

Modest Exercise Prevents the Progressive Disease Associated with Physical Inactivity

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SLENTZ, C.A., J.A. HOUMARD, and W.E. KRAUS. Modest exercise prevents the progressive disease associated with physical inactivity. *Exerc. Sport Sci. Rev.*, Vol. 35, No. 1, pp. 18–23, 2007. *Activity levels continue to decline as technology continues to engineer movement out of our environment. We summarize the findings from Studies Targeting Risk Reduction Interventions through Defined Exercise (STRRIDE) emphasizing the high cost of even short-term continued inactivity in sedentary, overweight, or mildly obese individuals. There seems to be a critical minimal level of physical activity required to maintain metabolic health. A modest amount of exercise seems to prevent metabolic deterioration. Key Words:* metabolic health, lipoproteins, insulin sensitivity, visceral fat, exercise training

INTRODUCTION

It is generally accepted that regular physical activity and exercise are an important part of a healthy lifestyle and that physical inactivity increases the risk of disease over the long term (2). The high cost of physical inactivity, even during the short term, is less well known and appreciated (2). Average daily physical activity levels continue to decline as we permit technological progress to engineer the need for movement out of our environment. For the last few years, we have published a number of observations from Studies Targeting Risk Reduction Interventions through Defined Exercise (STRRIDE), a randomized controlled trial designed to investigate the effects of different amounts and intensities of exercise on risk factors for cardiovascular disease (CVD) (3,4,6,7,12,13). What we did not appreciate at first, but which now has become very evident, was that the so-called control group did not represent a metabolically stable group of individuals. Indeed, the STRRIDE “control” group experienced metabolic deterioration in numerous CVD risk factors for only a 6-month

time. The major purpose of this review is to summarize the findings from STRRIDE with respect to the high cost of continued physical inactivity in sedentary, overweight, or mildly obese men and women.

Also, we address the question, if inactivity is more rapidly detrimental than previously realized, how much exercise is needed to prevent metabolic deterioration? The amount of physical activity and exercise needed for health maintenance has, in the past few years, become quite controversial, with different national organizations disagreeing on a minimal recommended amount of exercise to maintain health and wellness. Despite a number of excellent exercise training studies, uncertainty persists about how much exercise is enough for health benefits and how physical inactivity acts to worsen risk profiles. We address this also with observations from the STRRIDE study.

LONG-TERM COST OF PHYSICAL INACTIVITY—INCREASED PREMATURE MORTALITY

For decades, low levels of fitness and low levels of physical activity and sedentary living have been known to be associated with increased risk of CVD, cancer, and all-cause mortalities. In 1989, a landmark study (1) on 10,224 men and 3120 women who were followed on an average of 8 yr showed that all-cause, CVD, and even cancer mortalities are highest in both men and women in the lowest quintile compared with those in the higher quintiles of fitness as determined by treadmill exercise time to fatigue. Risk of premature mortality from all causes decreases further

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as fitness increases. Particularly interesting is the observation that the greatest reduction in risk seems to occur between the lowest fitness quintile and the next lowest fitness quintile. These findings have been interpreted to suggest that modest increases in physical activity might be especially beneficial in the most sedentary individuals. Indeed, in a recent and particularly compelling article, Mark and Lauer (9) argue that an overwhelming amount of observational data shows that cardiorespiratory fitness (exercise capacity) is a potent indicator of future health for both men and women.

INTERMEDIATE-TERM COST OF PHYSICAL INACTIVITY—INCREASED DISEASE (TYPE 2 DIABETES)

Recently, two landmark randomized controlled intervention studies have observed that modest lifestyle changes (including moderate nutritional changes and modest increases in physical activity that lead to small amounts of weight loss) can prevent much (and perhaps almost all) of the progression from impaired glucose intolerance to diabetes (5,15). A summary of the major findings from these two studies is presented in Figure 1A, B. The data from both studies illustrate the substantial benefits of even modest lifestyle changes. In the Diabetes Prevention Program, the results show not only the clear benefit of lifestyle modification over “usual care” (a 58% reduction in

diabetes incidence) but also that this intervention was nearly twice as effective as medical therapy in preventing the progression to overt diabetes mellitus in an at-risk population. In the Finnish Diabetes Prevention Study (FDPS), diabetes incidence was 33% for subjects who failed to make any of five possible lifestyle changes. However, even subjects who successfully made only one or two lifestyle changes greatly reduced their risk of diabetes. Particularly instructive was the finding that no one, in either group, developed diabetes if they were successful in making four or five lifestyle changes. Importantly, in the FDPS, the weight loss difference between the controls and lifestyle intervention group was only 3.4 kg (7.5 lb) at the end of year 1 and only 2.8 kg (6.2 lb) at the end of year 2, further emphasizing the benefits of even modest weight loss in this population.

Laaksonen *et al.* (8), in a recent *post hoc* analysis of the FDPS data aimed at isolating the effect of physical activity alone, found that individuals who increased their total leisure time physical activity the most during the intervention (highest tertile compared with lowest tertile) were 74% less likely to develop diabetes during the trial period. When adjusted for changes in diet (including total energy intake, total fat, saturated fat, and fiber changes), the risk was only slightly adjusted to a 71% reduction in risk. These studies clearly emphasize the high cost of physical inactivity and the benefits of modest lifestyle changes—particularly increases in physical activity—risk of developing diabetes in a susceptible population.

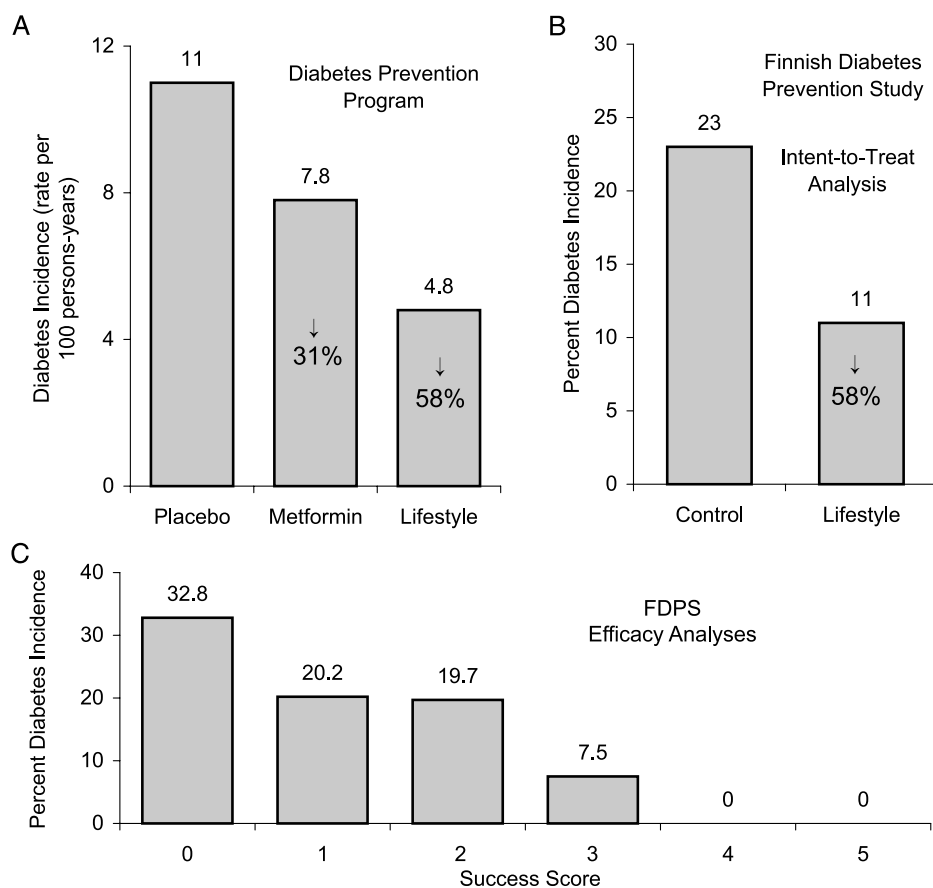


Figure 1. A. The main results from the Diabetes Prevention Program (5) are presented. B. The main results from the FDPS (15) are presented using “intent-to-treat” analyses. With intent-to-treat analysis, the data are analyzed based on which group each subject is assigned to without regard to whether they complied with their group assignment. So, for example, if a control subject started exercising and dieting, the data would still be analyzed as a control group, although the subject followed the instructions for the lifestyle group. Similarly, if a subject assigned to the lifestyle group did not exercise, change their diet, or lose weight, the data would still be analyzed in the lifestyle group. C. The efficacy analyses of diabetes incidence based on the number of successful lifestyle changes out of five are achieved (15). Efficacy analyses does not rely on group assignment but rather simply determines the number of successful lifestyle changes that were made, regardless of which group the subject was initially assigned to.

SHORT-TERM COSTS OF PHYSICAL INACTIVITY—METABOLIC DETERIORATION AND WEIGHT GAIN

It is obvious that physical activity levels are too low for many Americans and that these low activity levels play a major, some suggest perhaps a dominant, role in the obesity and diabetes epidemic in the United States and in the entire developing world. The overriding conceptual scheme that we propose is as follows:

1. There is a minimal level of physical activity required to maintain body weight and metabolic health, and most American adults (and an increasing percentage of children) have reduced their activity levels below this critical level (Fig. 2).
2. Both genetics and the level of sustained discipline around dietary choices (both the amount and types of foods) are key determinants of the minimal physical activity level required to prevent weight gain and premature metabolic deterioration.
3. Body weight changes likely serve as a reasonable, albeit imperfect, surrogate of the degree to which physical activity levels are adequate or not for maintenance of metabolic health (Figs. 2,3).
4. Data from STRRIDE now suggest that, in sedentary individuals, the current levels of physical activity may be so low that significant metabolic deterioration occurs in numerous health-related parameters in as little as 6 months of continued inactivity (Table 1).
5. Metabolic deterioration and weight gain, resulting from continued physical inactivity, can be prevented with a modest amount of dedicated physical activity.
6. In light of the apparently high percentage rate of weight regain after weight loss diets, it would seem prudent to adopt a major paradigm shift away from emphasizing

weight loss toward a much stronger emphasis on the prevention of weight gain in the first place.

LESSONS FROM THE STRRIDE STUDY

A detailed description of the STRRIDE is presented elsewhere (7). Subjects who were 40–65 yr old, sedentary, overweight or mildly obese (body mass index, 25–35 kg·m⁻²), and dyslipidemic (either LDL cholesterol 130–190 mg·dL⁻¹ or HDL cholesterol <40 mg·dL⁻¹ for men or <45 mg·dL⁻¹ for women) were randomly assigned to one of three training groups or a nonexercising control group. Subjects for this cohort were recruited continuously between January 1999 and June 2002, with exercise training completed by April 2003. The final number of subjects that completed the study was 260. The breakdown for each group was as follows: control, 61 (30 men and 31 women); low amount/moderate intensity, 61 (31 men and 30 women); low amount/vigorous intensity, 68 (38 men and 30 women); and high amount/vigorous intensity, 70 (41 men and 29 women). The exercise groups were as follows:

1. High-amount/vigorous-intensity individuals were assigned to do 23 kcal·kg⁻¹ of body weight per week (the caloric equivalent of walking/jogging approximately 20 miles·wk⁻¹ for a 90-kg person (range, 19.2–20.6 miles·wk⁻¹ for a 70- to 110-kg person)) at 65–80% peak $\dot{V}O_2$.
2. Low-amount/vigorous-intensity individuals were assigned to do 14 kcal·kg⁻¹ of body weight per week, (the caloric equivalent of walking/jogging approximately 12 miles·wk⁻¹) at 65–80% peak $\dot{V}O_2$.
3. Low-amount/moderate-intensity individuals were assigned the same amount of exercise as the low-amount/vigorous-intensity group, but the prescribed

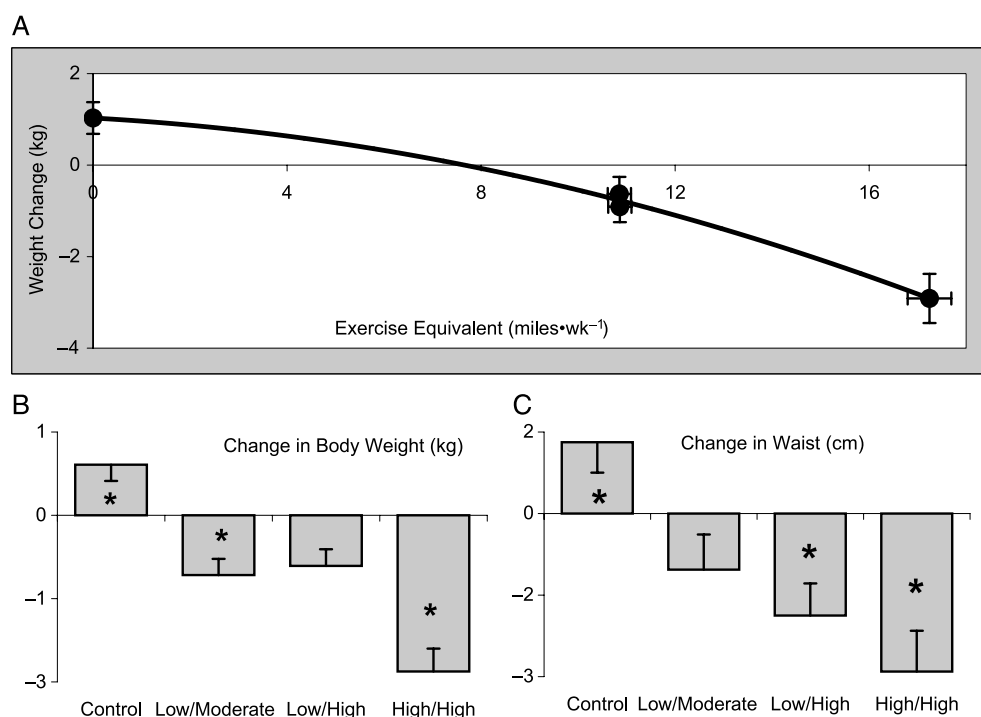


Figure 2. A. The figure presents the relation between average weight change (with vertical SE bars) for each group and average exercise (walking/jogging) equivalent in miles per week (with horizontal SE bars) (13). A curvilinear model is fitted to the group data indicating that the x-intercept is at approximately 8 miles and indicates the theoretical minimal exercise amount required for weight maintenance. B. Body weight change is represented in the bar graph with the change scores for each group represented. C. The figure shows change in waist circumference for each group. *Indicates a significant change score within a particular group, $P < 0.05$.

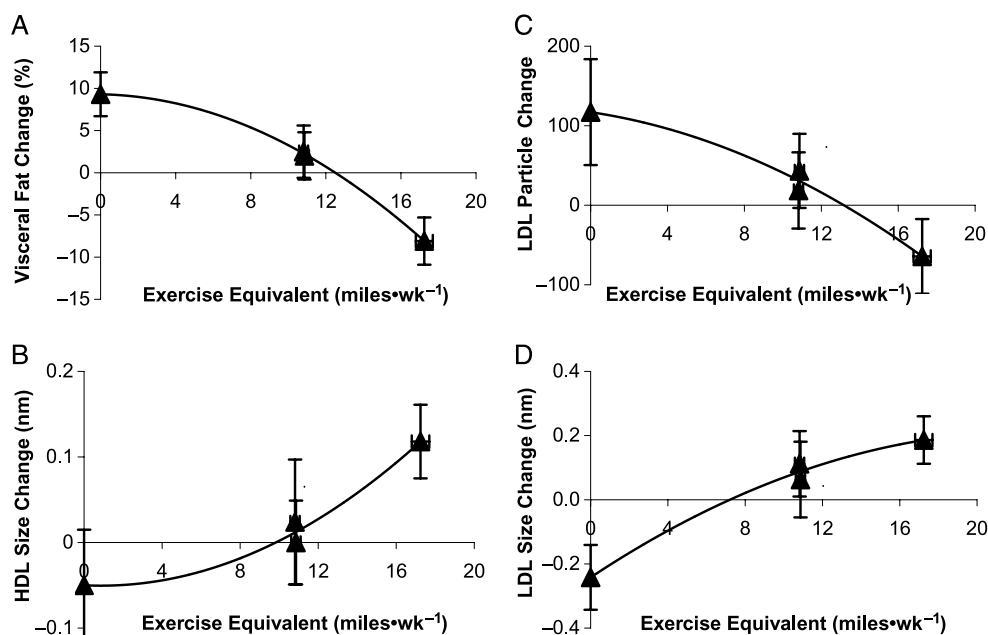


Figure 3. The change data (postintervention score – preintervention score) for the inactive controls and each of the three exercise groups, plotted based on exercise (walking/jogging) equivalent in miles per week, are shown for visceral fat (%) (A) (12), HDL size (B) 6, LDL particle number (C) 6, and LDL size (D) (6). See legend for Figure 2 and “Lessons from STRRIDE” section for a more complete description of the exercise groups.

intensity was lower and ranged between 40% and 55% of peak $\dot{V}O_2$.

The exercise modes included cycle ergometer, treadmill, and elliptical trainers. There was an initial ramp period (gradual increase of exercise minutes and intensity) of 2 to 3 months, followed by 6 months at the appropriate exercise prescription. All exercise sessions were verified by direct supervision or by heart rate monitors that provided recorded data.

The STRRIDE study was designed to investigate the effects of different amounts and different intensities of exercise on metabolic risk factors for cardiovascular disease and diabetes. As mentioned previously, we failed to anticipate the speed and degree to which numerous health-related variables worsened in the inactive control group. In Table 1, we identify 12 variables that were shown to significantly deteriorate for only 6 months. These health-related variables were wide ranging and included, in addition to body weight, both general and specific measures of central obesity, carbohydrate metabolism, lipid metabolism, and cardiorespiratory fitness.

One of the important findings in the STRRIDE trial was that the inactive group gained a small but statistically significant amount of weight (approximately 1% body weight gain for 6 months), whereas all the three exercise groups lost weight in a dose-response manner in the absence of reduced caloric intake. These observations support a number of conclusions. First, the weight gain in the inactive individuals was almost certainly due to a small daily imbalance of caloric intake over expenditure. Unfortunately, this small caloric imbalance can contribute to weight gain that may occur at a relatively rapid rate (2% per year, as estimated from our observations), which would be anticipated to ultimately affect metabolic health. However, a small amount of exercise eliminated the weight gain seen in the inactive group, which lends support to the hypothesis that there is a minimal amount of physical activity required for adequate weight control and that,

below this critical level of activity, weight gain occurs. This hypothesis was first proposed by Mayer *et al.* (10). The observation that all three exercise groups in STRRIDE lost a modest amount of weight supports this concept. A summary of the STRRIDE data in relation to exercise volume (amount per week) and weight loss or maintenance is presented in Figure 2. As indicated in this figure, the relationship between exercise amount per week and weight loss has an x-intercept at approximately 8 miles of walking or jogging per week or energy expenditure equivalent. To us, this suggests that this volume is the minimal level of activity that theoretically will produce weight maintenance in overweight and obese middle-aged sedentary men and women (13).

In Figure 3, we display the results of four of the 12 variables that worsened during the inactive control period. For visceral fat, HDL size, LDL particle number, or LDL size, it is clear that even a modest amount of exercise abrogated the deterioration in these variables observed in the inactive group. The dose-response effect observed across the three different amounts of exercise (control, low amount, and high amount) was by far the predominant pattern in most of the variables studied in STRRIDE. This consistent finding adds strong support to the concept of a minimal amount of exercise necessary for metabolic health. Figure 2 illustrates

TABLE 1. Effects of 6 months of continued physical inactivity in sedentary individuals.

↑ Body weight	↑ Total abdominal fat	↑ LDL particle no.
↑ Waist circumference	↑ Fasting insulin	↑ Small dense LDL
↑ Waist/hip ratio	↓ Insulin sensitivity	↓ LDL size
↑ Visceral fat amount	↓ Fitness (TTE)	↑ LDL cholesterol

Results above were taken from previously published results from STRRIDE (3,4,6,12,13). TTE indicates time to exhaustion, LDL, Low Density Lipoprotein.

that the theoretical minimal physical activity level for weight maintenance occurs at around 8 miles·wk⁻¹ (or equivalent energy expenditure). Examination of the other dose-response variables in a similar manner reveals that the theoretical minimal activity to maintain health parameters is approximately 7–12 miles of walking or jogging per week or other energy expenditure equivalent, somewhat higher levels for some variables and lower levels for others.

Recent findings from the Coronary Artery Risk Development in Young Adults study add strong support for the concept that weight maintenance is a reasonable surrogate for maintenance of metabolic health (14). In this study, the authors reported that weight gain for 15 yr was associated with unfavorable changes in numerous risk factors, whereas weight maintenance resulted in stable levels for fasting glucose, total cholesterol, LDL cholesterol, and HDL cholesterol, with only minimal increases in triglycerides (approximate increase of 6–10 mg/dL) and, in African Americans, a small increase in blood pressure (approximate increase of 7 mm Hg). Furthermore, they found that whether the group was normal weight or overweight at baseline, the beneficial effects of weight maintenance on cardiovascular risk factors were essentially the same.

It is important to interpret the relationship between volume of exercise and weight maintenance with the realization that the theoretical minimal amount of exercise is different for each individual. This is illustrated by understanding that if everyone in our study did the theoretical minimal amount of exercise (e.g., 8 miles·wk⁻¹), some proportion of individuals would still gain weight, and some proportion would lose weight. In theory, this would be true for each of the variables that displayed a dose-response relationship.

So, how much exercise is enough to prevent inactivity-related metabolic worsening, weight gain, diabetes, and premature mortality? Is 30 min·d⁻¹ enough as the 1995 U.S. Centers for Disease Control & Prevention/American College of Sports Medicine recommendation suggests, or is 60 min·d⁻¹ the necessary amount as some national organizations suggest? How do we reconcile these vastly different public recommendations? One prudent approach would be to recommend that all adults aim for 30 min of moderate intensity activity each day and then let body weight changes be the surrogate measure for determining if this amount of activity is adequate. For individuals who still gain weight at this activity level without significant dietary changes, then perhaps increasing to 40–45 min of daily activity would be the next step. This approach is not novel but rather is similar to titrating pharmacologic agents (e.g., statins) for desired effect on clinical risk factors (e.g., LDL cholesterol). We offer that this individualized approach might be an important component of national activity recommendations that would greatly minimize the confusion surrounding the seemingly contradictory recommendations for physical activity levels required to maintain health and wellness.

CONCLUSIONS AND SUMMARY

It is increasingly evident that inactivity is unhealthy and that the detrimental effects appear to be occurring more

quickly than previously realized. A modest amount of daily exercise (equivalent to the 1995 CDC/American College of Sports Medicine recommendations of 30 min a day of moderate-intensity exercise (11)) seems to be effective in most overweight and mildly obese sedentary individuals for preventing further inactivity-related metabolic deterioration. Therefore, this amount of daily activity would seem to be a very appropriate starting point for a national recommendation with the caveat that, on an individual basis, the adequacy of this amount could be judged based on its effect on body weight, which appears to serve as a reasonable surrogate measure for general metabolic health. In individuals who still experience weight gain at this dose, as with other medical therapies, the dose might be titrated to a level that is effective for prevention of further weight gain. Finally, as epidemiological research has previously suggested, results from STRRIDE demonstrate that modest increases above this minimal recommendation generally lead to additional significant and widespread improvements in numerous health measures.

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