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**Leisure-time physical activity, cardiovascular risk factors and mortality
during a 34-year follow-up in men**

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Abbreviations:

BMI: Body mass index

CI: Confidence interval

CVD: Cardiovascular disease

HR: Hazard ratio

SE: Standard error

SD: Standard deviation

Introduction

Given that physical activity affects several cardiovascular disease (CVD) risk factors, it is possible that exercise prevents deaths simply through risk factor modification. [1] However, the known risk associations may be confounded through several pathways including lifestyle choices, social class [2] and varying adherence - or more broadly the “healthy user effect”. In other words, people who initiate and adhere to preventive habits may be systemically healthier and more health-seeking than others.[3] Furthermore, the physical activity of work and leisure time, lifestyle and other stress factors differ in both their prevalence and modifiability in various socioeconomic groups, and consequently, population-based studies may not reflect the effects of physical activity as such. In order to reduce some of these caveats, we studied the associations between leisure-time physical activity and 34-year mortality in an initially healthy and socioeconomically homogeneous cohort of middle-aged men in Helsinki, Finland.

Methods

Baseline examinations in 1974 and questionnaire surveys in 1985-1986 and 2000

The cohort and examinations have been described earlier [4]. The study procedures have been approved by the Ethics Committee of the Department of Medicine, University of Helsinki. In brief, initially healthy men of high socioeconomic status, mostly business executives born in 1919-1934, had participated in structured health check-ups during the 1960s and early 1970s at the Institute of Occupational Health in Helsinki, Finland. They were evaluated with questionnaires and clinical and laboratory examinations in 1974, whereupon 1,815 men were found to be actively working and healthy without diabetes, clinical cardiovascular disease or regular medications. Of the 1,815 men, a structured questionnaire about details of their physical activity is available for 782 men. In 1974, this detailed information was mostly (90.7%, n=709) gathered from men who had at least one of the following risk factors: (1) serum cholesterol level 7.0 mmol/L (270mg/dL) or higher; (2) serum triglyceride level 1.7mmol/L (150mg/dL) or higher; (3) systolic blood pressure 160mmHg or higher; (4) diastolic blood pressure 95 mmHg or higher; (5) smoking more than ten cigarettes per day; (6) relative body weight (weight relative to mean weight for height) 120% or higher (indicating overweight); (7) one-hour glucose tolerance 9.0 mmol/L (162mg/dL) or higher. These men were assessed to be at higher cardiovascular risk [5]. However, their age

distribution as well as long-term mortality were not statistically different from those men without detailed physical activity assessment.

Although part of the men had participated in a controlled multifactorial prevention trial during the 1970s [5], our preliminary analyses showed that participation in the 1970s trial did not affect the present long-term results. Therefore, all the 782 men with detailed exercise information form the population of the present analyses.

In 1974, weight and height were measured and body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. In 1974, the men also reported their weight at 25 years of age, which was used to calculate midlife weight gain (weight in 1974 minus reported weight at 25 years of age). In 1974 the men were also asked questions on how they rated their present health and physical fitness on a 5-step scale ("very good", "good", "fair", "poor", "very poor"). To reflect composite risk of coronary artery disease, the Keys' risk score [6] including age, BMI, smoking, cholesterol and systolic blood pressure was calculated in 1974. The Framingham risk score could not be calculated because HDL cholesterol was not available in 1974.

The men were also asked to give a global description of their leisure-time physical activity on a 4-step scale:

- 1) Reading, watching television, going to the cinema or other sedentary activity.
- 2) Walking, cycling, skiing, gardening, bowling, fishing or other light exercise weekly.
- 3) Jogging, running, skiing, swimming, tennis, badminton, heavy gardening or similar exercise weekly on a regular basis.
- 4) Regular vigorous/competitive exercise several times a week on a regular basis.

Because only 11 men reported competitive activity, groups 3 and 4 were combined in the analyses. Men answering yes to question 1 were categorized as low activity; 2 as moderate; and 3 and 4 as high activity group. Preliminary analyses showed that global description differentiated mortality risk most consistently, and therefore more detailed analyses were performed comparing these groups.

Of the 782 men, 80.7% (n=631) and 70.6% (n=552) could be re-assessed with questionnaires in the 11-year (1985-1986) and 26-year surveys (2000), respectively, but questions about exercise were less comprehensive than in 1974: In the 11-year survey, men were asked whether they exercised regularly and weekly, and if yes, how many hours per week; in the 26-year survey, men were asked whether they exercised regularly and weekly, and if yes, how many hours per week. However, in the 26-year survey men were also asked how many times per week they exercised with an intensity leading to sweating and breathlessness (“vigorous” activity).

Mortality follow-up

Total mortality of the study cohort up to 31 March 2007 was retrieved from the Central Population Register, which keeps registry of all Finnish citizens. According to the Register, assessment of vital status is very reliable for people having their permanent place of residence in Finland (over 95% of the present cohort) irrespective of whether they die in Finland or abroad. Moreover, the assessment of the vital status is also quite reliable for Finnish citizens living permanently abroad. Causes of death up to 31 December 2006 were determined from the countrywide computerized Cause-of-Death Register of Statistics Finland, in which trained

nosologists code the causes of death. The causes were categorized into 5 groups: cardiovascular, cancer, accidents, suicides, and other causes.

Statistical methods

NCSS statistical software (2004 version, www.ncss.com) was used for the analyses. In the analyses, global level of physical activity was categorized as described above. T-tests, nonparametric tests and analyses of covariance (ANCOVA) were used where appropriate to compare continuous variables; chi-square and trend tests were used to compare proportions. Differences in survival curves were analyzed with log rank test. Hazard ratios (HR) with their 95% confidence intervals (CI) for mortality associated with physical activity at baseline were calculated using Cox's proportional hazards regression. Other risk factors were adjusted for in respective models. In statistical analyses 2-tailed tests were used, and P values < 0.05 were taken as significant.

Results

The baseline characteristics of the study population are shown in Table 1. Of the various CVD risk factors, physical activity was inversely associated with weight gain during adulthood, BMI in midlife, and with one-hour post-load glucose concentration. Sedentary men smoked more than other groups, but serum lipid levels and blood pressure were only weakly associated with physical activity.

As a global description of physical activity, 148 (18.9%), 398 (50.9%), and 236 (30.2%) men reported low (sedentary), moderate, and high leisure-time physical activity, respectively. Most men (80.5%, n=630) had sedentary work and commuted to work by car or public

transportation. No association was observed between physical activity groups and the type of work.

Physical activity was measured three times: at baseline and in the 11- and 26-year surveys, yet the questions about physical activity were most detailed at baseline, as described above.

Tracking of the baseline physical activity was good during the follow-up in the 11-year and 26-year surveys. (Table 2). The reported regular weekly exercise in the 11-year and 26-year surveys was 50-70%, 69-80% and 92-85% for low, moderate and high physical activity groups, respectively (Table 2). The continuity of initially reported regular weekly exercise was significantly higher among the most physically active men in both subsequent surveys ($P < 0.001$ and < 0.002 , respectively). “Vigorous” exercise leading to sweating and breathlessness was reported by 56%, 68% and 79% men in the low, moderate and high physical activity groups in the 26-year survey, while 35%, 45% and 60%, respectively, performed vigorous exercise more than twice a week.

During the 34-year follow-up, 295 men died (37.8%), with the cause of death available for 282 deaths (95.6% of total). Mortality was not significantly associated with type of work (sedentary, mobile) or type of commuting to work (walking or cycling).

Global description of leisure-time physical activity significantly predicted death: mortality per 1,000 person years was 16.5, 12.9, and 10.8 ($P = 0.01$) in the low, moderate and high physical activity groups, respectively. Unadjusted survival curves are shown in Figure 2, demonstrating the consistent difference between the groups. Causes of deaths are shown in Table 4, suggesting that especially CVD deaths were associated with physical activity. Multivariable analyses (Table 4) indicate that the protective effect of physical activity was independent of traditional CVD risk factors (age, BMI, cholesterol, smoking and systolic

blood pressure) reflected by Keys' risk index. The result did not change after one-hour glucose and triglycerides were added to the model.

Discussion

The self-reported "global" leisure time physical activity was strongly associated with 34-year mortality independently of traditional CVD risk factors in a socioeconomically homogeneous cohort of men. Comparison of the causes of death showed that especially CVD mortality was associated with physical activity, supporting the findings of earlier Finnish [7-9] and other population studies in Western countries [1,10-24].

While the difference in total work load showed the largest predictive power between the sedentary and active tertile, significant differences in mortality rates became evident after approximately 15 years of surveillance, and were interestingly shown to increase with time through the 34-year follow-up. The weekly physical activity was assessed twice during the follow-up and was shown to increase in all activity groups in both the 11-year and the 26-year survey. These findings can be accounted for by the positive effect of increasing exercise, and increasing selection through excessive mortality of sedentary participants. At the 26-year survey, vigorous exercise on a weekly basis was reported by 59% and 79% and the frequency of three times or more per week by 35% and 60% in the low and high activity groups, respectively. The exercise habit seemed to track best among the initially most active men in both surveys. An increase in both intensity and amount of exercise in all groups can be suggested to account for the dose-related decrease in mortality in relation to increased exercise.

Our results indicating that approximately 15 years of surveillance is needed before the differences between mortality rates of the low and high activity groups become evident are in accordance with a recent Swedish follow-up study [13]. It showed that an average of 10 years of increased physical activity after midlife is required to reduce excessive mortality in physically inactive men to the level of those who are physically active. Additionally, our results suggest that training has an independent dose-response effect in reducing mortality, which can even increase with time at least up to 34 years.

Both aerobic fitness and physical activity have been shown to associate with mortality. In a 16-year follow-up of Norwegian men the relative risk of death from any cause in the highest fitness quartile as compared with the lowest quartile was significantly reduced by 46% after adjustment for age, smoking status, serum lipids, blood pressure, resting heart rate, vital capacity, BMI, level of physical activity, and glucose tolerance. A high level of leisure time physical activity was strongly associated with fitness, but was not found to have an independent prognostic value. [11] In another 5.5-year prospective study with age-adjusted quartiles, a multivariate analysis including clinical characteristics, risk factors, exercise test data and activity patterns revealed that exercise capacity (HR per quartile 0.62; CI: 0.47-0.82) and energy expenditure from adulthood recreational activity (HR per quartile 0.72; CI: 0.58-0.89, $P=0.002$) were the sole significant predictors of mortality [25]. It should be noted, however, that in addition to exercise training, physical fitness level is markedly influenced by hereditary factors, which can affect survival. On the other hand, regular exercise is a prerequisite for the maintenance of individual fitness level. The constancy and even increasing tendency of regular physical activity during our 34-year follow-up probably have a crucial impact on the observed mortality benefit, emphasizing the importance of a life-long sporty lifestyle.

In the present study, physical activity was inversely associated with weight gain during adulthood, BMI in midlife, and with one-hour post-load glucose concentration. Nevertheless, BMI or even one-hour glucose did not show an independent effect on mortality, in evidence against reverse causality. Our findings are in line with a follow-up study of 9.8 years in middle-aged Finnish women and men, which showed that physical inactivity has an independent effect on increased CVD risk, while obesity was concluded to increase the risk partly through the modification of other risk factors [7]. The education level included in multivariate analysis was not found to have an independent effect on CVD risk, even though it was speculated that unmeasured components of socio-economic status may strengthen the positive effect of leisure-time activity and weaken the protective effects of occupational activity [7].

It has been suggested that public health programs may be of benefit by advising each socioeconomic status group separately while considering the country's level of development [2]. A combination of high stress levels and smoking or physical inactivity has been revealed to be especially harmful among individuals with low socioeconomic status [26]. The present study is unique in terms of a very long follow-up in a socioeconomically homogeneous cohort of men of high socioeconomic status, and it can be considered as being dated in a phase of constant and quite rapid social upswing and increasing awareness of health concerns in the Finnish society. The similarity of the results of our study with earlier Finnish population studies [7] suggests that the adoption of life-style and physical activity habits among high-economy social class of men were not markedly different from the whole population.

The distinct strength of this primary prevention study is the long follow-up time, which reduces the confounding effect of subclinical diseases at baseline. The fact that our cohort consisted of healthy men of high socioeconomic class can be considered to further reduce

confounding. Most studies concerning physical activity and mortality are based on a single estimate of activity [7,8,14,15,20,24,27,28], while in our study physical activity was also assessed during follow-up. Response rates to the surveys were high.

Our study also has some limitations. Physical activity was determined by self-report, which is considered to overestimate actual amounts of physical activity and thus underestimate the benefits of physical activity among older adults [10]. Despite this, our study shows a graded and independent association between physical activity and reduced long-term mortality.

Another limitation is that the questionnaires sent during the follow-up were not as detailed as the questionnaire at baseline. Generally, physical activity nevertheless seems to track well during the decades in our cohort. The fact that the physical activity pattern remained largely unchanged suggests that the physical activity habits were correctly reported. A clear limitation is that our cohort consisted only of men of high socioeconomic status. However, relations between physical activity and mortality have been reported to be considerably similar between sexes [8]. Another recent study showed no significant association between leisure-time physical activity and mortality in women, but the statistical power was limited by the small number of deaths among women [23].

Conclusions

In our 34-year follow-up study, leisure-time physical activity in midlife was associated with better long-term prognosis in a stepwise manner, irrespective of CVD risk factors and BMI among men with a homogeneous socioeconomic status. Whether this longer life achieved by physical activity is also associated with better quality of life in old age is important from the compression of morbidity viewpoint and needs to be investigated further.

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Legends to the figures

Figure 1. Flow chart of the study

Figure 2. Unadjusted survival curves according to baseline global physical activity

Table 1. Characteristics of the study group according to the level of physical activity at baseline in 1974

Variable	Whole group, n=782	Low physical activity, n=148	Moderate physical activity, n=398	High physical activity, n=236
Age, yr	47.8 (4.1)	48.4 (3.9)	47.9 (4.1)	47.4 (4.1)
Body mass index at 25 years of age, kg/m ²	22.2 (2.2)	22.0 (2.1)	22.2 (2.3)	22.4 (2.2)
Body mass index in 1974, kg/m ²	25.8 (2.9)	26.0 (3.0)	26.1 (2.9)	25.2 (2.6)
Weight gain from 25 years of age until 1974, kg	11.3 (8.4)	12.6 (8.9)	12.3 (8.8)	8.8 (6.6)
Perceived health, n (%)				
- very good or good	410 (53.9)	69 (48.6)	196 (50.5)	145 (63.0)
- fair	320 (42.1)	69 (48.6)	175 (45.1)	76 (33.0)
- poor or very poor	30 (3.9)	4 (2.8)	17 (4.4)	9 (3.9)
Perceived fitness, n (%)				
- very good or good	231 (30.3)	24 (16.9)	86 (22.1)	121 (52.6)
- fair	420 (55.2)	77 (54.2)	243 (62.5)	100 (43.5)
- poor or very poor	110 (14.5)	91 (28.9)	60 (15.5)	9 (3.9)
Keys' risk index, %/5 years, median (interquartile range)	1.7 (1.1-2.8)	1.9 (1.3-3.1)	1.7 (1.0-2.8)	1.6 (1.1-2.7)
Blood pressure, mm Hg				
Systolic	145.7 (18.6)	145.9 (17.4)	144.8 (19.2)	147.0 (18.2)
Diastolic	94.1 (10.7)	94.3 (10.1)	93.9 (10.9)	94.2 (10.8)
Pulse rate, per min	64.6 (10.8)	67.8 (11.8)	64.8 (10.3)	62.2 (10.5)

Cholesterol, mmol/L	5.9 (1.1)	6.1 (1.1)	5.9 (1.1)	5.9 (1.0)
Triglycerides, mmol/L, median (interquartile range)	1.0 (1.0-2.0)	1.1 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)
One-hour glucose, mmol/L median (interquartile range)	7.0 (5.0-8.0)	7.0 (6.0-8.0)	7.0 (5.0-9.0)	6.0 (5.0-8.0)
Smokers, %	275.0 (35.2)	66.0 (44.6)	132.0 (33.7)	77.0 (32.6)
Alcohol, g/week median (interquartile range)	126.0 (56.0-252.0)	126.0 (42.0-252.0)	126.0 (70.0-252.0)	136.0 (63.0-280.0)

Units in parentheses: Mean (SD) unless otherwise stated

Table 2. Reported regular weekly exercise in the 11-year (1985) and 26-year (2000) surveys, n (%)

	Low physical activity in 1974, n=148	Moderate physical activity in 1974, n=398	High physical activity in 1974, n=236	P-value
Weekly exercise in the 11-year survey, n (%)	59 (49.6)	220 (69.2)	176 (91.7)	<0.001
Weekly exercise in the 26-year survey, n (%)	64 (70.0)	216 (80.0)	157 (85.3)	0.002
“Vigorous” exercise * in the 26-year survey, n (%)	51 (56.0)	184 (68.1)	146 (79.3)	<0.001
“Vigorous” exercise * ≥3 times/week in the 26-year survey	18 (35.3)	82 (44.6)	88 (60.3)	<0.001

* Reported exercise intensity leading to sweating and breathlessness

Table 3. Causes of deaths in the study groups in 1974-2007

Cause of death	Low physical activity in 1974, n=148 (4162 person-years)	Moderate physical activity in 1974, n=398 (11,768 person-years)	High physical activity in 1974, n=236 (7310 person-years)
Cardiovascular disease	24 (57.7; 37.0-85.7)*	51 (43.3;32.3-56.9)	24 (32.8; 21.1-48.8)
Cancer	18 (43.2; 25.7-68.3)	54 (45.9: 34.5-59.8)	29 (39.7; 26.6-56.9)
Accidents	7 (16.8; 6.8-34.6)	5 (4.2; 0.5-8.0)	3 (4.1; 0.9-12.0)
Suicide	1 (2.4; 0.6-13.4)	4 (3.4; 0.9-8.7)	1 (1.4; 0.3-7.6)
Other causes	16 (38.4; 22.0-62.4)	28 (23.8; 15.8-34.4)	17 (23.3; 13.6-37.2)

* Number, deaths per 10,000 person-years with 95% CI in parentheses. Cause of death was undetermined in 13 men.

Table 4. Multivariate-adjusted hazard ratios of total mortality in physical activity groups during 34-year follow-up

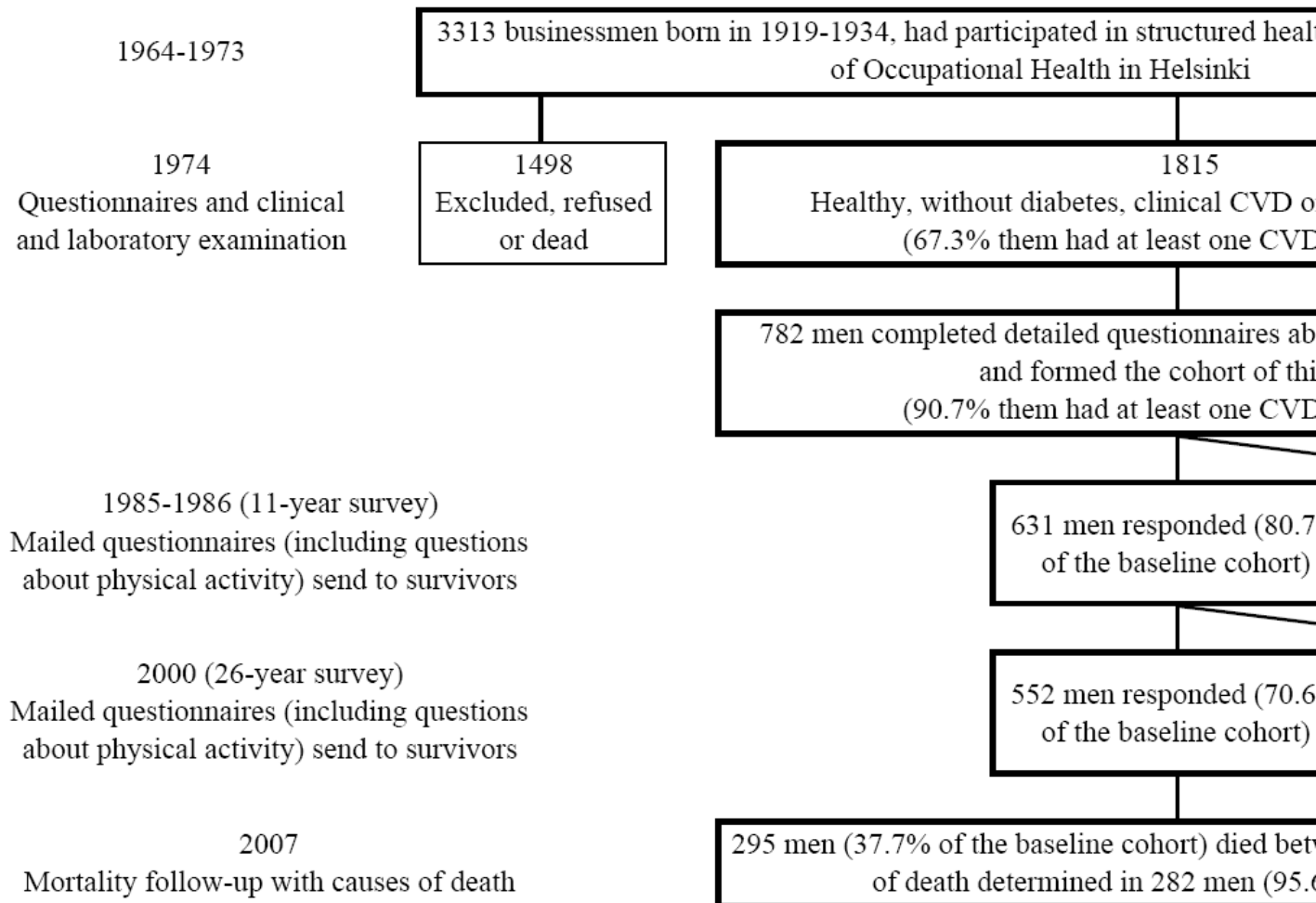
	Hazard ratio with 95% CI*		
	Low physical activity in 1974, n=148	Moderate physical activity in 1974, n=398	High physical activity in 1974, n=236
Model A+	1.52 (1.10, 2.11)	1.21 (0.92, 1.59)	1.0 (referent)
Model B**	1.68 (1.18, 2.39)	1.26 (0.93, 1.69)	1.0
Model C++	1.64 (1.15-2.34)	1.22 (0.90-1.64)	1.0

*Hazard ratio was calculated using the Cox proportional hazards model. CI denotes confidence interval.

+Model A: adjusted for age.

**Model B: adjusted for Keys' risk index, perceived health, and perceived physical fitness in 1974.

++Model C: adjusted as in B plus log triglycerides and log one-hour glucose in 1974



*Hypertension, dyslipidemia, overweight, glucose intolerance or smoking

