The association between physical inactivity and increased risk of coronary heart disease (CHD) has been clearly demonstrated\(^1,2\) and is of growing importance as physical inactivity becomes more prevalent.\(^3-5\) An association between vigorous activity and reduced risk of CHD is consistently reported.\(^6\) The US Surgeon General’s recommendations on physical activity were revised in 1996 to include moderate as well as vigorous intensity activity, but evidence for the benefit of moderate intensity activity is less robust\(^7-10\) and has been questioned.\(^7,11\)

The metabolic syndrome (MS) is distinguished by the biological markers of dyslipidaemia, hypertension, glucose intolerance, and insulin resistance that tend to cluster together in some individuals.\(^12\) Those with MS are at risk of developing cardiovascular disease and type 2 diabetes.\(^13,14\) Physical inactivity may be important in the aetiology of the syndrome.\(^15,16\) Total physical activity (measured as habitual energy expenditure) and fitness (measured as maximal oxygen consumption per kilogram) have independent effects on the components of MS.\(^17\) Body weight and physical fitness modulate insulin action, a core feature of MS.\(^18\) Modulation of MS is thus a plausible biological pathway through which physical inactivity may affect CHD risk. However, it is not known at what intensity activity may be of benefit in reducing the risk of MS and, more precisely, whether both moderate and vigorous activity are beneficial.

Within the Whitehall II cohort the components of MS were measured at 5- and 10-year follow-up. An inverse social gradient...
in the prevalence of MS at 5-year follow-up was not well explained by the social distribution of health behaviours including vigorous activity.19 More detailed measurement of physical activity was undertaken at 10-year follow-up.

This paper examines the association between both moderate and vigorous activity and MS. It also evaluates cardiovascular fitness and BMI as possible mediators of the association.

**Methods**

**Participants**

All non-industrial civil servants aged 35–55 years working in the London offices of 20 departments were invited to participate in this study. Recruitment (phase 1) took place during 1985–1988 and the final cohort consisted of 10 308 (3414 women) with an overall response rate of 73%. The actual rate is likely to be higher because 4% of those on the employee list had moved before the study had begun, and were thus not eligible for inclusion. Data presented are from screening at the fifth phase (1997–1998). Of the 10 308 participants from Phase 1, 7273 returned the physical activity questionnaire and 6554 attended the screening clinic at Phase 5. At Phase 5 92% of participants were white European. No other ethnic group was large enough for separate analysis (Afro-Caribbean = 210 and South Asian = 350). The clustering of components of MS20–22 and the most suitable cut points for them23 vary across ethnic groups. Our analysis is restricted to 5153 white European participants with complete data on metabolic variables.

**Screening examination**

At the screening examination, height, weight, and waist and hip circumferences were measured. Waist circumference was taken as the smallest circumference at or below the costal margin and hip circumference at the level of the greater trochanter using a fibreglass tape measure at 600 g tension. BMI from weight and height was calculated (kg/m²). Blood pressure was measured twice after 5 minutes rest with the Hawksley random-zero sphygmomanometer and the mean value taken (mmHg). High density lipoprotein (HDL) cholesterol concentration was determined from fasting blood samples. The oral glucose tolerance test was administrated following an overnight fast or in the afternoon after no more than a light fat-free breakfast eaten before 08.00 a.m. After the initial venous blood sample, participants drank 389 ml 'Lucozade' (equivalent to 75 g anhydrous glucose) over 5 minutes. A second blood sample was taken 2 hours later and analysed using the electrochemical glucose oxidase method. A 12-lead electrocardiogram was recorded after participants had rested for at least 5 minutes, supine in a quiet room to give a measure of resting heart rate (HR). In all, 4956 participants undertook HR measurements due to staff availability. Participants who did undergo a resting electrocardiogram did not differ from those who did not with respect to age, sex, employment grade, or physical characteristics.

Participants completed a questionnaire that included questions on smoking and alcohol consumption (units per week). High alcohol intake was defined as ≥31 units/week for men and ≥21 units/week for women. On the basis of the participant’s civil service grade title, each participant was assigned to one of six grade groups. Grade 1 represents the highest status jobs and Grade 6 the lowest.24 Details of these methods are described elsewhere.25

Individuals were classified as having MS if they fell into the most adverse sex-specific quintile for three or more of the risk factors; 2-hour glucose, systolic blood pressure, fasting triglycerides, waist-hip ratio (highest quintiles), and HDL cholesterol (lowest quintile).19 Individuals taking anti-hypertensive treatment were assigned to the adverse systolic blood pressure quintile.

**Physical activity questionnaire**

The questionnaire included 20 items on the amounts of time spent walking, cycling, in sports, gardening activities, housework, and house maintenance and was a modified version of the previously validated Minnesota leisure-time physical activity questionnaire.20 Open items allowed the participants to report further activities. Participants were asked about their activity in the last 4 weeks in order to give an indication of usual activity. Total hours per week were calculated for each activity and a MET value assigned to each using a compendium of activity energy costs.27 One MET is the metabolic energy expenditure of lying quietly and is equivalent to 1 kcal per kg per hour. The MET value reflects the intensity of the activity relative to lying quietly and is a multiple of one MET. Therefore a 70 kg person walking at a moderate pace (MET value of 3.5) for 1 hour expends 3.5 METS or 245 kcal. Time spent per week in each item was multiplied by the MET value of the activity to give MET hours per week. The items were divided into two groups based upon the MET value for the activity item; moderate (MET ≥3 to <5), which included activities such as walking and gardening, and vigorous (MET ≥5), including activities such as cycling and swimming. Moderate activity was divided into two categories <24 and ≥24 MET hours per week, the cut point equivalent to approximately 1 hour of moderate activity for 6 days a week. For vigorous activity we used four categories; no vigorous activity, <5, ≥5 and <12.5, or ≥12.5 MET hours per week. These cut points are approximately equivalent to <1 hour, 1–2½ hours, or >2½ hours a week of vigorous activity (on the basis that the mean intensity of vigorous activity is 5 MET).

**Statistical analysis**

The associations between physical activity levels and age, gender, smoking, and high alcohol consumption were evaluated using χ² tests and tests for linear trend. Age-adjusted means of risk factors were also assessed using tests for linear trend between vigorous activity categories and t-tests for moderate activity categories. Participants who reported vigorous activity were excluded from the analyses of moderate activity and cardiovascular risk factors to minimize the potential confounding effect of vigorous activity. However, since all participants reported some moderate activity, the analyses of vigorous activity were adjusted for moderate activity.

Logistic regression was used to estimate the odds of having MS in each activity category. Effects were similar in men and women so analyses were combined. To test for a linear trend across the categories of physical activity, the four categories of vigorous activity were treated as a single ordinal variable. Sex, age, current smoking, and high alcohol consumption were entered in a stepwise manner. The analyses were further adjusted for grade, as an indicator of socioeconomic status. As in the above analyses, only those participants who reported no vigorous activity were included in the moderate activity analyses and the
vigorous activity analyses were adjusted for reported moderate activity. To assess BMI and HR as possible biological intermediates in the pathway between physical activity and MS, these variables were added to the model both separately and combined in the group that had heart rate recordings (n = 4956) as indicators of body fatness and cardiovascular fitness respectively.

Results

Participants were aged 45–68 years (mean 55.5 years). Men reported vigorous activity more than women (49.7% versus 34.8% respectively P < 0.001). Women reporting vigorous activity were younger than those reporting none (mean (SD): 55.1 years (5.8) versus 56.4 years (6.1) P < 0.001). No difference was found in men. Men and women in the top category of moderate activity were significantly older than those in the low category (both P < 0.001).

A higher proportion of people who reported no vigorous activity were current smokers than those reporting some vigorous activity (men 11.7% and 6.3%, women 15.8% and 8.6% respectively). The proportion of men or women who smoked did not vary with moderate activity category. High alcohol intake was not associated with physical activity category in men or women.

Associations between work grade and reported participation in moderate and vigorous activity were observed. In men, 44.7% of the lowest grade was in the top moderate activity category compared with 56.9% of the highest grade. Conversely, in women 52.7% of the lowest grade and 34.9% of the highest grade were in the top category. Of men, 67.3% and 74.9% of women in the lowest grade reported no vigorous activity compared with 45.6% of men and 52.3% of women in the highest grade.

Associations between moderate activity and risk factors for cardiovascular disease are shown in Table 1. Lower waist-hip ratios were observed with the higher category of moderate activity in men and women. Significantly lower BMI, fasting triglycerides and HR values, and higher HDL cholesterol levels with the higher activity category were observed in men, but not in women. No associations were seen with 2-hour glucose or systolic blood pressure.

For vigorous activity, linear trends of lower BMI, fasting triglycerides, HR, and higher HDL cholesterol were observed with increasing activity categories in men and women (Table 2). Statistically significant linear trends of lower waist-to-hip ratio, 2-hour glucose, and systolic blood pressure with increasing vigorous activity categories were observed only in men.

In all, 470 men (12.6%) and 200 women (14.0%) were classified as having MS. Increasing moderate and vigorous physical activity levels were each associated with reduced odds of MS in analyses adjusted for age and sex (Table 3). These trends remained significant after adjustment for other health behaviours and work grade, where the odds ratios of MS in the top compared with the bottom categories of vigorous and moderate activity were 0.52 (95% CI: 0.40, 0.67) and 0.78 (95% CI: 0.63, 0.96) respectively.

BMI and HR attenuated the effect of activity on the odds of having MS (Table 4). The correlation between BMI and HR was 0.15 (P < 0.001). Inclusion of BMI in the model reduced the \( \beta \) coefficient of moderate activity by 30% and vigorous activity by 37%. HR reduced the \( \beta \) coefficients by 17% and 24% respectively. Inclusion of both HR and BMI reduced the \( \beta \) coefficients by 46% (moderate) and 51% (vigorous). The residual trend of the odds between activity categories remained significant for vigorous activity but not for moderate.

Discussion

The frequency of MS is lower among those reporting moderate or vigorous physical activity. This association persists after adjustment for age, smoking, high alcohol intake, and socioeconomic status. This is the first study, that we are aware of, to examine the association between both moderate and vigorous activity separately with MS in a large cohort. The age range of the cohort studied (45–68 years) represents that of a population in which disability and premature mortality from CHD are important concerns. Attenuation of the observed association by both BMI and HR suggests that body fatness and cardiovascular fitness are important mediators of the benefit conferred by both moderate and vigorous activity.

Strengths and limitations of the study

The questionnaire was designed to measure not only vigorous physical activity. This association persists after adjustment for other risk factors. However, we did not include a measure of diet. Any confounding effects of diet on the relationship between physical activity and MS need to be investigated. In addition, the cross-sectional form of the analysis limits causal inference and it is
Table 2. Means of metabolic syndrome factors and related cardiovascular risk factors adjusted for age and moderate activity by vigorous activity category: men = 3724 women = 1429

<table>
<thead>
<tr>
<th>Vigorous activity category (MET h/week)</th>
<th>Sex</th>
<th>None</th>
<th>&lt;5</th>
<th>≥5–&lt;12.5</th>
<th>≥12.5</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td>M</td>
<td>26.4</td>
<td>25.9</td>
<td>25.7</td>
<td>25.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>W</td>
<td>26.5</td>
<td>25.2</td>
<td>25.5</td>
<td>25.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>M</td>
<td>0.932</td>
<td>0.917</td>
<td>0.920</td>
<td>0.904</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>W</td>
<td>0.796</td>
<td>0.786</td>
<td>0.787</td>
<td>0.787</td>
<td>0.12</td>
</tr>
<tr>
<td>HDL&lt;sup&gt;a&lt;/sup&gt; cholesterol</td>
<td>M</td>
<td>1.36</td>
<td>1.36</td>
<td>1.39</td>
<td>1.44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>W</td>
<td>1.67</td>
<td>1.76</td>
<td>1.78</td>
<td>1.72</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Triglycerides&lt;sup&gt;b&lt;/sup&gt;</td>
<td>M</td>
<td>1.31</td>
<td>1.26</td>
<td>1.23</td>
<td>1.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>W</td>
<td>1.07</td>
<td>0.94</td>
<td>0.92</td>
<td>0.98</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2-hour glucose&lt;sup&gt;b&lt;/sup&gt;</td>
<td>M</td>
<td>5.92</td>
<td>5.83</td>
<td>5.64</td>
<td>5.67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>W</td>
<td>6.04</td>
<td>6.14</td>
<td>5.87</td>
<td>5.81</td>
<td>0.23</td>
</tr>
<tr>
<td>Resting heart rate&lt;sup&gt;b, c&lt;/sup&gt;</td>
<td>M</td>
<td>68.7</td>
<td>67.1</td>
<td>65.3</td>
<td>63.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>W</td>
<td>69.6</td>
<td>67.2</td>
<td>67.7</td>
<td>67.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Systolic blood pressure&lt;sup&gt;b&lt;/sup&gt;</td>
<td>M</td>
<td>124.2</td>
<td>121.9</td>
<td>122.8</td>
<td>122.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>W</td>
<td>121.5</td>
<td>118.6</td>
<td>120.6</td>
<td>121.4</td>
<td>0.27</td>
</tr>
</tbody>
</table>

<sup>a</sup> High density lipoprotein.

<sup>b</sup> Geometric mean.

<sup>c</sup> In sub-group men = 3563, women = 1382.

Table 3. Odds ratios (and 95% CI) for metabolic syndrome for vigorous activity (n = 5153) and moderate activity<sup>a</sup> (n = 2806)

<table>
<thead>
<tr>
<th>Model</th>
<th>Vigorous activity category (MET h/week)</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D1</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>&lt;5 (n = 620)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>≥5–&lt;12.5 (n = 761)</td>
<td>0.66 (0.50, 0.88)</td>
<td>0.66 (0.50, 0.88)</td>
<td>0.67 (0.51, 0.89)</td>
<td>0.69 (0.52, 0.91)</td>
</tr>
<tr>
<td></td>
<td>≥12.5 (n = 966)</td>
<td>0.50 (0.39, 0.64)</td>
<td>0.50 (0.38, 0.63)</td>
<td>0.50 (0.39, 0.64)</td>
<td>0.52 (0.40, 0.67)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Only those who reported no vigorous activity included in the moderate activity analyses.

Model A—sex, age.
Model B—sex, age, smoking, and high alcohol intake.
Model C—sex, age, smoking, high alcohol intake, and moderate activity.
Model D1—sex, age, smoking, high alcohol intake, and grade.
Model D2—sex, age, smoking, high alcohol intake, and grade.

Table 4. Odds ratios (and 95% CI) for metabolic syndrome for vigorous activity (n = 4945) and moderate activity adjusted for body mass index (BMI) and resting heart rate (HR)<sup>a</sup> (n = 2722)

<table>
<thead>
<tr>
<th>Model</th>
<th>Vigorous activity category (MET h/week)</th>
<th>Base</th>
<th>Base + BMI</th>
<th>Base + HR</th>
<th>Base + BMI + HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>&lt;5 (n = 592)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>≥5–&lt;12.5 (n = 718)</td>
<td>0.70 (0.52, 0.94)</td>
<td>0.88 (0.65, 1.21)</td>
<td>0.75 (0.55, 1.01)</td>
<td>0.91 (0.67, 1.25)</td>
</tr>
<tr>
<td></td>
<td>≥12.5 (n = 913)</td>
<td>0.53 (0.41, 0.69)</td>
<td>0.64 (0.47, 0.85)</td>
<td>0.61 (0.47, 0.80)</td>
<td>0.69 (0.51, 0.92)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Only those who reported no vigorous activity included in the moderate activity analyses. Base—sex, age, smoking, high alcohol intake, and grade (and moderate activity in vigorous activity models).
possible that those participants who reported low levels of moderate and vigorous activity may have reduced their activity as a result of having MS. Longitudinal data is required to assess whether low levels of moderate and vigorous activity do increase the risk of MS.

Comparison between studies is difficult, as studies in this area have used different risk factors to define MS and different thresholds for each risk factor. Similar to other studies, we have used cut-off points for risk factors based on the population distribution, which gives consistency to the approach longitudinally. However, our definition does differ from those of other researchers, including the Adult Treatment Program III (ATPIII) and WHO 1999 proposed criteria. A comparison of the definition of MS used in Whitehall II and the ATPIII definition was made in a nested case-control study within this cohort. Very similar effects were observed with both definitions of MS and hypothalamic-pituitary-adrenocortical measures.

Physical activity was expressed in MET hours per week rather than energy expenditure (kcal). Kilocalories depend on body weight which prevents direct comparison between participants with different body sizes and would confound the analyses between physical activity and MS.

Physical activity, cardiovascular disease, and MS

Low levels of physical activity are associated with increased CHD risk with a well-established dose—response relationship. Studies have largely examined self-reported vigorous activity, predominantly sport activities. Evidence that moderate exercise, including walking, is associated with substantial reduction in CHD is increasing, though not observed in all populations. Some authors emphasize additional benefits of vigorous activities mediated through increased cardiorespiratory fitness. Vigorous activity (5–9 MET) but not moderate activity (3–4.5 MET) was associated with significantly lower prevalence of two or more of the following risk factors: high BMI, HR, diastolic and systolic blood pressure, and low HDL cholesterol in the German Cardiovascular Prevention Study. MS is similarly associated with low physical activity levels and low cardiorespiratory fitness. However, these studies categorized people according to total activity rather than the intensities of activity.

Mediation of the effects of moderate and vigorous physical activity

A study using heart rate monitoring to measure physical activity concluded that total energy expenditure and fitness were independently associated with the probability of having MS; total energy expenditure having a greater effect than fitness. We used BMI as an indicator of body fatness; those with a BMI ≥25 kg/m² having excess body fatness and being defined as overweight or obese. We used HR as a measure of fitness. Both of these factors were used to investigate probable pathways for the effects of physical activity. HR has been shown to correlate with cardiovascular fitness in a variety of populations. In middle-aged men HR was negatively correlated with treadmill exercise capacity and observed to decrease with increased fitness following an exercise programme. It therefore provides a useful proxy for cardiovascular fitness in large population-based studies. In our population it correlated weakly with BMI, consistent with findings in a principal component analysis of cardiorespiratory fitness in which it consistently loaded in a separate component to BMI. HR can thus act as an indicator of fitness independent of BMI. Both BMI and HR attenuated the association between both moderate and vigorous exercise and MS. This suggests that both body fatness and fitness are mediators of the benefits of both activity intensities in this middle-aged population.

Others have observed that moderate physical activity may act on CHD risk almost completely through increased energy expenditure and reduction of body fat, and that additional reduction in disease risk is mediated by cardiovascular fitness due to vigorous activity. Our results suggest instead that both mechanisms operate for both moderate and vigorous activity. This may not generalize to other, for example younger, populations. However, middle-aged individuals in sedentary occupations form a large and important group in terms of CHD risk and understanding the effects of different intensities of activity in this group is especially important. Longitudinal studies with accurate measures of moderate and vigorous activity, body fatness, and cardiovascular fitness are needed to extend this understanding.

Socioeconomic factors

Occupational grade, a precise indicator of socioeconomic status in the Whitehall II cohort, slightly attenuated the association between physical activity and MS. This suggests that other factors associated with socioeconomic status only weakly confounded the association. High occupational grade was associated with higher levels of vigorous activity in men and women and with higher levels of moderate activity in men. Women in lower grades reported higher levels of moderate activity. Moderate activities most frequently reported in women, such as walking and housework, may be more related to low socioeconomic status than activities reported by men, such as home improvements and mowing the grass.

Public health recommendations

It is important for public health recommendations to be able to quantify benefit from moderate as well as vigorous activity. Recommendations from the US Surgeon General were changed to include moderate activity, in part to give a more attainable goal, especially to those at highest risk, overweight adults. This may also reduce the possible adverse health effects of intense activity among previously inactive individuals. In our study population, participants in the top category of self-reported vigorous activity meet the Surgeon General's criteria for vigorous activity. After adjustment for other risk factors, this group reduced their odds of having MS by 50% compared with those who reported no vigorous activity. Those in the high category for moderate activity, attaining more than 24 MET hours per week, equivalent to an hour a day of moderate activity for 6 days a week, reduced their odds by 22% compared with the low group. These results support the recommendations and suggest that moderate levels of activity may have a protective effect against the risk of CHD in populations similar to this cohort for individuals not participating in vigorous activity.

In conclusion, acknowledging study limitations and the cross-sectional nature of this analysis, this study suggests that both vigorous and moderate leisure-time activities may be beneficial to the metabolic syndrome cluster of cardiovascular
risk factors, and in middle-aged populations with sedentary occupations both body fatness and cardiovascular fitness are involved in mediating the benefits of both moderate and vigorous activity. Even modest increases in activity are therefore worthwhile public health targets.

Acknowledgements

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KEY MESSAGES

• Both moderate and vigorous activity may reduce the risk of the metabolic syndrome in middle-aged people.

• Body fatness and cardiovascular fitness are important mediators of the benefits of both moderate and vigorous activity.

References


