BMJ open

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Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2011-000279
Article Type:	Research
Date Submitted by the Author:	29-Jul-2011
Complete List of Authors:	Holtermann, Andreas Mortensen, Ole Søgaard, Karen Gyntelberg, Finn Suadicani, Poul
Primary Subject Heading:	Occupational & environmental medicine
Keywords:	Ischaemic heart disease < CARDIOLOGY, EPIDEMIOLOGY, OCCUPATIONAL & INDUSTRIAL MEDICINE

Risk factors for ischaemic heart disease mortality among men with different occupational physical demands. A 30-year prospective cohort study

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Keywords: Cardiovascular health; occupational health; cardiorespiratory fitness; physical activity

Word count: 2597

ABSTRACT

Objectives Men with high physical work demands have elevated cardiovascular strain. Theoretically, the impact of risk factors for ischaemic heart disease (IHD) may thus depend on physical work demands. We investigate if established hazards for IHD impose different risk for IHD mortality depending on level of occupational physical activity.

Design Prospective 30-year follow-up in the Copenhagen Male Study of 5,249 gainfully employed men aged 40-59 years; 311 men with cardiovascular disease/diabetes were excluded. Physical fitness was recorded using the Åstrand cycling test, and information on physical work demands obtained from the questionnaire.

Results 579 men (11.8%) died due to IHD and 2,628 (53.7%) from all-cause mortality. Similarities and differences in risk predictors between men with low (n=1,219), medium (n=2,636), and high (n=846) physical work demands were found. After control for potential confounders, high physical fitness conferred a reduced risk of IHD mortality among men with high physical work demands only (HR:0.48,CI95%:0.24-0.96), a moderate or high level of leisure time physical activity was associated with a reduced risk of IHD mortality among men with moderate and high physical work demands only. High systolic blood pressure and smoking were risk factors in all groups. Similar, but less pronounced differences in risk factors for all-cause mortality between groups were found.

Conclusion Risk factors for IHD and all-cause mortality are not identical for men with different physical work demands. Preventive initiatives for IHD ought to be tailored to the physical work demands.

ARTICLE SUMMARY

Article focus

- Men with high physical work demands have elevated cardiovascular strain and risk for ischaemic heart disease (IHD)
- Unknown if established hazards for IHD impose different risk for IHD mortality depending on level of occupational physical activity

Key messages

- Risk factors for IHD and all-cause mortality are not identical for men with different physical work demands
- Low physical fitness and leisure time physical activity particularly increase the risk for IHD mortality among men with high physical work demands
- Preventive initiatives for IHD ought not to be general, but tailored to the physical work demands of employees

Strengths and limitations

Study strengths are the 30-years follow-up on objective outcomes, inclusion of several objectively measured risk factors for IHD and mortality, and exclusion of workers with pre-existing cardiovascular disease at baseline. Study limitations are that physical work demands was based on self-assessment, and lacking repeated measures of exposure during the relatively long follow-up period

INTRODUCTION

Cardiovascular diseases are among the leading cause of death worldwide and account for about 30% of all deaths.[1] Occupational factors may be responsible for up to about 20% of all ischaemic heart disease (IHD) incidents.[2] Exposure to high physical work demands is an independent risk factor for IHD mortality and carotid arterial atherosclerosis.[3-5]

Physiologically, dynamic or static occupational physical activity several hours per day may induce a prolonged intravascular turbulence and increased wall shear stress,[6] inducing inflammatory processes in the arterial walls that may potentially lead to atherosclerosis.[5] These acute adverse effects of occupational physical activity may be modified by leisure time physical activity known to promote cardio-respiratory physical fitness [7] and reduce heart rate and blood pressure during daily activities.[8] A higher cardio-respiratory physical fitness and lower heart rate provides a longer period in the diastolic phase of the cardiac circle, causing better myocardium perfusion and a favourable intravascular turbulence and wall shear stress, reducing risk for inflammation and atherosclerosis.[5, 6] Previous results from the Copenhagen Male Study support this rationale [4] showing that high physical work demands confer an increased risk of IHD mortality among men with a low physical fitness, but not among men with high physical fitness.

The theoretical implication is that those exposed to high physical demands and cardiovascular strain at work might be particularly vulnerable when exposed to other established risk factors for IHD mortality like smoking, high blood pressure and low leisure time physical activity. Therefore, these risk factors for IHD and all-cause mortality may impose a divergent impact on people with different physical activity levels at work. This hypothesis has not previously been addressed in the scientific medical literature although, if supported, it may have important public health implications and be relevant in an occupational health context.

MATERIALS AND METHODS

Study design and population

The Copenhagen Male Study was established in 1970–1971. At 14 companies in Copenhagen, covering the railway, public road construction, military, post, telephone, customs, national bank, and the medical industry, all men aged 40–59 years were invited; 5,249 men, 87% of potential participants, agreed to participate.[9, 10]

The examination consisted of a questionnaire, a short interview, and a clinical examination including measurements of height, weight and blood pressure, and measurement of cardiorespiratory (physical) fitness following a bicycle ergometer test. Indirect measurement of physical fitness (VO_2Max) was performed with a bicycle ergometer. Thirty-five men with orthopaedic problems unable to perform the bicycle test were excluded from the study.

From the questionnaire, information about working conditions including perceived psychosocial pressure during work, lifestyle, and general health, including history of myocardial infarction, angina pectoris, and intermittent claudication was obtained. The information given in the questionnaire was clarified with each subject in the ensuing interview by one of the authors (FG). Details on the questionnaire have already been published [11] and are elaborated in more detail below.

Weekly work hours

Participants reported their weekly number of work hours in categories: 1) < 30, 2) 30-35, 3) 36-40, 4) 41-45, and 5) > 45. The distributions of answers in these groups were: 0.2%, 0.6%, 12.1%, 68.6%, and 18.6%, respectively, among men eligible for study. Due to the small number of men working less than 36 hours/week, the first three groups were pooled.

Markers of psychosocial pressure at work and leisure

"Are you under psychological pressure when performing your work?" Answer options were: "rarely" and "regularly".

"Do you take sedatives or sleep medicine?" Answer options were: "rarely", "regularly" and "never".

"Are you under psychological pressure in your leisure time?" Answer options were: "rarely" and "regularly".

Physical fitness

Heart rate was measured during submaximal bicycle work in a steady state with the aid of a stopwatch and stethoscope. The loads used were 100, 150 and 200 W. One, two or in a few cases three different loads were used. The load chosen in each case was based on weight and age of the person or heart rate during the first minute of the test, and the estimation of VO_2Max was accomplished with the aid of Åstrand's nomogram.[12] The correlation between directly and indirectly measured VO_2Max is high. The method used has previously been described in detail.[9]

Physical activity in leisure time

Which description most precisely covers your pattern of physical activity in leisure time?

1. You are mainly sedentary *e.g.* you read, watch television, go to the pictures. In general you spend most of your leisure time performing sedentary tasks.
2. You go for a walk, use your bicycle a little or perform activity for at least 4 hours/week. e.g. light gardening, leisure-time building activity, table tennis and bowling.
3. You are an active athlete, run, play tennis or badminton for at least 3 hours/week. If you frequently perform heavy gardening, you also belong to this group.

4. You take part in competitive sports, swim, play European football, handball or run long distances regularly i.e. several times/week.

In the analyses group 1 is referred to as Low and group 2 as Moderate; since only 0.4% belonged to group 4, groups 3 and 4 were pooled and are referred to as High.

Lifestyle factors

Smoking

The men reported if they smoked currently, previously or had never smoked.

Alcohol

Participants reported their daily average alcohol consumption as the number of alcoholic beverages consumed per day in categories: 0, 1-2, 3-5, 6-10, and > 10.

Clinical and health related factors

Body Mass Index (BMI)

Based on height and weight measurements BMI was calculated as kg/m^2.

Blood pressure

Measurements of blood pressure were carried out with the subject seated and after at least 5 min rest. A 12-cm wide, 26-cm-long cuff was firmly and evenly applied to the subject's right upper arm with the lower edge of the cuff placed 2 cm antecubitally. Diastolic blood pressure was recorded at the point where the Korotkoff sounds disappeared (phase 5).

Hypertension treatment

The participants were asked if they received treatment due to hypertension from their physician or elsewhere. Answer options were yes and no.

Diabetes treatment

The participants were asked if they received treatment due to diabetes mellitus from their physician or elsewhere. Whether their diabetes was type 1 or 2 was not recorded, and neither was their actual medication. Answer options were yes and no.

Social class

The men were divided into five social classes according to a system originally elaborated by Svalastoga, later adjusted by Hansen.[13, 14] This classification system is based on education level, and job position in terms of number of subordinates. Typical jobs in the study cohort were, in social class I: officer, civil engineer, office executive, head of department; social class II: head clerk, engineer; social class III: engine driver, train guard; social class IV: machine fitter in a telephone company; social class V: unskilled laborer, mechanic, driver.

Eligibility

In addition to the 35 men unable to carry out the bicycle test, men with a history of myocardial infarction (n=74), angina pectoris (n=165) or intermittent claudication (n=105) and 37 men receiving treatment due to diabetes were excluded from the prospective study. In total this latter group comprised 311 men and 9 men with missing answers leaving 4,906 men for the incidence study. With respect to all variables included, missing values ranged from 0 to 2.7%.

End-points

Information on death diagnoses within the period 1970-71 to end of 2001 was obtained from official national registers. The ischaemic heart disease mortality diagnoses used encompassed ICD-8 codes : 410-14, and (from 1994) ICD-10: I20-I25.

Statistical analyses

Basic statistical analyses, including Chi-squared analysis (likelihood ratio), unpaired (Student's) t test, and regression analyses, were performed. Relative risks were estimated by exp(β), where β is the

hazard coefficient for the variable of interest in a Cox's proportional hazards regression model with the maximum likelihood ratio method. Assumptions regarding the use of Cox's proportional hazards were met by inspection of the log minus log function at the covariate mean. A two-sided probability value of $p \leq 0.05$ was a priori taken as significant.

RESULTS

In the eligible study population of male employees who had completed the ergometer test and were without a history of myocardial infarction, angina pectoris, intermittent claudication or diabetes, 579 died (11.8%) from IHD during the period 1970/1971 to 2001. During the same period, 2,628 (53.7%) died in total.

Table 1 shows the association between lifestyle and other potential predictors with risk of IHD mortality including the entire population eligible for study. Hazard ratios (95%CI) are presented for each factor following different adjustment criteria: control for age only, age plus lifestyle, age plus clinical factors, and, finally, a model including all available potential risk factors/confounders. In the final model controlling for all factors, significant risk factors of IHD mortality were age, smoking, low leisure time physical activity, high systolic and diastolic blood pressure, and low social class.

Table 2 presents the results of a similar analysis including only men with low physical work demands. In the final, fully adjusted model, significant associations with risk of IHD mortality were found for age, alcohol consumption - with a lower risk among those consuming 1-2 beverages, systolic and diastolic blood pressure. Never smokers had half the risk of IHD mortality compared to current smokers, HR = 0.51(0.25-1.02).

Table 3 presents the association between lifestyle and other potential predictors and risk for IHD mortality among men with moderate physical work demands. In the final model, significant positive associations with risk of IHD mortality were found for age, smoking, low leisure time physical activity, high systolic blood pressure, and low social class. Surprisingly, perceived psychological pressure at work conferred a lower risk of IHD mortality.

Table 4 shows the association between lifestyle and other potential predictors and risk for IHD mortality among men with high physical work demands. In the final model, significant positive associations with risk of IHD mortality were found for age, smoking, low leisure time physical activity, high systolic blood pressure and low physical fitness.

Among the total eligible study population, significant multi-adjusted (i.e. age, lifestyle, clinical factors, psychosocial stress at work and leisure, number of work hours, and social class) positive associations with risk of all-cause mortality were found for smoking, alcohol consumption, low leisure time physical activity, high systolic and diastolic blood pressure, low physical fitness, and low social class (data on all-cause mortality not shown). An inverse multi-adjusted association was found for number of weekly work hours and all-cause mortality. Among males with low physical work demands, multi-adjusted significant positive associations with risk of all-cause mortality were found for age, smoking, low leisure time physical activity, high systolic and diastolic blood pressure, and low social class. Among males with moderate physical work demands, significant multi-adjusted positive associations with risk of all-cause mortality were found for age, smoking, alcohol consumption, low leisure time physical activity, high systolic blood pressure, and low physical fitness. Among males with high physical work demands, significant multi-adjusted positive associations with risk of all-cause mortality were found for age, smoking, alcohol consumption, high diastolic blood pressure, low physical fitness, and low social class.

COMMENTS

The findings of this study support the hypothesis that risk factors for IHD and all-cause mortality have a divergent impact on people with different physical activity levels at work. However, the well-established risk factors smoking and high blood pressure were strongly associated with IHD mortality risk whether physical work demands were low, moderate, or high. With respect to alcohol consumption, we confirmed the well-known U- or J-shaped relationship with cardiovascular mortality risk,[15] with a lower risk among those with a moderate daily consumption. This relationship was consistent among those with low and moderate physical work demands, but absent among the group with the highest physical work demands.

Surprisingly, among men with moderate physical work demands, but not among others, those who reported exposure to regular psychological work pressure had a lower risk of IHD mortality than those who did not. This lower risk could not be attributed to underlying risk factor characteristics of men with and without perceived psychological work pressure. A biologically plausible explanation for this observation will be speculative.

Low physical activity in leisure time was a statistically significant risk factor among those with a moderate or high level of physical work demands. Among those with low physical work demands, the association was weaker and did not reach statistical significance. Only among men with high physical work demands, those with highest level of physical fitness had a significantly lower risk of IHD mortality compared to those with a low fitness level.

Physical fitness is a well established predictor of cardiovascular disease and mortality.[7, 16-18] In our study, considerable differences were found between men with different occupational physical demands in the predictive role of physical fitness for both IHD and all-cause mortality (data not shown). High physical fitness was found to reduce the risk for IHD mortality among men with high

physical work demands with as much as 52%, but only modestly (22%) and non-significantly (9%) among men with low and moderate physical work demands, respectively. Among men with moderate physical work demands, a high physical fitness was though associated with reduced all-cause mortality risk (38%). These findings add further support to our previous observation that men with high physical work demands and high physical fitness do not have an increased risk of IHD mortality in contrast to men with high physical work demands and low physical fitness.[4]

Also the inverse association between leisure time physical activity and risk of IHD mortality was most pronounced among men with moderate and high occupational physical activity. High or medium leisure time physical activity reduced the risk of IHD mortality among men with moderate and high occupational physical demands, with 63% and 44%, respectively. These findings indicate that it is particularly important to be physically active during leisure time when having moderate or high occupational physical activity for preventing IHD mortality.[3] The particular importance of leisure time physical activity and high physical fitness among men with high physical work demands may be because it will lower heart rate during daily activities and therefore improving myocardium perfusion, intravascular turbulence and wall shear stress among these workers with high cardiovascular strain several hours per day.

A methodological aspect of this study is that the information regarding physical work demands was based on self-assessment, which invariably entails some degree of misclassification.[19] However, no technical equipment for measuring daily physical activity at work and in leisure was available in 1970, at least not in Denmark. In addition, the lack of continuous exposure data and repeated measures of exposure during the relatively long follow-up period may have contributed to misclassification of exposure. The study population of the Copenhagen Male Study is urban Danish male workers between 40-59 years of age in 1970-1971. It is unknown whether the findings of this study are relevant also for females, younger workers, self-employed or workers from other (e.g. rural) com-

munities and nationalities. Moreover, the workers with pre-existing cardiovascular disease were excluded from this study.

In conclusion, risk factors for IHD and all-cause mortality are not identical for men with different physical work demands. Low physical fitness and low leisure time physical activity was observed to only increase the risk for IHD mortality among men with high physical work demands. Preventive initiatives for IHD ought to be tailored to the physical work demands.

Table 1. All men eligible for the incidence study. Lifestyle and other predictors of IHD mortality (n = 579, 11.8%) during the 30-year follow-up 1970/71 to 2001. Statistically significant results are highlighted (bold).

	Cumulative incidence, %	Hazard Ratio[c]	Hazard Ratio[d]	Hazard Ratio[e]	Hazard Ratio[f]
Age					
Youngest half (max 48 y), n=2,436	7.6%	na	1[a]	1[a]	1[a]
Oldest half (> 48 y), n=2,470	16.0%		**2.72(2.27-3.26)**	**2.33(1.95-2.79)**	**2.42(2.01-2.92)**
Smoking					
Current, n=3,522	12.7%	1[a]	1[a]	1[a]	1[a]
Previous, n=937	9.9%	**0.66(0.53-0.82)**	**0.68(0.54-0.86)**	**0.57(0.45-0.71)**	**0.60(0.47-0.75)**
Never, n=446	9.0%	**0.59(0.43-0.81)**	**0.63(0.44-0.86)**	**0.50(0.36-0.69)**	**0.51(0.36-0.71)**
Alcohol, beverages/d					
0, n=1,658	12.6%	1[a]	1[a]	1[a]	1[a]
1-2, n=2,315	10.6%	0.84(0.70-1.01)	**0.82(0.68-0.99)**	**0.84(0.69-1.00)**	0.84(0.69-1.02)
3-5, n=764	13.1%	1.18(0.93-1.49)	1.06(0.83-1.36)	1.07(0.84-1.36)	0.87(0.68-1.13)
6 +, n=151	16.6%	1.97(1.30-2.99)	1.73(1.13-2.65)	1.63(1.06-2.50)	1.14(0.73-1.77)
Leisure time physical activity					
Low, n=798	15.4%	1[a]	1[a]	1[a]	1[a]
Medium, n=3,478	11.3%	**0.68(0.56-0.84)**	**0.71(0.58-0.87)**	**0.70(0.57-0.86)**	**0.73(0.59-0.89)**
High, n=498	8.1%	**0.51(0.35-0.73)**	**0.54(0.38-0.78)**	**0.57(0.40-0.82)**	**0.62(0.43-0.90)**
BMI					
- 25, n=2,358	10.1%	1[a]	1[a]	1[a]	1[a]
> 25 – 28, n=1,710	11.9%	1.11(0.92-1.34)	1.14(0.94-1.38)	0.97(0.80-1.18)	0.96(0.79-1.56)
> 28, n=829	16.7%	**1.66(1.34-2.04)**	**1.67(1.34-2.08)**	**1.25(1.0-1.56)**	1.23(0.97-1.56)
Systolic BP, mm Hg					
- 120, n=1,383	6.4%	1[a]	1[a]	1[a]	1[a]
> 120 – 150, n=2,869	12.6%	**2.01(1.59-2.53)**	**2.09(1.65-2.66)**	**1.65(1.29-2.11)**	**1.80(1.40-2.34)**
> 150, n=650	20.2%	**3.32(2.52-4.36)**	**3.54(2.67-4.70)**	**2.02(1.44-2.85)**	**2.42(1.72-3.41)**
Diastolic BP mm Hg					
- 75, n=1,421	8.3%	1[a]	1[a]	1[a]	1[a]
>75-90, n=2,736	11.4%	**1.38(1.11-1.70)**	**1.48(1.19-1.84)**	1.16(0.93-1.45)	1.12(0.89-1.42)
> 90, n=745	20.0%	**2.79(2.12-3.44)**	**2.91(2.26-3.75)**	**1.66(1.21-2.27)**	**1.74(1.27-2.37)**
Hypertension[b]					
No, n=4,826	11.6%	1[a]	1[a]	1[a]	1[a]
Yes, n=77	27.3%	**2.41(1.56-3.73)**	**2.36(1.52-3.66)**	1.38(0.87-2.17)	1.46(0.92-2.30)
Physical fitness (VO_2Max)					
15-26, n=882	16.7%	1[a]	1[a]	1[a]	1[a]
27-38, n=3,017	11.5%	**0.74(0.61-0.90)**	**0.76(0.62-0.93)**	0.88(0.71-1.07)	0.88(0.71-1.08)
39-78, n=1,007	8.5%	**0.56(0.43-0.73)**	**0.60(0.45-0.80)**	0.77(0.57-1.02)	0.78(0.58-1.05)
Psychological pressure at work					
No, n=3,834	12.2%	1[a]	1[a]	1[a]	1[a]
Yes, n=1,060	10.5%	0.86(0.70-1.05)	0.86(0.70-1.07)	0.84(0.68-1.04)	0.88(0.70-1.10)
Psychological pressure at leisure					
No, n=4,556	11.8%	1[a]	1[a]	1[a]	1[a]
Yes, n=332	12.7%	1.11(0.81-1.53)	1.04(0.75-1.44)	1.17(0.85-1.60)	1.14(0.81-1.61)
Work hours/week					
< 40, n=628	8.3%	1[a]	1[a]	1[a]	1[a]
40-45, n=3,366	12.9%	**1.62(1.22-2.16)**	**1.57(1.17-2.10)**	**1.57(1.17-2.09)**	1.25(0.92-1.69)
> 45, n=911	10.2%	1.28(0.91-1.79)	1.33(0.94-1.88)	1.26(0.89-1.77)	1.12(0.79-1.59)
Social class					
High (I,II,III), n=2,196	9.1%	1[a]	1[a]	1[a]	1[a]
Low (IV,V), n=2,688	14.0%	**1.72(1.45-2.05)**	**1.61(1.35-1.93)**	**1.72(1.45-2.05)**	**1.48(1.22-1.79)**

[a]: reference category
[b]: receives doctor's treatment due to hypertension
[c]: adjusted for age; [d]: adjusted for age + lifestyle (smoking, LTPA, alcohol); [e]: adjusted for age + clinical factors (BMI, blood pressure including treatment for, physical fitness); [f]: age + all other confounders/risk factors (lifestyle, clinical factors, psychosocial stress at work and leisure, number of work hours, and social class
na: not applicable

Table 2. ***Men with low physical work demands only, n= 1,219.*** **Lifestyle and other predictors of IHD mortality (n = 118, 9.7%) during the 30-year follow-up 1970/71 to 2001. Statistically significant results are highlighted (bold).**

	Cumulative incidence, %	Hazard Ratio[c]	Hazard Ratio[d]	Hazard Ratio[e]	Hazard Ratio[f]
Age					
Youngest half (max 48 y), n=602	7.5%	na	1[a]	1[a]	1[a]
Oldest half (> 48 y), n=617	11.9%		**1.90(1.31-2.76)**	**1.72(1.17-2.52)**	**1.75(1.19-2.58)**
Smoking					
Current, n=808	9.5%	1[a]	1[a]	1[a]	1[a]
Previous, n=275	11.7%	1.12(0.74-1.69)	1.07(0.71-1.62)	1.03(0.68-1.56)	0.96(0.63-1.47)
Never, n=135	7.4%	0.67(0.35-1.30)	0.58(0.30-1.14)	0.56(0.29-1.10)	0.51(0.25-1.02)
Alcohol, beverages/d					
0, n=478	12.0%	1[a]	1[a]	1[a]	1[a]
1-2, n=617	7.5%	**0.59(0.40-0.88)**	**0.58(0.40-0.86)**	**0.56(0.38-0.83)**	**0.59(0.40-0.88)**
3-5, n=110	13.6%	1.26(0.72-2.23)	1.15(0.65-2.05)	1.08(0.60-1.91)	1.04(0.57-1.89)
6 +, n=12	0%	na	na	na	na
Leisure time physical activity					
Low, n=227	12.8%	1[a]	1[a]	1[a]	1[a]
Medium, n=859	8.9%	0.66(0.43-1.02)	**0.65(0.42-1.0)**	0.74(0.48-1.15)	0.74(0.47-1.15)
High, n=130	10.0%	0.74(0.38-1.42)	0.70(0.36-1.35)	0.86(0.44-1.68)	0.76(0.38-1.53)
BMI					
- 25, n=690	8.2%	1[a]	1[a]	1[a]	1[a]
> 25 – 28, n=381	10.3%	1.25(0.83-1.89)	1.30(0.86-1.96)	0.99(0.65-1.52)	1.04(0.68-1.60)
> 28, n=146	15.8%	**1.93(1.19-3.15)**	**1.79(1.09-2.92)**	1.35(0.81-2.26)	1.17(0.69-1.98)
Systolic BP, mm Hg					
- 120, n=337	4.5%	1[a]	1[a]	1[a]	1[a]
> 120 – 150, n=720	10.4%	**2.62(1.50-4.56)**	**2.46(1.41-4.29)**	**1.90(1.07-3.39)**	1.62(0.89-2.95)
> 150, n=160	17.5%	**4.50(2.38-8.49)**	**4.55(2.41-8.60)**	1.80(0.81-4.02)	**2.34(1.10-4.99)**
Diastolic BP mm Hg					
- 75, n=338	4.5%	1[a]	1[a]	1[a]	1[a]
>75-90, n=680	9.9%	**2.42(1.38-4.24)**	**2.43(1.39-4.27)**	**2.04(1.15-3.64)**	**1.94(1.07-3.53)**
> 90, n=199	18.2%	**5.03(2.75-9.20)**	**4.90(2.67-9.0)**	**2.93(1.40-6.12)**	**3.21(1.56-6.60)**
Hypertension[b]					
No, n=1196	9.5%	1[a]	1[a]	1[a]	1[a]
Yes, n=23	21.7%	1.85(0.75-4.56)	2.28(0.91-5.66)	0.92(0.36-2.33)	1.20(0.46-3.12)
Physical fitness (VO_2Max)					
15-26, n=238	13.9%	1[a]	1[a]	1[a]	1[a]
27-38, n=749	8.7%	**0.65(0.42-0.99)**	0.67(0.44-1.03)	0.81(0.52-1.26)	0.82(0.53-1.27)
39-78, n=232	8.7%	0.68(0.38-1.19)	0.70(0.39-1.25)	0.98(0.54-1.78)	0.91(0.49-1.66)
Psychological pressure at work					
No, n=830	9.6%	1[a]	1[a]	1[a]	1[a]
Yes, n=386	10.2%	1.15(0.79-1.70)	1.11(0.76-1.64)	1.10(0.74-1.61)	1.02(0.68-1.55)
Psychological pressure at leisure					
No, n=1,107	9.6%	1[a]	1[a]	1[a]	1[a]
Yes, n=109	11.1%	1.18(0.65-2.15)	1.09(0.59-2.01)	1.34(0.73-2.45)	1.35(0.71-2.58)
Work hours/week					
< 40, n=209	8.1%	1[a]	1[a]	1[a]	1[a]
40-45, n=738	10.9%	1.35(0.80-2.29)	1.31(0.78-2.23)	1.26(0.74-2.13)	1.11(0.65-1.90)
> 45, n=272	7.7%	0.95(0.50-1.80)	0.93(0.48-1.77)	0.98(0.51-1.86)	0.84(0.43-1.63)
Social class					
High (I,II,III), n=946	8.5%	1[a]	1[a]	1[a]	1[a]
Low (IV,V), n=260	13.8%	**1.69(1.14-2.51)**	**1.61(1.08-2.41)**	**1.69(1.13-2.53)**	1.45(0.96-2.20)

[a]: reference category
[b]: receives doctor's treatment due to hypertension
[c]: adjusted for age; [d]: adjusted for age + lifestyle (smoking, LTPA, alcohol); [e]: adjusted for age + clinical factors (BMI, blood pressure including treatment for, physical fitness); [f]: age + all other confounders/risk factors (lifestyle, clinical factors, psychosocial stress at work and leisure, number of work hours, and social class
na: not applicable

Table 3. ***Men with moderate physical work demands only, n= 2,636.*** **Lifestyle and other predictors of IHD mortality (n = 312, 11.8%) during the 30-year follow-up 1970/71 to 2001. Statistically significant results are highlighted (bold).**

	Cumulative incidence, %	Hazard Ratio[c]	Hazard Ratio[d]	Hazard Ratio[e]	Hazard Ratio[f]
Age					
Youngest half (max 48 y), n=1,316	7.2%	na	1[a]	1[a]	1[a]
Oldest half (> 48 y), n=1,320	16.6%		**2.98(2.33-3.81)**	**2.69(2.10-3.45)**	**2.74(2.13-3.52)**
Smoking					
Current, n=1,901	13.0%	1[a]	1[a]	1[a]	1[a]
Previous, n=502	8.8%	**0.57(0.41-0.78)**	**0.59(0.43-0.82)**	**0.47(0.34-0.65)**	**0.52(0.38-0.73)**
Never, n=233	9.0%	**0.57(0.37-0.89)**	**0.60(0.39-0.95)**	**0.52(0.33-0.81)**	**0.53(0.33-0.83)**
Alcohol, beverages/d					
0, n=898	13.1%	1[a]	1[a]	1[a]	1[a]
1-2, n=1,250	10.7%	0.82(0.64-1.05)	0.83(0.64-1.06)	0.83(0.64-1.06)	0.84(0.65-1.09)
3-5, n=404	11.7%	1.00(0.71-1.41)	0.95(0.68-1.34)	0.93(0.66-1.31)	0.82(0.58-1.17)
6 +, n=74	18.9%	2.25(1.29-3.92)	2.06(1.17-3.60)	1.85(1.03-3.32)	1.31(0.72-2.38)
Leisure time physical activity					
Low, n=409	14.9%	1[a]	1[a]	1[a]	1[a]
Medium, n=1,978	12.1%	**0.73(0.55-0.96)**	0.76(0.57-1.01)	**0.73(0.55-0.97)**	0.78(0.59-1.04)
High, n=240	4.6%	**0.29(0.15-0.55)**	**0.32(0.17-0.60)**	**0.32(0.17-0.60)**	**0.37(0.19-0.72)**
BMI					
- 25, n=1,220	10.0%	1[a]	1[a]	1[a]	1[a]
> 25 – 28, n=957	12.3%	1.13(0.87-1.45)	1.12(0.87-1.45)	1.03(0.79-1.34)	1.02(0.78-1.32)
> 28, n=454	16.1%	**1.56(1.16-2.09)**	**1.54(1.14-2.08)**	1.21(0.88-1.65)	1.19(0.86-1.65)
Systolic BP, mm Hg					
- 120, n=757	6.9%	1[a]	1[a]	1[a]	1[a]
> 120 – 150, n=1,523	12.5%	**1.77(1.30-2.41)**	**1.93(1.41-2.63)**	**1.54(1.11-2.13)**	**1.82(1.31-2.54)**
> 150, n=355	19.5%	**2.87(1.99-4.12)**	**3.27(2.26-4.73)**	**2.00(1.27-3.16)**	**2.56(1.64-4.01)**
Diastolic BP mm Hg					
- 75, n=768	8.9%	1[a]	1[a]	1[a]	1[a]
>75-90, n=1,491	11.7%	1.26(0.95-1.67)	**1.35(1.02-1.80)**	1.07(0.80-1.44)	1.01(0.75-1.37)
> 90, n=376	18.6%	**2.25(1.61-3.14)**	**2.50(1.78-3.52)**	1.42(0.92-2.20)	1.39(0.91-2.12)
Hypertension[b]					
No, n=2,592	11.6%	1[a]	1[a]	1[a]	1[a]
Yes, n=41	26.8%	**2.95(1.61-5.40)**	**2.90(1.58-5.32)**	1.74(0.92-3.32)	1.51(0.80-2.87)
Physical fitness (VO_2Max)					
15-26, n=465	16.4%	1[a]	1[a]	1[a]	1[a]
27-38, n=1,616	11.8%	0.79(0.60-1.03)	0.78(0.60-1.03)	0.89(0.67-1.18)	0.92(0.69-1.22)
39-78, n=555	8.3%	**0.56(0.39-0.82)**	**0.59(0.41-0.86)**	0.73(0.49-1.09)	0.78(0.53-1.17)
Psychological pressure at work					
No, n=2,133	12.6%	1[a]	1[a]	1[a]	1[a]
Yes, n=496	8.5%	**0.65(0.47-0.90)**	**0.70(0.48-0.93)**	**0.64(0.46-0.89)**	**0.68(0.48-0.96)**
Psychological pressure at leisure					
No, n=2,462	11.9%	1[a]	1[a]	1[a]	1[a]
Yes, n=163	11.7%	1.12(0.71-1.79)	1.14(0.72-1.83)	1.17(0.73-1.87)	1.26(0.77-2.06)
Work hours/week					
< 40, n=341	7.9%	1[a]	1[a]	1[a]	1[a]
40-45, n=1,865	13.1%	**1.71(1.14-2.54)**	**1.61(1.08-2.40)**	**1.66(1.11-2.47)**	1.31(0.87-1.96)
> 45, n=429	9.8%	1.26(0.78-2.04)	1.34(0.82-2.17)	1.25(0.77-2.06)	1.16(0.71-1.89)
Social class					
High (I,II,III), n=1,075	9.2%	1[a]	1[a]	1[a]	1[a]
Low (IV,V), n=1,554	13.7%	**1.64(1.29-2.08)**	**1.53(1.20-1.95)**	**1.62(1.27-2.07)**	**1.35(1.05-1.75)**

[a]: reference category
[b]: receives doctor's treatment due to hypertension
[c]: adjusted for age; [d]: adjusted for age + lifestyle (smoking, LTPA, alcohol); [e]: adjusted for age + clinical factors (BMI, blood pressure including treatment for, physical fitness); [f]: age + all other confounders/risk factors (lifestyle, clinical factors, psychosocial stress at work and leisure, number of work hours, and social class
na: not applicable

Table 4. ***Men with high physical work demands only, n= 846.*** **Lifestyle and other predictors of IHD mortality (n = 119, 14.1%) during the 30-year follow-up 1970/71 to 2001. Statistically significant results are highlighted (bold).**

	Cumulative incidence, %	Hazard Ratio[c]	Hazard Ratio[d]	Hazard Ratio[e]	Hazard Ratio[f]
Age					
Youngest half (max 48 y), n=420	8.6%	na	1[a]	1[a]	1[a]
Oldest half (> 48 y), n=426	19.5%		**3.16(2.12-4.71)**	**2.48(1.64-3.73)**	**2.52(1.66-3.83)**
Smoking					
Current, n=648	15.3%	1[a]	1[a]	1[a]	1[a]
Previous, n=131	9.2%	**0.46(0.25-0.84)**	**0.45(0.24-0.82)**	**0.40(0.22-0.73)**	**0.38(0.20-0.71)**
Never, n=67	11.9%	0.67(0.32-1.37)	0.71(0.34-1.46)	0.47(0.22-1.03)	0.49(0.22-1.09)
Alcohol, beverages/d					
0, n=218	12.4%	1[a]	1[a]	1[a]	1[a]
1-2, n=355	15.2%	1.23(0.78-1.96)	1.23(0.77-1.95)	1.31(0.81-2.11)	1.41(0.87-2.29)
3-5, n=208	13.0%	1.11(0.65-1.90)	1.00(0.58-1.72)	1.14(0.65-1.98)	0.95(0.53-1.67)
6 +, n=60	16.7%	**2.10(1.01-4.35)**	1.84(0.88-3.84)	2.05(0.97-4.33)	1.43(0.67-3.05)
Leisure time physical activity					
Low, n=144	20.8%	1[a]	1[a]	1[a]	1[a]
Medium, n=586	12.6%	**0.62(0.40-0.95)**	**0.59(0.38-0.90)**	**0.62(0.40-0.96)**	**0.56(0.36-0.88)**
High, n=114	13.2%	0.67(0.36-1.26)	0.64(0.34-1.21)	0.80(0.42-1.52)	0.77(0.40-1.48)
BMI					
- 25, n=351	12.8%	1[a]	1[a]	1[a]	1[a]
> 25 – 28, n=299	12.0%	0.82(0.53-1.28)	0.87(0.56-1.36)	0.66(0.42-1.05)	0.73(0.45-1.17)
> 28, n=194	18.6%	1.37(0.88-2.13)	1.34(0.84-2.12)	1.02(0.64-1.62)	1.08(0.66-1.76)
Systolic BP, mm Hg					
- 120, n=238	7.1%	1[a]	1[a]	1[a]	1[a]
> 120 – 150, n=499	15.2%	**2.02(1.19-3.42)**	**2.16(1.27-3.68)**	1.68(0.96-2.95)	**1.93(1.07-3.46)**
> 150, n=108	24.1%	**3.20(1.72-5.95)**	**3.41(1.81-6.44)**	2.13(0.97-4.66)	2.14(0.98-4.66)
Diastolic BP mm Hg					
- 75, n=253	11.5%	1[a]	1[a]	1[a]	1[a]
>75-90, n=455	12.5%	1.05(0.67-1.64)	1.05(0.67-1.66)	0.90(0.55-1.46)	0.79(0.47-1.30)
> 90, n=137	24.1%	**2.18(1.32-3.60)**	**2.53(1.51-4.23)**	1.43(0.73-2.78)	1.60(0.83-3.09)
Hypertension[b]					
No, n=834	13.8%	1[a]	1[a]	1[a]	1[a]
Yes, n=12	33.3%	2.32(0.85-6.30)	2.12(0.76-5.90)	1.80(0.64-5.13)	1.82(0.62-5.34)
Physical fitness (VO_2Max)					
15-26, n=125	23.2%	1[a]	1[a]	1[a]	1[a]
27-38, n=531	13.9%	**0.65(0.42-1.00)**	**0.63(0.40-0.99)**	0.73(0.46-1.16)	0.70(0.43-1.13)
39-78, n=190	8.4%	0.41(0.22-0.76)	0.39(0.21-0.74)	0.54(0.27-1.06)	**0.48(0.24-0.96)**
Psychological pressure at work					
No, n=708	13.8%	1[a]	1[a]	1[a]	1[a]
Yes, n=136	14.7%	1.01(0.62-1.63)	1.08(0.66-1.76)	0.98(0.60-1.60)	1.04(0.61-1.78)
Psychological pressure at leisure					
No, n=795	14.0%	1[a]	1[a]	1[a]	1[a]
Yes, n=47	17.0%	1.11(0.54-2.27)	1.15(0.56-2.37)	1.04(0.50-2.14)	1.09(0.51-2.30)
Work hours/week					
< 40, n=51	9.8%	1[a]	1[a]	1[a]	1[a]
40-45, n=618	14.6%	1.50(0.61-3.70)	1.68(0.68-4.19)	1.47(0.60-3.63)	1.54(0.62-3.85)
> 45, n=177	13.6%	1.49(0.57-3.89)	1.81(0.68-4.86)	1.38(0.52-3.64)	1.58(0.70-3.18)
Social class					
High (I,II,III), n=74	10.8%	1[a]	1[a]	1[a]	1[a]
Low (IV,V), n=771	14.3%	1.47(0.72-3.01)	1.43(0.69-2.96)	1.55(0.75-3.18)	1.49(0.70-3.18)

[a]: reference category
[b]: receives doctor's treatment due to hypertension
[c]: adjusted for age; [d]: adjusted for age + lifestyle (smoking, LTPA, alcohol); [e]: adjusted for age + clinical factors (BMI, blood pressure including treatment for, physical fitness); [f]: age + all other confounders/risk factors (lifestyle, clinical factors, psychosocial stress at work and leisure, number of work hours, and social class
na: not applicable

CONTRIBUTORS All authors contributed to the conception, design, interpretation of data, and writing or critically revising the manuscript. PS made the statistical analyses. AH and PS are guarantors.

ACKNOWLEDGEMENT The King Christian X's Foundation, The Danish Medical Research Council, The Danish Heart Foundation, and The Else & Mogens Wedell-Wedellsborg Foundation.

CONFLICTS OF INTEREST None

COMPETING INTEREST STATEMENT None. All authors declare that the answer to the questions on your competing interest form Exclusive licence (http://bmj.com/cgi/content/full/317/7154/291/DC1) are all No and therefore have nothing to declare.

FUNDING The study is a part of the Physical work demands and fitness project, financed by the Danish Working Environment Research Foundation.

ETHICAL APPROVAL When the Copenhagen Male Study (CMS) was initiated as a closed cohort study in 1970-71 no ethics committee for medical research had been established in Denmark. However, in 1985-86, when survivors from the first baseline were re-examined, the study was approved by the ethics committee for medical research in the county of Copenhagen, and all participants in the study gave informed consent to participate, as stated in many previous publications from the CMS based on analyses using the 1985-86 baseline.

ORIGINALE STUDY PROTOCOL It does not exist

DATA SHARING STATEMENT Technical appendix and statistical code available from the corresponding author at aho@nrcwe.dk. Consent was not obtained, but the presented data are anonymised and risk of identification is very low. No additional data available.

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	Page 1
		Page 2
Introduction		
Background/rationale	2	Page 3
Objectives	3	Page 3
Methods		
Study design	4	Page 4 and 7
Setting	5	Page 4
Participants	6	Page 4
Variables	7	Page 4, 5 and 6
Data sources/ measurement	8	Page 4, 5 and 6
Bias	9	Page 7
Study size	10	Page 4 and 7
Quantitative variables	11	Page 4, 5 and 6
Statistical methods	12	Page 7
		Page 7
		Page 7
		Page 7
		Page 7
Results		
Participants	13	Page 8
		Page 8
Descriptive data	14	Page 8
		Page 8
		Page 8
Outcome data	15	Page 8 and table 1-5
Main results	16	Table 1-5
		Page 8 and 9
		Table 1-5
Other analyses	17	No other analyses were done
Discussion		
Key results	18	Page 9
Limitations	19	Page 11
Interpretation	20	Page 10 and 11
Generalisability	21	Page 10 and 11
Other information		
Funding	22	Page 19

BMJ open

Risk factors for ischaemic heart disease mortality among men with different occupational physical demands. A 30-year prospective cohort study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2011-000279.R1
Article Type:	Research
Date Submitted by the Author:	01-Nov-2011
Complete List of Authors:	Holtermann, Andreas Mortensen, Ole Søgaard, Karen Gyntelberg, Finn Suadicani, Poul
Primary Subject Heading:	Occupational & environmental medicine
Secondary Subject Heading:	Epidemiology, Occupational & environmental medicine
Keywords:	Ischaemic heart disease < CARDIOLOGY, EPIDEMIOLOGY, OCCUPATIONAL & INDUSTRIAL MEDICINE

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Title and abstract	1	Page 1
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Introduction		
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Methods		
Study design	4	Page 4 and 7
Setting	5	Page 4
Participants	6	Page 4
Variables	7	Page 4, 5 and 6
Data sources/ measurement	8	Page 4, 5 and 6
Bias	9	Page 7
Study size	10	Page 4 and 7
Quantitative variables	11	Page 4, 5 and 6
Statistical methods	12	Page 7
		Page 7
		Page 7
		Page 7
		Page 7
Results		
Participants	13	Page 8
		Page 8
Descriptive data	14	Page 8
		Page 8
		Page 8
Outcome data	15	Page 8 and table 1-5
Main results	16	Table 1-5
		Page 8 and 9
		Table 1-5
Other analyses	17	No other analyses were done
Discussion		
Key results	18	Page 9
Limitations	19	Page 11
Interpretation	20	Page 10 and 11
Generalisability	21	Page 10 and 11
Other information		
Funding	22	Page 19

MS.ID:BMJOPEN-2011-000279

MS.TITLE: Risk factors for ischaemic heart disease mortality among men with different occupational physical demands. A 30-year prospective cohort study.

Dear Managing Editor, BMJ Open, Richard Sands

Thank you for the clear and constructive comments from the reviewers to our paper. We have revised the paper taking into account all suggestions to the extent possible. Moreover, we have modified the abstract in accordance with the new guidelines.

How we addressed the points made by the reviewers appears below. The changes performed in the manuscript are marked with MS Word "track changes".

Ad reviewer Alex Burdorf.

We would like to thank you for the positive and constructive comments, improving our paper.

Comment:

- Overall, a nice paper with some suggestions for improvements.
- I think the authors should consider an analysis with an interaction term. But..this is my preference, but may be not of the authors.

Response:

In previous papers from the Copenhagen male Study, which are referred to in the present paper, using the same baseline, cohort, and duration of follow-up, we addressed the interaction of occupational physical activity and leisure time physical activity as a predictor of IHD and all-cause mortality, and also the interaction of occupational physical activity and physical fitness (VO_2max). As described, the purpose of the present paper was to address in a much broader sense if established and potential risk factors for IHD mortality might differ between groups with different occupational physical work demands since, due to the load on the cardiovascular system induced by these demands, this may have influenced their vulnerability to risk factors. In the context of the present

paper, interaction analyses would thus be either post hoc or superfluous, so we prefer to maintain the analysis strategy we have already applied.

Comment:

1. The interesting observation that physical load and physical activity/fitness seem to interact to some extent was reported earlier, e.g. Russo OEM 2006 and a related commentary with other references. I think the authors could draw attention to the observation that PA (preventive factor) is something else than physical load (risk factor), and the current work presents some explanation for this.

Response:

We agree. This aspect is now included in the discussion section.

Comment:

2. The physical work demands are not defined in the methods with sufficient details, please present more information

Response:

This is now explicitly described in the method section

Comment:

3. The Cox regression presents HR, which may be interpreted as a proxy for RR, but the results should be presented as HR, since that is the measure of association in the analysis.

Response:

We agree with the reviewer that HR is a measure of relative risk. This is already briefly addressed in the Statistical analysis section, and in presentation of the results in the tables we present these as HR.

Comment:

4. The authors should consider a formal analysis of interaction, which could be presented in a single table, instead of the current stratification. The slight disadvantage with the current approach is that adjustment is done for the same variable but with another distribution, since essentially we have 3 different populations with different size, which may complicate the picture of relevant (i.e. not only significant) variables.

Response:

Please see our previous response to your comment concerning choice of analysis strategy.

Comment:

5. The statement that "Surprisingly, among men with moderate physical work demands, but not among others, those who reported exposure to regular psychological work pressure" may be partly due to the suggestion in remark 4.

Response:

We find it unlikely that data manipulation would contribute to answer the observation and prefer to keep the expression used.

Comment:

6. In the discussion the authors could pay attention to the distribution of men with good physical fitness cq PA over the 3 levels of physical work demands. This gives some input into the interesting results that physically demandings jobs will certainly not lead to physically healthy persons.

Response:

This important aspect is now described in the discussion section.

Comment:

7. Is there any information on change of job during the -70s and -80s, since it may very well be that a single measure in 1970 will be a good proxy for the next 20 years and, thus, the statement on misclassification on exposure could be substantiated.

Response:

Information on job title was available only from the first baseline in the cohort, i.e. 1970-71.

****

Ad reviewer Marco M Ferrario

We would like to thank you for the positive and constructive comments, improving the paper.

Comment:

The study question is not clear. Please explain it better.

Response:

We see your point. The study question and hypothesis are now clarified in the abstract and introduction sections.

Comment:

Physical fitness. Add "maximum" to "The load chosen..". In addition: are you sure of the three step levels? Are not too high?

Response:

"maximum" is now included in the sentence.

The three steps were applied in only a very few cases.

Comment:

Alcohol consumption in the weekends not given. Why?

Response:

Unfortunately, we don't have specific information about alcohol consumption during the weekends.

Comment:

Why lipid measurements are not included. Which might be the effect(s) of not having them.

Response:

Unfortunately, lipid measurements are not available at baseline. Lipids could therefore be a potential confounder/risk factor in this study. However, the direction of its effect is uncertain. This is now included as a methodological aspect in the discussion section.

Comment:

Blood pressure: only one measurement? This should be discussed base on the Results showing a strong effect of BP levels, both of systolic and diastolic BP.

Response:

We have added a brief statement in the results section addressing table 1 that despite the fact that blood pressure was measured only once, the predictive strength of systolic as well as diastolic was strong.

Comment:

I suggest to include in Table 1 in addition to the listed independent variables physical work demand, which is the stratifying variable for the following tables. I do not think it is meaningful to add models adjusting also for the independent variables.

Response:

The idea of the paper is to challenge the relative importance of a number of risk factors for IHD mortality among men with different occupational physical work demands. Thus, table 1 presents the role of these factors, when they "stand alone", *i.e.* are adjusted for age only, and in various other models taking into account factors associated with these single items. We believe that keeping the table as it is will uphold the flow of the presentation from a logical narrative point of view.

Comment:

Not clear why social class is added to the last model only, in all tables.

Response:

Social class is included in the last model only to explicitly show the independent results (after adjusting for the potential confounders) with and without adjustment for social class. This is chosen because social class may be considered an "over-adjustment", since social class is strongly associated with physical work demands.

Comment:

The worker healthy effect bias may play some role? Please add some considerations in Discussion.

Response:

Yes, the healthy worker effect may impose a significant bias of the result. This is now considered in the discussion section.

Comment:

Conclusions are too general, please be more specific.

Response:

We want to be careful with providing very specific conclusions. However, we have specified the conclusions in the abstract and discussion sections.

Risk factors for ischaemic heart disease mortality among men with different occupational physical demands. A 30-year prospective cohort study

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Keywords: Cardiovascular health; occupational health; cardiorespiratory fitness; physical activity

Word count: 2597

ABSTRACT

Objectives Men with high physical work demands have elevated cardiovascular strain, which may lead to enhanced atherosclerosis. Theoretically, the impact of risk factors for ischaemic heart disease (IHD) may thus depend on physical work demands. We investigated this hypothesis.

Design Prospective 30-year follow-up

Setting The Copenhagen Male Study

Participants 5,249 gainfully employed men aged 40-59 years; 311 men with cardiovascular disease/diabetes were excluded.

Primary and secondary outcome measures IHD and all-cause mortality

Results 579 men (11.8%) died due to IHD and 2,628 (53.7%) from all-cause mortality. Similarities and differences in risk predictors were found between men with low (n=1,219), medium (n=2,636), and high (n=846) physical work demands. After control for potential confounders, high physical fitness conferred a reduced risk of IHD mortality only among men with high physical work demands (HR:0.48,CI95%:0.24-0.96), a moderate/high level of leisure time physical activity was associated with reduced risk of IHD mortality only among men with moderate and high physical work demands. High systolic blood pressure and smoking were risk factors in all groups. Similar, but less pronounced differences in risk factors for all-cause mortality between groups were found.

Conclusion The risk factors for IHD and all-cause mortality, low physical fitness and low leisure time physical activity, are not identical for men with different physical work demands. Preventive initiatives for IHD should be tailored to the physical work demands.

ARTICLE SUMMARY

Article focus

- Men with high physical work demands have elevated cardiovascular strain and risk of ischaemic heart disease (IHD)
- Unknown if established risk factors for IHD impose divergent risk for IHD mortality among men with different levels of occupational physical activity

Key messages

- Risk factors for IHD and all-cause mortality are not identical for men with different physical work demands
- Low physical fitness and leisure time physical activity particularly increase the risk of IHD mortality among men with high physical work demands
- Preventive initiatives for IHD ought not to be general, but tailored to the physical work demands of employees

Strengths and limitations

Study strengths are the 30-years follow-up on objective outcomes, inclusion of several objectively measured risk factors for IHD and mortality, and exclusion of workers with pre-existing cardiovascular disease at baseline. Study limitations are that physical work demands was based on self-assessment, and lacking repeated measures of exposure during the relatively long follow-up period

INTRODUCTION

Cardiovascular diseases are leading causes of death worldwide and account for about 30% of all deaths.[1] Occupational factors may be responsible for up to about 20% of all ischaemic heart disease (IHD) incidents.[2] Exposure to high physical work demands is an independent risk factor for IHD mortality and carotid arterial atherosclerosis.[3-5]

Physiologically, dynamic or static occupational physical activity several hours per day may induce a prolonged intravascular turbulence and increased wall shear stress,[6] inducing inflammatory processes in the arterial walls that may potentially lead to atherosclerosis.[5] These acute adverse effects of occupational physical activity may be modified by leisure time physical activity known to promote cardio-respiratory physical fitness [7] and reduce heart rate and blood pressure during daily activities.[8] A higher cardio-respiratory physical fitness and lower heart rate provides a longer period in the diastolic phase of the cardiac circle, causing better myocardium perfusion and a favourable intravascular turbulence and wall shear stress, reducing risk for inflammation and atherosclerosis.[5, 6] Previous results from the Copenhagen Male Study support this rationale [4] showing that high physical work demands confer an increased risk of IHD mortality among men with a low physical fitness, but not among men with high physical fitness.

The theoretical implication is that those exposed to high physical demands and cardiovascular strain at work might be particularly vulnerable when exposed to other established risk factors for IHD mortality like smoking, high blood pressure and low leisure time physical activity. Therefore, these risk factors for IHD and all-cause mortality may impose a divergent impact on people with different physical activity levels at work. The hypothesis of the study is that established hazards for IHD impose a divergent risk for IHD mortality among men with different level of occupational physical activity. This hypothesis has not previously been addressed in the scientific medical literature although, if supported, it may have important public health implications and be relevant in an occupational health context.

MATERIALS AND METHODS

Study design and population

The Copenhagen Male Study was established in 1970–1971. At 14 companies in Copenhagen, covering the railway, public road construction, military, post, telephone, customs, national bank, and the medical industry, all men aged 40–59 years were invited; 5,249 men, 87% of potential participants, agreed to participate.[9, 10]

The examination consisted of a questionnaire, a short interview, and a clinical examination including measurements of height, weight and blood pressure, and measurement of cardiorespiratory (physical) fitness following a bicycle ergometer test. Indirect measurement of physical fitness (VO_2Max) was performed with a bicycle ergometer. Thirty-five men with orthopaedic problems unable to perform the bicycle test were excluded from the study.

From the questionnaire, information about working conditions including perceived psychosocial pressure during work, lifestyle, and general health, including history of myocardial infarction, angina pectoris, and intermittent claudication was obtained. The information given in the questionnaire was clarified with each subject in the ensuing interview by one of the authors (FG). Details on the questionnaire have already been published [11] and are elaborated in more detail below.

Weekly work hours

Participants reported their weekly number of work hours in categories: 1) < 30, 2) 30-35, 3) 36-40, 4) 41-45, and 5) > 45. The distributions of answers in these groups were: 0.2%, 0.6%, 12.1%, 68.6%, and 18.6%, respectively, among men eligible for study. Due to the small number of men working less than 36 hours/week, the first three groups were pooled.

Markers of psychosocial pressure at work and leisure

"Are you under psychological pressure when performing your work?" Answer options were: "rarely" and "regularly".

"Do you take sedatives or sleep medicine?" Answer options were: "rarely", "regularly" and "never".

"Are you under psychological pressure in your leisure time?" Answer options were: "rarely" and "regularly".

Physical work demands

Physical activity at work was estimated using the following questions:

Which description most precisely covers your pattern of physical activity at work?

1. You are mainly sedentary and do not walk much around at your workplace. *E.g.* desk work, work including assembling of minor parts.
2. You walk around quite a bit at your workplace but do not have to carry heavy items. *E.g.* light industrial work, non-sedentary office work, inspection and the like.
3. Most of the time you walk, and you often have to walk up stairs and lift various items. Examples include mail delivery and construction work.
4. You have heavy physical work. You carry heavy burdens and carry out physically strenuous work. *E.g.* work including digging and shoveling.

In the analyses group 1 is referred to as Low and group 2 as moderate; since only 2.4% belonged to group 4, groups 3 and 4 were pooled and are referred to as high.

In addition, the following question on physical strenuous work was used:

"Do you perform strenuous work (work resulting in sweating)?" Answer options were: "often", "occasionally" and "seldom or never", and coded as 1= seldom or never, 2= occasionally and 3= often.

In order to discriminate between men with presence or absence of physically demanding work, we constructed an additional variable based on the two described above. With respect to physical activity at work, groups were coded: low=1, moderate=2 and high=3. With respect to physical strenuous work, groups were coded: often=3, occasionally=2, and seldom or never=1. Summing up the two gave values from 2 to 6. A low combined score of 2 was defined as low physical work demands, a score of 3 or 4 was defined as moderate physical work demands, and a score of 5 or 6 was defined as high physical work demands.

Physical fitness

Heart rate was measured during submaximal bicycle work in a steady state with the aid of a stopwatch and stethoscope. The loads used were 100, 150 and 200 W. One, two or in a few cases three different loads were used. The maximum load chosen in each case was based on weight and age of the person or heart rate during the first minute of the test, and the estimation of VO_2Max was accomplished with the aid of Åstrand's nomogram.[12] The correlation between directly and indirectly measured VO_2Max is high. The method used has previously been described in detail.[9]

Physical activity in leisure time

Which description most precisely covers your pattern of physical activity in leisure time?

1. You are mainly sedentary *e.g.* you read, watch television, go to the pictures. In general you spend most of your leisure time performing sedentary tasks.
2. You go for a walk, use your bicycle a little or perform activity for at least 4 hours/week. e.g. light gardening, leisure-time building activity, table tennis and bowling.
3. You are an active athlete, run, play tennis or badminton for at least 3 hours/week. If you frequently perform heavy gardening, you also belong to this group.
4. You take part in competitive sports, swim, play European football, handball or run long distances regularly i.e. several times/week.

In the analyses group 1 is referred to as Low and group 2 as Moderate; since only 0.4% belonged to group 4, groups 3 and 4 were pooled and are referred to as High.

Lifestyle factors

Smoking

The men reported if they smoked currently, previously or had never smoked.

Alcohol

Participants reported their daily average alcohol consumption as the number of alcoholic beverages consumed per day in categories: 0, 1-2, 3-5, 6-10, and > 10.

Clinical and health related factors

Body Mass Index (BMI)

Based on height and weight measurements BMI was calculated as kg/m^2.

Blood pressure

Measurements of blood pressure were carried out with the subject seated and after at least 5 min rest. A 12-cm wide, 26-cm-long cuff was firmly and evenly applied to the subject's right upper arm with the lower edge of the cuff placed 2 cm antecubitally. Diastolic blood pressure was recorded at the point where the Korotkoff sounds disappeared (phase 5).

Hypertension treatment

The participants were asked if they received treatment due to hypertension from their physician or elsewhere. Answer options were yes and no.

Diabetes treatment

The participants were asked if they received treatment due to diabetes mellitus from their physician or elsewhere. Whether their diabetes was type 1 or 2 was not recorded, and neither was their actual medication. Answer options were yes and no.

Social class

The men were divided into five social classes according to a system originally elaborated by Svalastoga, later adjusted by Hansen.[13, 14] This classification system is based on education level, and job position in terms of number of subordinates. Typical jobs in the study cohort were, in social class I: officer, civil engineer, office executive, head of department; social class II: head clerk, engineer; social class III: engine driver, train guard; social class IV: machine fitter in a telephone company; social class V: unskilled laborer, mechanic, driver.

Eligibility

In addition to the 35 men unable to carry out the bicycle test, men with a history of myocardial infarction (n=74), angina pectoris (n=165) or intermittent claudication (n=105) and 37 men receiving treatment due to diabetes were excluded from the prospective study. In total this latter group comprised 311 men and 9 men with missing answers leaving 4,906 men for the incidence study. With respect to all variables included, missing values ranged from 0 to 2.7%.

End-points

Information on death diagnoses within the period 1970-71 to end of 2001 was obtained from official national registers. The ischaemic heart disease mortality diagnoses used encompassed ICD-8 codes : 410-14, and (from 1994) ICD-10: I20-I25.

Statistical analyses

Basic statistical analyses, including Chi-squared analysis (likelihood ratio), unpaired (Student's) t test, and regression analyses, were performed. Relative risks were estimated by exp(β), where β is the hazard coefficient for the variable of interest in a Cox's proportional hazards regression model with the maximum likelihood ratio method. Assumptions regarding the use of Cox's proportional hazards were met by inspection of the log minus log function at the covariate mean. A two-sided probability value of $p \leq 0.05$ was a priori taken as significant.

RESULTS

In the eligible study population of male employees who had completed the ergometer test and were without a history of myocardial infarction, angina pectoris, intermittent claudication or diabetes, 579 died (11.8%) from IHD during the period 1970/1971 to 2001. During the same period, 2,628 (53.7%) died in total.

Table 1 shows the association between lifestyle and other potential predictors with risk of IHD mortality including the entire population eligible for study. Hazard ratios (95%CI) are presented for each factor following different adjustment criteria: control for age only, age plus lifestyle, age plus clinical factors, and, finally, a model including all available potential risk factors/confounders. In the final model controlling for all factors, significant risk factors of IHD mortality were age, smoking, low leisure time physical activity, high systolic and diastolic blood pressure, and low social class. Despite the fact that blood pressure was measured only once, the predictive strength of systolic as well as diastolic was strong.

Table 2 presents the results of a similar analysis including only men with low physical work demands. In the final, fully adjusted model, significant associations with risk of IHD mortality were found for age, alcohol consumption - with a lower risk among those consuming 1-2 beverages, systolic and diastolic blood pressure. Never smokers had half the risk of IHD mortality compared to current smokers, HR = 0.51(0.25-1.02).

Table 3 presents the association between lifestyle and other potential predictors and risk for IHD mortality among men with moderate physical work demands. In the final model, significant positive associations with risk of IHD mortality were found for age, smoking, low leisure time physical ac-

tivity, high systolic blood pressure, and low social class. Surprisingly, perceived psychological pressure at work conferred a lower risk of IHD mortality.

Table 4 shows the association between lifestyle and other potential predictors and risk for IHD mortality among men with high physical work demands. In the final model, significant positive associations with risk of IHD mortality were found for age, smoking, low leisure time physical activity, high systolic blood pressure and low physical fitness.

Among the total eligible study population, significant multi-adjusted (i.e. age, lifestyle, clinical factors, psychosocial stress at work and leisure, number of work hours, and social class) positive associations with risk of all-cause mortality were found for smoking, alcohol consumption, low leisure time physical activity, high systolic and diastolic blood pressure, low physical fitness, and low social class (data on all-cause mortality not shown). An inverse multi-adjusted association was found for number of weekly work hours and all-cause mortality. Among males with low physical work demands, multi-adjusted significant positive associations with risk of all-cause mortality were found for age, smoking, low leisure time physical activity, high systolic and diastolic blood pressure, and low social class. Among males with moderate physical work demands, significant multi-adjusted positive associations with risk of all-cause mortality were found for age, smoking, alcohol consumption, low leisure time physical activity, high systolic blood pressure, and low physical fitness. Among males with high physical work demands, significant multi-adjusted positive associations with risk of all-cause mortality were found for age, smoking, alcohol consumption, high diastolic blood pressure, low physical fitness, and low social class.

COMMENTS

The findings of this study support the hypothesis that risk factors for IHD and all-cause mortality have a divergent impact on people with different physical activity levels at work. However, the

well-established risk factors smoking and high blood pressure were strongly associated with IHD mortality risk whether physical work demands were low, moderate, or high. With respect to alcohol consumption, we confirmed the well-known U- or J-shaped relationship with cardiovascular mortality risk,[15] with a lower risk among those with a moderate daily consumption. This relationship was consistent among those with low and moderate physical work demands, but absent among the group with the highest physical work demands.

Surprisingly, among men with moderate physical work demands, but not among others, those who reported exposure to regular psychological work pressure had a lower risk of IHD mortality than those who did not. This lower risk could not be attributed to underlying risk factor characteristics of men with and without perceived psychological work pressure. A biologically plausible explanation for this observation will be speculative.

Low physical activity in leisure time was a statistically significant risk factor among those with a moderate or high level of physical work demands. Among those with low physical work demands, the association was weaker and did not reach statistical significance. Only among men with high physical work demands, those with highest level of physical fitness had a significantly lower risk of IHD mortality compared to those with a low fitness level. This finding supports previous observations that physical work demands have may generally have the opposite effect on cardiovascular health, general health and physical function than that of leisure time physical activity. [3, 16, 17]

Physical fitness is a well established predictor of cardiovascular disease and mortality.[7, 18-20] In our study, considerable differences were found between men with different occupational physical demands in the predictive role of physical fitness for both IHD and all-cause mortality (data not shown). High physical fitness was found to reduce the risk for IHD mortality among men with high physical work demands with as much as 52%, but only modestly (22%) and non-significantly (9%)

among men with low and moderate physical work demands, respectively. Among men with moderate physical work demands, a high physical fitness was though associated with reduced all-cause mortality risk (38%). These findings add further support to our previous observation that men with high physical work demands and high physical fitness do not have an increased risk of IHD mortality in contrast to men with high physical work demands and low physical fitness.[4] The results also show that those with high physical work demands do not have a higher level of physical fitness compared to those with low physical work demands, indicating that high physical work demands do not lead to improvements in physical fitness.

Also the inverse association between leisure time physical activity and risk of IHD mortality was most pronounced among men with moderate and high occupational physical activity. High or medium leisure time physical activity reduced the risk of IHD mortality among men with moderate and high occupational physical demands, with 63% and 44%, respectively. These findings indicate that it is particularly important to be physically active during leisure time when having moderate or high occupational physical activity for preventing IHD mortality.[3] The particular importance of leisure time physical activity and high physical fitness among men with high physical work demands may be due to a lower heart rate during daily activities and a subsequent improvement of myocardial perfusion, and a lower intravascular turbulence and wall shear stress among these workers with high cardiovascular strain several hours per day.

A methodological aspect of this study is that the information regarding physical work demands was based on self-assessment, which invariably entails some degree of misclassification.[21] However, no technical equipment for measuring daily physical activity at work and in leisure was available in 1970, at least not in Denmark. In addition, the lack of continuous exposure data and repeated measures of exposure during the relatively long follow-up period may have contributed to misclassification of exposure. The study population of the Copenhagen Male Study is urban Danish male

workers between 40-59 years of age in 1970-1971. It is unknown whether the findings of this study are relevant also for females, younger workers, self-employed or workers from other (e.g. rural) communities and nationalities. The healthy worker effect may be particularly strong among the men with high physical work demands, and therefore reduced differences in risk estimates between the groups of physical work demands. Information about lipids was not available, which may have induced some confounding effect on the results. Moreover, the workers with pre-existing cardiovascular disease were excluded from this study.

In conclusion, well-established risk factors like smoking and high blood pressure were strongly associated with IHD mortality risk among all groups of physical work demands. However, other risk factors for IHD and all-cause mortality were not identical for men with different physical work demands. Low physical fitness and low leisure time physical activity was observed to only increase the risk for IHD mortality among men with high physical work demands. Preventive initiatives for IHD ought to be tailored to the physical work demands.

Table 1. All men eligible for the incidence study. Lifestyle and other predictors of IHD mortality (n = 579, 11.8%) during the 30-year follow-up 1970/71 to 2001. Statistically significant results are highlighted (bold).

	Cumulative incidence, %	Hazard Ratio[c]	Hazard Ratio[d]	Hazard Ratio[e]	Hazard Ratio[f]
Age					

Youngest half (max 48 y), n=2,436	7.6%	na	1[a]	1[a]	1[a]
Oldest half (> 48 y), n=2,470	16.0%		**2.72(2.27-3.26)**	**2.33(1.95-2.79)**	**2.42(2.01-2.92)**
Smoking					
Current, n=3,522	12.7%	1[a]	1[a]	1[a]	1[a]
Previous, n=937	9.9%	**0.66(0.53-0.82)**	**0.68(0.54-0.86)**	**0.57(0.45-0.71)**	**0.60(0.47-0.75)**
Never, n=446	9.0%	**0.59(0.43-0.81)**	**0.63(0.44-0.86)**	**0.50(0.36-0.69)**	**0.51(0.36-0.71)**
Alcohol, beverages/d					
0, n=1,658	12.6%	1[a]	1[a]	1[a]	1[a]
1-2, n=2,315	10.6%	0.84(0.70-1.01)	**0.82(0.68-0.99)**	**0.84(0.69-1.00)**	0.84(0.69-1.02)
3-5, n=764	13.1%	1.18(0.93-1.49)	1.06(0.83-1.36)	1.07(0.84-1.36)	0.87(0.68-1.13)
6 +, n=151	16.6%	1.97(1.30-2.99)	1.73(1.13-2.65)	1.63(1.06-2.50)	1.14(0.73-1.77)
Leisure time physical activity					
Low, n=798	15.4%	1[a]	1[a]	1[a]	1[a]
Medium, n=3,478	11.3%	**0.68(0.56-0.84)**	**0.71(0.58-0.87)**	**0.70(0.57-0.86)**	**0.73(0.59-0.89)**
High, n=498	8.1%	**0.51(0.35-0.73)**	**0.54(0.38-0.78)**	**0.57(0.40-0.82)**	**0.62(0.43-0.90)**
BMI					
- 25, n=2,358	10.1%	1[a]	1[a]	1[a]	1[a]
> 25 – 28, n=1,710	11.9%	1.11(0.92-1.34)	1.14(0.94-1.38)	0.97(0.80-1.18)	0.96(0.79-1.56)
> 28, n=829	16.7%	**1.66(1.34-2.04)**	**1.67(1.34-2.08)**	**1.25(1.0-1.56)**	1.23(0.97-1.56)
Systolic BP, mm Hg					
- 120, n=1,383	6.4%	1[a]	1[a]	1[a]	1[a]
> 120 – 150, n=2,869	12.6%	**2.01(1.59-2.53)**	**2.09(1.65-2.66)**	**1.65(1.29-2.11)**	**1.80(1.40-2.34)**
> 150, n=650	20.2%	**3.32(2.52-4.36)**	**3.54(2.67-4.70)**	**2.02(1.44-2.85)**	**2.42(1.72-3.41)**
Diastolic BP mm Hg					
- 75, n=1,421	8.3%	1[a]	1[a]	1[a]	1[a]
>75-90, n=2,736	11.4%	**1.38(1.11-1.70)**	**1.48(1.19-1.84)**	1.16(0.93-1.45)	1.12(0.89-1.42)
> 90, n=745	20.0%	**2.79(2.12-3.44)**	**2.91(2.26-3.75)**	**1.66(1.21-2.27)**	**1.74(1.27-2.37)**
Hypertension[b]					
No, n=4,826	11.6%	1[a]	1[a]	1[a]	1[a]
Yes, n=77	27.3%	**2.41(1.56-3.73)**	**2.36(1.52-3.66)**	1.38(0.87-2.17)	1.46(0.92-2.30)
Physical fitness (VO_2Max)					
15-26, n=882	16.7%	1[a]	1[a]	1[a]	1[a]
27-38, n=3,017	11.5%	**0.74(0.61-0.90)**	**0.76(0.62-0.93)**	0.88(0.71-1.07)	0.88(0.71-1.08)
39-78, n=1,007	8.5%	**0.56(0.43-0.73)**	**0.60(0.45-0.80)**	0.77(0.57-1.02)	0.78(0.58-1.05)
Psychological pressure at work					
No, n=3,834	12.2%	1[a]	1[a]	1[a]	1[a]
Yes, n=1,060	10.5%	0.86(0.70-1.05)	0.86(0.70-1.07)	0.84(0.68-1.04)	0.88(0.70-1.10)
Psychological pressure at leisure					
No, n=4,556	11.8%	1[a]	1[a]	1[a]	1[a]
Yes, n=332	12.7%	1.11(0.81-1.53)	1.04(0.75-1.44)	1.17(0.85-1.60)	1.14(0.81-1.61)
Work hours/week					
< 40, n=628	8.3%	1[a]	1[a]	1[a]	1[a]
40-45, n=3,366	12.9%	**1.62(1.22-2.16)**	**1.57(1.17-2.10)**	**1.57(1.17-2.09)**	1.25(0.92-1.69)
> 45, n=911	10.2%	1.28(0.91-1.79)	1.33(0.94-1.88)	1.26(0.89-1.77)	1.12(0.79-1.59)
Social class					
High (I,II,III), n=2,196	9.1%	1[a]	1[a]	1[a]	1[a]
Low (IV,V), n=2,688	14.0%	**1.72(1.45-2.05)**	**1.61(1.35-1.93)**	**1.72(1.45-2.05)**	**1.48(1.22-1.79)**

[a]: reference category
[b]: receives doctor's treatment due to hypertension
[c]: adjusted for age; [d]: adjusted for age + lifestyle (smoking, LTPA, alcohol); [e]: adjusted for age + clinical factors (BMI, blood pressure including treatment for, physical fitness); [f]: age + all other confounders/risk factors (lifestyle, clinical factors, psychosocial stress at work and leisure, number of work hours, and social class
na: not applicable

Table 2. ***Men with low physical work demands only, n= 1,219.*** **Lifestyle and other predictors of IHD mortality (n = 118, 9.7%) during the 30-year follow-up 1970/71 to 2001. Statistically significant results are highlighted (bold).**

	Cumulative incidence, %	Hazard Ratio[c]	Hazard Ratio[d]	Hazard Ratio[e]	Hazard Ratio[f]
Age					

Youngest half (max 48 y), n=602	7.5%	na	1[a]	1[a]	1[a]
Oldest half (> 48 y), n=617	11.9%		**1.90(1.31-2.76)**	**1.72(1.17-2.52)**	**1.75(1.19-2.58)**
Smoking					
Current, n=808	9.5%	1[a]	1[a]	1[a]	1[a]
Previous, n=275	11.7%	1.12(0.74-1.69)	1.07(0.71-1.62)	1.03(0.68-1.56)	0.96(0.63-1.47)
Never, n=135	7.4%	0.67(0.35-1.30)	0.58(0.30-1.14)	0.56(0.29-1.10)	0.51(0.25-1.02)
Alcohol, beverages/d					
0, n=478	12.0%	1[a]	1[a]	1[a]	1[a]
1-2, n=617	7.5%	**0.59(0.40-0.88)**	**0.58(0.40-0.86)**	**0.56(0.38-0.83)**	**0.59(0.40-0.88)**
3-5, n=110	13.6%	1.26(0.72-2.23)	1.15(0.65-2.05)	1.08(0.60-1.91)	1.04(0.57-1.89)
6 +, n=12	0%	na	na	na	na
Leisure time physical activity					
Low, n=227	12.8%	1[a]	1[a]	1[a]	1[a]
Medium, n=859	8.9%	0.66(0.43-1.02)	**0.65(0.42-1.0)**	0.74(0.48-1.15)	0.74(0.47-1.15)
High, n=130	10.0%	0.74(0.38-1.42)	0.70(0.36-1.35)	0.86(0.44-1.68)	0.76(0.38-1.53)
BMI					
- 25, n=690	8.2%	1[a]	1[a]	1[a]	1[a]
> 25 – 28, n=381	10.3%	1.25(0.83-1.89)	1.30(0.86-1.96)	0.99(0.65-1.52)	1.04(0.68-1.60)
> 28, n=146	15.8%	**1.93(1.19-3.15)**	**1.79(1.09-2.92)**	1.35(0.81-2.26)	1.17(0.69-1.98)
Systolic BP, mm Hg					
- 120, n=337	4.5%	1[a]	1[a]	1[a]	1[a]
> 120 – 150, n=720	10.4%	**2.62(1.50-4.56)**	**2.46(1.41-4.29)**	**1.90(1.07-3.39)**	1.62(0.89-2.95)
> 150, n=160	17.5%	**4.50(2.38-8.49)**	**4.55(2.41-8.60)**	1.80(0.81-4.02)	**2.34(1.10-4.99)**
Diastolic BP mm Hg					
- 75, n=338	4.5%	1[a]	1[a]	1[a]	1[a]
>75-90, n=680	9.9%	**2.42(1.38-4.24)**	**2.43(1.39-4.27)**	**2.04(1.15-3.64)**	**1.94(1.07-3.53)**
> 90, n=199	18.2%	**5.03(2.75-9.20)**	**4.90(2.67-9.0)**	**2.93(1.40-6.12)**	**3.21(1.56-6.60)**
Hypertension[b]					
No, n=1196	9.5%	1[a]	1[a]	1[a]	1[a]
Yes, n=23	21.7%	1.85(0.75-4.56)	2.28(0.91-5.66)	0.92(0.36-2.33)	1.20(0.46-3.12)
Physical fitness (VO_2Max)					
15-26, n=238	13.9%	1[a]	1[a]	1[a]	1[a]
27-38, n=749	8.7%	**0.65(0.42-0.99)**	0.67(0.44-1.03)	0.81(0.52-1.26)	0.82(0.53-1.27)
39-78, n=232	8.7%	0.68(0.38-1.19)	0.70(0.39-1.25)	0.98(0.54-1.78)	0.91(0.49-1.66)
Psychological pressure at work					
No, n=830	9.6%	1[a]	1[a]	1[a]	1[a]
Yes, n=386	10.2%	1.15(0.79-1.70)	1.11(0.76-1.64)	1.10(0.74-1.61)	1.02(0.68-1.55)
Psychological pressure at leisure					
No, n=1,107	9.6%	1[a]	1[a]	1[a]	1[a]
Yes, n=109	11.1%	1.18(0.65-2.15)	1.09(0.59-2.01)	1.34(0.73-2.45)	1.35(0.71-2.58)
Work hours/week					
< 40, n=209	8.1%	1[a]	1[a]	1[a]	1[a]
40-45, n=738	10.9%	1.35(0.80-2.29)	1.31(0.78-2.23)	1.26(0.74-2.13)	1.11(0.65-1.90)
> 45, n=272	7.7%	0.95(0.50-1.80)	0.93(0.48-1.77)	0.98(0.51-1.86)	0.84(0.43-1.63)
Social class					
High (I,II,III), n=946	8.5%	1[a]	1[a]	1[a]	1[a]
Low (IV,V), n=260	13.8%	**1.69(1.14-2.51)**	**1.61(1.08-2.41)**	**1.69(1.13-2.53)**	1.45(0.96-2.20)

[a]: reference category
[b]: receives doctor's treatment due to hypertension
[c]: adjusted for age; [d]: adjusted for age + lifestyle (smoking, LTPA, alcohol); [e]: adjusted for age + clinical factors (BMI, blood pressure including treatment for, physical fitness); [f]: age + all other confounders/risk factors (lifestyle, clinical factors, psychosocial stress at work and leisure, number of work hours, and social class
na: not applicable

Table 3. ***Men with moderate physical work demands only, n= 2,636.*** **Lifestyle and other predictors of IHD mortality (n = 312, 11.8%) during the 30-year follow-up 1970/71 to 2001. Statistically significant results are highlighted (bold).**

	Cumulative incidence, %	Hazard Ratio[c]	Hazard Ratio[d]	Hazard Ratio[e]	Hazard Ratio[f]
Age					
Youngest half (max 48 y), n=1,316	7.2%	na	1[a]	1[a]	1[a]
Oldest half (> 48 y), n=1,320	16.6%		**2.98(2.33-3.81)**	**2.69(2.10-3.45)**	**2.74(2.13-3.52)**
Smoking					
Current, n=1,901	13.0%	1[a]	1[a]	1[a]	1[a]
Previous, n=502	8.8%	**0.57(0.41-0.78)**	**0.59(0.43-0.82)**	**0.47(0.34-0.65)**	**0.52(0.38-0.73)**
Never, n=233	9.0%	**0.57(0.37-0.89)**	**0.60(0.39-0.95)**	**0.52(0.33-0.81)**	**0.53(0.33-0.83)**
Alcohol, beverages/d					
0, n=898	13.1%	1[a]	1[a]	1[a]	1[a]
1-2, n=1,250	10.7%	0.82(0.64-1.05)	0.83(0.64-1.06)	0.83(0.64-1.06)	0.84(0.65-1.09)
3-5, n=404	11.7%	1.00(0.71-1.41)	0.95(0.68-1.34)	0.93(0.66-1.31)	0.82(0.58-1.17)
6 +, n=74	18.9%	2.25(1.29-3.92)	2.06(1.17-3.60)	1.85(1.03-3.32)	1.31(0.72-2.38)
Leisure time physical activity					
Low, n=409	14.9%	1[a]	1[a]	1[a]	1[a]
Medium, n=1,978	12.1%	**0.73(0.55-0.96)**	0.76(0.57-1.01)	**0.73(0.55-0.97)**	0.78(0.59-1.04)
High, n=240	4.6%	**0.29(0.15-0.55)**	**0.32(0.17-0.60)**	**0.32(0.17-0.60)**	**0.37(0.19-0.72)**
BMI					
- 25, n=1,220	10.0%	1[a]	1[a]	1[a]	1[a]
> 25 – 28, n=957	12.3%	1.13(0.87-1.45)	1.12(0.87-1.45)	1.03(0.79-1.34)	1.02(0.78-1.32)
> 28, n=454	16.1%	**1.56(1.16-2.09)**	**1.54(1.14-2.08)**	1.21(0.88-1.65)	1.19(0.86-1.65)
Systolic BP, mm Hg					
- 120, n=757	6.9%	1[a]	1[a]	1[a]	1[a]
> 120 – 150, n=1,523	12.5%	**1.77(1.30-2.41)**	**1.93(1.41-2.63)**	**1.54(1.11-2.13)**	**1.82(1.31-2.54)**
> 150, n=355	19.5%	**2.87(1.99-4.12)**	**3.27(2.26-4.73)**	**2.00(1.27-3.16)**	**2.56(1.64-4.01)**
Diastolic BP mm Hg					
- 75, n=768	8.9%	1[a]	1[a]	1[a]	1[a]
>75-90, n=1,491	11.7%	1.26(0.95-1.67)	**1.35(1.02-1.80)**	1.07(0.80-1.44)	1.01(0.75-1.37)
> 90, n=376	18.6%	**2.25(1.61-3.14)**	**2.50(1.78-3.52)**	1.42(0.92-2.20)	1.39(0.91-2.12)
Hypertension[b]					
No, n=2,592	11.6%	1[a]	1[a]	1[a]	1[a]
Yes, n=41	26.8%	**2.95(1.61-5.40)**	**2.90(1.58-5.32)**	1.74(0.92-3.32)	1.51(0.80-2.87)
Physical fitness (VO_2Max)					
15-26, n=465	16.4%	1[a]	1[a]	1[a]	1[a]
27-38, n=1,616	11.8%	0.79(0.60-1.03)	0.78(0.60-1.03)	0.89(0.67-1.18)	0.92(0.69-1.22)
39-78, n=555	8.3%	**0.56(0.39-0.82)**	**0.59(0.41-0.86)**	0.73(0.49-1.09)	0.78(0.53-1.17)
Psychological pressure at work					
No, n=2,133	12.6%	1[a]	1[a]	1[a]	1[a]
Yes, n=496	8.5%	**0.65(0.47-0.90)**	**0.70(0.48-0.93)**	**0.64(0.46-0.89)**	**0.68(0.48-0.96)**
Psychological pressure at leisure					
No, n=2,462	11.9%	1[a]	1[a]	1[a]	1[a]
Yes, n=163	11.7%	1.12(0.71-1.79)	1.14(0.72-1.83)	1.17(0.73-1.87)	1.26(0.77-2.06)
Work hours/week					
< 40, n=341	7.9%	1[a]	1[a]	1[a]	1[a]
40-45, n=1,865	13.1%	**1.71(1.14-2.54)**	**1.61(1.08-2.40)**	**1.66(1.11-2.47)**	1.31(0.87-1.96)
> 45, n=429	9.8%	1.26(0.78-2.04)	1.34(0.82-2.17)	1.25(0.77-2.06)	1.16(0.71-1.89)
Social class					
High (I,II,III), n=1,075	9.2%	1[a]	1[a]	1[a]	1[a]
Low (IV,V), n=1,554	13.7%	**1.64(1.29-2.08)**	**1.53(1.20-1.95)**	**1.62(1.27-2.07)**	**1.35(1.05-1.75)**

[a]: reference category
[b]: receives doctor's treatment due to hypertension
[c]: adjusted for age; [d]: adjusted for age + lifestyle (smoking, LTPA, alcohol); [e]: adjusted for age + clinical factors (BMI, blood pressure including treatment for, physical fitness); [f]: age + all other confounders/risk factors (lifestyle, clinical factors, psychosocial stress at work and leisure, number of work hours, and social class
na: not applicable

Table 4. ***Men with high physical work demands only, n= 846.*** **Lifestyle and other predictors of IHD mortality (n = 119, 14.1%) during the 30-year follow-up 1970/71 to 2001. Statistically significant results are highlighted (bold).**

	Cumulative incidence, %	Hazard Ratio[c]	Hazard Ratio[d]	Hazard Ratio[e]	Hazard Ratio[f]
Age					
Youngest half (max 48 y), n=420	8.6%	na	1[a]	1[a]	1[a]
Oldest half (> 48 y), n=426	19.5%		**3.16(2.12-4.71)**	**2.48(1.64-3.73)**	**2.52(1.66-3.83)**
Smoking					
Current, n=648	15.3%	1[a]	1[a]	1[a]	1[a]
Previous, n=131	9.2%	**0.46(0.25-0.84)**	**0.45(0.24-0.82)**	**0.40(0.22-0.73)**	**0.38(0.20-0.71)**
Never, n=67	11.9%	0.67(0.32-1.37)	0.71(0.34-1.46)	0.47(0.22-1.03)	0.49(0.22-1.09)
Alcohol, beverages/d					
0, n=218	12.4%	1[a]	1[a]	1[a]	1[a]
1-2, n=355	15.2%	1.23(0.78-1.96)	1.23(0.77-1.95)	1.31(0.81-2.11)	1.41(0.87-2.29)
3-5, n=208	13.0%	1.11(0.65-1.90)	1.00(0.58-1.72)	1.14(0.65-1.98)	0.95(0.53-1.67)
6 +, n=60	16.7%	**2.10(1.01-4.35)**	1.84(0.88-3.84)	2.05(0.97-4.33)	1.43(0.67-3.05)
Leisure time physical activity					
Low, n=144	20.8%	1[a]	1[a]	1[a]	1[a]
Medium, n=586	12.6%	**0.62(0.40-0.95)**	**0.59(0.38-0.90)**	**0.62(0.40-0.96)**	**0.56(0.36-0.88)**
High, n=114	13.2%	0.67(0.36-1.26)	0.64(0.34-1.21)	0.80(0.42-1.52)	0.77(0.40-1.48)
BMI					
- 25, n=351	12.8%	1[a]	1[a]	1[a]	1[a]
> 25 – 28, n=299	12.0%	0.82(0.53-1.28)	0.87(0.56-1.36)	0.66(0.42-1.05)	0.73(0.45-1.17)
> 28, n=194	18.6%	1.37(0.88-2.13)	1.34(0.84-2.12)	1.02(0.64-1.62)	1.08(0.66-1.76)
Systolic BP, mm Hg					
- 120, n=238	7.1%	1[a]	1[a]	1[a]	1[a]
> 120 – 150, n=499	15.2%	**2.02(1.19-3.42)**	**2.16(1.27-3.68)**	1.68(0.96-2.95)	**1.93(1.07-3.46)**
> 150, n=108	24.1%	**3.20(1.72-5.95)**	**3.41(1.81-6.44)**	2.13(0.97-4.66)	2.14(0.98-4.66)
Diastolic BP mm Hg					
- 75, n=253	11.5%	1[a]	1[a]	1[a]	1[a]
>75-90, n=455	12.5%	1.05(0.67-1.64)	1.05(0.67-1.66)	0.90(0.55-1.46)	0.79(0.47-1.30)
> 90, n=137	24.1%	**2.18(1.32-3.60)**	**2.53(1.51-4.23)**	1.43(0.73-2.78)	1.60(0.83-3.09)
Hypertension[b]					
No, n=834	13.8%	1[a]	1[a]	1[a]	1[a]
Yes, n=12	33.3%	2.32(0.85-6.30)	2.12(0.76-5.90)	1.80(0.64-5.13)	1.82(0.62-5.34)
Physical fitness (VO_2Max)					
15-26, n=125	23.2%	1[a]	1[a]	1[a]	1[a]
27-38, n=531	13.9%	**0.65(0.42-1.00)**	**0.63(0.40-0.99)**	0.73(0.46-1.16)	0.70(0.43-1.13)
39-78, n=190	8.4%	0.41(0.22-0.76)	0.39(0.21-0.74)	0.54(0.27-1.06)	**0.48(0.24-0.96)**
Psychological pressure at work					
No, n=708	13.8%	1[a]	1[a]	1[a]	1[a]
Yes, n=136	14.7%	1.01(0.62-1.63)	1.08(0.66-1.76)	0.98(0.60-1.60)	1.04(0.61-1.78)
Psychological pressure at leisure					
No, n=795	14.0%	1[a]	1[a]	1[a]	1[a]
Yes, n=47	17.0%	1.11(0.54-2.27)	1.15(0.56-2.37)	1.04(0.50-2.14)	1.09(0.51-2.30)
Work hours/week					
< 40, n=51	9.8%	1[a]	1[a]	1[a]	1[a]
40-45, n=618	14.6%	1.50(0.61-3.70)	1.68(0.68-4.19)	1.47(0.60-3.63)	1.54(0.62-3.85)
> 45, n=177	13.6%	1.49(0.57-3.89)	1.81(0.68-4.86)	1.38(0.52-3.64)	1.58(0.70-3.18)
Social class					
High (I,II,III), n=74	10.8%	1[a]	1[a]	1[a]	1[a]
Low (IV,V), n=771	14.3%	1.47(0.72-3.01)	1.43(0.69-2.96)	1.55(0.75-3.18)	1.49(0.70-3.18)

[a]: reference category
[b]: receives doctor's treatment due to hypertension
[c]: adjusted for age; [d]: adjusted for age + lifestyle (smoking, LTPA, alcohol); [e]: adjusted for age + clinical factors (BMI, blood pressure including treatment for, physical fitness); [f]: age + all other confounders/risk factors (lifestyle, clinical factors, psychosocial stress at work and leisure, number of work hours, and social class
na: not applicable

CONTRIBUTORS All authors contributed to the conception, design, interpretation of data, and writing or critically revising the manuscript. PS made the statistical analyses. AH and PS are guarantors.

ACKNOWLEDGEMENT The King Christian X's Foundation, The Danish Medical Research Council, The Danish Heart Foundation, and The Else & Mogens Wedell-Wedellsborg Foundation.

CONFLICTS OF INTEREST None

COMPETING INTEREST STATEMENT None. All authors declare that the answer to the questions on your competing interest form Exclusive licence (http://bmj.com/cgi/content/full/317/7154/291/DC1) are all No and therefore have nothing to declare.

FUNDING The study is a part of the Physical work demands and fitness project, financed by the Danish Working Environment Research Foundation.

ETHICAL APPROVAL When the Copenhagen Male Study (CMS) was initiated as a closed cohort study in 1970-71 no ethics committee for medical research had been established in Denmark. However, in 1985-86, when survivors from the first baseline were re-examined, the study was approved by the ethics committee for medical research in the county of Copenhagen, and all participants in the study gave informed consent to participate, as stated in many previous publications from the CMS based on analyses using the 1985-86 baseline.

ORIGINALE STUDY PROTOCOL It does not exist

DATA SHARING STATEMENT Technical appendix and statistical code available from the corresponding author at aho@nrcwe.dk. Consent was not obtained, but the presented data are anonymised and risk of identification is very low. No additional data available.

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