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The Disease-Specific Benefits and Risks of Physical Activity and Exercise

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Synopsis

Physical inactivity has been related to the occurrence of coronary heart disease, hypertension, diabetes mellitus, and osteoporosis. The literature was reviewed to determine what is and what is not known about the efficacy and safety of physical activity in each of these conditions.

Although there is a transient increase in the risk of sudden cardiac death during vigorous activity, there is mounting evidence that habitual vigorous activity is associated with an overall reduced risk of coronary heart disease. It is unlikely that this association merely reflects the "selection" that results from sick persons who tend to be less active.

Several studies suggest that physical activity may be related to the prevention and control of hypertension, diabetes mellitus, and osteoporosis. However, additional research is needed to make explicit the risks and benefits of physical activity in each of these conditions.

Finally, future efforts should determine the type, intensity, frequency, and duration of activity required to maximize the benefits and minimize the hazards of physical activity. The public health and clinical significance of these questions requires that they be examined in the most rigorous manner feasible.

THERE IS MOUNTING EPIDEMIOLOGIC evidence that physical inactivity and a lack of exercise are related to the occurrence of several diseases that are major causes of death and disability in the United States. Although the relationship between the level of physical activity and the risk of coronary heart disease has been the most extensively investigated, studies have suggested that physical activity may contribute to the prevention and control of several other diseases as well.

We restricted our review to four diseases that are of major public health importance and that have been related to physical activity and exercise in clinical-epidemiologic literature: coronary heart disease, hypertension, diabetes mellitus, and osteoporosis. We critically reviewed the literature that examines potential disease-specific effects of physical activity and exercise to identify what is and what is not known about these relationships. Our review focused on four questions related to each condition:

1. Are physical activity and exercise associated with the occurrence of the specific condition?
2. Is there evidence that the association is potentially causal, or is it merely related to the selection that results from sick persons who tend to be less active?
3. Are there groups of persons who particularly benefit from physical activity and others who benefit little or not at all?
4. Is there a disease-specific hazard related to physical activity, and to what extent does it detract from the potential benefits of physical activity?

Our review was limited to the major clinical-epidemiologic literature related to these questions.

Disease-Specific Effects

Coronary heart disease. Although numerous studies have focused on the relationship between physical activity and coronary heart disease, we used the findings from four studies to address the previously noted questions. Details of these studies are summarized in table 1. Each study determined whether a form of physical activity was associated with the risk of coronary heart disease.

Paffenbarger prospectively assessed the relationship between work activity and coronary heart disease mortality among San Francisco longshoremen (*1*). The risk of coronary heart disease mortality was higher for workers with lower levels of work-related activity, compared with workers who were more vigorous at work. Morris examined the relationship between leisure-time activity and initial clinical coronary heart disease events, both fatal and nonfatal, in a large cohort of British civil servants (*2*). Civil servants who reported that they did not engage in vigorous leisure-time activity had a higher risk of clinical coronary heart disease compared with those who reported vigorous activity.

The relationship between leisure-time physical activity and first clinical heart attacks, both fatal and nonfatal, was also examined in a large cohort of Harvard College alumni (*3*). The risk of first heart attack was higher in those alumni with low levels of contemporary leisure-time physical activity, compared with alumni who were more active. In addition, the risk of first heart attacks seemed to be lower for those who engaged in strenuous sports play than with more casual activities, at any given level of energy expenditure.

A recent population-based case-control study from metropolitan Seattle, WA, examined the relationship between habitual leisure-time activity and primary cardiac arrest among persons without a known history of heart disease or major comorbidity (*4*). Among persons who habitually engaged in low levels of vigorous activity, the overall risk of primary cardiac arrest was increased, compared with persons who were more vigorous. The findings from these four studies and others (*5,6*), therefore, suggest that there is an association between the level of habitual vigorous activity and the overall risk of coronary heart disease, as reflected in the relative risk estimates in table 1.

There are two possible explanations for these observations. On the one hand, if habitual vigorous activity leads to a lower risk of coronary heart disease, then exercise might be "protective." On the other hand, if either prior morbidity or other factors lead to a lack of vigorous activity, then the association may reflect the "selection" associated with "sick" or "unfit" persons who tend to be less active.

The four studies cited addressed the issue of "selection versus protection" in several different ways. First, each study started with a healthy population, minimizing the potential confounding that results from sick persons who tend to be less active. Second, other potential confounding factors, such as age, smoking, obesity, hypertension, and family history, were examined in the data analyses; they did not appear to account for the observed inverse relationship between the level of physical activity and the risk of coronary heart disease.

Table 1. Physical activity and coronary heart disease, comparison of four studies

Study population and reference	*Number*	*Design*	*Activity*	*Coronary disease*	*Number of events*	*Relative risk*[1]
Longshoremen (*1*)						
Men 35–74 years	6,351	Cohort	Work	Fatal	598	1.8
Civil servants (*2*)						
Men 40–65 years	17,944	Cohort	Leisure	Fatal and nonfatal	1,138	1.4 fatal and 2.0 nonfatal
Harvard alumni (*3*)						
Men 35–74 years	16,936	Cohort	Leisure	Fatal and nonfatal	572	2.0 fatal and 1.5 nonfatal
Primary cardiac arrest (*4*)	163	Population-based, case-control				
Men and women 25–75 years			Leisure	Primary cardiac arrest	163	2.4

[1] Relative risk = incidence among nonvigorous ÷ incidence among vigorous.

Third, the possibility that constitutional differences between persons who chose to be active and those who are sedentary might explain the association between physical activity and coronary heart disease was examined in the Harvard College alumni study. Activity in adult life appeared independent of activity during college in predicting a lower risk of heart attack, suggesting that constitutional differences did not account for the association.

Fourth, neither exluding cases of coronary heart disease that occurred early in the followup period (*7*) nor accounting for changes in job classification (*8*) altered the relationship between activity and coronary heart disease. For these reasons, it seems unlikely that the association between a lack of habitual vigorous activity and an increased risk of coronary heart disease merely reflects "selection."

Even though habitual activity is associated with an overall reduced risk of coronary heart disease in the population as a whole, it is possible that the presence or absence of other risk factors for coronary heart disease might modify this relationship. To determine whether there are groups of persons who particularly benefit from habitual vigorous activity, and others who benefit little or not at all, the difference in risk of coronary heart disease related to exercise for persons with or without other factors needs to be examined.

The relative risk of coronary heart disease was reduced among persons who engaged in high levels of physical activity compared with more sedentary persons both in the presence and absence of other risk factors such as age, smoking, hypertension, obesity (body-mass index), and family history (*2,3,9,10*). However, the attributable risk, that is, the difference in incidence potentially related to habitual activity, was greatest for persons who were older (*2,10*), hypertensive (*3,9,10*), or obese (*10*). Thus, habitually active persons with these other risk factors may benefit the most.

Finally, the relationship between habitual activity and coronary heart disease has not been assessed among persons with hypercholesterolemia. Whether the relationship differs among persons with this major coronary heart disease risk factor remains unclear.

Based on numerous case reports and series, and given biological plausibility, there is concern that vigorous activity might precipitate sudden cardiac death. The observation that habitual activity may protect overall from coronary heart disease does not preclude the possibility that there is a transient increase in the risk of sudden cardiac death during the act of exercise itself.

Data from the community-based study of primary cardiac arrest make explicit the two components of the overall effect of physical activity, that is, the cardiac risk and benefit, by examining the incidence of cardiac arrest during and not during vigorous activity in relation to the level of habitual physical activity (*11*).

At each level of habitual activity, the risk of cardiac arrest during activity was higher than during inactivity. However, the magnitude of the increased risk during activity was reduced with increasing levels of habitual activity. Finally, these data further suggest that among persons in the upper levels of habitual vigorous activity, their transient increase in risk during activity was outweighed by a decrease in risk during nonexercise periods; thus, their overall risk of primary cardiac arrest was lower than that of men in the lower levels of habitual activity.

The figure illustrates the cardiac risks and benefits of vigorous activity that relate to the occur-

Table 2. Physical activity, fitness, and blood pressure in healthy men and women, comparison of 11 studies

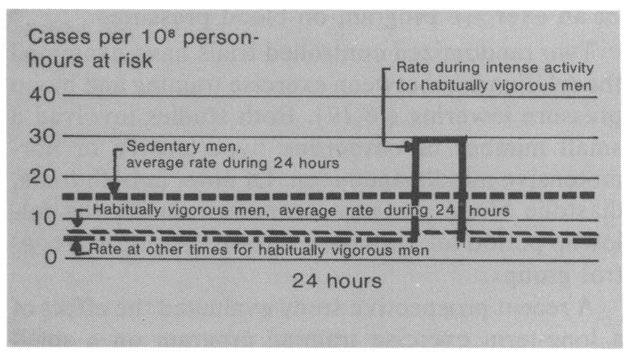
Study population and reference	Number	Design	Activity	Significant BP decrease	Comments
Hinkley (*12*) men 25–74	15,171	Cross-sectional	Work, leisure	No	Adjusted for age only
Cooper (*13*) men 45	3,000	Cross-sectional	Fitness level	Yes	Adjusted for age, weight, percent body fat
Gibbons (*14*) women 18–65	1,700	Cross-sectional	Fitness level	Yes	Adjusted for age, body mass index, examination year
Boyer (*15*) men 35–61[1]	45	Prospective	Fitness program	Yes	Uncontrolled
Choquette (*16*) men 42[1]	165	Prospective	Fitness program	Yes	Uncontrolled
Stamler (*17*) men 40–59	216	Prospective	Leisure	Yes	Uncontrolled, combined exercise nutrition intervention
Mann (*18*) men 25–60	82	Randomized trial	Fitness program	No	Both intervention and control groups' blood pressure decreased
Kukkonen (*19*) men 35–50[1]	59	Randomized trial	Fitness program	No	Both intervention and control groups' blood pressure decreased
Roman (*20*) women 35–74[2]	55	Prospective	Fitness program	Yes	Cross-over design
Paffenbarger (*21*) men 35–74	14,998	Prospective	Leisure	Yes	Adjusted for body mass index, weight gain since college, history of parental hypertension
Blair (22):					
Men 20–65	4,820	Prospective	Fitness level	Yes	Adjusted for sex, age, followup interval, baseline blood pressure, and baseline body mass index
Women 20–65	1,219				

[1] Included both normotensive and hypertensive men. [2] Hypertensive women.

rence of primary cardiac arrest. It shows the incidence per person-hour at risk for sedentary men, for habitually vigorous men overall, and the two components of the overall risk for habitually vigorous men, that is, the risk during intense activity and at other times. As shown, although the risk of primary cardiac arrest is transiently increased during the act of vigorous exercise, men who are habitually vigorous have a lower overall risk of primary cardiac arrest than sedentary men.

Hypertension. Several studies have suggested that increased levels of physical activity and exercise are associated with lower levels of blood pressure (table 2). Large cross-sectional studies have demonstrated an inverse relationship between the level of physical activity (*12*) or physical fitness (*12,14*) and systolic and diastolic blood pressure levels among apparently healthy, primarily normotensive, persons. Although blood pressure was lower among persons who were active or fit, compared with nonactive or unfit persons, the magnitude of the effect in the populations appeared small; persons who were active had an average diastolic blood pressure that was from 2 to 5 mmHg less than inactive persons. These differences persisted after statistical adjustments for potential confounding re-

Risk of primary cardiac arrest during vigorous physical activity and at other times, by level of habitual physical activity



lated to age (*12*), weight (*13,14*), and percent body fat (*13*). Unfortunately, the cross-sectional design of these studies makes them particularly vulnerable to the potential confounding related to the fact that sick persons may tend to be less active.

Two prospective studies examined the effect of exercise training to achieve fitness on the blood pressure levels of normotensive and hypertensive middle-aged men (*15,16*). Both studies suggested that systolic and diastolic blood pressure decreased with exercise training; the magnitude of the reductions in blood pressure was significantly greater for hypertensives compared to normotensives. Be-

'It appears that physical activity early in life, for example, during college years, is not necessary or sufficient to achieve the cardiac benefits of activity. However, it is not known at what point in life and for how long one needs to be physically active to achieve these benefits.'

cause these studies did not include control groups for comparison, it is unclear to what extent the observed decrease in blood pressure can be attributed to the exercise training.

A recent report of a prospective evaluation of a nutritional-exercise regimen among men with high normal diastolic blood pressure or mild hypertension suggested that improvements in exercise habits and nutrition were useful in preventing high blood pressure in hypertension-prone persons and in controlling established "mild" hypertension (*17*). The change in blood pressure observed in this study significantly correlated with change in weight. The absence of a control group in this study limits the ability of these data to determine the potential effect of an exercise program on blood pressure.

Two randomized controlled trials have examined the relationship between exercise training and blood pressure lowering (*18,19*). Both studies involved a small number of borderline hypertensive or normotensive middle-aged men. Of note, in both trials, diastolic blood pressure decreased during the followup period for both the exercise training and control groups.

A recent prospective study evaluated the effect of a long-term exercise training program on a small group of women with chronic hypertension (*20*). Among the 30 subjects in this study, blood pressure decreased during a 3–month training period, increased when training was discontinued for 3 months, and decreased again when training was reinstituted for 1 year.

To determine if habitual physical activity is associated with a reduced risk of developing hypertension, a large cohort study of Harvard college alumni assessed the relationship between physical activity and the incidence of physician-diagnosed hypertension (*21*). Alumni who did not currently engage in vigorous sports play were at 35 percent greater risk of hypertension than those who were active. This relationship was independent of other predictors of increased risk of hypertension such as higher body mass index, weight gain since college, and history of parental hypertension. Of note, the inverse relationship between contemporary vigorous activity and hypertension risk was primarily among those alumni who were overweight-for-height, suggesting that this group might particularly benefit from activity.

Finally, a large cohort of healthy normotensive men and women were followed to determine if the level of physical fitness, assessed by maximal treadmill testing, was related to the incidence of physician-diagnosed hypertension (*22*). In this cohort, physical fitness was related to the incident of hypertension, and the relationship appeared to be independent of sex, age, followup interval, baseline blood pressure, and baseline body–mass index. When compared with highly "fit" persons, persons with low levels of fitness were at 52 percent greater risk for the development of hypertension.

These cohort studies suggest that habitual activity and physical fitness may reduce the risk of developing hypertension. In addition, the clinical studies cited previously suggest that habitual exercise may improve the control of high blood pressure. The lack of consistency in the findings of some studies may relate to differences in the prevalence of high blood pressure in the populations studied, the range of physical activity or fitness within each population, and small sample sizes in several of the prospective studies.

Further research will be needed to determine the extent of the association between physical activity or fitness and blood pressure level, to exclude potential confounding from other factors, and to determine if there are groups of persons who particularly benefit from physical activity, for example, obese persons, in terms of the prevention and control of hypertension. In addition, although there is clinical concern that vigorous exercise may be less safe for persons with high blood pressure than for those who are normotensive, there is little empiric evidence relating to the hazards of vigorous activity among this population.

Diabetes mellitus. Considerable research has been done on the acute effect of physical activity on noninsulin-dependent diabetics (*23*). Exercise appears to reduce blood glucose levels, increase insulin receptors, and increase the effectiveness of insulin. Because of these metabolic and hormonal effects, it has been suggested that habitual physical activity might prevent or postpone the development of noninsulin-dependent diabetes. Unfortunately, few controlled studies have assessed the relationship between habitual physical activity and the risk of noninsulin-dependent diabetes.

A cross-sectional study from the South Pacific examined this relationship. In this study, populations that were sedentary had a much higher prevalence of noninsulin-dependent diabetes, compared with active populations, and the association was independent of differences in obesity (*24*). In addition, it has been suggested that the higher risk of noninsulin-dependent diabetes among urban populations, compared with rural populations, may be related to differences in habitual physical activity (*25*).

Based on clinical observations that higher levels of physical activity appear to improve glucose control in diabetic children and that severe degrees of physical inactivity, for example, bed rest, seem to worsen glucose control, exercise has been stressed as an important part of the treatment of insulin-dependent diabetes. However, we are unaware of any controlled studies that have demonstrated the efficacy of physical activity in the control of insulin-dependent diabetes.

The potential long-term benefits and risks of habitual physical activity related to the complications of diabetes are of particular importance. On the one hand, a recent unpublished case-control study by R. E. LaPorte, Graduate School of Public Health, University of Pittsburgh, suggested that higher levels of physical activity may be associated with a reduced risk of macrovascular disease and death, but that they did not appear to be associated with the risk of microvascular disease. On the other hand, based on several case reports, there is concern that increased physical activity may be associated with adverse diabetic consequences, especially for insulin-dependent diabetics with proliferative retinopathy. Clearly, further research is needed to define better the efficacy and safety of different patterns of physical activity among both noninsulin-dependent and insulin-dependent diabetics.

Osteoporosis. Physical activity may be inversely related to the development of osteoporosis and the risk of fracture. Studies of populations have suggested that the incidence of fracture is lower in active populations, compared with less active populations (*26*). In addition, studies of individuals have demonstrated a relationship between physical activity and bone density.

Female and male marathon runners appear to have higher bone densities than nonrunners (*27,28*) and, in two nonrandomized prospective trials, exercise training programs seemed to retard bone loss in older women (*29,30*). In addition, several studies have shown that a marked reduction in activity to the levels characteristic of disabled persons is associated with a decrease in bone density (*31–35*). When persons who have experienced a severe reduction in their activity level because of immobilization return to their normal daily activity, bone density increases (*36*). These clinical studies and others have suggested that physical activity that involves the pull of gravity, that is, weight-bearing, is the type of activity that is necessary to affect bone density; aerobic activity that is nonweight bearing, such as swimming, may not reduce bone loss.

Randomized controlled trials of activity interventions designed to increase weight-bearing are needed to clarify the relationship between this type of activity and bone density and to exclude the potential distortion from confounding factors. In addition, it will be important to determine whether there are groups of persons who particularly benefit and others who benefit little or not at all from physical activity in their risk of osteoporosis. For example, excessive running leading to amenorrhea appears to be associated with reduced bone density (*37*). Finally, the risk of fracture during activity in relation to the level of habitual activity needs to be determined, so that the risks and benefits of activity related to osteoporosis and fracture can be made explicit.

Table 3. Evidence assessing the disease-specific effects of physical activity and exercise, graded on quality of evidence from A to D[1]

Disease	*Efficacy of exercise*	*Safety of exercise*
Coronary disease	B[2]	B
Hypertension	B[2]C[3]	NA
Diabetes mellitus	D[3]	NA
Osteoporosis	C[2]	NA

[1] A—evidence from randomized controlled trials, B—evidence from well-designed cohort or case-controlled analytic studies, C—evidence from cross-sectional studies, D—evidence from clinical experience or descriptive studies, NA—no data available.
[2] In relation to prevention of specific disease.
[3] In relation to treatment of specific disease.

Discussion

Our overall assessment of the quality of the evidence that examines the disease-specific effects of physical activity is shown in table 3. This review suggests that habitual vigorous activity is associated

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with an overall reduced risk of coronary heart disease. Although a randomized controlled trial might more completely address the concern that self-selection of activity level accounts for these findings, mounting evidence from nonexperimental studies suggests that this association is not merely the result of sick persons tending to be less active. In addition, men with and without other coronary heart disease risk factors seem to benefit from physical activity; those with hypertension or obesity may particularly benefit.

It appears that physical activity early in life, for example during college years, is not necessary or sufficient to achieve the cardiac benefits of activity. However, it is not known at what point in life and for how long one needs to be physically active to achieve these benefits.

Finally, data pertaining to the safety of physical activity related to coronary heart disease indicate that the risk of primary cardiac arrest is transiently increased during vigorous activity. However, because the increase in risk during activity is outweighed by the reduced risk during nonexercise periods, persons who are habitually vigorous have a reduced overall risk of cardiac arrest. Nevertheless, it remains unclear whether there are groups of apparently healthy persons who have a particuarly large increase in risk during vigorous activity.

Although there is some evidence suggesting that physical activity is associated with the prevention or control of high blood pressure, osteoporosis, and diabetes mellitus, major questions regarding the efficacy and safety of physical activity related to each of these conditions remain unresolved. In these conditions, the effects of physical activity may be reflected in relatively sensitive physiologic or metabolic outcome measures, for example, blood pressure, blood glucose, and bone density, that do not require prolonged periods of followup. Therefore, it should be possible to begin to address more fully questions relating to the efficacy of physical activity in these conditions through randomized controlled trials. However, surveillance of larger populations with these conditions and research designs other than randomized trials will be needed to determine if there are groups of persons who particularly benefit from activity and to demonstrate the risks, for example, the safety of physical activity, since clinically important hazards may be rare events.

The disease-specific effects of physical activity need to be examined in a variety of populations, for example, among women and the elderly. In addition, the potential complexity of these relationships needs to be considered: issues related to the measurement of physical activity, potential confounding and interaction related to other factors, and the assessment of the risks as well as the benefits of physical activity.

Whether vigorous activity, such as jogging, that results in physical fitness is necessary to achieve the disease-specific benefits of physical activity remains unclear, because previous studies have not adequately examined the relationship between less intense activity, such as walking, and these diseases. There is a need for research that clarifies the type, intensity, frequency, and duration of activity required to maximize the potential disease-specific benefits and minimize the hazards of physical activity.

We did not review the evidence that relates physical activity and exercise to a variety of other potential disease-specific effects including obesity, peripheral vascular disease, stroke, lipid disorders, chronic obstructive pulmonary disease, asthma, musculoskeletal disorders, arthritis, and cancer. The potential role of physical activity in either the prevention or treatment (or both) of each of these conditions remains unresolved; so it is not possible at present to weigh the potential risks and benefits of physical activity in these diseases.

The lessons learned from more than 30 years of investigations related to physical activity and coronary heart disease should guide the research activities that address these issues. The public health and clinical significance of these questions requires that they be examined in the most rigorous manner feasible.

Summary

Based on our critical review, what is known about the relationship between habitual physical activity and coronary heart disease?

1. Habitual vigorous physical activity is associated with a reduced overall risk of coronary heart disease (CHD) and sudden cardiac death.
2. The effect of vigorous physical activity on CHD is independent of its effects on other known CHD risk factors such as hypertension, cigarette smoking, and obesity.
3. There is some evidence of potentially important interactions between habitual vigorous activity and other risk factors, particularly hypertension and obesity, on the risk of CHD.
4. Although there is a transient increase in the risk of sudden cardiac death during the act of vigorous activity itself, habitual activity is associated with an overall reduced risk of CHD and sudden cardiac death.

Because many important questions remain unresolved, we recommend that future research:

1. Determine the dose-response effects of physical activity, such as type, frequency, intensity, an duration, on the prevention of CHD.
2. Determine the effects on CHD of beginning physical activity at different ages.
3. Determine the interrelationships between physical activity, characteristics that affect CHD risk, and CHD.
4. Determine the factors that affect the risk of CHD during exercise, like interactions with dose, other risk factors, drugs, or the environment.
5. Determine the effects of physical activity on longevity.
6. Determine if the CHD benefits can be maximized and the risks minimized through pre-exercise evaluation and exercise prescription.
7. Determine if the same relationships are found in men and women.

What is known about the relationship between physical activity or fitness and hypertension, diabetes mellitus, and osteoporosis?

1. Cohort studies suggest that habitual physical activity and physical fitness reduce the risk of de-

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veloping hypertension. Clinical studies suggest that habitual physical activity improves the control of hypertension.

2. Clinical observations suggest that habitual activity improves the control of the blood sugar in type II diabetes.
3. Observational studies suggest that habitual physical activity slows the loss of bone density in post-menopausal women.

As with coronary heart disease, we recommend that future research:

1. Determine the dose-response effects of physical activity on both the prevention and control of hypertension, diabetes, and osteoporosis.
2. Determine the effects of starting a physical activity program at different ages on the prevention and on the control of these diseases.
3. Determine the interrelationships between physical activity, other risk factors, and the prevention and control of these diseases. For example, do obese persons at risk for hypertension and diabetes benefit the most?
4. Determine the risks during physical activity for people with these diseases, the cofactors of these risks. Determine if these risks are outweighed by the overall benefits of physical activity.
5. Determine the answers to similar questions related to a variety of other diseases,—obesity, lipid disorders, arthritis, respiratory disease, and cancer.

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