Physical Activity and Coronary Event Incidence in Northern Ireland and France

The Prospective Epidemiological Study of Myocardial Infarction (PRIME)

Aline Wagner, MD; Chantal Simon, MD, PhD; Alun Evans, MD; Jean Ferrières, MD; Michèle Montaye, MD; Pierre Ducimetière, PhD; Dominique Arveiler, MD; on behalf of the PRIME Study Group

Background—The influence of physical activity on the incidence of angina pectoris and hard coronary events (myocardial infarction and coronary deaths) was examined in Northern Ireland and France at contrasting risk for coronary heart disease (CHD) and with different physical activity patterns.

Methods and Results—Participants of the Prospective Epidemiological Study of Myocardial Infarction (PRIME) (n=9758; age, 50 to 59 years), free of CHD at baseline, were followed up for 5 years: 167 hard CHD and 154 angina events were recorded. Net energy expenditure (EE) as the result of physical activity was assessed by means of the MONICA Optional Study of Physical Activity Questionnaire (MOSPA-Q). Leisure-time physical activity EE was calculated; subjects were also categorized as to whether they performed high-intensity leisure-time activities or walked or cycled to work. After multivariate adjustment, leisure-time physical activity EE was associated with a lower risk of hard CHD events (P<0.04), whereas walking or cycling to work was not independently related to hard CHD events. No interaction by country was found. The beneficial effect of leisure-time physical activity was also present among subjects who did not report high-intensity activities (P<0.04), with similar results in France and Northern Ireland. In contrast, an increasing level of leisure-time physical activity was associated with a higher risk of angina in both countries.

Conclusions—These data indicate a beneficial effect of leisure-time physical activity EE on hard CHD incidence in middle-aged men, which could partly explain the unfavorable rate of CHD in Northern Ireland. The higher level of leisure-time activities in France could, in part, explain its lower rate of CHD. (Circulation. 2002;105:2247-2252.)

Key Words: angina ■ coronary disease ■ follow-up studies ■ men ■ exercise

Inverse associations have been reported between regular physical activity and all-cause mortality as well as cardiovascular morbidity and mortality. For a long period, only vigorous activity was considered to confer health benefits. More recently, walking has been found to be associated with a decreased risk of coronary heart disease (CHD) and of death from all causes. Nevertheless, there still remains uncertainty about the physical activity that influences cardiovascular health. The relation between physical activity and angina pectoris is less well established. Nearly all the published studies have assessed the effect of physical activity on the incidence of a combined end point such as cardiovascular disease morbidity, death from CHD, or death from all causes. Data explaining the associations of physical activity with angina alone are scant and somewhat contradictory.

France and Northern Ireland, two geographically close countries, are characterized by contrasting risk for CHD, unexplained by traditional risk factors. Recently, we highlighted disparities in physical activity patterns in middle-aged men from these two countries. Despite similar levels of total physical activity, a higher prevalence of walking or cycling to work was noted in Northern Ireland, whereas French men expended more energy as the result of leisure-time physical activity and had a higher rate of high-intensity leisure-time activities (A. Wagner, MD, unpublished data, 2001).

Hence, the aim of this study was to investigate if the associations between physical activity patterns and incidence of coronary events could explain, at least partly, the gradient in CHD observed between the two countries. The PRIME Study (Prospective Epidemiological Study of Myocardial Infarction) afforded us the opportunity of examining the effects of physical activity levels and patterns, not only on major coronary events but on angina.
Methods

Study Sample
Subjects were participants in the PRIME Study, which was established in 1991 to investigate risk factors for CHD in middle-aged men in 4 collaborating WHO MONICA centers: Belfast (United Kingdom), the Urban Community of Lille, and the Departments of Bas-Rhin and Haute-Garonne (France). Detailed information on the aims and methods are available elsewhere.8 Briefly, this cohort of 10,600 men, 50 to 59 years of age, was recruited between 1991 and 1993 to match broadly the social class structure of the background population. Participation was voluntary, and each study center obtained local approval from the appropriate ethics committee. Subjects who agreed to take part in the study were given a morning appointment. Men with a history of CHD or a positive Rose Chest pain questionnaire9 or clinical signs of CHD at baseline were excluded (n = 9756), leaving 9758 participants for the present analysis.

Study Design and Assessment of Cardiovascular Risk Factors
Questionnaires relating to past medical history, demographic and socioeconomic factors, tobacco consumption, and alcohol habits were obtained, and clinical examination was performed with standardized anthropometric measurements.

Physical activity was assessed for the year preceding recruitment by means of the MONICA Optional Study of Physical Activity Questionnaire (MOSPA-Q), whose validity and reliability have been reported.10 This administered questionnaire evaluated time and mean energy expenditure during leisure time, at work, and during walking or cycling to and from work. Leisure-time walking and the two activities that were most frequently performed (sport or others, such as gardening) were taken into account. The intensities of the activities were derived from the Compendium11 and expressed in metabolic equivalents (MET). The average weekly net energy expenditure (EE) as the result of leisure-time physical activity was not violated, multivariate models were computed with leisure-time physical activity EE expressed in MET· h/week was computed.12 Participants were also categorized as to whether they walked or cycled to work (yes or no) or if they took part in regular high-intensity leisure-time activities (≥6 MET).

Follow-Up
Annual questionnaires were mailed to the participants asking about disease events. In the event of no reply, a phone contact was established with the subject or his practitioner. For all possible events, clinical information was sought directly from the practitioners’ notes. Death certificates were checked for supporting information on cause of death. After 5 years, follow-up was achieved in >98% of the cohort.

Ascertainment of End Points
Two primary end points were studied: angina pectoris and hard coronary events (fatal or nonfatal myocardial infarction and coronary deaths). Coronary deaths comprised definite coronary death, possible coronary death, and sudden death. Fuller details on the determination of these outcomes have been previously described.6 All these events were checked by a Medical Committee to provide an independent validation of the coronary event.

Statistical Analyses
The distribution of sociodemographic and behavioral factors according to categories of physical activity (tertiles of leisure-time physical activity EE, participation or not in high-intensity leisure-time activities, and in walking or cycling to work) was assessed by means of χ² tests and ANOVA. Cox proportional hazards model was used to investigate the associations between different physical activity indexes and the outcome variables. Angina was only considered in the absence of previous myocardial infarction. When studying the association of physical activity and the incidence of angina, subjects were censored at the time that the myocardial infarction developed. We computed 3 models, with adjustment of different sets of covariates: (1) age, country, and employment status; (2) further adjustment for tobacco and alcohol consumption; and (3) further adjustment for educational level and body mass index (BMI). Estimated relative risks are presented with 95% confidence intervals. Because the assumption of log linearity for leisure-time physical activity EE was not violated, multivariate models were computed with leisure-time physical activity EE entered as a continuous variable. Assumptions of the proportional hazards model were checked and found to be true. Analyses were conducted with the use of BMDP Statistical Software.

Results
Baseline Characteristics
The baseline characteristics of participants are detailed in Table 1, according to physical activity patterns. Subjects in the highest tertile of leisure-time physical activity EE were significantly older and currently unemployed, were more likely to be French, and were more likely to be higher drinkers but not smokers. Participation in regular high-intensity leisure-time activities was higher in 50- to 54-year-olds than in those who were not active, and was associated with significantly higher socioeconomic status and fewer smokers but not with higher alcohol consumption. These results are consistent with previous studies, which have shown that higher socioeconomic status is associated with higher levels of physical activity20 and that socioeconomic status is also associated with lower risk of coronary heart disease.21

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=9756)</th>
<th>Lowest (n=3433)</th>
<th>Middle (n=3194)</th>
<th>Highest (n=3129)</th>
<th>P</th>
<th>No (n=6730)</th>
<th>Yes (n=3026)</th>
<th>P</th>
<th>No (n=4332)</th>
<th>Yes (n=3450)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, % 55–59 y</td>
<td>48.5</td>
<td>46.1</td>
<td>45.6</td>
<td>54.0</td>
<td>&lt;10⁻⁴</td>
<td>50.0</td>
<td>45.1</td>
<td>&lt;10⁻⁴</td>
<td>41.3</td>
<td>41.4</td>
<td>0.95</td>
</tr>
<tr>
<td>Northern Ireland, %</td>
<td>24.6</td>
<td>28.4</td>
<td>25.6</td>
<td>19.3</td>
<td>&lt;10⁻⁵</td>
<td>23.8</td>
<td>16.3</td>
<td>&lt;10⁻⁵</td>
<td>10.6</td>
<td>47.7</td>
<td>&lt;10⁻⁵</td>
</tr>
<tr>
<td>Currently employed, % yes</td>
<td>79.8</td>
<td>84.4</td>
<td>83.8</td>
<td>70.6</td>
<td>&lt;10⁻⁵</td>
<td>78.5</td>
<td>82.6</td>
<td>&lt;10⁻⁵</td>
<td>10.6</td>
<td>47.7</td>
<td>&lt;10⁻⁵</td>
</tr>
<tr>
<td>Alcohol, % ≥30 g/d</td>
<td>40.4</td>
<td>39.1</td>
<td>39.8</td>
<td>42.5</td>
<td>0.02</td>
<td>41.3</td>
<td>38.6</td>
<td>0.02</td>
<td>43.5</td>
<td>33.5</td>
<td>&lt;10⁻⁵</td>
</tr>
<tr>
<td>Tobacco, % smokers</td>
<td>27.6</td>
<td>30.4</td>
<td>27.4</td>
<td>24.7</td>
<td>&lt;10⁻⁴</td>
<td>30.1</td>
<td>22.0</td>
<td>&lt;10⁻⁴</td>
<td>26.4</td>
<td>27.8</td>
<td>0.75</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Secondary</td>
<td>59.3</td>
<td>56.4</td>
<td>58.5</td>
<td>63.3</td>
<td>&lt;10⁻⁴</td>
<td>58.2</td>
<td>61.8</td>
<td>&lt;10⁻⁴</td>
<td>61.3</td>
<td>59.6</td>
<td>&lt;10⁻²</td>
</tr>
<tr>
<td>% University</td>
<td>15.0</td>
<td>15.1</td>
<td>18.4</td>
<td>11.4</td>
<td></td>
<td>11.6</td>
<td>22.6</td>
<td></td>
<td>17.4</td>
<td>16.0</td>
<td></td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>26.6 (3.4)</td>
<td>26.6 (3.6)</td>
<td>26.4 (3.3)</td>
<td>26.7 (3.3)</td>
<td>0.02</td>
<td>26.7 (3.6)</td>
<td>26.3 (3.1)</td>
<td>0.02</td>
<td>26.7 (3.5)</td>
<td>26.2 (3.3)</td>
<td>&lt;10⁻⁵</td>
</tr>
</tbody>
</table>
old subjects, in France, in subjects with a university education, and in nonsmokers and was associated with lower alcohol consumption and BMI. Walking or cycling to work was more frequent in Northern Ireland and was associated with lower alcohol consumption and lower BMI.

Follow-Up
During the 5-year follow-up period, 321 coronary events were recorded: 167 hard CHD (106 in France, 61 in Northern Ireland) and 154 angina pectoris (94 in France and 60 in Northern Ireland). Table 2 describes the distribution of these events by physical activity patterns with the unadjusted relative risk of hard CHD and angina. Subjects in the two highest tertiles of leisure-time physical activity EE had a lower risk of hard CHD ($P$ for trend: 0.04); participation in high-intensity leisure-time activities was associated with a lower risk of hard CHD (relative risk, 0.72; 95% CI, 0.50 to 1.02), although statistical significance was not achieved. By contrast, walking or cycling to work was unrelated to the incidence of hard CHD. A higher risk of angina was observed, but only in the highest tertile of leisure-time physical activity EE, with a $P$ for trend approaching statistical significance ($P=0.10$), whereas intensity of leisure-time activities was not associated with the incidence of angina. Those who walked or cycled to work tended to have a higher incidence of angina ($P=0.08$). Job-related physical activity EE was not associated either with hard CHD or angina incidence (results not shown).

Leisure-Time Physical Activities and Coronary Events Incidence
Table 3 shows crude and adjusted relative risks of hard CHD and angina pectoris according to leisure-time physical activity EE. An increasing level of leisure-time physical activity was associated with a lower risk of hard CHD ($P<0.03$), which persisted after controlling for several potential confounders, including use of tobacco and alcohol and BMI. Likewise, the crude positive association between leisure-time physical activity EE and the incidence of angina ($P<0.02$) was strengthened ($P<10^{-2}$) after multivariate adjustment. Different interactions between leisure-time physical activity EE and other variables were tested, in particular alcohol consumption, educational level, and country, but none of these was significant. Hence, when analyses were computed separately in France and Northern Ireland, associations with outcomes were of the same magnitude in the two countries, although statistical significance relating to hard CHD events was lost (results not shown).

To assess whether the intensity of leisure-time activities has an effect on the incidence of hard CHD, after removing the contribution of EE, these two dimensions of physical activity were entered in the same models with adjustment for

**TABLE 2. Distribution of Coronary Events According to Physical Activity: Unadjusted Relative Risk and 95% Confidence Interval**

<table>
<thead>
<tr>
<th>Tertile of Leisure-Time Physical Activity EE</th>
<th>High-Intensity Leisure-Time Activities</th>
<th>Walking or Cycling to Work</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
<td>Lowest (n=3433)</td>
<td>Middle (n=3194)</td>
</tr>
<tr>
<td>Hard CHD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>74</td>
<td>48</td>
</tr>
<tr>
<td>RR</td>
<td>1</td>
<td>0.73</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.51–1.05</td>
<td>0.46–0.96</td>
</tr>
<tr>
<td>Angina</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>51</td>
<td>40</td>
</tr>
<tr>
<td>RR</td>
<td>1</td>
<td>0.83</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.55–1.25</td>
<td>0.88–1.86</td>
</tr>
</tbody>
</table>

EE indicates net energy expenditure.

**TABLE 3. Crude and Adjusted Relative Risk for Incidence of Hard CHD Events and Angina According to Leisure-Time Physical Activity EE (MET h/week)**

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Hard CHD Events</th>
<th>Angina</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR*</td>
<td>95% CI</td>
</tr>
<tr>
<td>Crude</td>
<td>0.92</td>
<td>(0.86–0.99)</td>
</tr>
<tr>
<td>t Model 1</td>
<td>0.91</td>
<td>(0.85–0.98)</td>
</tr>
<tr>
<td>t Model 2</td>
<td>0.92</td>
<td>(0.86–0.99)</td>
</tr>
<tr>
<td>t Model 3</td>
<td>0.92</td>
<td>(0.86–0.99)</td>
</tr>
</tbody>
</table>

*RRs are computed for a difference of 10 MET h/week.†Adjusted for age, country, and employment status.‡Additional adjustment for tobacco and alcohol consumption.§Additional adjustment for educational level and BMI.
walking or cycling to work. The fully adjusted model is presented in Table 4. Higher levels of leisure-time physical activity EE were associated with a lower incidence of hard CHD (relative risk for a difference of 10 MET·h/week: 0.92; 95% CI, 0.86 to 0.99; \( P = 0.04 \)), but performing high-intensity leisure-time activities was not independently associated with hard CHD. Interactions between physical activity variables were tested and were found to be nonsignificant.

**Incidence of CHD in Subjects Without High-Intensity Leisure-Time Activities**

To further evaluate the effects of light-to-moderate intensity activities on the incidence of hard CHD, we analyzed separately the subjects who did not report regular high-intensity leisure-time activities (\( n = 6730 \)). Results of the various models are presented in Table 5. An increasing level of leisure-time physical activity was associated with a lower risk of hard CHD incidence even after multivariate adjustment. For each additional 10 MET·h/week of leisure-time physical activity EE, the equivalent of approximately half an hour of brisk walking per day or 2.5 hours of gardening per week, the risk of hard CHD decreased by 11% in the crude model (\( P < 0.02 \)). The same associations persisted after controlling for several potential confounders. Separated analyses of France and Northern Ireland gave the same results (not shown).

**Discussion**

This prospective study, conducted in a cohort of 9756 middle-aged men free of CHD, indicates that subjects with higher regular leisure-time physical activity EE had a lower incidence of coronary events such as fatal or nonfatal myocardial infarction and coronary deaths over a 5-year follow-up. This graded beneficial effect of EE also held when subjects did not perform high-intensity leisure-time activities. Taking into account the differences in physical activity patterns between France and Northern Ireland, these results may partly explain the higher incidence of CHD in Northern Ireland compared with France. By contrast, higher leisure-time physical activity EE was positively associated with the incidence of angina pectoris.

Many prospective studies have demonstrated a negative association between physical activity or fitness and hard CHD events in various subgroups of the population. Uncertainty remains about the specific effect of physical activity intensity. In our cohort, the beneficial effect of intensity was no longer present after removing the contribution of physical activity EE, indicating that intensity may be favorable through its effect on physical activity EE. Our finding that light-to-moderate activities performed on a regular basis lower the risk of acute coronary events among subjects who do not engage in vigorous activities is in agreement with previous reports. These results are important for public health policy, bearing in mind that a substantial part of the population may not engage in high-intensity leisure-time activities or could not maintain these activities in the long term.

Associations between quantity of energy expended and incidence of hard CHD events went in the same direction and were of the same magnitude in France and in Northern Ireland. We showed differences in physical activity patterns between the two countries. Although total physical activity levels were similar, French men performed more leisure-time physical activity, which may contribute to their lower incidence of CHD in comparison to Northern Ireland. Physical activity patterns are often associated with socioeconomic status and behavioral factors such as alcohol consumption, which may confound the relation between physical activity and coronary events. However, the associations between leisure-time physical activity and incidence of hard CHD persisted after controlling for several potential confounders such as smoking, alcohol habits, and educational level. We recently demonstrated that relations between leisure-time physical activity and educational level or alcohol consumption differ in France and Northern Ireland. Moreover, patterns of alcoholic beverage consumption were found to differ...
between the two countries. However, interaction terms between these factors were all nonsignificant, implying that the associations observed between leisure-time physical activity EE and hard CHD could not be explained by a modifying effect of these factors.

In our study, surprisingly, a significant increase in the incidence of angina was observed for the most active subjects. This was after independent validation of this outcome and exclusion of all borderline cases. In the literature, scant data exist on the association between physical activity and the incidence of angina alone, and, where they do exist, the results are inconclusive. Generally, angina is included in a combined end point such as CHD morbidity, which does not enable the assessment of the effect of physical activity on this specific coronary event, which is also probably harder to ascertain. The pathophysiology is somewhat different from that of acute coronary events such as myocardial infarction or sudden death. Whereas angina symptoms express the development of coronary atherosclerosis, a process over a lifetime, thrombosis on atherosclerotic lesions represents the triggering factor in myocardial infarction. Since physical activity has been shown to reduce thrombotic mechanisms by inhibiting platelet aggregation and reducing clotting factors concentration, this may explain the favorable effect of leisure-time physical activity specifically on hard CHD. Otherwise, we may hypothesize that angina pectoris is less often diagnosed in sedentary subjects because they do not attain sufficiently high levels of exercise to induce ischemic pain.

Some limitations of our study should be considered. Misclassification of the intensity level of physical activity could not be excluded because only the two most frequent leisure-time activities were taken into account in the MOSPA-Q. Hence, the third most frequently performed activity may be of high intensity. However, this could only concern subjects who reported two activities, that is, ≈35% of the subjects, and, among them, those who had not already reported an activity ≥6 MET (only 15% of the total sample). Underestimation also may have concerned light-to-moderate intensity physical activities that have been shown to be less accurately reported. Also in this study, we did not measure the effect of changes in physical activity during follow-up. Such changes may have occurred in our cohort, although the follow-up period was relatively short. However, a subsequent measurement of physical activity would probably have strengthened the relations between leisure-time physical activity and CHD.

The strengths of our study include the high rate of follow-up and the quality control in the ascertainment of endpoints, with validation by an independent committee of all coronary events. Another positive aspect was the assessment of the various forms of physical activity over a 1-year period, thereby taking the seasonal variations into account and better reflecting the average leisure-time physical activity EE.

In conclusion, these prospective data from a European cohort of middle-aged men show a beneficial effect of leisure-time physical activity EE on the incidence of fatal or nonfatal myocardial infarction and coronary deaths. These results could partly explain the unfavorable rate of CHD in Northern Ireland compared with France.

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References


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