Physical Activity and Coronary Heart Disease in Men
The Harvard Alumni Health Study

Howard D. Sesso, ScD; Ralph S. Paffenbarger, Jr, MD, DrPH; I-Min Lee, MBBS, ScD

Background—The quantity and intensity of physical activity required for the primary prevention of coronary heart disease (CHD) remain unclear. Therefore, we examined the association of the quantity and intensity of physical activity with CHD risk and the impact of other coronary risk factors.

Methods and Results—We followed 12,516 middle-aged and older men (mean age 57.7 years, range 39 to 88 years) from 1977 through 1993. Physical activity was assessed at baseline in kilojoules per week (4.2 kJ = 1 kcal) from blocks walked, flights climbed, and participation in sports or recreational activities. During follow-up, 2,135 cases of incident CHD, including myocardial infarction, angina pectoris, revascularization, and coronary death, occurred. Compared with men expending <2,100 kJ/wk, men expending 2,100 to 4,199, 4,200 to 8,399, 8,400 to 12,599, and ≥12,600 kJ/wk had multivariate relative risks of 0.90, 0.81, 0.80, and 0.81, respectively (P for trend = 0.003). When we considered the independent effects of specific physical activity components, only total sports or recreational activities (P for trend = 0.042) and vigorous activities (P for trend = 0.02) were inversely associated with the risk of CHD. These associations did not differ within subgroups of men defined by coronary risk factors. Finally, among men with multiple coronary risk factors, those expending ≥4,200 kJ/wk had reduced CHD risk compared with men expending <4,200 kJ/wk.

Conclusions—Total physical activity and vigorous activities showed the strongest reductions in CHD risk. Moderate and light activities, which may be less precisely measured, showed nonsignificant inverse associations. The association between physical activity and a reduced risk of CHD also extends to men with multiple coronary risk factors.


Key Words: exercise ★ coronary disease ★ epidemiology ★ risk factors ★ men

Coronary heart disease (CHD) is the leading cause of death in the United States, accounting for >700,000 deaths in 1996.1 Several studies have confirmed the overall benefit of physical activity in reducing the risk of CHD.2 Still, more than 60% of American adults are not regularly active.3 The necessary quantity and intensity of physical activity for the primary prevention of CHD remain unclear. Few studies have simultaneously considered physical activity of different intensities with the risk of CHD. Some reports suggest that only participation in vigorous activities is associated with reductions in CHD risk,4-8 whereas others extend benefits to moderate activities.9-12 Two recent trials indicate that incorporating moderate-intensity activities into the lifestyle may have benefits on coronary risk factors comparable to those derived from structured exercise programs.13,14

Therefore, we sought to update earlier findings on physical activity and risk of CHD in the Harvard Alumni Study15 by examining the quantity, type, and intensity of physical activity in 1977. We also assessed whether, given the multifactorial etiology of CHD, physical activity impacts the risk of CHD in the presence of other coronary risk factors.

Methods

Subjects
The Harvard Alumni Study is an ongoing cohort study of men matriculating as undergraduates at Harvard University between 1916 and 1950 that was initiated in 1962. For the present study, we were interested in 17,835 men who returned the 1977 questionnaire. We excluded 2,863 men reporting physician-diagnosed cardiovascular disease or cancer and 607 men with missing data on physical activity or other coronary risk factors. We successfully followed 12,516 (87.1%) of the remaining 14,365 men; those successfully followed were the men who returned questionnaires in 1988 or 1993 or died by the end of 1993.

Assessment of Physical Activity and Other CHD Risk Factors
We estimated an index of weekly energy expenditure in 1977 from the reported daily number of flights of stairs climbed, city blocks...
walked, and sports or recreational activities engaged in during the past year. For each sport or activity, we asked for details regarding the frequency (weeks per year) and duration (time per week when active). This assessment of physical activity is both reliable and valid. We estimated that climbing up and down a flight of stairs (1 flight=10 steps) daily expended 59 kJ/wk (4.2 kcal=1 kcal) and that walking a city block (1 block=1/12 mile=0.13 km) daily expended 235 kJ/wk. Each activity was assigned a multiple of resting metabolic rate (MET score). Because resting metabolic rate is ~4.2 kJ/kg body wt per hour, we estimated the average weekly energy expenditure for each activity by multiplying its MET score by body weight and hours per year and then dividing by 52. We summed kilojoules per week from flights climbed, blocks walked, and all sports or recreational activities and categorized this into <2100, 2100 to 4199, 4200 to 8399, 8400 to 12 599, and ≥16 000 kJ/wk (or <500, 500 to 999, 1000 to 1999, 2000 to 2999, and ≥3000 kcal/wk, respectively).

We next examined the type and intensity of physical activity. Men were categorized into approximate fifths of flights climbed (2 flights=1 story), walking (1 block=0.13 km), and total energy expended from sports or recreational activities. We then separately calculated and categorized energy expenditure from vigorous (>6 METs), moderate (4 to <6 METs), and light (<4 METs) activities.

The On the 1977 questionnaire, we also collected information on age (in years), cigarette smoking (nonsmoker or current smoker [≥20 or >20 cigarettes/d]), alcohol consumption (none, <100, or ≥100 g/wk), early parental death at <65 years (yes or no), weight and height (combined into body mass index [kg/m²] and categorized as ≤22.5, 22.5 to <25.5, 25.5 to <28.5, 28.5 to <31.5, and ≥31.5 kg/m²), physician-diagnosed hypertension (yes or no), and physician-diagnosed diabetes mellitus (yes or no).

Ascertainment of CHD Occurrence
We ascertained cases of first CHD (including myocardial infarction, angina pectoris, coronary artery bypass graft surgery, and percutaneous transluminal coronary angioplasty) through self-reports on follow-up questionnaires sent in 1988 and 1993. The year of diagnosis was taken as the earliest reported year of diagnosis for any event from the 2 questionnaires. If different events occurred in the same year, the event was selected in hierarchical fashion: myocardial infarction, angina pectoris, revascularization, and then death. Self-reported physician-diagnosed CHD has been validated in this cohort. In addition, deaths were compiled continuously by the Harvard Alumni Office, which maintains a listing of deceased alumni. We traced deaths through the end of 1993. For each reported death, we requested and obtained death certificates from the appropriate state. We included deaths with either underlying or contributory death, we requested and obtained death certificates from the appropriate state. We included deaths with either underlying or contributory causes from CHD. To verify an earlier observation that mortality from CHD increased with increasing levels of energy expenditure, we distributed CHD events and enhanced power.

In secondary analyses, we excluded men developing CHD during the first 3 years of follow-up to minimize any bias due to illnesses that might have affected baseline physical activity. Sensitivity analyses assessed whether altering the cut points for the various types of physical activity appreciably altered the RR estimates. Finally, we updated physical activity in a subset of 6897 men returning both the 1977 and 1988 questionnaires who were free of CHD through 1988 and followed them for 5 years through the end of 1993 (424 cases).

Results
The mean±SD age at baseline in 1977 was 57.7±9.0 years (range 39 to 88 years), and the mean±SD body mass index was 24.4±2.8 kg/m². Table 1 compares men by physical activity category according to coronary risk factors at baseline. Men with higher levels of energy expenditure tended to be younger (P<0.001), to consume more alcohol (P<0.001), and to be less likely to smoke (P<0.001) and have diabetes mellitus (P=0.01) and hypertension (P<0.001). There were no appreciable differences in baseline coronary risk factors comparing men in the study population with those excluded because of loss to follow-up (data not shown).

The mean±SD physical activity level was 8362±8215 kJ/wk. On average, the relative contribution of energy from flights climbed, blocks walked, and total sports or recreational activities was 5.7%, 36.8%, and 57.4%, respectively. Sports or recreational activities were reported by 74.1% of the men. Most of the energy was expended on moderate (4 to <6 METs) and vigorous (≥6 METs) activities, which contributed 37.4% and 56.1%, respectively, to the total energy expended from sports or recreational activities.

During 166 410 person-years of follow-up, 2135 CHD cases (1295 identified through questionnaires and 840 from death certificates) occurred. Of the 2135 cases, 512 were from angina pectoris, 576 from myocardial infarction, 207 from revascularizations, and 840 from CHD death (709 as the primary cause). We found an L-shaped association between increasing levels of physical activity and the risk of CHD in the age-adjusted model (Table 2) (P for trend<0.001), with no additional reduction in risk of CHD for levels >8400 kJ/wk. The addition of coronary risk factors to the model modestly attenuated the age-adjusted RRs, but the L-shaped association remained. We found no appreciable difference in the RRs when we considered CHD identified from questionnaires versus death certificates, when we excluded men with CHD during the first 3 years of follow-up, or when we did not adjust for body mass index, hypertension, or diabetes, which are biological mediators. When a stricter definition of CHD (angina pectoris, myocardial infarction, or CHD death as the primary cause) was used, the RRs also changed little. Finally,
we found no significant evidence that coronary risk factors modified the inverse association of physical activity with CHD risk.

We then considered whether specific components of physical activity were associated with the risk of CHD (Figure). In multivariate models, we found significant associations of increasing levels of total activities and vigorous activities with the risk of CHD. The lack of a linear association (P = 0.08) in multivariate models between kilometers walked per week and CHD may have been due to a threshold effect beyond walking 5 km/wk. In fact, men walking ≥5 km/wk had a significant (13%) reduced risk of CHD compared with those walking <5 km/wk.

In sensitivity analyses, cut points >8400 kJ/wk for total energy expended from sports or recreational activities did not result in greater reductions in CHD risk. Levels of energy expenditure >8400 kJ/wk for vigorous activities were associated with a 10% to 20% reduction in the risk of CHD. We found a possible U-shaped association (P for nonlinear trend = 0.10) between moderate activity and the risk of CHD, with a nadir in risk among men expending 2100 to 4199 kJ/wk compared with men reporting no moderate activities. Increasing the cut point for the highest category of moderate activity did not result in an elevated risk of CHD compared with the referent category. For light activities, the lack of an association with the risk of CHD remained at even higher cut points.

Next, we examined the association between physical activity and CHD in the presence of other coronary risk factors, stratifying the results according to men aged <60 and ≥60


<table>
<thead>
<tr>
<th>Physical Activity Index,* kJ/wk</th>
<th>&lt;2100 (n=2002)</th>
<th>2100–4199 (n=2354)</th>
<th>4200–8399 (n=3481)</th>
<th>8400–12 599 (n=2145)</th>
<th>≥12 600 (n=2534)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>60.4±9.6</td>
<td>58.0±9.1</td>
<td>57.1±8.7</td>
<td>56.4±8.4</td>
<td>57.0±8.6</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>24.7±3.3</td>
<td>24.0±3.0</td>
<td>24.4±2.7</td>
<td>24.4±2.5</td>
<td>24.4±2.7</td>
</tr>
<tr>
<td>Alcohol consumption, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 g/wk</td>
<td>16.9</td>
<td>13.0</td>
<td>10.5</td>
<td>10.8</td>
<td>9.3</td>
</tr>
<tr>
<td>&lt;100 g/wk</td>
<td>31.3</td>
<td>32.5</td>
<td>30.8</td>
<td>27.2</td>
<td>26.8</td>
</tr>
<tr>
<td>≥100 g/wk</td>
<td>51.9</td>
<td>54.5</td>
<td>58.6</td>
<td>62.0</td>
<td>63.9</td>
</tr>
<tr>
<td>Smoking status, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>79.4</td>
<td>80.3</td>
<td>83.5</td>
<td>82.8</td>
<td>85.7</td>
</tr>
<tr>
<td>Current smoker</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 cigarettes/d</td>
<td>10.5</td>
<td>9.6</td>
<td>8.7</td>
<td>9.6</td>
<td>8.3</td>
</tr>
<tr>
<td>≥20 cigarettes/d</td>
<td>10.1</td>
<td>10.1</td>
<td>7.8</td>
<td>7.6</td>
<td>6.0</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>25.1</td>
<td>21.6</td>
<td>19.4</td>
<td>17.8</td>
<td>17.5</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>13.6</td>
<td>11.5</td>
<td>10.3</td>
<td>10.9</td>
<td>10.1</td>
</tr>
<tr>
<td>Early parental death, &lt;65 y, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No parents</td>
<td>64.6</td>
<td>67.0</td>
<td>65.7</td>
<td>67.4</td>
<td>66.1</td>
</tr>
<tr>
<td>One parent</td>
<td>30.8</td>
<td>29.1</td>
<td>30.0</td>
<td>28.3</td>
<td>29.7</td>
</tr>
<tr>
<td>Both parents</td>
<td>4.6</td>
<td>4.0</td>
<td>4.3</td>
<td>4.3</td>
<td>4.2</td>
</tr>
</tbody>
</table>

Values for age and body mass index are mean±SD.

*Estimated from flights climbed, blocks walked, and sports played (4.2 kJ=1 kcal).


<table>
<thead>
<tr>
<th>Physical Activity Index,* kJ/wk</th>
<th>&lt;2100 (n=2002)</th>
<th>2100–4199 (n=2354)</th>
<th>4200–8399 (n=3481)</th>
<th>8400–12 599 (n=2145)</th>
<th>≥12 600 (n=2534)</th>
<th>P for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>438</td>
<td>429</td>
<td>552</td>
<td>322</td>
<td>394</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted RR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RR</td>
<td>1.00 (referent)</td>
<td>0.85</td>
<td>0.75</td>
<td>0.73</td>
<td>0.73</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>95% CI</td>
<td>...</td>
<td>0.74–0.97</td>
<td>0.66–0.85</td>
<td>0.63–0.84</td>
<td>0.64–0.84</td>
<td></td>
</tr>
<tr>
<td>Multivariate RR†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RR</td>
<td>1.00 (referent)</td>
<td>0.90</td>
<td>0.81</td>
<td>0.80</td>
<td>0.81</td>
<td>0.003</td>
</tr>
<tr>
<td>95% CI</td>
<td>...</td>
<td>0.79–1.03</td>
<td>0.71–0.92</td>
<td>0.69–0.93</td>
<td>0.71–0.94</td>
<td></td>
</tr>
</tbody>
</table>

*Estimated from flights climbed, blocks walked, and sports played (4.2 kJ=1 kcal).

†Adjusted for age, body mass index, alcohol intake, hypertension, diabetes mellitus, smoking status, and early parental death (<65 years).
years (Table 3). The lower case counts among men with specific single risk factors limited our ability to make definitive conclusions in these categories. Among men aged <60 years, those who were active (≥4200 kJ/wk) had lower magnitudes of increased CHD risk compared with those who were inactive. Men with single coronary risk factors expending ≥4200 kJ/wk also had lower RRs of CHD compared with those expending <4200 kJ/wk, with the exceptions of diabetics and smokers. Among men aged ≥60 years compared with younger men, the magnitudes of RRs of CHD for increasing numbers of coronary risk factors were lower. Compared with physically active men with no risk factors, older men with single coronary risk factors expending ≥4200 kJ/wk had no increased risk of CHD.

Finally, we considered the joint effect of physical activity measured in 1977 and 1988 on the risk of CHD among 6959 men (424 CHD cases) free of CHD through 1988. Models with physical activity and other coronary risk factors as time-dependent variables did not appreciably alter the main results for physical activity.

Discussion

The present study provides new data from the Harvard Alumni Study on both the quantity and intensity of physical activity and CHD risk among older men, in the context of the new Surgeon General’s recommendations. We found an L-shaped association between physical activity and risk of CHD.

RRs of CHD, 1977 through 1993, among Harvard alumni, according to types of physical activity in 1977. RRs were adjusted for age, other components of physical activity, body mass index, alcohol intake, hypertension, diabetes mellitus, smoking status, and early parental death (<65 years). Types of physical activity were categorized as follows: vigorous activity, ≥6 METs; moderate activity, 4 to <6 METs; and light activity, <4 METs (4.2 kJ=1 kcal).

TABLE 3. RRs of CHD, 1977 Through 1993, Among Harvard Alumni by Age and Physical Activity Index, According to Coronary Risk Factor Profile

<table>
<thead>
<tr>
<th>Coronary Risk Factor Profile</th>
<th>Cases, n</th>
<th>RR* for Men Aged &lt;60 y</th>
<th>RR* for Men Aged ≥60 y</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PAI &lt;4200 kJ/wk</td>
<td>PAI ≥4200 kJ/wk</td>
<td>PAI &lt;4200 kJ/wk</td>
</tr>
<tr>
<td>No risk factors</td>
<td>315</td>
<td>1.00 (referent)</td>
<td>1.00 (referent)</td>
</tr>
<tr>
<td>Specific single risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cigarette smoker</td>
<td>81</td>
<td>1.60 (0.85–3.01)</td>
<td>1.63 (1.05–2.55)</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>101</td>
<td>2.42 (1.22–4.82)</td>
<td>2.06 (1.29–3.29)</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>63</td>
<td>1.36 (0.42–4.45)</td>
<td>2.15 (1.24–3.73)</td>
</tr>
<tr>
<td>Body mass index ≥25 kg/m²</td>
<td>236</td>
<td>2.10 (1.32–3.35)</td>
<td>1.67 (1.23–2.26)</td>
</tr>
<tr>
<td>No alcohol consumption</td>
<td>58</td>
<td>2.05 (1.00–4.18)</td>
<td>1.32 (0.72–2.41)</td>
</tr>
<tr>
<td>Any early parental death</td>
<td>206</td>
<td>1.93 (1.12–3.34)</td>
<td>1.53 (1.10–2.13)</td>
</tr>
<tr>
<td>Any 1 risk factor</td>
<td>745</td>
<td>1.97 (1.32–2.95)</td>
<td>1.65 (1.29–2.12)</td>
</tr>
<tr>
<td>Any 2 risk factors</td>
<td>656</td>
<td>2.73 (1.82–4.09)</td>
<td>2.34 (1.81–3.02)</td>
</tr>
<tr>
<td>Any 3 risk factors</td>
<td>318</td>
<td>4.25 (2.75–6.56)</td>
<td>3.02 (2.23–4.09)</td>
</tr>
<tr>
<td>Any 4 or more risk factors</td>
<td>101</td>
<td>5.56 (3.29–9.43)</td>
<td>5.03 (3.17–7.97)</td>
</tr>
</tbody>
</table>

PAI indicates physical activity index, estimated from flights climbed, blocks walked, and sports played (4.2 kJ=1 kcal). Values in parentheses are 95% CIs.

*Adjusted for age.
CHD, with an $\sim 20\%$ reduction in CHD risk for total physical activity levels $>4200$ kJ/wk. A physical activity level of 4200 kJ/wk is consistent with the Surgeon General’s recommendation and can be attained by performing activities such as brisk walking, recreational cycling and swimming, home repair, and yard work for 30 min/d on most days of the week. In addition, there was a nonsignificant 10% reduction in men expending 2100 to 4199 kJ/wk.

The present study also suggests that vigorous activities are associated with a reduced risk of CHD, whereas moderate or light activities have no clear association with the risk of CHD. Finally, physical activity may favorably affect CHD risk even in the presence of other coronary risk factors. Therefore, an active lifestyle may ameliorate the deleterious effect of concomitant coronary risk factors. In particular, men aged $\geq 60$ years who expended $\geq 4200$ kJ/wk may have smaller increases in CHD risk in the presence of coronary risk factors.

The most relevant previous publication from this cohort was published in 1978 with the use of data from the 1962/1966 questionnaire in relation to the risk of myocardial infarction. This and other reports on morbidity and mortality from this cohort of Harvard alumni have contributed, in part, to the development of the Surgeon General’s recommendations. In the 1978 article, the cohort consisted of middle-aged men, and information on physical activity was coded in far less detail. Risk estimates were also calculated without adjustment for potential coronary risk factors. The present study adds valuable new information on the association between physical activity and risk of CHD with the use of detailed coding of physical activity from the 1977 questionnaire in relation to CHD risk. As a result, the present cohort consists of older men, with sufficient detail on the quantity, intensity, and type of physical activity to directly address the Surgeon General’s recommendations. Furthermore, we adjusted for known coronary risk factors that confounded the association between physical activity and CHD. Because there are few studies on quantity, type, and intensity of physical activity and the risk of CHD among older men, the present study provided an excellent opportunity to explore these hypotheses.

Recent statements from the Surgeon General, the National Institutes of Health Consensus Development Panel on Physical Activity and Cardiovascular Health, and the Centers for Disease Control and Prevention and the American College of Sports Medicine recommend that every adult should accumulate at least 30 minutes of moderate-intensity physical activity on most, preferably all, days of the week to prevent CHD and other chronic diseases. The decision to expand the recommendation for physical activity to include moderate activities, in addition to vigorous activities, was based on the assumptions that moderate physical activity would be more easily attainable and can be accumulated in either several small daily doses or a single large daily dose. Two recent intervention trials indicate that moderate-intensity physical activity may have benefits on coronary risk factors that are similar to those provided by structured, more vigorous activities. However, these results applied to previously sedentary, overweight, and obese individuals. It remains unclear whether short-term improvements in coronary risk factors result in long-term reductions in CHD risk.

The few studies that have focused on the intensity of physical activity in relation to CHD have yielded inconsistent results. Differences in intensity classifications, adjustment for confounders, and CHD numbers and definitions across studies may account for these results. Whereas the benefits of vigorous-intensity physical activity appear clear, the benefits of moderate-intensity activities have been observed in some but not all studies. We did not find equivalent benefits for vigorous and moderate physical activity in relation to CHD risk. Greater energy expended from vigorous activities was inversely associated with the risk of CHD. In contrast, we found a possible U-shaped association for moderate activities, with the lowest risk of CHD among men expending 2100 to 4199 kJ/wk. This lack of association for moderate activities may reflect the imprecise measurement of these activities compared with vigorous activities or the difficulty in achieving such high levels of energy expenditure from moderate activities.

Clinical studies have demonstrated that exercise lowers blood pressure and improves body composition, glucose tolerance, and insulin sensitivity. In the present study, when we adjusted for some of these biological effects, the RR estimates were only modestly confounded. Other pathways leading to a reduction in CHD risk may be responsible for the observed inverse association, including improvements in HDL cholesterol and thrombotic function, including hematocrit, fibrinogen, platelet function, and fibrinolysis.

Some limitations should be considered in light of our results. First, the measurement of physical activity may be susceptible to misclassification, which would, if random with respect to CHD risk, bias our results toward the null. However, a previous validation study suggests that the average magnitude of misclassification of nonresting energy expenditure may be $\sim 630$ kJ/wk (150 kcal/wk); thus, we do not expect misclassification to greatly affect our risk estimates. Second, we followed men over a long period, during which physical activity levels likely fluctuated. However, when we updated information on physical activity, our findings were little changed. Third, we are unclear whether our results extend to women. Recent studies have shown both an inverse association and no association with CHD risk. Finally, the lack of control for dietary factors and lipids may introduce residual confounding.

In conclusion, we found an L-shaped association between physical activity and the risk of CHD. Older men should expend at least 4200 kJ/wk in total physical activity to potentially reduce their risk of CHD by $\sim 20\%$. Those expending 2100 to 4199 kJ/wk, slightly lower than that recommended by the Surgeon General, had a possible nonsignificant 10% reduction in the risk of CHD. Future research must improve the assessment of moderate and light physical activity to better distinguish whether particular types and intensities of activities derive reductions in CHD risk.

**Acknowledgments**

This study was supported by grants CA-44854 and HL-34174 from the National Cancer Institute and the National Heart, Lung, and...
Blood Institute, Bethesda, Md. We are grateful to Stacey DeCaro, Sarah E. Freeman, Tina Y. Ha, Marty Higgins, James B. Kampert, Rita W. Leung, Doris C. Rosoff, and Alvin L. Wing for their help with the College Alumni Health Study.

References
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Circulation. 2000;102:975-980
doi: 10.1161/01.CIR.102.9.975
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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