CARDIOVASCULAR MEDICINE

What level of physical activity protects against premature cardiovascular death? The Caerphilly study

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Heart 2003;**89**:502–506

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Accepted 14 January 2002

Objective: To examine the optimal intensity of leisure time physical activity (LTPA) to decrease the risk of all cause, cardiovascular disease (CVD), and coronary heart disease (CHD) mortality in a population sample of middle aged British men.
Design: Prospective study of middle aged men with an 11 year follow up.
Setting: A whole population sample of men from Caerphilly, South Wales, UK.
Subjects: 1975 men aged 49–64 years without historical or clinical evidence of CHD at baseline examination.
Main outcome measures: All cause, CVD, and CHD mortality.
Results: Total (cumulative) LTPA had a graded, significant relation with all cause, CVD, and CHD mortality but no trend with cancer deaths. When different intensities of activity were considered, light and moderate intensity LTPA had inconsistent and non-significant relations with all cause, CVD, or CHD mortality whether adjusted only for age or for other cardiovascular risk factors. In contrast a significant dose–response relation was found for heavy intensity LTPA for all cause, CVD, and CHD mortality fully adjusted for other risk factors.
Conclusions: These data suggest that, in a population of men without evidence of CHD at baseline, only leisure exercise classified as heavy or vigorous was independently associated with reduced risk of premature death from CVD.

Many studies have shown that physical activity during leisure is associated with a decrease in all cause mortality[1–10] and may extend life by 1–2 years.[1 2] Other studies have shown a reduction in premature death caused by cardiovascular disease (CVD)[11 12] and more specifically with coronary heart disease (CHD).[13–18] But the optimal intensity of leisure time physical activity (LTPA) is still unclear. Some studies indicate that only vigorous intensity activity is associated with decreased risk of death[2 9]; others also show associations with moderate or light intensity activity.[15 18] Also, studies of leisure physical activity and cancer death have yielded inconsistent findings.[3 13 19]

The first aim of the present study was to examine the association of LTPA with all cause mortality and cause specific mortality. It is also useful to know the required level and intensity of activity important in the prevention of premature death. We therefore assessed the effects of energy expenditure in various intensity activities (light, moderate, and heavy) during leisure on the risk of disease specific death in a prospective study of middle aged men in Caerphilly, South Wales, UK. Work related physical activity was also examined.

METHODS

Study population and design

The Caerphilly collaborative heart disease study began in 1979 with the overall objective of examining the determinants and predictive ability of new and classical risk factors for CHD. During the initial recruitment phase (1979–1983) 2512 men aged 45–59 years were examined, representing 90% of the population of men in this age group from the town of Caerphilly and its surrounding villages (total population 40 000). Since then they have been examined at five year intervals. At the first re-examination between 1984 and 1988, when the men were aged 49–64 years, men of the same age who had moved into the defined geographical area were also deemed to be eligible. A total of 2398 men were recruited into the reconstructed cohort between 1984 and 1988. All men gave informed consent to participate in the study, which received ethical approval from the South Glamorgan ethics committee.

Since pre-existent CHD and other diseases may influence physical activity patterns, and since men with these conditions have a high mortality, we excluded 393 men with mainly symptomatic evidence of CHD, a doctor diagnosed myocardial infarction, or grade 1 angina (chest pain on walking uphill only) or grade 2 angina (chest pain on walking on the level) as judged from the London School of Hygiene and Tropical Medicine (LSHTM) chest pain questionnaire, or probable ECG ischaemia (Minnesota codes 1–1, any; 1–2, any, major Q waves),[20] as well as 30 men who died within two years and may have been in poor health, leaving 1975 men for the current study.

At the baseline survey for the reconstructed cohort (between 1984 and 1988) men were invited to attend an afternoon or evening clinic. A detailed questionnaire derived from the Minnesota LTPA questionnaire[21] was used to estimate energy expenditure expressed as an activity index (AI) in kcal/day from a record of leisure activity during the preceding 12 months. A trained interviewer asked subjects about the type and duration of their leisure activities during the previous 12 months. Light AI was defined by summing those activities having intensity codes 2.0, 2.5, 3.0, 3.5, and 4.0 (for example, walking, bowling, sailing); moderate AI was obtained by summing activities with intensity codes of 4.5, 5.0, and 5.5 (for example, golfing, digging, dancing); and heavy AI was defined by summing all activities having intensity codes $\geqslant$ 6.0 (for

Abbreviations: AI, activity index; CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular disease; LSHTM, London School of Hygiene and Tropical Medicine; LTPA, leisure time physical activity; MRFIT, multiple risk factor intervention trial

Table 1 Energy expenditure expressed as activity index (AI, in kcal/day) of physical activity during leisure by activity intensity between 1984 and 1988 in men from Caerphilly, South Wales, UK

Variable	Number	Mean	Geometric mean	Median	Maximum	Q_1	Q_3
Total AI	1964	366.1	207.3	257.5	2747.2	122.0	486.0
Light AI	1964	152.1	52.4	81.9	2048.6	23.0	211.9
Moderate AI	1964	163.9	65.0	83.0	2113.6	29.6	204.2
Heavy AI	1964	50.1	9.1	8.1	2142.9	0.0	38.9

Q_1, 25th centile; Q_3, 75th centile.

example, climbing stairs, swimming, jogging). Four AI scores characterised each person, one for each class of intensity activity and their sum total AI. Because the intensity codes for each specific activity were based predominantly on the experience in middle aged American men, some minor modifications were made to adapt to the leisure activity of British men in this study.

Detailed medical and lifestyle histories were obtained and the LSHTM chest pain questionnaire was administered.[20] A full 12 lead ECG was recorded and height, weight, and blood pressure were measured.

The Health Insurance Plan questionnaire,[22] slightly modified, was used to assess physical activity at work, or previous work if unemployed or retired, by self administration. Job physical activity class was divided into four equally sized groups from low to high occupational physical activity. Subjects who did not answer one or more components of the job physical activity questionnaire were not classified (23 subjects, 1%).

Outcome variables

The mean period of follow up was 10.5 years. Deaths were included until 25 September 1997. All men were flagged with the National Health Service Central Registry and we used death certificates coded according to *International classification of diseases*, ninth revision (ICD-9). The main outcome measures were mortality from all causes, CVD (ICD-9 codes 390–458), CHD (ICD-9 codes 410–414), and cancer (ICD-9 codes 140–239).

Person years at risk were calculated from the date of examination between 1984 and 1988 to the date of death or 25 September 1997 for men still alive. For analyses of all cause mortality, deaths due to congenital anomalies (ICD-9 codes 740 to 759) and injury and poisoning (ICD-9 codes 800 to 999) were censored at the date of death (seven cases, or 3% of all deaths). For analyses of disease specific mortality, subjects who died of causes other than each disease specific cause were censored at the date of their death.

Statistical methods

For primary analysis, total, light, moderate, and heavy AI were logarithmically transformed because of their positively skewed distributions. Before taking logarithms, 1.0 was added to each value for total, light, moderate, and heavy AI because zero values were common in some subjects, particularly for heavy AI. This transformation produced a more symmetrical Gaussian distribution and stabilised variances.

The main analyses used a Cox proportional hazards model in survival analysis from the *Statistical package for the social sciences* (SPSS)[23] with the occurrence, or not, of disease specific mortality as the binary dependent variable. The distributions of total, light, moderate, and heavy AI were each divided into equal thirds and the results are presented as the hazard ratio for each disease category in each third relative to a baseline third, which was always taken as the 20% of men with the lowest levels. For heavy AI, in the first third there were 595 subjects who were inactive for vigorous activity. These subjects were referred to throughout as having the baseline value and, where appropriate, hazards for other thirds of the distribution are shown together with 95% confidence intervals (CIs) estimated from the Cox proportional hazards model.

The tests of linear trend for increasing thirds of total, light, moderate, and heavy AI were performed using Cox proportional hazards model by treating total, light, moderate, and heavy AI as an ordered variable in thirds as described on the relevant tables.

All tests are two sided significance levels of $p \leq 0.05$ calculated from SPSS. Partially missing values were automatically excluded from the analyses.

RESULTS

Of the total cohort of 1975 British men, 252 (13% of all men) died over the follow up period of 10 years. Among these 252, 111 (44%) deaths were caused by CVD, 82 (33%) by CHD, and 98 (39%) by cancer. Deaths resulting from congenital anomalies or injury and poisoning were censored for analyses of all cause mortality (seven cases).

Table 2 Total energy expenditure of physical activity during leisure time and all cause and selected cause specific mortality during 10 years of follow up

Total AI (kcal/day)	Person years	All cause		Cardiovascular disease		Coronary heart disease		Cancer	
		Number	Rate*	Number	Rate*	Number	Rate*	Number	Rate*
1 (0–161.8)	6804.6	97	14.3	47	6.9	36	5.3	31	4.6
2 (161.9–395.5)	6954.8	71	10.2	35	5.0	26	3.7	29	4.2
3 (395.6–2747.2)	6943.7	74	10.7	29	4.2	20	2.9	37	5.3
Test for trend†		p=0.047		p=0.028		p=0.025		p=0.526	
Total	20703.0	242‡	11.7	111	5.4	82	4.0	97§	4.7

*The crude mortality rates (1/1000 person years).
†Deaths caused by congenital anomalies and injuries and poisonings were censored at date of death (7 cases, 3% of all deaths).
‡p Value for trend from Cox proportional hazards model with total activity metabolic index (expressed as kcal/day) as an ordered variable from the lowest tertile to the highest tertile.
§AI data missing for three deaths, one of three deaths caused by cancer.

Table 3 Hazard ratios and 95% confidence intervals (CIs) of deaths in relation to total activity during leisure at baseline during a 10 year follow up

	Total activity tertile (kcal/day)			
Cause	1 (0.0–161.6)	2 (161.8–395.3)	3 (395.5–2747.2)	p Value for trend*
All causes				
Age adjusted	1.00	0.73 (0.54 to 0.99)	0.74 (0.55 to 1.00)	0.046
Fully adjusted†	1.00	0.79 (0.58 to 1.08)	0.76 (0.56 to 1.04)	0.083
CVD				
Age adjusted	1.00	0.74 (0.48 to 1.15)	0.60 (0.38 to 0.95)	0.028
Fully adjusted†	1.00	0.81 (0.51 to 1.27)	0.64 (0.40 to 1.04)	0.067
CHD				
Age adjusted	1.00	0.72 (0.43 to 1.19)	0.54 (0.31 to 0.93)	0.025
Fully adjusted†	1.00	0.74 (0.44 to 1.25)	0.55 (0.31 to 0.98)	0.039

*p Value for trend from Cox proportional hazards model with total activity metabolic index (kcal/day) as an ordered variable from the lowest to the highest tertile.
†Adjusted for age, diastolic blood pressure, and body mass index as continuous variables, smoking status (never smoked, previously smoked, or currently smokes cigars, pipe, or 1–14, 15–24, or ≥25 cigarettes per day), social class (manual), family history of CHD among first degree relatives before age 55, history of diabetes mellitus in the past five years, and job physical activity class (accumulated score 1–8, 9–12, 13–16, and 17–19).

Table 4 Hazard ratios and 95% CIs of deaths in relation to combined light and moderate activity during leisure at baseline during a 10 year follow up

	Combined light and moderate activity tertile (kcal/day)			
Cause	1 (0.0–133.0)	2 (133.1–342.6)	3 (342.7–2743.23)	p Value for trend*
All causes				
Age adjusted†	1.00	0.90 (0.65 to 1.23)	1.02 (0.75 to 1.39)	0.917
Fully adjusted‡	1.00	0.95 (0.69 to 1.31)	1.04 (0.76 to 1.43)	0.798
CVD				
Age adjusted†	1.00	1.02 (0.65 to 1.61)	0.94 (0.59 to 1.50)	0.800
Fully adjusted‡	1.00	1.09 (0.69 to 1.73)	1.01 (0.62 to 1.63)	0.958
CHD				
Age adjusted†	1.00	1.09 (0.65 to 1.84)	0.90 (0.52 to 1.57)	0.738
Fully adjusted‡	1.00	1.12 (0.66 to 1.92)	0.93 (0.52 to 1.66)	0.832

*p Value for trend from Cox proportional hazards model with combined light and moderate activity metabolic index (kcal/day) as an ordered variable from the lowest to the highest tertile.
†Adjusted for age and heavy intensity activity (expressed as AI (kcal/day) and logarithmic scale) as continuous variables.
‡Adjusted for age and heavy intensity activity (expressed as AI (kcal/day) and logarithmic scale) as continuous variables, and variables listed in footnote in table 3.

Table 1 presents basic descriptive data at baseline. LTPA measurements were missing for 11 men (0.6% of all men), of whom three had died, one from cancer. The total AI ranged from 0 to 2747.2 kcal/day with a median of 257.5 kcal/day. The medians for light, moderate, and heavy AI were 81.9, 83.0, and 8.1 kcal/day, respectively. The geometric means for total, light, moderate, and heavy AI were 207.3, 52.4, 65.0, and 9.1 kcal/day, respectively. The main energy expenditure during leisure was from light and moderate intensity activity in this population. The energy expenditure in vigorous intensity activity was the lowest, because there were 595 subjects (30% of all men) who reported no heavy intensity activity at all, and those who did take such exercise did so rarely.

Table 2 shows the crude mortality of all cause death and cause specific death according to thirds for total LTPA at baseline over 10.5 years of follow up. In all cases except for cancer mortality, men in the least active group had the highest mortality across the thirds. Men in the group immediately below the most active group of men had the lowest mortality from all causes.

Hazard ratios for all cause, CVD, and CHD mortality were calculated adjusted firstly only for age. Secondly, they were adjusted additionally for six major cardiovascular risk factors and job related physical activity. Table 3 shows these results.

Hazard ratios for higher levels of total activity are lower and show a significant trend with increasing levels of activity for all causes and CVD mortality. Hazard ratios for CHD mortality are lower than those for all causes and CVD mortality in the higher thirds of total activity. Full adjustment for multiple risk factors in addition tends to increase the size of the hazard ratios slightly.

Light and moderate intensity LTPA each showed inconsistent and non-significant trends with all cause, CVD, and CHD mortality and have therefore been combined in table 4. Age and multivariate adjusted hazard ratios and 95% CIs of all cause mortality and cause specific mortality by thirds of all non-heavy intensity (combined light and moderate intensity LTPA) are shown. The hazard ratios of all cause mortality showed no trend from the least to the most active group (p for trend 0.917) with the least active group as referent either after adjustment for age and heavy intensity activity or after multivariate adjustment (p for trend 0.734).

Similarly combined light and moderate intensity LTPA failed to show a trend with the risk of CVD or CHD mortality after adjustment for age or multiple risk factors.

Heavy intensity LTPA was significantly and inversely associated with the risk of all cause, CVD, and CHD death after adjustment for either age and combined light and moderate intensity activity or multiple risk factors (all tests for trend $p < 0.05$) (table 5).

Table 6 shows the relation between work related activity and all cause, CVD, CHD, and cancer mortality according to the four categories of job physical activity classes (the least active group as referent). This classification was based on the last

Table 5 Hazard ratios and 95% CIs of deaths in relation to energy expenditure of heavy intensity activity during leisure at baseline during 10 years follow up

	Heavy activity tertile (kcal/day)			
Cause	1 (0.0–0.6)	2 (0.7–23.8)	3 (23.9–2142.9)	p Value for trend*
All causes				
Age adjusted†	1.00	0.88 (0.66 to 1.18)	0.58 (0.41 to 0.82)	0.002
Fully adjusted‡	1.00	0.87 (0.65 to 1.17)	0.61 (0.43 to 0.86)	0.006
CVD				
Age adjusted†	1.00	0.87 (0.57 to 1.31)	0.39 (0.22 to 0.67)	0.001
Fully adjusted‡	1.00	0.86 (0.57 to 1.32)	0.38 (0.21 to 0.67)	0.001
CHD				
Age adjusted†	1.00	1.11 (0.69 to 1.78)	0.37 (0.19 to 0.73)	0.008
Fully adjusted‡	1.00	1.13 (0.69 to 1.85)	0.36 (0.18 to 0.73)	0.009

*p Value for trend from Cox proportional hazard model with heavy activity metabolic index (kcal/day) as an ordered variable from the lowest to the highest tertile.
†Adjusted for age and combined light and moderate intensity activity (logarithmic scale) as continuous variables.
‡Adjusted for age and combined light and moderate intensity activity (logarithmic scale) and variables listed in footnote in table 3.

Table 6 Hazard ratios and 95% CIs of deaths in relation to job physical activity at baseline during 10 years of follow up

	Job physical activity*				
Cause	1 (1–8)	2 (9–12)	3 (13–16)	4 (17–19)	p Value for trend†
All causes					
Age adjusted	1.00	1.31 (0.92 to 1.87)	1.46 (1.02 to 2.10)	1.24 (0.86 to 1.79)	0.19
Fully adjusted‡	1.00	1.38 (0.95 to 2.00)	1.38 (0.93 to 2.03)	1.10 (0.73 to 1.64)	0.71
CVD					
Age adjusted	1.00	1.42 (0.85 to 2.37)	1.68 (1.00 to 2.80)	0.87 (0.48 to 1.59)	0.99
Fully adjusted‡	1.00	1.59 (0.93 to 2.71)	1.75 (1.00 to 3.06)	0.73 (0.38 to 1.41)	0.52
CHD					
Age adjusted	1.00	1.46 (0.82 to 2.62)	1.32 (0.71 to 2.45)	0.94 (0.48 to 1.84)	0.87
Fully adjusted‡	1.00	1.68 (0.92 to 3.08)	1.43 (0.73 to 2.79)	0.80 (0.38 to 1.69)	0.54

*Job physical activity (expressed as job physical activity class, accumulated scores from low to high occupational physical activity) was divided into four equally sized groups.
†p Value for trend from Cox proportional hazard model with job physical activity as a ordinal variable (1, 2, 3, or 4 for four groups from low to high occupational physical activity).
‡Adjusted for total leisure activity (logarithmic scale), employment status (employed versus unemployed or retired) and variables listed in footnote in table 3.

employment for each man. Some 48% of men had retired or were unemployed and results were adjusted for employment status. There was no evidence of any association between job physical activity and all cause, CVD, CHD, and cancer deaths.

All analyses were repeated to include 30 men who died within two years who were initially excluded. The pattern and significance of the results were essentially unchanged.

To define more accurately the activity level associated with a reduction in risk of death or cardiovascular death, we divided the men according to fifths of the distribution of heavy intensity activity. Five hundred and ninety five men did no heavy intensity activity and a further 191 men expended less than 3.4 kcals/day on average (first two "fifths"). Of the upper two fifths the penultimate fifth (16.5–54.3 kcals/day) was associated with a hazard ratio of 0.86, 0.71, and 0.73 for all cause, cardiovascular, and coronary mortality, respectively, when fully adjusted for other risk factors (non-significant). The upper fifth (54.4–2142.9 kcals/day) was associated with a hazard ratio of 0.53, 0.37, and 0.38, respectively (fully adjusted) (all 95% CIs significant). In the upper fifth of the distribution all but 24 subjects had an energy expenditure of heavy intensity less than 500 kcals/day.

DISCUSSION

The purpose of this study was to examine the relation between habitual physical activity and all cause and cause specific mortality. We also assessed the effect of exercise at different levels of energy expenditure during leisure (light, moderate, and heavy) on all cause and disease specific mortality in middle aged British men.

We found strongly significant inverse associations between heavy LTPA and all cause, CVD, and CHD mortality after adjustment for either age or multiple risk factors, but neither LTPA of moderate nor of light intensity was consistently associated with all cause or cause specific mortality. Job related physical activity was not associated with all cause or cardiovascular mortality.

Current guidelines in the UK[24] recommend that adults accumulate at least 30 minutes of moderately intensive activity (such as brisk walking) on at least five days a week, which are similar to those recommended for US adults by the Surgeon General.[25] However, the number of studies that show that exercise of light or moderate intensity reduces risk of CHD is small.[4 15–18] The largest study[15] to show that moderate intensity activity is protective (MRFIT (multiple risk factor intervention trial)) is based on 12 866 men selected from 361 662 men initially screened and who were at relatively high risk of CHD with very few men engaging in heavy intensity activity. Two of the other studies[4 17] relate to increases in physical activity during middle age, which suggests that the type of population studied has a bearing on the generalisability of our present results. The present report supports the findings of other cohort studies[1 2 10 26–29] that habitual leisure exercise of vigorous intensity is associated with significantly reduced risk of all cause and cardiovascular death.

In additional analyses we examined risk of deaths by fifths of the distribution of men in this cohort according to their level of vigorous intensity leisure activity. Forty per cent of men reported no or very little vigorous activity while those in the upper fifth of the distribution (at 54 kcals/day or above) had a 10 year reduced risk of death of 47% and of a coronary death of 62%. In the next highest fifth (at 16–53 kcals/day) there was a 16% reduction in the risk of death and a 27% reduction in the risk of coronary death.

An energy expenditure of 54 kcals/day corresponds to an average of nine minutes of jogging or doubles tennis per day or seven minutes of climbing stairs, but this level and intensity of activity was achieved by only one fifth of our population. In contrast subsequent risk was not reduced in men in the upper third of the distribution of light and moderate intensity activity. This group had an energy expenditure of 343 kcals/day or more (table 4) equivalent to over one and a half hours of walking for pleasure or one hour of ballroom dancing a day.

The strengths of this study were a well defined prospective design, mid to long term follow up, and standardised and validated assessment of physical activity.[30–32] One limitation is that we measured physical activity during leisure only at the baseline survey and did not have information about changes of physical activity over time. This can cause misclassification of physical activity over time. Additionally, the bias in this type of study may be due to the possibility that men who had low levels of LTPA at baseline were already sick and that illness was the cause rather than the result of lack of physical activity. To reduce this potential source of bias we excluded from these analyses men with diagnosed myocardial infarction, angina, or probable ECG ischaemia and men who died during the first two years of follow up. Extending the exclusion period to four years did not alter the pattern of results. Finally, physical activity was measured by a self administered questionnaire, and despite the use of a previously validated LTPA questionnaire there was undoubtedly some misclassification, particularly as the initial validation was undertaken in a North American sample.[21] This misclassification most likely would attenuate the observed relative risks, especially for light and moderate intensity activity, and the true association may be stronger.

In conclusion, these data support the view that significant health benefits can be obtained by LTPA. We and others have recently shown LTPA to be independently linked with lower concentrations of thrombotic factors[33] and inflammatory markers,[34] which may provide an additional mechanism for these effects. This study also clearly showed that vigorous physical activity, such as climbing stairs, hiking, jogging, swimming, tennis, badminton, squash, and heavy digging, may independently prevent premature death, principally from CVD and CHD, in middle aged men who have no evidence of pre-existing CHD.

ACKNOWLEDGEMENTS
We thank the British Heart Foundation and the Medical Research Council for financial support.

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