Can Physical Activity Mitigate the Effects of Aging in Middle-Aged Women?

Jane F. Owens, DrPH; Karen A. Matthews, PhD; Rena R. Wing, PhD; and Lewis H. Kuller, MD, DrPH

Background. Aging is associated with an increased risk of women dying from coronary heart disease as well as from all causes combined. Alterations in the major biological risk factors for early coronary heart disease and all-cause mortality are frequently seen in aging.

Methods and Results. The present investigation tested the hypothesis that high levels of physical activity could protect against age-associated changes in biological risk factor levels. In the Healthy Women Study, 507 women were evaluated at study entry and 3 years later. Weekly physical activity level was measured at each examination via the Paffenbarger Physical Activity Questionnaire. During the 3-year period, women increased significantly in weight, blood pressure, levels of total and low-density lipoprotein cholesterol, triglycerides, and insulin and decreased significantly in levels of total high-density lipoprotein cholesterol (HDL-C) and HDL2-C.

Conclusions. Consistent with the study hypothesis, women who reported higher levels of activity at baseline had less weight gain over time. Furthermore, women who increased their activity during the 3-year interval had the smallest increases in weight and tended to have the smallest decreases in total HDL-C and HDL2-C. The changes in lipids due to activity were largely independent of changes in body weight. (Circulation 1992;85:1265-1270)

Key Words: exercise • coronary heart disease • gender • aging • risk factors

Aging is associated with an increased risk of women dying from coronary heart disease (CHD) as well as from all causes. With age, the magnitude of the sex difference in CHD and all-cause mortality decreases to when, at advanced age, the risk of dying is almost identical for men and women. Aging is associated with increased levels in women of many biological risk factors for CHD, including levels of blood pressure, weight, and lipids and lipoproteins. High levels of physical activity appear to protect men and women from cardiovascular morbidity and mortality, although few studies have included women. Physical activity may be in part health promoting through its effect on other biological and psychological risk factors for cardiovascular disease. We previously reported cross-sectional analyses of healthy middle-aged women; women who had higher levels of physical activity had lower weight, systolic and diastolic blood pressures, triglycerides, low-density lipoprotein cholesterol (LDL-C), fasting insulin, and 2-hour postprandial insulin levels and higher high-density lipoprotein cholesterol (HDL-C) and HDL2-C levels. Other cross-sectional studies of physical activity have also shown that more active women had lower blood pressure and less atherogenic lipid profiles.

Intervention studies have shown that middle-aged women who increase their activity levels lose weight and subcutaneous fat. Physical activity also improves insulin sensitivity and reduces the amount of insulin necessary to control glucose levels among insulin-dependent diabetic patients. However, intervention studies have not consistently demonstrated improvement in women's lipid and lipoprotein profiles with change in activity.

The primary objective of the present investigation was to test the hypothesis that high levels of physical activity would retard the adverse changes in women's biological risk factors associated with middle aging. Secondary objectives were to evaluate the effects of change in physical activity on change in psychological well-being and to describe the patterns of physical activity in healthy middle-aged women. The patterns of physical activity and levels of height, weight, lipids and lipoproteins, blood pressure, glucose, insulin, and depressive and stress symptoms were evaluated at study onset and approximately 3 years later in 500 healthy middle-aged women. The study design permitted simultaneous tests of the effects of initial level of physical activity and of change in physical activity level during the 3 years on change in biological and psychological characteristics.

Methods

Sample Characteristics

In 1983–1984, 541 women were enrolled in the Healthy Women Study, a prospective study of the effect of the menopause on biological and behavioral charac-
teristics of women. Women whose names appeared on a motor vehicle license data base were invited to enter the study, provided they met the eligibility criteria of ages of 42–50 years, menstrual bleeding within the past 3 months, no surgical menopause, diastolic blood pressure of less than 100 mm Hg, and not receiving medication known to influence the biological characteristics under study (e.g., lipid-lowering, insulin, thyroid, estrogen, antihypertensive, and psychotropic medications). Complete details regarding participant characteristics and recruitment are available elsewhere.  

Study Protocol

After the initial screening for eligibility criteria, all women completed a baseline clinic examination. After an overnight fast, women came to a morning appointment at the University of Pittsburgh. Heart rate and blood pressure were measured twice with a random zero muddler sphygmomanometer by two registered nurses trained by the MRFIT protocol. Blood was drawn for analysis of lipid, lipoprotein, insulin, and glucose levels, after which women ingested a 75-g glucose load. Blood was then drawn 2 hours later for determination of insulin and glucose levels. Certified clinical nutritionists measured the women’s height and weight on a standard balance scale. The women completed standardized psychosocial questionnaires. Approximately 3 years later, women were invited to return for an evaluation identical in form and content to the baseline examination. Four hundred ninety women completed the entire examination, with an additional 17 women completing all of the examination except the blood draw; of these 507 women, 500 (92% of the original sample) had complete physical activity data.

Measurement of Biological and Psychological Risk Factors

Physical activity was measured using the Paffenbarger Physical Activity Questionnaire, and kilocalories expended weekly were calculated by the method suggested by Paffenbarger et al.  

The calculation takes into account the energy exerted in climbing flights of stairs, walking city blocks, and participating in sports and recreational activities. The questionnaire was originally developed for use in assessing the physical activity levels of a cohort of Harvard College alumni and has subsequently been used in a variety of studies, including studies of physical activity in women.  

The questionnaire was administered both at the initial home visit and during the follow-up examination. The questionnaire, which measures habitual physical activity at leisure, has been shown to have good test-retest reliability over periods of time as diverse as 1 week (unpublished data, J.F. Owens, Department of Psychiatry, University of Pittsburgh), 4 weeks,  

and 1 year.  

The two blood pressure readings were averaged. Serum lipids were analyzed in the Nutrition Core Laboratory of the University of Pittsburgh Graduate School of Public Health. This laboratory participates in the Centers for Disease Control Standardization Program. Total cholesterol was determined using the enzymatic method, and HDL-C was determined using the heparin-manganese precipitation method. HDL-C was determined by the precipitation method using dextran sulfate, and HDL-C was found by subtracting HDL-C from the concentration of total HDL-C. Triglycerides were measured enzymatically. Plasma insulin levels were determined by radioimmunoassay, and plasma glucose was measured with the Abbot glucose UV test. The psychological tests used include the Beck Depression Inventory, a measure of depressive symptoms within the previous 2 weeks, and the Cohen Perceived Stress Scale, a measure of perceived stress within the previous 2 weeks.

Data Analysis

Distributions of kilocalories, insulin, triglycerides, and Beck Depression Inventory scores were skewed and subjected to log transformation before analysis. Change scores were created for kilocalories and risk factors by subtracting the level at the initial evaluation from the level 3 years later.

Paired t tests were conducted on the levels of risk factors at each evaluation to measure the effect of aging or repeated testing. Two-tailed p values of less than 0.05 were considered significant. Spearman rank order correlation coefficients assessed the relation between activity levels at the two examinations.

Multiple linear regression analyses determined the relative importance of baseline physical activity, change in physical activity, and hormonal and menopausal status in predicting change in risk factors. The baseline level of the risk factor was entered in the first step. Baseline activity level, change in activity level between evaluations, menopausal status (before and during versus after), and hormone use (yes versus no) were entered at the second step. Interaction terms for baseline activity and change in activity with menopausal status and hormone use were entered at step 3. The analyses were then repeated with change in weight and current smoking status included in the model at step 2. In addition, the analyses were repeated on Caucasian women only and reported when they showed a pattern of results different than that in the full analysis. Dietary factors such as change in grams of fat, percent of calories in fat, and total caloric intake were not significantly correlated with change in physical activity. Inclusion of smoking status in the analysis did not affect results and is not discussed further.

Results

Changes in Physical Activity and Biological Risk Factor Levels Across 3 Years

Mean energy expenditure in physical activity and mean risk factor levels at the baseline and 3-year examinations are shown in Table 1. The women were moderately active at the time of each examination, and their activity level did not change with aging. Their physical activity levels were substantially correlated during the 3-year interval (r = 0.49, p < 0.001).

In contrast to the nonsignificant change in energy expenditure, there were relatively large changes in biological risk factors during the 3-year period. Women experienced increases in weight, diastolic (not systolic) blood pressure, and levels of total cholesterol, LDL-C, triglycerides, HDL-C, and fasting and 2-hour postprandial insulin; they experienced decreases in height and...
levels of total HDL-C and HDL₂-C. No adverse changes were seen in fasting or 2-hour glucose levels. This pattern of results had been reported in a subsample of these women (i.e., 65 menopausal cases and age-matched controls).

**Association of Physical Activity and Changes in Biological Risk Factors**

We next addressed whether baseline physical activity or change in activity mitigated the changes in the biological risk factors that occurred over time. Regression analyses (see Table 2) on weight change showed that women who were less active at baseline and those who reported the greatest decreases in physical activity between the two examinations gained the most weight. Similar results were reported earlier in a subsample of 279 premenopausal women and 61 menopausal women.

Table 3 shows that women who increased their activity level also tended to exhibit a smaller decline in HDL-C ($p=0.06$, without adjustment for weight change). However, baseline activity level was not related to changes in HDL-C. To illustrate the association between change in physical activity and change in HDL-C, women were categorized into three groups: women who reported increasing their activity at least 300 kcal/wk, women who reported decreasing their physical activity at least that amount, and the remaining women who exhibited <300 kcal change in physical activity. (This energy expenditure is approximately the equivalent of walking three times per week for 20 minutes.) Figure 1 shows that women who increased their physical activity had essentially no change in HDL-C during the 3 years ($-0.6$ mg/dl), whereas those who reported decreasing their activity ≥300 kcal had a decline of $-1.9$ mg/dl. HDL-C declined more in postmenopausal women than in premenopausal women (Table 3). Postmenopausal women declined an average of $-1.6$ mg/dl, whereas premenopausal women declined $-0.85$ mg/dl.

Multiple regression analyses showed that the more women increased their level of activity between examinations, the smaller was the decline in HDL₂-C levels (Table 4). Women whose activity level increased at least 300 kcal/wk declined an average of only $-1.3$ mg/dl in HDL₂-C levels, whereas those who reported a decrease in activity level of the same amount declined $-3.5$ mg/dl in HDL₂-C (Figure 1). Weight change did not alter the effect of increasing activity on HDL₂-C. Although there

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**TABLE 1. Mean Biological Risk Factor Levels at Years 1 and 3 and Change Over Time**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Baseline examination</th>
<th>3-Year examination</th>
<th>Change from baseline</th>
<th>$p^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical activity (kcal/wk)</td>
<td>1,420</td>
<td>1,551</td>
<td>+131</td>
<td>0.11</td>
</tr>
<tr>
<td>Height (in.)</td>
<td>64.3</td>
<td>63.9</td>
<td>-0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (lb)</td>
<td>145.6</td>
<td>150.4</td>
<td>+4.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>107.8</td>
<td>108.3</td>
<td>+0.5</td>
<td>0.21</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>71.3</td>
<td>72.0</td>
<td>+0.73</td>
<td>0.01</td>
</tr>
<tr>
<td>Lipids (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>185.2</td>
<td>195.4</td>
<td>+10.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>83.2</td>
<td>92.0</td>
<td>+8.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL-C</td>
<td>108.9</td>
<td>118.4</td>
<td>+9.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL-C</td>
<td>59.6</td>
<td>58.5</td>
<td>-1.1</td>
<td>&lt;0.006</td>
</tr>
<tr>
<td>HDL₂-C</td>
<td>20.9</td>
<td>18.6</td>
<td>-2.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL₃-C</td>
<td>38.6</td>
<td>39.8</td>
<td>+1.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl)</td>
<td>87.6</td>
<td>88.0</td>
<td>+0.4</td>
<td>0.55</td>
</tr>
<tr>
<td>2-Hour glucose (mg/dl)</td>
<td>92.9</td>
<td>93.3</td>
<td>+0.4</td>
<td>0.84</td>
</tr>
<tr>
<td>Fasting insulin (µunits/l)</td>
<td>8.2</td>
<td>10.6</td>
<td>+2.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2-Hour insulin (µunits/l)</td>
<td>48.5</td>
<td>60.4</td>
<td>+11.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Beck Depression Inventory</td>
<td>4.4</td>
<td>5.0</td>
<td>+0.61</td>
<td>0.02</td>
</tr>
<tr>
<td>Cohen Perceived Stress</td>
<td>12.00</td>
<td>12.06</td>
<td>+0.04</td>
<td>0.74</td>
</tr>
</tbody>
</table>

LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

*p value from paired $t$ test.

**TABLE 2. Relation of Baseline Physical Activity, Change in Activity, and Hormonal Status to Change in Weight**

<table>
<thead>
<tr>
<th>Relation of change in weight (lb) to:</th>
<th>Regression coefficient</th>
<th>SEM of coefficient</th>
<th>$F$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline weight</td>
<td>0.02</td>
<td>0.014</td>
<td>2.3</td>
<td>0.12</td>
</tr>
<tr>
<td>Baseline kcal*</td>
<td>-1.29</td>
<td>0.440</td>
<td>8.5</td>
<td>0.003</td>
</tr>
<tr>
<td>Change in kcal</td>
<td>-5.84×10⁻⁴</td>
<td>2.36×10⁻⁴</td>
<td>6.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Menopausal status</td>
<td>-1.87</td>
<td>1.22</td>
<td>2.3</td>
<td>0.12</td>
</tr>
<tr>
<td>Hormone use</td>
<td>2.06</td>
<td>1.29</td>
<td>2.5</td>
<td>0.10</td>
</tr>
</tbody>
</table>

*kcal/wk, Data log transformed for analysis.

**TABLE 3. Relation of Physical Activity, Change in Activity, and Hormonal Status to Change in HDL-C**

<table>
<thead>
<tr>
<th>Relation of change in HDL-C (mg/dl) to:</th>
<th>Regression coefficient</th>
<th>SEM of coefficient</th>
<th>$F$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline HDL-C</td>
<td>-0.19</td>
<td>0.028</td>
<td>45.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline kcal*</td>
<td>0.51</td>
<td>0.433</td>
<td>1.4</td>
<td>0.23</td>
</tr>
<tr>
<td>Change in kcal</td>
<td>3.47×10⁻⁴</td>
<td>2.14×10⁻⁴</td>
<td>2.6</td>
<td>0.10</td>
</tr>
<tr>
<td>Change in weight</td>
<td>-0.07</td>
<td>0.041</td>
<td>3.3</td>
<td>0.07</td>
</tr>
<tr>
<td>Menopausal status</td>
<td>-2.65</td>
<td>1.12</td>
<td>5.5</td>
<td>0.02</td>
</tr>
<tr>
<td>Hormone use</td>
<td>2.10</td>
<td>1.17</td>
<td>3.1</td>
<td>0.07</td>
</tr>
</tbody>
</table>

HDL-C, high-density lipoprotein cholesterol.

*kcal/wk, Data log transformed for analysis.
The results of Symptoms Psychological use Hormone status x Menopausal Change in TABLE 4. had smaller increases in ties to: Relation of those (Table 1). and women greater decreases in premenopausal women, there was no relation between baseline physical activity and change in HDL-C (r=0.01). In the entire sample, postmenopausal women tended to have greater HDL-C decreases than premenopausal women (p=0.05; Table 4). Among Caucasian women only, those who were postmenopausal had significantly greater decreases in HDL-C than had premenopausal women (p=0.04). Neither physical activity at baseline nor change in activity between examinations predicted change in height, diastolic blood pressure, LDL-C, triglycerides, or insulin levels.

Association of Physical Activity and Change in Psychological Symptoms

Women reported a small increase during 3 years in depressive symptoms on the Beck Depression Inventory and in stress symptoms on the Cohen Perceived Stress Scale (Table 1). Multiple regression analyses showed that those women who reported increasing their activities had smaller increases in depressive symptoms (F=4.7, p=0.02) and in stress symptoms (F=5.3, p=0.02). The results were independent of change in body weight. Taken together, these results suggest that physical activity has a positive impact on indexes of mental health in middle-aged women.

Physical Activity Characteristics of Middle-Aged Healthy Women

We next examined the type of exercise and the reasons for exercise reported by the women. At both examinations, approximately 50% of the sample reported recreational sport or activity. The most prevalent sport at both examinations was walking, with calisthenics and aerobic exercise the next most common recreational activities. On average, the women reported walking three times per week, and most reported walking about 2 miles each time.

At the second examination, questions were asked regarding reasons for physical activity or inactivity. The most important reason given for exercise was to maintain fitness (28%); the next most important reason was to “feel good” (21%); and the third most important reason was to lose or maintain weight (15%). Seventy-three percent of the women did not feel that they exercised enough. Reasons given for why they were not getting enough exercise, in descending order of frequency, were lack of motivation, lack of time due to work obligations, and dislike of exercise. Very few women felt that lack of facilities or lack of a partner with whom to exercise were serious impediments to exercise.

Among women who reported a decrease in their regular patterns of activity in the previous year, the reason most often given was a lack of motivation or lack of time for exercise. The women who reported an increase in activity in the previous year most often cited a desire to lose or maintain weight as the reason for increasing activity. Thirty-eight women reported sustaining an injury directly related to their exercise that caused them to stop or change their regular exercise pattern; the most common sites involved were the knee and the foot. Seventy-three percent of the women injured sought medical care for their injury.

Discussion

The primary objective of the study was to test the hypothesis that high levels of physical activity would prevent or alter the adverse changes in women’s biological risk factors associated with midlife aging in women. Relatively healthy women were evaluated on major risk factors at study entry and 3 years later. Even though the duration of follow-up was short, women experienced substantial increases in weight; diastolic blood pressure; levels of total cholesterol, LDL-C, and triglycerides; and fasting and 2-hour postprandial insulin. They also experienced significant decreases in levels of total HDL-C and HDL2-C and in height. Support was found for the primary hypothesis with regard to HDL-C and HDL2-C. Women who increased, even slightly, physical activity during the 3 years tended to show the smallest decreases in total HDL-C and HDL2-C levels. These relations were maintained in analyses adjusted for menopausal status, hormone use, weight change, race, and smoking status. The inverse relation between physical activity at baseline and HDL2-C change at the second examination among postmenopausal women

Table 4. Relation of Physical Activity, Change in Activity, and Hormonal Status to Change in HDL-C

<table>
<thead>
<tr>
<th>Relation of change in HDL-C (mg/dl) to:</th>
<th>Regression coefficient</th>
<th>SEM of coefficient</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline HDL-C</td>
<td>-0.30</td>
<td>0.031</td>
<td>95.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline kcal*</td>
<td>0.29</td>
<td>0.347</td>
<td>0.73</td>
<td>0.39</td>
</tr>
<tr>
<td>Change in kcal</td>
<td>4.01 x 10^-4</td>
<td>1.71 x 10^-4</td>
<td>5.4</td>
<td>0.02</td>
</tr>
<tr>
<td>Change in weight</td>
<td>-0.08</td>
<td>0.033</td>
<td>5.8</td>
<td>0.02</td>
</tr>
<tr>
<td>Menopausal status</td>
<td>-1.75</td>
<td>0.902</td>
<td>3.7</td>
<td>0.05</td>
</tr>
<tr>
<td>Hormone use</td>
<td>-0.43</td>
<td>0.944</td>
<td>0.2</td>
<td>0.64</td>
</tr>
<tr>
<td>Menopausal status x kcal</td>
<td>-2.0</td>
<td>1.04</td>
<td>3.7</td>
<td>0.05</td>
</tr>
</tbody>
</table>

HDL-C, high density lipoprotein fraction 2 cholesterol. *kcal/wk, Data log transformed for analysis.
cannot be readily explained. The beneficial effects of physical activity on HDL-C and HDL₄-C are particularly noteworthy for two reasons. First, they occurred around the time of the menopause, when these lipoproteins are changing in response to a decline in levels of estradiol. Second, women’s greater protection from CHD relative to men appears to be due in part to their elevated HDL-C and HDL₄-C levels. Increasing physical activity in midlife may be a way to retain some of women’s relative health advantage.

Consistent with our previous report²³ is the finding that higher levels of physical activity are associated with less weight gain over time in the entire sample. Because weight gain leads to higher levels of blood pressure and insulin and a more atherogenic lipid profile, retarding the weight gain associated with aging may also reduce the incidence of cardiovascular diseases associated with these risk factors, as well as with other age-related chronic diseases, such as osteoarthritis.

Initial physical activity and change in activity did not effect change in triglycerides, LDL-C, and insulin. However, physical activity level covaried with these variables at each examination (data not shown). Perhaps larger changes in physical activity are necessary to effect change in insulin levels or certain lipids and lipoproteins. Or perhaps a change from premenopausal to postmenopausal status simply overpowers any influence of change in physical activity level, as women who became postmenopausal by the 3-year examination had greater increases in LDL-C over time than did age-matched premenopausal women, and women who became postmenopausal had higher levels of triglycerides at both study entry and the follow-up examinations.²²

A secondary objective of the present investigation was to assess the relation between change in physical activity and change in psychological well-being. We found that women who increased their activity the most had the smallest increases in symptoms of stress and depression between examinations. These findings are consistent with cross-sectional data from a sample of 401 adults,²⁴ in which self-reported usual physical activity was found to be negatively associated with measures of depression and anxiety. Even stronger evidence for a protective effect of physical activity on the incidence of depression was found in a prospective study where little or low levels of physical activity were found to be independent predictors of depression 8 years later.²⁵

Understanding the motives for engaging or not engaging in physical activity may be useful for implementing public health policy. The women in this study reported that the desire to achieve or maintain fitness was the primary reason for exercise, although a surprising percentage of the women reported that they exercised just to “feel good.” The majority of the women felt that they were not getting enough exercise and that a lack of motivation coupled with a lack of time were the greatest deterrents. These were the same reasons given for decreasing activity during the follow-up period. Weight gain or the desire to maintain current weight was the most common reason given for increasing exercise. The usefulness of exercise in maintaining weight has been demonstrated in other prospective studies.²⁶,²⁷

The present study is among the first to assess some of the risks associated with low-level exercise in a nonathletic population. This is of particular importance in this population of women because they are entering menopause, a time of accelerated bone loss in women. The accident or injury rate of 7% during the previous year was not remarkable. However, it is noteworthy that all of the reported accidents or injuries occurred among the women who reported increasing their activity during the 3-year period. Although the present study shows that increasing activity has a beneficial effect on selected risk factors, it is important to continue to monitor the risk associated with increasing activity to identify activities that would put women at risk for musculoskeletal injury.

A recent meta-analysis of studies of both men and women has confirmed the protective effect of physical activity against CHD.²⁸ The present study provides important evidence that modest increases in activity in middle-aged women can prevent some of the deleterious changes in risk factors known to be associated with CHD. Although modest increases are relatively easy to achieve, increasing the motivation for exercise and accurate and reliable methods of measuring physical activity in men and women remains a problem. Other related issues that remain to be addressed are the effects of increases in activity in older populations, determination of a threshold of physical activity that results in the greatest benefit for specific age groups, risks associated with increasing activity, and differences between men and women in the ability of physical activity to modify risk.

References

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