physical activity on diabetes are important in two ways. First, physical activity has been shown in several studies to reduce the incidence of Type II diabetes. Helmrich and colleagues evaluated the effects of physical activity in 5990 male University of Pennsylvania alumni over 20 years. They found that for every 500 kcal of increased energy expenditure per week, the age-adjusted risk of NIDDM was reduced by an average of 6% (RR 0.94). This protective effect was greatest among those with other risk factors for diabetes, such as obesity, hypertension or a family history of diabetes. Increased BMI was even more strongly correlated with incidence of diabetes, which increased 21% for each 2-unit increase in BMI. After correcting for the effect of obesity, the beneficial effects of activity were still statistically significant.[57]

Manson and coworkers evaluated 21,271 male physicians participating in the Physician's Health Study for 5 years. In this study, for men who exercised vigorously at least once weekly, the age-adjusted relative risk of developing NIDDM was 0.64 (95% CI 0.51-0.82). Increasing frequency of vigorous activity was inversely related to incidence with RR 0.77 for once weekly, 0.62 for 2 to 4 times weekly, and 0.58 for 5 or more times per week.[58] In a study of African-American men, those who were moderately physically active had one third the risk of developing NIDDM as those who were inactive.[59]

The effect of activity on incidence of diabetes in women was evaluated in the Nurses Health Study. During 8 years of follow-up of the 87,253 participants aged 34-59, women who exercised vigorously at least once weekly had an age-adjusted RR of NIDDM of 0.67 ($p<0.0001$). After adjusting for BMI, the benefit was reduced to 0.84, but remained statistically significant. In this study, vigorous activity more than twice weekly had no additional benefit.[60]

The second important effect of exercise is on the treatment of diabetes. The effects of both physical fitness and overall activity were evaluated in the Aerobics Center Longitudinal Study. In this study, 1263 men (mean age 50±10 years) with type II DM were followed for an average of 12 years. After adjustment for age and all other conventional cardiac risk factors, the relative risk of all-cause mortality for the least fit quintile, when compared to all others, was 2.1 (95% CI 1.5-2.9). Physical inactivity, adjusted for the same risk factors, was associated with a RR of 1.7 (95% CI 1.2-2.3).[61]

Persons With Established Cardiovascular Disease

Given that physical inactivity is a well-known risk for the development of coronary heart disease, it seems intuitive that increased physical activity would be beneficial for persons with established cardiovascular disease. Unfortunately, most of the large epidemiological studies excluded persons with established cardiovascular disease. The Lipid Research Clinics Mortality Follow-up Study included separate analyses of those with cardiovascular disease at baseline, and those without. In this study of physical fitness, lack of fitness had a more pronounced effect in those with CVD than those without as measured by death from all causes (RR 2.9 vs. 1.8), cardiovascular disease (RR 4.8 vs. 3.6), and coronary heart disease (RR 5.6 vs. 2.8).[62] The Iowa Women's Health Study also stratified women according to pre-existing disease (coronary heart disease and known cancer). Women with baseline disease derived greater benefit over all levels of activity.[43]

Table 11. ***Relative Risks of Death from Coronary Heart Disease (CHD), Cardiovascular Disease (CVD), and All Causes in Healthy Men and Men with Cardiovascular Disease over 8.5 Years of Follow-up, According to Exercise Time on the Treadmill.***

Cause of Death And Group	Relative Risk (95% Confidence Limits)	P Value
CHD		
Healthy	2.8 (1.3-6.1)	0.007
CVD	5.6 (2.5-12.6)	<0.0001
CVD		
Healthy	3.6 (1.6-5.6)	0.0004
CVD	4.8 (2.5-9.2)	<0.0001
All causes		
Healthy	1.8 (1.2-2.6)	0.006
CVD	2.9 (1.7-4.9)	0.0001

Source: Ekelund et al. N Engl J Med 1988;319:1379-84.

The effect of exercise on coronary heart disease has been studied extensively in cardiac rehabilitation programs. However, many of the studies have been small and of short duration which has made it difficult to demonstrate mortality benefits. Oldridge and colleagues performed a meta-analysis of 10 trials, only one of which was able to demonstrate a statistically significant mortality benefit. However, pooling the data produced clear reductions in all-cause mortality (OR 0.76) and in cardiovascular death (OR 0.75), both of which were statistically significant. It should also be noted that there was a non-significant trend to increased risk of reinfarction (OR 1.15). When stratified according to time at which intervention was initiated (≤ 8 weeks or > 8 weeks), statistical significance was only maintained for treatment initiated early, which was also associated with an even stronger trend to reinfarction.[63]

Just How Much Will It Help?

Longevity

Overall these studies suggest that if one stays active and fit, one will live longer. Two reviews have been influential in establishing estimates of excess mortality resulting from inactivity. Hahn compared death rates across all 50 states resulting from 9 chronic diseases. Based on the lowest death rates for each of the nine diseases reported from all of the states, he calculated a combined lowest state mortality rate of 284.1/100,000. The average for the U.S. was 427.4/100,000, representing 33.5% excess mortality. He also calculated a risk-eliminated death rate (the mortality rate that would be obtained if the most important risk factor for each disease were eliminated) of 224.5/100,000, indicating an excess mortality rate as high as 48% in the U.S. In 1986, this resulted in an estimated 524,000 premature deaths. Elimination of these factors could be associated with increased life expectancy of 4 years.[64]

Table 12. Population Attributable Risk of Coronary Heart Disease Deaths and Estimated Society Costs, by Selected Risk Factor—United States

Risk Factor	Attributable Risk Percent	Estimated Cost (billions)
Physical inactivity	34.6	$5.7
Obesity	32.1	$5.3
Smoking	25.0	$4.1
Hypertension	28.9	$4.7
Elevated serum cholesterol	42.7	$7.0

Costs include hospital, physician, and nursing services; medicines; and lost productivity.
Source: CDC. MMWR 1993;42:669-72.

McGinnis and Foege estimated that poor diet and sedentary life-style contributed to as many as 300,000 premature deaths per year, a number they believe is based on conservative data.[65] Other studies have associated dietary and sedentary lifestyles with attributable risks ranging from 22%-30%.[65] The CDC estimated the population attributable risk (a value that takes prevalence into account) of coronary heart disease to be 34.6%. Based on 1989 mortality estimates, physical inactivity resulted direct and indirect annualized costs of $5.7 billion.[66] Small improvements in physical activity, such as the goals established by the Healthy People 2000 and Healthy people 2010 campaigns could save 30,000-35,000 lives per year.[67]

The results of a 20 year Finnish study of 636 men aged 45-64 are shown in Figure 1. Participants were classified into two groups for comparison. The mortality curves for the two groups diverge very early and remain divergent for many years. However, the curves converge again at 17 years. Overall, the adjusted gain in average life-expectancy for men with high physical activity in middle age was 2.1 years. But in this study, the benefit was not maintained indefinitely. The authors concluded that physical activity does not extend the maximum life-span, but that it does reduce premature mortality. It has also been suggested that the convergence is a manifestation of changes in activity levels as the cohort aged, resulting in dilution of the data and inability to detect a difference that is in fact present.[68]

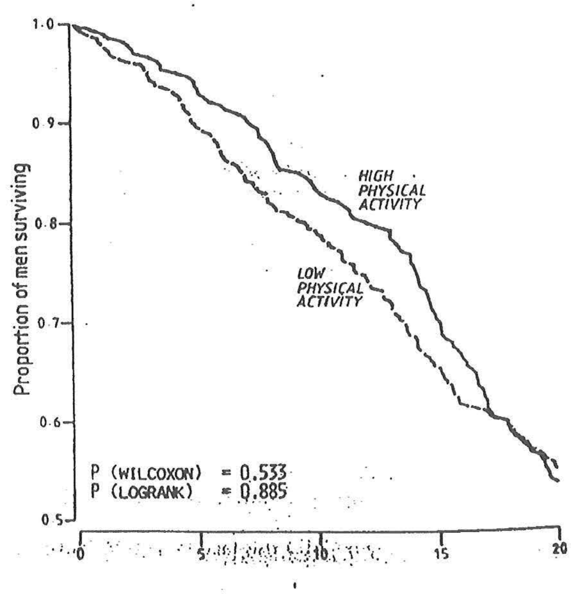

Fig 1 – Crude 20-year survival of a cohort of 636 men aged 45-64 at baseline according to physical activity at baseline.

Based on the data from the Harvard Alumni Study, Paffenbarger has estimated years of added life for various activity levels. These estimates are shown in Table 13.

Table 13. Added Life from an Active Life Style in Men up to the Age of 80, Estimated from Harvard Alumni Mortality, 1962 to 1978.

Age at Entry (Yr)	*Physical-activity Index** ≥ 2000 vs. <500* Crude	Adjusted†	*≥ 2000 vs. <2000* Crude	Adjusted†	*Vigorous Sports Play Present vs. Absent* Crude	Adjusted†
35-39	2.64	2.51	1.66	1.50	1.66	1.55
40-44	2.48	2.34	1.46	1.39	1.54	1.45
45-49	2.32	2.10	1.24	1.10	1.38	1.23
50-54	2.37	2.11	1.35	1.20	1.40	1.32
55-59	2.25	2.02	1.27	1.13	1.25	1.21
60-64	1.98	1.75	1.04	0.93	1.00	0.95
65-69	1.64	1.35	0.82	0.67	0.70	0.55
70-74	0.94	0.72	0.57	0.44	0.11	-0.11
75-79	0.35	0.42	0.29	0.30	0.01	-0.09
35-79	2.33	2.15	1.38	1.25	1.37	1.28

*Kilocalories expended per week in walking, climbing stairs, and playing sports.
†Adjusted for differences in blood-pressure status, cigarette smoking, net gain in body-mass index since college, and age of parental death.
Source: Paffenbarger et al. N Engl J Med 1986;314:605-13.

Effects on Disability

Aside from the potential to reduce premature mortality, exercise has important beneficial effects on maintaining functional capacity. Physical activity is associated with reduced total disability at any age, later onset of disability and total duration of disability.[69] High levels of activity nearly double the likelihood of death without disability,[70] and one study suggested that vigorous activity is more protective than moderate.[71] In short, even if physical activity does not add years to your life, "it will add life to your years."

Complications of Exercise: Is It Safe?

Injuries and Medical Complications of Exercise

The most common complication of exercise is injuries. The risk of injuries increases with the intensity, duration and frequency of exercise.[72] Other contributing factors include age, gender, body build, experience, poor flexibility, and prior injuries. Estimates of yearly rates of injuries among joggers ranges from 25-54%.[73] Incorporation of warm-up and cool-down, and the inclusion of flexibility exercises as part of regular exercise have been shown to decrease the risk of injuries.

Non-orthopedic complications are less common, but frequently much more serious. The types of complications that can occur include volume depletion, dehydration, rhabdomyolysis and renal failure, heat exhaustion, heat stroke, syncope, exercise induced asthma, and others. In a study by the National Center for Catastrophic Sports Injury Research, van Camp reviewed 37 cases of sports-related deaths not attributable to cardiovascular causes. Thirteen were caused by heat-related illness and seven more occurred as a result of rhabdomyolysis in persons with sickle cell trait. Other causes included asthma, GI bleeding, and exercise anaphylaxis.[74]

Cardiovascular Events

Sudden death is the most feared cardiac complication of exercise. Fortunately it is rare. Among high school and college athletes, sudden death occurs in approximately 1/133,000 young men and 1/769,000 young women. Among older athletes, the rate is 6/100,000.[75] The cause of sudden death varies depending on the age of the participants. Among younger athletes, the most common causes are related to congenital abnormalities, with hypertophic cardiomyopathy or probably cases of hypertophic cardiomyopathy accounting for over 50% of these. In a study of 134 sudden deaths among young athletes, only three had normal hearts. Even more concerning was the finding that 115 of the young athletes who died had pre-participation screening and only 4 (3%) were suspected of having a cardiovascular problem and only 1 was correctly diagnosed.[76]

The problem in older athletes is very different. Among older persons, by far the most common cause is coronary heart disease, accounting for as many as 80% of cases. The incidence of coronary heart disease in the older population is much higher than the incidence of congenital abnormalities in younger persons. Consequently, the burden of risk is much greater. In a study of joggers in Rhode Island, Thompson found that sudden death was 7 times more likely to occur during jogging than during other activities.[77] In a Seattle study, the risk of sudden death was 5 times higher during exercise for men who exercised regularly, but 56 times higher for those who infrequently participated in vigorous exercise.[78] Although regular exercise seems to add some protection, Thompson reviewed the causes of death in 18 jogging/running-related sudden deaths and found that most had exercised regularly for years.[79] Seventeen of the eighteen deaths were among men, thirteen of which were due to CHD. Among the 13 CHD-related deaths, only one had previously diagnosed CHD. Six of the 13 had prodromal symptoms but continued vigorous exercise. Willich et al., reviewed 1194 patients admitted with acute MI. They found that 7.1 percent of the patients had participated in vigorous activity (> 6 METS) at the onset of infarction, resulting in a RR of 2.1 (95% CI 1.1-3.6). For persons who exercised less than 4 times per week the RR was 6.9 (95% CI 4.1-12.2) and for those exercising 4 or more times it was 1.3 (95% CI 0.8-2.2).[80]

Interestingly, the pathological mechanism of sudden death is thought to differ between asymptomatic persons and those with known cardiovascular disease. Among asymptomatic persons, pathologic findings are most consistent with plaque rupture and acute coronary occlusion. In those with known coronary disease, autopsy studies frequently do not demonstrate evidence of acute coronary lesions, suggesting that scarring and arrhythmias are the more likely cause.[75] In a study of cardiovascular complications during supervised exercise training of cardiac patients, Haskell reported 50 cardiac arrests, only seven of which were related to acute MI.[81] In spite of the increased risk of acute events during vigorous exercise, the risk of physical inactivity outweighs the risk of the temporary increase in risk during exercise. What is yet to be determined, however, is what the optimal frequency and intensity of exercise is to minimize the risk of acute cardiovascular events.

Pre-Exercise Screening

Given the devastating consequences of acute cardiac events, much attention has been given to ways to reduce the risk of exercise related events. Thompson reviewed 5 studies of echocardiographic screening of asymptomatic young athletes. In the 5458 high school and college age participants, no cases of definite hypertrophic cardiomyopathy were identified. Consequently, screening echocardiography does not appear to be cost-effective. Routine physical examination has also been shown to be ineffective. Nevertheless, the author concluded that all young athletes undergo a pre-participation cardiovascular exam with careful cardiac inspection and auscultation, including maneuvers to increase the likelihood of detecting a murmur of HCM. This also underscores the need for coaches and trainers to be well-versed in techniques of CPR and basic life support.[75]

Exercise testing is the technique most often recommended to identify persons at increased risk prior to beginning an exercise program. The AHA recommends ETT for persons over age 40 who anticipate beginning vigorous exercise.[82] The ACSM has offered a tiered approach to pre-exercise screening, recommending ETT for men 45 and over and women 55 and over, or anyone with 2 or more cardiovascular risk factors. Pre-exercise testing prior to beginning moderate exercise is only necessary if one has active symptoms or has known cardiovascular or pulmonary disease.[83] Numerous studies have attempted to evaluate the effectiveness of testing at predicting events. Unfortunately, like echocardiography in younger athletes, exercise testing also suffers from lack of sensitivity. For instance, in an arm of the Lipid Research Clinics Coronary Primary Prevention Trial, 3617 asymptomatic men with hypercholesterolemia underwent screening submaximal exercise tolerance tests at baseline and annually for up to 10 years. Of 62 men who experienced a non-fatal MI or CHD-related death, 11 had evidence of ischemia on initial exercise testing and 227 had false positive tests. The sensitivity was 18%, specificity 92%, positive predictive value was 4%, and negative predictive value was 98%. Twenty-three of the 62 men had an abnormality on any one of the repeated exercise tests and 649 had false positive tests. This yielded a sensitivity of repeated testing of 37%, specificity of 79%, positive predictive value of 3% and negative predictive value of 98%.[84] In a study of Indian State Policemen followed with serial symptom-limited exercise tests for 8-15 years, positive tests were helpful at predicting future development of angina, but did not predict myocardial infarction or sudden death as initial cardiac events.[85]

Clinical Exercise Prescription

Traditional exercise prescription aimed at improving fitness has focused on the central components of type, intensity, frequency and duration. The discussion in this paper focuses on the health benefits of physical activity not necessarily intended to improve fitness. Rather than focusing on the issues of frequency, intensity and duration separately, the recent physical activity recommendations emphasize the total amount of activity required to derive benefit. All of the major medical organizations have come to essentially the same conclusion. They all recommended acquiring on average at least 30 minutes per day of moderate intensity activity roughly equivalent to 150-200 kcal of energy expenditure per day. This *dose* is largely based upon the results of the studies reviewed in this paper. For instance, in MRFIT, 30 minutes per day of light to moderate physical activity (roughly equivalent to 150 kcal/day) was associated with a 25% reduction in death from coronary heart disease, with no further benefit at levels above this. In the U.S. Railroad Study, the additional expenditure of 548 kcal/week (78 kcal/day) in otherwise sedentary individuals was associated with a 16% decrease in CHD-related mortality and 18% decrease in all cause mortality. Most of this activity was non-vigorous activity. Again, little benefit was obtained at levels above this. In the Harvard Alumni Study, the addition of 500 kcal/week reduced all-cause mortality by 22% and the addition of 1500kcal per week reduced the risk by 37%. In this study, additional benefit was achieved up to the addition of 3000 kcal per week. In short, the addition of as little as 500 kcal/week (or a total expenditure of 1000 kcal/week) of light to moderate activity may have substantial benefits.

This data has a profound influence on the way we prescribe exercise for our patients. There is no clear minimum threshold of activity which must be obtained to derive benefit. Consequently, since 60% of people are not regularly active, any increase in activity is potentially beneficial. Although establishing a goal to increase activity to a level of at least 1000 kcal/week is advisable, the most salient issue is to simply get moving. Increasing physical activity begins with a mindset that includes looking for opportunities. This is as simple as taking the stairs rather than the elevator or parking the car further away from the mall entrance and walking across the parking lot. The type of activity described can typically be performed without breaking a sweat. Consequently, it does not required setting aside a designated time or going to a special place to do it.

For those who want a more structured exercise plan, countless options are available. Recommendations should take into consideration the persons current level of activity and overall health. Any activity or combination of activities using large muscle groups can be performed with a combination of frequency, intensity and duration to result in the expenditure of enough calories to achieve the desired goals. Activity of higher intensity can be performed less frequently or of shorter duration and still accomplish the same goals. It should also be noted that about 50% of persons discontinue their exercise program within one year. Consequently, it is essential that the participant find something that he or she can do consistently. The least sophisticated exercise program, performed with vigor is better than the best program not performed infrequently or not at all.

One caveat to be remembered is that it is prudent to avoid the recommendation of absolute levels of intensity. For instance, the CDC report suggested that moderate activity is that which requires 3-6 METs, such as walking at a pace of 3-4 miles per hour. Although this may represent moderate activity for most people, for some it may represent vigorous activity, especially the elderly.

Since the current recommendations for physical activity emphasize the total amount of energy expended, it is useful to be able to estimate kcal expended based upon the intensity of exercise. The total kcal is directly proportional to weight. The following formula can be used to estimate the caloric expenditure.

Kcal = (METs x weight in kg x minutes of activity)/60 minutes

The formula can also be used to determine how long one must perform an activity to burn a desired number of calories.

Minutes = (desired # of calories x 60 minutes)/(METs x weight in kg)

The metabolic equivalents (METs) for various activities have been published in the form of a compendium for easy reference.[86]

The level of activity discussed here is primarily intended to reduce cardiovascular morbidity and mortality. For some people the goal of activity may be to lose weight. In this instance, it may be desirable to recommend an increased amount of activity commensurate with the amount of weight loss desired. It is also worth pointing out that these recommendations do not address the issue of weight bearing exercise which may be helpful in preventing or treating osteoporosis, or flexibility training which is beneficial in preventing falls and increasing mobility. It may be desirable to incorporate these types of activities into one's exercise regimen.

For those who wish to pursue more vigorous exercise for the purpose of increasing fitness, recommendations have been established by the AHA and ACSM and are available in other resources.[82,87]

Conclusion

Based upon the data reviewed, it is safe to draw the following conclusions.

1. Exercise of moderate intensity and of moderate amount has substantial health benefits, particularly for sedentary individuals.
2. Additional benefit may be obtained from vigorous activity.
3. Activity needs to be current to be helpful.
4. Moderate physical activity has been shown to be beneficial in the prevention and treatment of both diabetes and cardiovascular disease.
5. Although the data is somewhat inconsistent, the beneficial effects appear to be similar in both men and women.

Exercise does not have to be painful to produce gain. It simply has to be done. The "treatment" of inactivity is as important as treating hypertension, hyperlipidemia. Physicians can have a major influence on the willingness of their patients to become more active. Discussions about physical activity should be a frequent part of office visits and specific goals for physical activity should be discussed with patients, particularly those who are least active. So to quote a famous slogan, it is time that we all get moving and "**just do it**."

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