

Physical Activity and Health: Dose-Response Issues

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Over the past two decades, compelling scientific evidence has accumulated demonstrating that regular participation in physical activity provides important health benefits. As a result, promotion of physical activity has become recognized as a public health issue, and in recent years several prominent health organizations have issued pronouncements noting the disease prevention and health promotion benefits of physical activity (Fletcher et al., 1992; Killoran, 1994; Pate et al., 1995).

In communicating the significance of regular physical activity to the public, it is important to indicate the types and amounts of physical activity that are needed for health benefits. This need raises several important questions and these include (a) how much and what types of physical activity are needed for each of the specific health benefits that have been associated with physical activity? (b) is there an optimal amount of physical activity that can be recommended? and (c) is there a minimal amount of activity that could be endorsed? A strategy that could be employed in answering these questions is to study the so-called dose-response relationship between physical activity and health (Blair, Wells, Weathers, & Paffenbarger, 1994; Haskell, 1994). This relationship describes the level of health benefits associated with various levels of physical activity. Because health is a multifactorial construct and because physical activity has been shown to affect numerous health parameters, a study of the global dose-response relationship for physical activity and health requires examining numerous specific dose-response gradients.

The purpose of this paper is to examine our current knowledge of the dose-response relationship between physical activity and health. This examination will involve reviewing the dose-response relationships for several specific health outcomes that are known to be associated with habitual physical activity. These include (a) one physical fitness parameter (cardiorespiratory fitness);

(b) three physiological factors associated with chronic disease risk (high-density lipoprotein cholesterol [HDL-C], resting blood pressure, and glucose tolerance); (c) morbidity from three chronic diseases (coronary heart disease, Type II diabetes, and hypertension); and (d) all-cause mortality.

To the extent allowed by the existing scientific literature, the effects of two markers of physical activity "dose" will be considered for each health outcome. First, the effect of the amount of physical activity performed, as indicated by estimated weekly caloric expenditure (or a surrogate measure thereof), will be considered. Second, the effect of exercise intensity, independent of overall amount of activity, will be examined.

Cardiorespiratory Fitness

Of all the various health parameters, cardiorespiratory fitness may be the one for which the dose-response relationship with physical activity is best understood. Numerous controlled training studies have examined the effects of various combinations of frequency, intensity, and duration of exercise on maximal aerobic power ($VO_2\text{max}$). These studies have shown that in initially inactive adults, endurance exercise training produces increases in $VO_2\text{max}$ that are directly related to the overall amount of work performed (American College of Sports Medicine [ACSM], 1990). However, with higher doses of activity, there is a diminishing return such that a given increase in dose elicits a smaller response. The traditional exercise prescription recommendation is based on this observation. The recommended minimum of 20 min of aerobic activity, at 50% or more of individual $VO_2\text{max}$, on three or more days per week is based on the observation that this dose of activity produces a 10-20% increase in $VO_2\text{max}$ in most initially inactive persons (ACSM, 1991). Higher doses of activity produce greater, but not proportionally greater, increases in $VO_2\text{max}$.

The scientific literature provides clear evidence that intensity of exercise training is directly related to

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(ACSM, 1993; Fagard & Tipton, 1994). Most of the pertinent studies have examined this effect in borderline or fully hypertensive individuals. Hence, in this population, the dose-response curve for intensity of exercise and change in blood pressure may take the shape of an inverted U.

Glucose Tolerance

There is substantial evidence, in normal individuals, that endurance exercise training increases tolerance to an oral or intravenous glucose load by increasing insulin sensitivity (Sutton, Farrell, & Harber, 1990). In addition, reviewers of the available literature have concluded that this effect is observed in people who are borderline diabetic (Gudat, Berger, & Lefèbvre, 1994). However, to date, studies of exercise training in patients with full-blown diabetes have yielded inconsistent results (Wallberg-Henriksson, 1992; Young & Ruderman, 1993). The experimental literature provides little information about the dose-response curve, as few pertinent studies have used more than one amount or intensity of training. Further, the epidemiological literature is not helpful on this point, perhaps because measures of glucose tolerance are impractical in large scale surveys.

Chronic Disease Morbidity and Mortality

The past two decades have witnessed an impressive expansion in the scientific literature linking regular participation in physical activity to reduced risk for development of chronic diseases. This growth in the body of knowledge has been most dramatic for CHD, but also has been extensive for several other chronic diseases. This section overviews the epidemiological literature that addresses the possible existence of a dose-response relationship for physical activity and three chronic diseases: CHD, hypertension, and non-insulin-dependent diabetes mellitus.

CHD

Lack of physical activity is now considered a major risk factor for development of CHD (Fletcher et al., 1992). This conclusion has been based, in large part, on the fact that the pertinent epidemiological literature has been found to meet the criteria for establishing a causal relationship between physical inactivity and CHD. One of these criteria is that a dose-response relationship (or biological gradient) has been convincingly documented (Pate et al., 1995; Powell et al., 1987). It seems clear that a gradient does exist, although its exact pattern remains uncertain. Powell et al. (1987), in an extensive review, concluded that studies employing the best epidemiological research methods tended to observe an inverse relationship between the amount of

habitual physical activity and CHD risk. In a more recent review, Blair (1994) also concluded that such a trend exists and noted that the relationship may be curvilinear—CHD risk decreasing steeply at the lower end of the physical activity (or fitness) continuum—but reaching an asymptote in the midrange for physical activity or fitness. However, it should be noted that not all studies agree on this point.

The literature also includes conflicting evidence concerning the role of exercise intensity in determining CHD risk. Haskell (1994) and Blair (1994) noted that several key studies have shown substantial reductions in CHD risk with accumulation of physical activity, most of which was of moderate intensity. However, the work of Morris (Morris, Clayton, Everitt, Semmence, & Burgess, 1990) and the recently published study by Lee, Hsieh, and Paffenbarger (1995) argue that more vigorous physical activity may provide unique benefits. Clearly, the role of exercise intensity in reducing CHD risk requires further research.

Hypertension

Several well-designed epidemiological studies have observed reduced risk for the development of hypertension in physically active versus inactive persons (Blair, Goodyear, Gibbons, & Cooper, 1984; Paffenbarger, Wing, Hyde, & Jung, 1983). However, these studies were not designed to address the possible existence of a dose-response gradient. Also, none of the available studies examined the possible independent role of exercise intensity in determining risk of developing hypertension.

Non-Insulin-Dependent Diabetes Mellitus (NIDDM)

Three recently published epidemiological studies provide strong evidence that habitual physical activity is inversely related to risk of developing NIDDM (Helmrich, Ragland, Leung, & Paffenbarger, 1991; Manson et al., 1991, 1992). In all three studies, there was evidence of a dose-response relationship, though the shape of the curve was not consistent across the studies.

Helmrich et al. (1991) examined the dose-response relationship between physical activity and risk of NIDDM for both total physical activity and for only vigorous activity. They observed a steeper decline in risk for vigorous activity than for total activity. In both of the studies by Manson et al. (1991, 1992), only frequency of participation in vigorous physical activity was reported. Clearly, existing evidence points to important benefits of vigorous physical activity. Vigorous activity may be more beneficial than moderate physical activity, but to date only the study of Helmrich et al. has examined this issue.

the change in VO_2 max that is induced by the training (Gossard et al., 1986; Karvonen, Kentala, & Mustala, 1957). So it seems certain that exercise intensity, acting either independently or as a contributor to the overall amount of activity, is related to change in physical fitness. However, one of the dogmas of exercise physiology has been that the dose-response relationship for physical activity and physical fitness, described earlier, applies only for intensities of exercise above a threshold at approximately 50% of individual VO_2 max. Indeed, the ACSM's (1990) current position stand on the recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness in healthy adults states that ". . . present evidence suggests that, when exercise is performed above the minimum threshold, the total amount of work accomplished is an important factor in fitness development" (p. 266). For two reasons, it seems appropriate to challenge the assumption that there is a "threshold" exercise intensity. First, very few studies have examined the effects of exercise training at intensities lower than 50% VO_2 max and, second, there is some evidence that training at intensities lower than 50% VO_2 max may increase VO_2 max (although the increases may be statistically insignificant because of limited statistical power; Duncan, Gordon, & Scott, 1991).

Physiological Risk Factors

Both cross-sectional comparisons of physically active and inactive persons and controlled, longitudinal exercise training studies have examined the relationship between physical activity and an array of physiological factors that are associated with chronic disease risk. This section provides a concise review of the available literature pertinent to the dose-response relationship for physical activity and three key physiological variables: HDL-C, resting blood pressure, and glucose tolerance.

HDL-C

It is well established that plasma HDL-C concentration is inversely related to risk of future development of coronary heart disease (CHD; Gordon, Castelli, Hjortland, Kannel, & Dawber, 1977). In addition, it is now well documented that regular participation in endurance exercise is associated with increases in HDL-C (Stefanick & Wood, 1994; Wood, Williams, & Haskell, 1984). Because of the magnitude and biological impact of the observed associations, increased HDL-C is generally considered to be one of the most important physiological mechanisms whereby physical activity reduces CHD risk (Powell, Thompson, Caspersen, & Kendrick, 1987).

Although it is clear that endurance exercise training increases HDL-C in most initially inactive persons, the dose-response relationship between physical activity and HDL-C has not been fully described. Some cross-sectional studies, in which more than one level of habitual physical activity have been examined, have shown a dose-response gradient (Durstine et al., 1987; Rotkis, Cote, Coyle, & Wilmore, 1982). Likewise, some longitudinal training studies have observed dose-response gradients (Wood et al., 1983). Available evidence does not allow a detailed characterization of the shape of the dose-response curve for physical activity and HDL-C. However, it has been suggested that a weekly energy expenditure of 1,000 or more kilocalories in physical activity may be needed to generate a significant increase in HDL-C (Durstine & Haskell, 1994).

It is not clear that intensity of exercise, independent of its effect on total energy expenditure, is related to HDL-C in a dose-response manner. Duncan et al. (1991) addressed this issue directly and observed similar increases in HDL-C in three groups that trained by performing the same amounts of walking exercise but at three different intensities. Therefore, at present it appears that total amount of exercise performed in training is a more important determinant of HDL-C than is the intensity at which the training is performed.

Resting Blood Pressure

Several epidemiological studies have observed significant associations between either habitual physical activity or physical fitness level and resting systolic blood pressure (Montoye, Metzner, & Keller, 1972; Reaven, Barrett-Conner, & Edelstein, 1991). These observations suggest the presence of a dose-response relationship. In addition, recent reviews of the scientific literature have consistently concluded that structured exercise training decreases resting blood pressure (Tipton, 1991). The magnitude of the decrease in systolic pressure has typically approximated 5 mmHg in normotensive individuals and 10 mmHg in hypertensive individuals. The prevailing consensus, as summarized in a recently published position stand, is that the standard exercise prescription produces the aforementioned decreases in resting systolic blood pressure (ACSM, 1993). Unfortunately, few controlled exercise training studies have used more than one amount of exercise training. Consequently, at the present time, it is not possible to describe the dose-response curve for physical activity and blood pressure on the basis of experimental evidence.

The relationship between intensity of exercise training and resting blood pressure has been addressed in several experimental studies. Reviewers of these studies have concluded that moderate-intensity exercise (40-70% VO_2 max) tends to produce greater decreases in resting blood pressure than higher intensity exercise

All-Cause Mortality

Arguably the most important recent additions to the body of knowledge on physical activity and health have been several investigations exploring the effect of physical activity on the incidence of death from all causes. In essence these studies address the critical question: Does regular physical activity affect longevity? Although the pertinent studies differ considerably in populations observed, nature of exposure variables, and analytic methodologies, just two fundamental research designs have been employed. Most of the available studies have examined the effect of either habitual physical activity or physical fitness, measured at baseline, on incidence of death during the follow-up period (Blair et al., 1989; Leon, Connett, Jacobs, & Rauramaa, 1987). With considerable consistency, these studies have reported that physical activity (or fitness) was inversely related to risk of mortality (Blair et al., 1989; Paffenbarger et al., 1993). In general, a dose-response gradient is evident across the range of values for activity or fitness, with the greatest reductions in risk of mortality falling at the lower end of the activity/fitness continuum.

A second research design, which now has been used in two studies, has examined the relationship between change in physical activity (Paffenbarger et al., 1993) or physical fitness (Blair et al., 1995) and risk of mortality during a follow-up period. In both studies, increases in activity or fitness were associated with lower risk of mortality than maintenance of low status or decreased status. Collectively, these studies provide important evidence that regular physical activity extends life and that a dose-response gradient exists.

Few studies have examined the possible independent effect of intensity of physical activity on all-cause mortality. The recently published work of Lee et al. (1995) showed a strong dose-response gradient for vigorous physical activity and mortality, but did not find a significant gradient for nonvigorous activity. However, some earlier studies have shown reduced risk of mortality with the accumulation of moderate-intensity physical activity (e.g., Leon et al., 1987). Clearly, the role of intensity of exercise warrants further investigation.

Summary

The depth of our current knowledge of the dose-response gradient for physical activity and health is highly variable across the different health parameters. To the extent that the existing literature allows conclusions, it appears that (a) most health parameters are related to the amount of habitual physical activity in a graded fashion; (b) intensity of physical activity may be independently related, in a graded fashion, to some health parameters but unrelated to others; and (c) for

some variables, the dose-response relationship is linear but, in other cases, is curvilinear. At present, these conclusions must be considered tentative, and most experts agree that further elucidation of dose-response relationships should be a major thrust of future research on physical activity and health.

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