BMJ open

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Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004355
Article Type:	Research
Date Submitted by the Author:	29-Oct-2013
Complete List of Authors:	Torén, Kjell; Medicine, Schiöler, Linus; Medicine, Occupational and environmental medicine Kok, Wai; Medicine, Novak, Masuma; Medicine, Söderberg, Mia; Medicine, Occupational and environmental medicine Rosengren, Annika
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Cardiovascular medicine, Epidemiology
Keywords:	STROKE MEDICINE, PUBLIC HEALTH, OCCUPATIONAL & INDUSTRIAL MEDICINE

A longitudinal general-population based study of job strain and risk for coronary heart disease and stroke in Swedish men.

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The authors declare no conflicts of interest

Word count (body of test); 2 365

Keywords

Epidemiology, job strain, longitudinal, cerebrovascular disease

Abstract

Objectives

The aim was to investigate whether psycho-social stress based on the job-demand-control model increased the risk for coronary heart disease (CHD) and stroke.

Setting

Swedish men

Participants

The Primary Prevention Study comprise 6 070 men born between 1915 and 1925 free from previous history of coronary heart disease and stroke at baseline (1974-1977). Psychosocial workplace exposure was assessed using a job-exposure matrix for the job-demand-control model based on occupation at baseline. The participants were followed from baseline examination, until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register for non-fatal and fatal stroke and CHD events. Cox regression models were used with stroke or CHD as the outcome using job-demand-control model and age as explanatory variables, as well as stratified models with regard to smoking, self-reported stress, socio-economic status, obesity, hypertension, and diabetes.

Primary and secondary outcome measures

Risk for stroke and coronary heart disease

Results

There was an increased risk (HR) for CHD in relation to high strain, HR 1.31, 95% CI 1.01-1.70. The risk was further increased among ever-smokers and among blue-collar workers. There was no increased risk for stroke in any of the job-demand-control categories.

Conclusions

Exposure to occupational psycho-social stress defined as job strain increased the risk for CHD, especially among smokers and blue-collar workers. There was no increased risk for stroke in any of the job-demand-control categories.

Introduction

During the last decades a growing body of evidence have accumulated showing that psychosocial stress is associated with adverse health outcomes, especially coronary heart disease (CHD) (1). Psycho-social stress as a risk factor has been studied both as a general factor and linked to the work-place. The most studied definition of work-place related stress has been the job-demand-control model (2). In this model is postulated that the combination of high demands and low decision latitude at work results in high strain (job-strain) which increase the risk of cardiovascular diseases. There are studies showing that high strain is associated with a doubled risk of coronary heart disease. However, in a recent meta-analysis of 13 studies the association was rather modest, hazard ratio 1.23. The used models were adjusted for sex and age, and in some cases also for socioeconomic status. The authors concluded that adjustments for life style factors did not substantially affect the association (3). However, in a previous meta-analysis it was found that the risk of coronary heart disease was further increased among subjects with job-strain in combination with current smoking, being obese or reporting low physical activity (4). Hence, it seems to clear that job strain is associated with an increased risk for coronary heart disease, and there may also exist interactions with life-style factors.

There are studies indicating that self-reported psychosocial stress increase the risk for stroke (5, 6). However, the evidence between occupational exposure to psycho-social stress and stroke is less clear. There are a few longitudinal studies showing slightly increased risk for stroke associated with low control (7, 8). The association with job-strain is also unclear, some studies show an association (9, 10) and one study did not find any association (11). In a prospective general-population based study from Japan it was found that men, but not women, with high-strain job had an increased risk for stroke, with more than doubled risks among those with active, passive or high-strain jobs (12).

The aim of the present study was to investigate whether psycho-social stress based on the job-demand-control model increased the risk for coronary heart disease and stroke. The study base is a longitudinal general population based study of 6 070 Swedish men followed from 1975 to 2008.

Methods

Study population

The Primary Prevention Study (PPS) is a population-based cohort study from Gothenburg, Sweden. It was established in 1970 as previously described (13). The source population comprised all men living in Gothenburg born between 1915 and 1925. The initial study population was a random sample of 10 000 men, and 7494 men (75% of the sample) participated in screening examinations between January 1970 and March 1973 (14, 15). Three years later, 1975-1976, a clinical follow-up investigation was performed where 7 133 men participated. In the present study we are using data from the first follow-up investigation, because in that round there were complete occupational data. All participants gave their informed consent to participate in the study and it was approved by the Ethics Committee for Medical Research at Gothenburg University.

The current occupation at baseline (1974-1977) was classified at three-digit level according to the Nordic Classification of Occupations, NYK-74 (16). For assessing the psychosocial workplace exposure we used a previously published job-exposure matrix (17, 18). This JEM was developed in late 1970s based on information from large Swedish population surveys where around 12 000 randomly selected subjects aged 25 to 74 years were classified for psychological demands and decision latitude. The JEM gives separate estimates of demand and control for 261 occupations separated into gender and age (25-44 and 45 to 74). Socioeconomic status, high or low, was obtained based on one-digit level of occupations, i e blue-collar vs. white-collar workers

Psychological job demands and decision latitude were explored with four items each. All items were scored using a scale (1-10), with a score of 10 indicating high psychological demands or high decision latitude. Each subject was assigned a certain score based on occupation and age. The scores were then dichotomized into high and low, using the median of the distribution as cut-off. Combining demand and control with the median cut-offs divides the participants into four categorical quadrants; high strain (high demand-low control), active (high demand-high control), passive (low demand-low control) and low-strain (low demand-high control).

In the present study there was information at baseline about age, country of birth (Sweden/other), body mass index (BMI), serum cholesterol (s-cholesterol) level, systolic blood pressure, diastolic blood pressure, use of antihypertensive medication (yes/no), history of diabetes (yes/no), coronary heart disease (yes/no), hypertension (yes/no) or stroke (yes/no) at baseline and smoking as previously described (19).

Subjects with coronary heart disease or stroke at baseline were excluded resulting in a study population of 6 070 subjects (Table 1). Based on unique personal identification numbers, participants were followed from the date of their baseline examination until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register. The hospital discharge register has operated on a nationwide basis since 1987, but all discharges from Gothenburg hospitals have been entered in the national register since 1970 (except for 1976, because of a legislative change for that year). Additional data from the Gothenburg stroke register were used to identify strokes from the start of the study until 1983. The International Classification of Disease (ICD) codes listed in the registries were used to identify stroke events (both non-fatal and fatal events) and coronary heart disease during the entire follow-up period. The eighth version of the ICD code was used until 1986, ICD-9 was used from 1987 to 1996, and ICD-10 was used from 1997 onwards. Ischemic stroke was defined as ICD codes 431-438 and I61-I69. Non-fatal CHD was defined as 410 and I21. Fatal CHD was defined as 410-414 and I20-I25.

Statistical analysis

Descriptive statistics are presented as percentages or mean values with standard deviations (SD). All analyses were performed using the SAS statistical package (version 9.3) and R (version 3.0.1). The material were analysed with Cox regression models using SAS (the PHREG procedure). The proportional hazards assumptions were investigated using tests and plots based on weighted residuals (20) using the R package Survival. All assumptions were found reasonable except for the analysis if baseline diabetes. Hospital care or mortality (whatever came first) from stroke or coronary heart disease were events and time were measured as months since baseline. The observation period stopped at the age of 75. In the crude model hazard ratios were calculated using age the job-demand-control model and age as explanatory variables. The low strain group

was used as reference group. There were also models using high strain vs. all other subjects as an independent variable. There were also separate models stratifying for ever-smoking and never-smoking, adiposity (body mass index ≥30) or not, hypertension or not at baseline and diabetes or not at baseline. There was also one model with five years latency time, i.e excluding subject with any event occurring during the five first year during the follow-up.

Results

For the follow-up period 1976-2008 there were 1 052 events due to coronary heart disease. The Cox regression models adjusted for age showed an increased risk (HR) for coronary heart disease in relation to high job strain, HR 1.31, 95% CI 1.01-1.70 (Table 2). In the stratified analysis high strain was associated with an even slightly higher risk for coronary heart disease among ever-smokers, (HR 1.37, 95% CI 1.02-1.83) and among blue-collar-workers (HR 1.36, 95% CI 1.01-1.84). Among obese subjects there was an indication of increased risk in relation to high-strain (HR 2.05, 95% CI 0.93-4.81) but with wide confidence intervals. In other strata there was an increased risk for coronary heart disease in the active group among those with hypertension (HR 1.50, 95% CI 1.00-2.33) (Table 2).

For the follow-up period 1976-2008 there were 549 events due to stroke. In the total population there was no increased risk for stroke in any of the job-demand-control categories. In the stratified analyses those with self-reported stress at baseline seem to have increased risk, both in the active group (HR 1.98, 95% CI 1.09-4.05) and in the passive group as well (HR 2.15, 95% CI 1.17-4.44) (Table 2).

In the additional analyses subjects with five years latency time the results were similar. The risk for coronary heart disease among subjects with high strain was slightly higher (HR 1.34, 95% CI 1.00-1.80) (Table 3). In the final full model, adjusted age, adiposity, diabetes, smoking and hypertension, there was an indication of increased risk of CHD in relation to high strain (HR 1.29, 95% CI 0.97-1.72). There were no increased risks for stroke.

Discussion

Principal findings

In line with the other studies an increased risk for coronary heart disease was found in relation to high strain, job-strain. Of interest is that job strain risks increased further among ever-smokers, obese subjects and among subjects with low socioeconomic status. Active subjects with hypertension also ran an increased risk for coronary heart disease. Of interest, even if it is a negative report, is that there was no increased risk for stroke in most of the job-demand control groups. In the strata with high levels of self-reported stress there was an increased risk for stroke in all job-demand categories.

Methodological considerations

This study has several strengths, a general-population sample with a long period of follow-up and use of a national mortality register and hospital discharge register with high coverage. The assessment of psycho-social stress is based on occupations, which probably is less biased than self-reports of demand and control. Further, the population was in their fifties at baseline, meaning that they are quite stable in their occupations. Finally, the study comprises only men which limit the external validity.

The regression models have been adjusted for age. The study population comprises only men. In the literature it has been discussed that further adjustments for different lifestyle factors marginally decreased the risk estimates, which is in line with the findings from a large metaanalyses (3). There is also a possibility that that smoking, adiposity and hypertension can be part of the causal chain act and hence stratifications are to prefer. Further, there were no separate adjustments for socioeconomic position. The reason is that the exposure for psychosocial stress is based on occupational titles and the socioeconomic position is part of the occupational classification. However, in the stratified analysis, the risk for CHD was increased among blue-collar workers (low SES), but not among the white-collar works (high SES). In the literature, the job-demand-control model mostly predict to ill-health associations among blue-collar workers, often men (2, 17, 21, 22, 23, 24). One plausible explanation is that the development of the JDC model was mainly conducted among male blue-collar jobs, and is consequently adjusted to such

job characteristics. When broadening study populations, more conflicting findings emerge. For example, little support has been found for female high-strain related ill-health (25).

The effect of psycho-social stress

The results from the present study indicate that exposure to occupational psycho-social stress is not increasing the risk for stroke. The study is rather large, 549 stroke events, and there was neither no increased risks in different lifestyle strata. Previously the association with job-strain has been unclear with both positive (9-12) and negative studies (11). There is probably a publication bias as studies with no or weak associations may not be published, as it has been shown for job strain and coronary heart disease (3). Hypertension has been associated with occupational psycho-social stress, especially among men (26). However, job strain was not associated with stroke among men with hypertension at baseline. Hence, the present study indicates that stroke has a different pattern of risk factors compared to coronary heart disease.

Self-reported stress have been associated with stroke, both in cohort studies (5, 27, 28) and in case-control studies (6, 29). Self-reported stress is a global composite item reflecting both occupational and non-occupational exposure. In the present study, increased risks for stroke was among subjects reporting stress at baseline and belonging to either the active, high strain or passive strata (compared to low strain). This may indicate an interaction between occupational and non-occupational stress in relation to stroke.

One limitation of our study is that there was only one assessment of the exposure the occupational psychosocial stress. There are indications in the literature that psychosocial stress occurs late in the causal chain for stroke as indicated by the observation that studies with short period of follow-up have higher risks of stroke in relation to psychosocial stress (8, 9). We have a rather long observation period, which may result in low risk estimates due to misclassification of the exposure.

The study confirms the previous findings of an association with job strain and risk for coronary heart disease. Compared to some other studies the risk levels were quite modest, which may reflect non-differential misclassification of the exposure assessment or may reflect the true underlying risk (3, 30). There was a slight interaction with lifestyle factors, especially smoking

and to some extent also obesity, as the risks were further increased among smoking subjects and obese subjects. Positive interaction with both smoking and obesity was recently shown in a meta-analysis (4). A finding that needs to be replicated is that active subjects with hypertension had a high risk for coronary heart disease.

Conclusions

Exposure to occupational psycho-social stress defined as job strain increased the risk for CHD, especially among smokers and blue-collar workers. There was no increased risk for stroke in any of the job-demand-control categories.

Acknowledgements

The study was funded by the Swedish Research Council (VR), the Swedish Research Council for Health, Working Life and Welfare (FORTE) and the Swedish Heart and Lung Foundation

Strengts and limitations of the paper;

Job strain increase the risk for coronary heart disease but the relation to stroke is uncertain. There is a need for longitudinal general-population based studies in this field. This study confirms that job strain increase the risk for coronary heart disease, but the risk seems to be limited to blue-collar workers. There was no clear relation between job strain and risk for stroke. The risk pattern for stroke seems to be different compared to coronary heart disease.

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Table 1. Baseline characteristics of a general population study of 6 070 Swedish men.

	Active N=2357	High strain N=671	Low strain N=679	Passive N=2363	Overall N=6070
Age (yrs)	55.2 (2.1)	55.3 (2)	55.2 (2)	55.4 (2)	55.3 (2.1)
Cholesterol (mmol/L)	6.37 (1.05)	6.45 (1.1)	6.37 (0.99)	6.43 (1.05)	6.4 (1.05)
SBP, mm Hg (SD)	145.1 (19.5)	147.2 (20.5)	145.2 (18.8)	146.8 (19.7)	146 (19.6)
BMI (kg/m^2)	25.5 (3.1)	25.6 (3.4)	25.8 (3.2)	25.8 (3.4)	25.6 (3.3)
Diabetes, % (N)	2.8 (65)	3.6 (24)	2.5 (17)	2.7 (64)	2.8 (170)
Hypertension, % (N)	21.8 (512)	23.9 (160)	22.5 (152)	21.9 (517)	22.1 (1341)
Hypertensive medication, % (N)	15.2 (358)	16.5 (111)	14.6 (99)	13.9 (328)	14.8 (896)
Smoking status					
Never % (N) N=1437	25.8 (607)	21 (141)	25.2 (171)	21.9 (518)	23.7 (1437)
Current % (N) N=2460	37.3 (879)	47.4 (318)	39.0 (265)	42.2 (998)	40.5 (2460)
Former % (N) N=1890	32.7 (771)	27 (181)	31.4 (213)	30.7 (725)	31.1 (1890)
Unknown % (N) N=283	4.2 (100)	4.6 (31)	4.4 (30)	5.2 (122)	4.7 (283)
Number of events					
Coronary heart disease	384	131	104	433	1052
Stroke	208	64	65	212	549
Mean follow-up time, months					
Coronary heart disease	200	193	199	192	196
Stroke	204	195	203	197	200

Table 2. Cox Regression models 6070 men followed from 1974 to 2008. All models are adjusted for age.

Strain group	Coronary heart disease		Stroke	
	N (N Events)	Hazard ratio (95% CI)	N (N Events)	Hazard ratio (95% CI)
All	6070 (1052)		6070 (549)	
Active	2357 (384)	1.06 (0.85-1.32)	2357 (208)	0.91 (0.70-1.22)
High strain	671 (131)	1.31 (1.01-1.70)	671 (64)	1.05 (0.74-1.48)
Passive	2363 (433)	1.23 (1.00-1.53)	2363 (212)	0.96 (0.74-1.28)
Ever-smokers	4350 (826)		4350 (406)	
Active	1650 (277)	1.00 (0.78-1.29)	1650 (152)	0.87 (0.64-1.20)
High strain	499 (109)	1.37 (1.02-1.83)	499 (46)	0.92 (0.62-1.38)
Passive	1723 (361)	1.31 (1.03-1.68)	1723 (158)	0.90 (0.66-1.25)
Never-smokers	1437 (184)		1437 (113)	
Active	607 (88)	1.21 (0.76-1.99)	607 (46)	1.11 (0.61-2.18)
High strain	141 (18)	1.04 (0.55-1.96)	141 (13)	1.39 (0.63-3.08)
Passive	518 (57)	0.90 (0.55-1.52)	518 (42)	1.18 (0.64-2.35)
Blue-collar	3020 (555)		3020 (279)	
Active	41 (7)	1.04 (0.44-2.11)	41 (5)	1.30 (0.45-2.906)
High strain	492 (101)	1.36 (1.01-184)	53 (492)	1.22 (0.82-1.82)
Passive	2008 (372)	1.20 (0.94-1.55)	2008 (75)	0.93 (0.68-1.30)
White-collar	3050 (497)		3050 (270)	
Active	2316 (377)	1.14 (0.80-1.71)	2316 (203)	0.93 (0.60-1.54)
High strain	179 (30)	1.15 (0.69-1.92)	179 (11)	0.63 (0.29-1.30)
Passive	355 (612)	1.24 (0.80-1.95)	355 (37)	1.16 (0.68-2.06)
Self-reported stress at baseline	2177 (381)		2177 (201)	
Active	1014 (170)	1.01 (0.70-1.49)	1014 (98)	1.98 (1.09-4.05)
High strain	236 (47)	1.28 (0.82-2.02)	236 (20)	1.92 (0.92-4.28)
Passive	722 (131)	1.13 (0.78-1.69)	722 (73)	2.15 (1.17-4.44)

No self-reported stress at baseline	3742 (381)		3742 (330)	
Active	1304 (203)	1.00 (0.77-1.32)	1304 (105)	0.67 (0.49-0.94)
High strain	411 (77)	1.23 (0.89-1.70)	411 (40)	0.84 (0.56-1.26)
Passive	1568 (635)	1.21 (0.94-1.58)	1568 (131)	0.72 (0.53-1.00)
Hypertension at baseline	1341 (314)		1341 (201)	
Active	512 (129)	1.50 (1.00-2.33)	512 (78)	0.86 (0.56-1.35)
High strain	160 (37)	1.37 (0.84-2.29)	160 (22)	0.79 (0.45-1.38)
Passive	517 (122)	1.41 (0.94-2.20)	517 (74)	0.81 (0.53-1.29)
No hypertension at baseline	4715 (736)		4715 (347)	
Active	1840 (254)	0.93 (0.72-1.21)	1840 (129)	0.96 (0.68-1.39)
High strain	509 (94)	1.30 (0.96-1.76)	509 (42)	1.21 (0.78-1.88)
Passive	1842 (311)	1.18 (0.93-1.53)	1842 (138)	1.07 (0.76-1.55)
Body mass index<30	5544 (938)		5544 (499)	
Active	2188 (343)	0.99 (0.79-1.25)	2188 (196)	0.97 (0.72-1.31)
High strain	598 (113)	1.23 (0.94-1.62)	598 (57)	1.08 (0.75-1.57)
Passive	2150 (387)	1.18 (0.95-1.48)	2150 (190)	0.99 (0.74-1.34)
Body mass index ≥30	516 (113)		516 (50)	
Active	167 (41)	1.92 (0.98-4.21)	167 (12)	0.54 (0.23-1.33)
High strain	70 (17)	2.05 (0.93-4.81)	70 (7)	0.88 (0.31-2.35)
Passive	209 (46)	1.76 (0.90-3.84)	209 (22)	0.83 (0.40-1.91)
No Diabetes at baseline	5900 (989)		5900 (515)	
Active	2292 (357)	1.04 (0.84-1.31)	2292 (194)	0.91 (0.69-1.22)
High strain	647 (123)	1.31 (1.01-1.72)	647 (60)	1.05 (0.74-1.50)
Passive	2299 (411)	1.24 (1.00-1.55)	2299 (200)	0.97 (0.73-1.30)

Diabetes at baseline	170 (63)		170 (34)	
Active	65 (27)	1.26 (0.56-3.39)	65 (14)	1.02 (0.36-3.59)
High strain	24 (8)	1.08 (0.37-3.28)	24 (4)	0.96 (0.23-4.09)
Passive	64 (22)	1.00 (0.43-2.73)	64 (12)	0.96 (0.33-3.43)

Table 3. Cox Regression models 6070 men followed from 1974 to 2008. Subjects with events the first five years after baseline are excluded. Models adjusted for age, adiposity, diabetes, smoking and hypertension.

Strain group	Coronary heart disease		Stroke	
	N (N Events)	Hazard ratio (95% CI)	N (N Events)	Hazard ratio (95% CI)
Low strain	642 (85)	1.00	642 (60)	1.00
Active	2247 (312)	1.08 (0.85-1.38)	2275 (189)	0.93 (0.70-1.25)
High strain	630 (109)	1.29 (0.97-1.72)	640 (54)	0.91 (0.63-1.32)
Passive	2208 (351)	1.22 (0.97-1.56)	2248 (190)	0.94 (0.70-1.26)

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Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004355.R1
Article Type:	Research
Date Submitted by the Author:	08-Jan-2014
Complete List of Authors:	Torén, Kjell; Medicine, Schiöler, Linus; Medicine, Occupational and environmental medicine Kok, Wai; Medicine, Novak, Masuma; Medicine, Söderberg, Mia; Medicine, Occupational and environmental medicine Rosengren, Annika; Medicine,
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Cardiovascular medicine, Epidemiology
Keywords:	STROKE MEDICINE, PUBLIC HEALTH, OCCUPATIONAL & INDUSTRIAL MEDICINE

A longitudinal general-population based study of job strain and risk for coronary heart disease and stroke in Swedish men.

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The authors declare no conflicts of interest

Word count (body of test); 2 621

Keywords

Epidemiology, job strain, longitudinal, cerebrovascular disease

Abstract

Objectives

The aim was to investigate whether psycho-social stress based on the job-demand-control model increased the risk for coronary heart disease (CHD) and stroke.

Setting

Swedish men

Participants

The Primary Prevention Study comprise 6 070 men born between 1915 and 1925 free from previous history of coronary heart disease and stroke at baseline (1974-1977). Psychosocial workplace exposure was assessed using a job-exposure matrix for the job-demand-control model based on occupation at baseline. The participants were followed from baseline examination, until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register for non-fatal and fatal stroke and CHD events. Cox regression models were used with stroke or CHD as the outcome using job-demand-control model and age as explanatory variables, as well as stratified models with regard to smoking, self-reported stress, socio-economic status, obesity, hypertension, and diabetes.

Primary and secondary outcome measures

Risk for stroke and coronary heart disease

Results

There was an increased risk (HR) for CHD in relation to high strain, HR 1.31, 95% CI 1.01-1.70. The risk was further increased among ever-smokers and among blue-collar workers. There was a relation between low control and increased risk for CHD, HR 1.19, 95% CI 1.06-1.35. There was no increased risk for stroke in any of the job-demand-control categories.

Conclusions

Exposure to occupational psycho-social stress defined as job strain or low control increased the risk for CHD, especially among smokers and blue-collar workers. There was no increased risk for stroke in any of the job-demand-control categories.

Strengths and limitations of the paper;

Job strain increase the risk for coronary heart disease but the relation to stroke is uncertain. There is a need for longitudinal general-population based studies in this field. This study confirms that job strain increase the risk for coronary heart disease, but the risk seems to be limited to blue-collar workers. There was no clear relation between job strain and risk for stroke.

Introduction

During the last decades a growing body of evidence have accumulated showing that psychosocial stress is associated with adverse health outcomes, especially coronary heart disease (CHD) (1). Psycho-social stress as a risk factor has been studied both as a general factor and linked to the work-place. The most studied definition of work-place related stress has been the job-demand-control model (2). According to Karasek the job demand variable constitutes volume and intensity of workload and job control referred to the working individual's potential control over pace and content of their tasks (2). In this model it is postulated that the combination of high demands and low decision latitude at work results in high strain (job-strain) which increase the risk of cardiovascular diseases. There are studies showing that high strain is associated with a doubled risk of coronary heart disease. However, in a recent meta-analysis of 13 studies the association was rather modest, hazard ratio 1.23. The used models were adjusted for gender and age, and in some cases also for socioeconomic status. The authors concluded that adjustments for life style factors did not substantially affect the association (3). However, in an additional paper from the previous meta-analysis it was found that the risk of coronary heart disease was further increased among subjects with job-strain in combination with current smoking, being obese or reporting low physical activity (4). Hence, it seems to clear that job strain is associated with an increased risk for coronary heart disease, and there may also exist interactions with life-style factors.

There are studies indicating that self-reported psychosocial stress increase the risk for stroke (5, 6). However, the evidence between occupational exposure to psycho-social stress and stroke is less clear. There are a two longitudinal studies showing slightly increased risk for stroke associated with low control (7, 8). One study showed an increased risk in working Finnish men (7) and in one study based on the Swedish working population there was an increased risk among women, but not among men (8). The association with job-strain is also unclear, two studies in women show an association (9, 10) and one study in the general population did not find any association, either among women or among men (11). In a prospective general-population based study from Japan it was found that men, but not women, with high-strain job had an increased

risk for stroke, with more than doubled risks among those with active, passive or high-strain jobs (12).

The aim of the present study was to investigate whether psycho-social stress based on the job-demand-control model increased the risk for coronary heart disease and stroke. The study base is a longitudinal general population study of 6 070 Swedish men followed from baseline examination (1974-1977), until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register.

Methods

Study population

The Primary Prevention Study (PPS) is a population-based cohort study from Gothenburg, Sweden. It was established in 1970 as previously described (13). The source population comprised all men living in Gothenburg born between 1915 and 1925. The initial study population was a random sample of 10 000 men, and 7494 men (75% of the sample) participated in screening examinations between January 1970 and March 1973 (14, 15). Three years later, 1974-1977, a clinical follow-up investigation was performed where 7 133 men participated. In the present study we are using data from the first follow-up investigation, because in that round there were complete occupational data. All participants gave their informed consent to participate in the study and it was approved by the Ethics Committee for Medical Research at Gothenburg University.

The current occupation at baseline (1974-1977) was classified at three-digit level according to the Nordic Classification of Occupations, NYK-74 (16). For assessing the psychosocial workplace exposure we used a previously published job-exposure matrix (17, 18). This JEM was developed in late 1970s based on information from large Swedish population surveys where around 12 000 randomly selected subjects aged 25 to 74 years were classified for psychological demands and decision latitude. The JEM gives separate estimates of demand and control for 261 occupations separated into gender and age (25-44 and 45 to 74). Socioeconomic status, high or low, was obtained based on one-digit level of occupations, i e blue-collar vs. white-collar workers

Psychological job demands and decision latitude were explored with four items each. All items were scored using a scale (1-10), with a score of 10 indicating high psychological demands or high decision latitude. Each subject was assigned a certain score based on occupation and age. The scores were then dichotomized into high and low, using the median of the distribution as cut-off. Combining demand and control with the median cut-offs divides the participants into four categorical quadrants; high strain (high demand-low control), active (high demand-high control), passive (low demand-low control) and low-strain (low demand-high control).

In the present study there was information at baseline about age, country of birth (Sweden/other), body mass index (BMI), serum cholesterol (s-cholesterol) level, systolic blood pressure, diastolic blood pressure, use of antihypertensive medication (yes/no), history of diabetes (yes/no), coronary heart disease (yes/no), hypertension (yes/no) or stroke (yes/no) at baseline and smoking as previously described (19).

Subjects with coronary heart disease or stroke at baseline (1974-1977) were excluded resulting in a study population of 6 070 subjects (Table 1). Based on unique personal identification numbers, participants were followed from the date of their baseline examination until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register. The hospital discharge register has operated on a nationwide basis since 1987, but all discharges from Gothenburg hospitals have been entered in the national register since 1970 (except for 1976, because of a legislative change for that year). Additional data from the Gothenburg stroke register were used to identify strokes from the start of the study until 1983. The International Classification of Disease (ICD) codes listed in the registries were used to identify stroke events (both non-fatal and fatal events) and coronary heart disease during the entire follow-up period. The eighth version of the ICD code was used until 1986, ICD-9 was used from 1987 to 1996, and ICD-10 was used from 1997 onwards. Ischemic stroke was defined as ICD codes 431-438 and I61-I69. Non-fatal CHD was defined as 410 and I21. Fatal CHD was defined as 410-414 and I20-I25. Each type of event was treated separately and only the first event of each type was used in the analysis.

Statistical analysis

Descriptive statistics are presented as percentages or mean values with standard deviations (SD). All analyses were performed using the SAS statistical package (version 9.3) and R (version 3.0.1). The material were analysed with Cox regression models using SAS (the PHREG procedure). The proportional hazards assumptions were investigated using tests and plots based on weighted residuals (20) using the R package Survival. All assumptions were found reasonable except for the analysis of baseline diabetes. Hospital care or mortality (whatever came first) from stroke or coronary heart disease were events and time were measured as months since baseline. The observation period stopped at the age of 75. In the crude model hazard ratios were calculated using the job-demand-control model and age as explanatory variables. The low strain group was used as reference group. There were also models using high strain vs. all other subjects as an independent variable. There were also separate models stratifying for ever-smoking and never-smoking, adiposity (body mass index ≥30) or not, hypertension or not at baseline and diabetes or not, self-reported stress or not at baseline and finally status as white-collar worker or blue-collar worker at baseline. There was also one model with five years latency time, i.e excluding subject with any event occurring during the five first year during the follow-up.

Results

For the follow-up period there were 1 052 events due to coronary heart disease. The Cox regression models adjusted for age showed an increased risk (HR) for coronary heart disease in relation to high job strain, HR 1.31, 95% CI 1.01-1.70 (Table 2). In the stratified analysis high strain was associated with an even slightly higher risk for coronary heart disease among ever-smokers, (HR 1.37, 95% CI 1.02-1.83) and among blue-collar-workers (HR 1.36, 95% CI 1.01-1.84). Among obese subjects there was an indication of increased risk in relation to high-strain (HR 2.05, 95% CI 0.93-4.81) but with wide confidence intervals. In other strata there was an increased risk for coronary heart disease in the active group among those with hypertension (HR 1.50, 95% CI 1.00-2.33) (Table 2).

For the follow-up period there were 549 events due to stroke. In the total population there was no increased risk for stroke in any of the job-demand-control categories. In the stratified analyses those with self-reported stress at baseline seem to have increased risk, both in the active group (HR 1.98, 95% CI 1.09-4.05) and in the passive group as well (HR 2.15, 95% CI 1.17-4.44) (Table 2).

In the additional analyses subjects with five years latency time the results were similar. The risk for coronary heart disease among subjects with high strain was slightly higher (HR 1.34, 95% CI 1.00-1.80) (Table 3). In the final full model, adjusted age, adiposity, diabetes, smoking and hypertension, there was an indication of increased risk of CHD in relation to high strain (HR 1.29, 95% CI 0.97-1.72). There were no increased risks for stroke.

Further additional analyses explored the relations between low control and high demands, respectively. There was a clear relation between low control and increased risk for coronary heart disease (Table 4). This was found among all subjects, but also among smokers and in subjects without hypertension, without diabetes, without self-reported stress or with BMI<30. There were no clear signals regarding high demands and risk for coronary heart disease. There were no significant relations between low control or high demands and the risk for stroke (Table 4).

Discussion

Principal findings

In line with the other studies an increased risk for coronary heart disease was found in relation to high strain, job-strain. Of interest is that job strain risks increased further among ever-smokers, obese subjects and among subjects with low socioeconomic status. Active subjects with hypertension also ran an increased risk for coronary heart disease. There was also a clear association between low control and increased risk for coronary heart disease. Of interest, even if it is a negative report, is that there was no increased risk for stroke in most of the job-demand control groups. In the strata with high levels of self-reported stress there was an increased risk for stroke in all job-demand categories.

Methodological considerations

This study has several strengths, a general-population sample with a long period of follow-up and use of a national mortality register and hospital discharge register with high coverage. The assessment of psycho-social stress is based on occupations, which probably is less biased than self-reports of demand and control. Further, the population was in their fifties at baseline, meaning that they are quite stable in their occupations. Finally, the study comprises only men which limit the external validity.

The regression models have been adjusted for age. The study population comprises only men. In the literature it has been discussed that further adjustments for different lifestyle factors marginally decreased the risk estimates, which is in line with the findings from a large metaanalyses (3). There is also a possibility that that smoking, adiposity and hypertension can be part of the causal chain act and hence stratifications are to prefer. Further, there were no separate adjustments for socioeconomic position. The reason is that the exposure for psychosocial stress is based on occupational titles and the socioeconomic position is part of the occupational classification. However, in the stratified analysis, the risk for CHD was increased among blue-collar workers (low SES), but not among the white-collar works (high SES). In the literature, the job-demand-control model mostly predicts to ill-health associations among blue-collar workers, often men (2, 17, 21, 22, 23, 24). One plausible explanation is that the development of the JDC model was mainly conducted among male blue-collar jobs, and is consequently adjusted to such

job characteristics. When broadening study populations, more conflicting findings emerge. For example, little support has been found for female high-strain related ill-health (25).

The effect of psycho-social stress

It is evident from this study that both high strain and the passive dimension increase the risk for coronary heart disease. It is of interest that low control, the common denominator for job-strain and the passive dimension, was clearly related to increased risk for coronary heart disease.

The results from the present study indicate that exposure to occupational psycho-social stress is not increasing the risk for stroke. The study is rather large, 549 stroke events, and there was no increased risks in different lifestyle strata. Previously the association with job-strain has been unclear with both positive (9, 10, 12) and negative studies (11). There is probably a publication bias as studies with no or weak associations may not be published, as it has been shown for job strain and coronary heart disease (3). Hypertension has been associated with occupational psycho-social stress, especially among men (26). However, job strain was not associated with stroke among men with hypertension at baseline. Hence, the present study indicates that stroke has a different pattern of risk factors compared to coronary heart disease.

Self-reported stress has been associated with stroke, both in cohort studies (5, 27, 28) and in case-control studies (6, 29). Self-reported stress is a global composite item reflecting both occupational and non-occupational exposure. In the present study, increased risks for stroke was among subjects reporting stress at baseline and belonging to either the active, high strain or passive strata (compared to low strain). This may indicate an interaction between occupational and non-occupational stress in relation to stroke.

One limitation of our study is that there was only one assessment of the exposure the occupational psychosocial stress. There are indications in the literature that psychosocial stress occurs late in the causal chain for stroke as indicated by the observation that studies with short period of follow-up have higher risks of stroke in relation to psychosocial stress (8, 9). We have a rather long observation period, which may result in low risk estimates due to misclassification of the exposure.

Another limitation of this study is that the sample consisted only of men. Previous studies have indicated that health outcomes differ between men and women when exposed to Job demand-control (8, 9, 10, 11, 22, 25). Since the cohort was established with only men it was not possible to include women in our study, but we recommend that future similar analyzes include women as to investigate gender differences

The study confirms the previous findings of an association with job strain and risk for coronary heart disease. Compared to some other studies the risk levels were quite modest, which may reflect non-differential misclassification of the exposure assessment or may reflect the true underlying risk (3, 30). There was a slight interaction with lifestyle factors, especially smoking and to some extent also obesity, as the risks were further increased among smoking subjects and obese subjects. Positive interaction with both smoking and obesity was recently shown in a meta-analysis (4). A finding that needs to be replicated is that active subjects with hypertension had a high risk for coronary heart disease.

Conclusions

Exposure to occupational psycho-social stress defined as job strain increased the risk for CHD, especially among smokers and blue-collar workers. Low control was also related to increased risk for CHD. There was no increased risk for stroke in any of the job-demand-control categories.

Acknowledgements

The study was funded by the Swedish Research Council (VR), the Swedish Research Council for Health, Working Life and Welfare (FORTE) and the Swedish Heart and Lung Foundation

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Table 1. Baseline characteristics of a general population study of 6 070 Swedish men.

	Active N=2357	High strain N=671	Low strain N=679	Passive N=2363	Overall N=6070
Age, yrs (SD)	55.2 (2.1)	55.3 (2)	55.2 (2)	55.4 (2)	55.3 (2.1)
Cholesterol, mmol/L (SD)	6.37 (1.05)	6.45 (1.1)	6.37 (0.99)	6.43 (1.05)	6.4 (1.05)
SBP, mm Hg (SD)	145.1(19.5)	147.2 (20.5)	145.2 (18.8)	146.8 (19.7)	146 (19.6)
BMI, kg/m^2 (SD)	25.5 (3.1)	25.6 (3.4)	25.8 (3.2)	25.8 (3.4)	25.6 (3.3)
Diabetes, % (N)	2.8 (65)	3.6 (24)	2.5 (17)	2.7 (64)	2.8 (170)
Hypertension, % (N)	21.8 (512)	23.9 (160)	22.5 (152)	21.9 (517)	22.1 (1341)
Hypertensive medication, % (N)	15.2 (358)	16.5 (111)	14.6 (99)	13.9 (328)	14.8 (896)
Smoking status					
Never % (N) N=1437	25.8 (607)	21 (141)	25.2 (171)	21.9 (518)	23.7 (1437)
Current % (N) N=2460	37.3 (879)	47.4 (318)	39.0 (265)	42.2 (998)	40.5 (2460)
Former % (N) N=1890	32.7 (771)	27 (181)	31.4 (213)	30.7 (725)	31.1 (1890)
Unknown % (N) N=283	4.2 (100)	4.6 (31)	4.4 (30)	5.2 (122)	4.7 (283)
Number of events (mean age, yrs, at event)					
Coronary heart disease	384 (66.2)	131 (66.4)	104 (65.9)	433 (65.9)	1052 (66.0)
Stroke	208	64	65	212	549
Mean follow-up time, months					
Coronary heart disease	200	193	199	192	196
Stroke	204	195	203	197	200

Table 2. Cox Regression models 6070 men followed from 1974-1977 until event or until 75 years of age. All models are adjusted for age. Low strain group is used as the reference group in all analyses.

Strain group	Coronary heart disease		Stroke	
	N (N Events)	Hazard ratio (95% CI)	N (N Events)	Hazard ratio (95% CI)
All	6070 (1052)		6070 (549)	
Active	2357 (384)	1.06 (0.85-1.32)	2357 (208)	0.91 (0.70-1.22)
High strain	671 (131)	1.31 (1.01-1.70)	671 (64)	1.05 (0.74-1.48)
Passive	2363 (433)	1.23 (1.00-1.53)	2363 (212)	0.96 (0.74-1.28)
Ever-smokers	4350 (826)		4350 (406)	
Active	1650 (277)	1.00 (0.78-1.29)	1650 (152)	0.87 (0.64-1.20)
High strain	499 (109)	1.37 (1.02-1.83)	499 (46)	0.92 (0.62-1.38)
Passive	1723 (361)	1.31 (1.03-1.68)	1723 (158)	0.90 (0.66-1.25)
Never-smokers	1437 (184)		1437 (113)	
Active	607 (88)	1.21 (0.76-1.99)	607 (46)	1.11 (0.61-2.18)
High strain	141 (18)	1.04 (0.55-1.96)	141 (13)	1.39 (0.63-3.08)
Passive	518 (57)	0.90 (0.55-1.52)	518 (42)	1.18 (0.64-2.35)
Blue-collar	3020 (555)		3020 (279)	
Active	41 (7)	1.04 (0.44-2.11)	41 (5)	1.30 (0.45-2.906)
High strain	492 (101)	1.36 (1.01-184)	53 (492)	1.22 (0.82-1.82)
Passive	2008 (372)	1.20 (0.94-1.55)	2008 (75)	0.93 (0.68-1.30)
White-collar	3050 (497)		3050 (270)	
Active	2316 (377)	1.14 (0.80-1.71)	2316 (203)	0.93 (0.60-1.54)
High strain	179 (30)	1.15 (0.69-1.92)	179 (11)	0.63 (0.29-1.30)
Passive	355 (612)	1.24 (0.80-1.95)	355 (37)	1.16 (0.68-2.06)
Self-reported stress at baseline	2177 (381)		2177 (201)	
Active	1014 (170)	1.01 (0.70-1.49)	1014 (98)	1.98 (1.09-4.05)
High strain	236 (47)	1.28 (0.82-2.02)	236 (20)	1.92 (0.92-4.28)

Passive	722 (131)	1.13 (0.78-1.69)	722 (73)	2.15 (1.17-4.44)
No self-reported stress at baseline	3742 (381)		3742 (330)	
Active	1304 (203)	1.00 (0.77-1.32)	1304 (105)	0.67 (0.49-0.94)
High strain	411 (77)	1.23 (0.89-1.70)	411 (40)	0.84 (0.56-1.26)
Passive	1568 (635)	1.21 (0.94-1.58)	1568 (131)	0.72 (0.53-1.00)
Hypertension at baseline	1341 (314)		1341 (201)	
Active	512 (129)	1.50 (1.00-2.33)	512 (78)	0.86 (0.56-1.35)
High strain	160 (37)	1.37 (0.84-2.29)	160 (22)	0.79 (0.45-1.38)
Passive	517 (122)	1.41 (0.94-2.20)	517 (74)	0.81 (0.53-1.29)
No hypertension at baseline	4715 (736)		4715 (347)	
Active	1840 (254)	0.93 (0.72-1.21)	1840 (129)	0.96 (0.68-1.39)
High strain	509 (94)	1.30 (0.96-1.76)	509 (42)	1.21 (0.78-1.88)
Passive	1842 (311)	1.18 (0.93-1.53)	1842 (138)	1.07 (0.76-1.55)
Body mass index<30	5544 (938)		5544 (499)	
Active	2188 (343)	0.99 (0.79-1.25)	2188 (196)	0.97 (0.72-1.31)
High strain	598 (113)	1.23 (0.94-1.62)	598 (57)	1.08 (0.75-1.57)
Passive	2150 (387)	1.18 (0.95-1.48)	2150 (190)	0.99 (0.74-1.34)
Body mass index ≥30	516 (113)		516 (50)	
Active	167 (41)	1.92 (0.98-4.21)	167 (12)	0.54 (0.23-1.33)
High strain	70 (17)	2.05 (0.93-4.81)	70 (7)	0.88 (0.31-2.35)
Passive	209 (46)	1.76 (0.90-3.84)	209 (22)	0.83 (0.40-1.91)
No Diabetes at baseline	5900 (989)		5900 (515)	
Active	2292 (357)	1.04 (0.84-1.31)	2292 (194)	0.91 (0.69-1.22)
High strain	647 (123)	1.31 (1.01-1.72)	647 (60)	1.05 (0.74-1.50)

Passive	2299 (411)	1.24 (1.00-1.55)	2299 (200)	0.97 (0.73-1.30)
Diabetes at baseline	170 (63)		170 (34)	
Active	65 (27)	1.26 (0.56-3.39)	65 (14)	1.02 (0.36-3.59)
High strain	24 (8)	1.08 (0.37-3.28)	24 (4)	0.96 (0.23-4.09)
Passive	64 (22)	1.00 (0.43-2.73)	64 (12)	0.96 (0.33-3.43)

Table 3. Cox Regression models 6070 men followed from 1974-1977 until event or until 75 years of age. Subjects with events the first five years after baseline are excluded. Models adjusted for age, adiposity, diabetes, smoking and hypertension.

Strain group	Coronary heart disease		Stroke	
	N (N Events)	Hazard ratio (95% CI)	N (N Events)	Hazard ratio (95% CI)
Low strain	642 (85)	1.00	642 (60)	1.00
Active	2247 (312)	1.08 (0.85-1.38)	2275 (189)	0.93 (0.70-1.25)
High strain	630 (109)	1.29 (0.97-1.72)	640 (54)	0.91 (0.63-1.32)
Passive	2208 (351)	1.22 (0.97-1.56)	2248 (190)	0.94 (0.70-1.26)

Table 4. Cox regression models of 6070 men followed from 1974-1977 until event or until 75 years of age showing hazard ratios (HR) for low control and high demands in relation to coronary heart disease and stroke for different subgroups. All models are adjusted for age.

Subgroup	Coronary heart disease		Stroke	
	Low Control vs. high control	HR High Demands vs. low demands	HR Low Control vs. high control	HR High Demands vs. low demands
All	1.19 (1.06-1.35)	0.94 (0.84-1.07)	1.05 (0.89-1.24)	0.97 (0.82-1.15)
Never smokers	0.80 (0.60-1.07)	1.27 (0.95-1.71)	1.13 (0.78-1.64)	1.02 (0.70-1.48)
Ever smokers	1.32 (1.15-1.52)	0.87 (0.76-1.00)	1.01 (0.83-1.23)	0.95 (0.79-1.16)
No hypertension	1.28 (1.11-1.48)	0.88 (0.76-1.02)	1.14 (0.92-1.40)	0.96 (0.78-1.18)
Hypertension	1.02 (0.81-1.27)	1.12 (0.89-1.39)	0.91 (0.69-1.20)	0.98 (0.74-1.30)
BMI<30	1.20 (1.05-1.36)	0.92 (0.81-1.04)	1.03 (0.87-1.23)	1.00 (0.84-1.19)
BMI>=30	1.11 (0.77-1.61)	1.25 (0.86-1.81)	1.25 (0.72-2.22)	0.72 (0.40-1.26)
No diabetes	1.22 (1.07-1.38)	0.93 (0.82-1.05)	1.06 (0.89-1.26)	0.96 (0.81-1.14)
Diabetes	0.85 (0.51-1.40)	1.21 (0.74-2.01)	0.95 (0.47-1.87)	1.04 (0.52-2.07)
No stress	1.21 (1.04-1.42)	0.91 (0.78-1.06)	0.99 (0.80-1.23)	0.90 (0.73-1.12)
Self reported stress	1.16 (0.95-1.42)	0.96 (0.78-1.17)	1.15 (0.87-1.52)	1.04 (0.79-1.39)
Blue Collar	1.23 (0.98-1.56)	1.15 (0.93-1.41)	0.96 (0.72-1.31)	1.31 (0.97-1.73)
White collar	1.06 (0.84-1.33)	1.00 (0.80-1.26)	1.04 (0.75-1.40)	0.83 (0.62-1.12)

A longitudinal general-population based study of job strain and risk for coronary heart disease and stroke in Swedish men.

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The authors declare no conflicts of interest

Word count (body of test); 2 621

Keywords

Epidemiology, job strain, longitudinal, cerebrovascular disease

Abstract

Objectives

The aim was to investigate whether psycho-social stress based on the job-demand-control model increased the risk for coronary heart disease (CHD) and stroke.

Setting

Swedish men

Participants

The Primary Prevention Study comprise 6 070 men born between 1915 and 1925 free from previous history of coronary heart disease and stroke at baseline **(1974-1977)**. Psychosocial workplace exposure was assessed using a job-exposure matrix for the job-demand-control model based on occupation at baseline. The participants were followed from baseline examination, until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register for non-fatal and fatal stroke and CHD events. Cox regression models were used with stroke or CHD as the outcome using job-demand-control model and age as explanatory variables, as well as stratified models with regard to smoking, self-reported stress, socio-economic status, obesity, hypertension, and diabetes.

Primary and secondary outcome measures

Risk for stroke and coronary heart disease

Results

There was an increased risk (HR) for CHD in relation to high strain, HR 1.31, 95% CI 1.01-1.70. The risk was further increased among ever-smokers and among blue-collar workers. **There was a relation between low control and increased risk for CHD, HR 1.19, 95% CI 1.06-1.35.** There was no increased risk for stroke in any of the job-demand-control categories.

Conclusions

Exposure to occupational psycho-social stress defined as job strain **or low control** increased the risk for CHD, especially among smokers and blue-collar workers. There was no increased risk for stroke in any of the job-demand-control categories.

Introduction

During the last decades a growing body of evidence have accumulated showing that psychosocial stress is associated with adverse health outcomes, especially coronary heart disease (CHD) (1). Psycho-social stress as a risk factor has been studied both as a general factor and linked to the work-place. The most studied definition of work-place related stress has been the job-demand-control model (2). **According to Karasek the job demand variable constitutes volume and intensity of workload and job control referred to the working individual's potential control over pace and content of their tasks (2).** In this model **it** is postulated that the combination of high demands and low decision latitude at work results in high strain (job-strain) which increase the risk of cardiovascular diseases. There are studies showing that high strain is associated with a doubled risk of coronary heart disease. However, in a recent meta-analysis of 13 studies the association was rather modest, hazard ratio 1.23. The used models were adjusted for **gender** and age, and in some cases also for socioeconomic status. The authors concluded that adjustments for life style factors did not substantially affect the association (3). However, in **an additional paper from the** previous meta-analysis it was found that the risk of coronary heart disease was further increased among subjects with job-strain in combination with current smoking, being obese or reporting low physical activity (4). Hence, it seems to clear that job strain is associated with an increased risk for coronary heart disease, and there may also exist interactions with life-style factors.

There are studies indicating that self-reported psychosocial stress increase the risk for stroke (5, 6). However, the evidence between occupational exposure to psycho-social stress and stroke is less clear. There are a **two** longitudinal studies showing slightly increased risk for stroke associated with low control (7, 8). **One study showed an increased risk in working Finnish men (7) and in one study based on the Swedish working population there was an increased risk among women, but not among men (8).** The association with job-strain is also unclear, **two** studies **in women** show an association (9, 10) and **one study in the general population did not find any association, either among women or among men (11)**. In a prospective general-population based study from Japan it was found that men, but not women, with high-strain job

had an increased risk for stroke, with more than doubled risks among those with active, passive or high-strain jobs (12).

The aim of the present study was to investigate whether psycho-social stress based on the job-demand-control model increased the risk for coronary heart disease and stroke. **The study base is a longitudinal general population study of 6 070 Swedish men followed from baseline examination (1974-1977), until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register.**

Methods

Study population

The Primary Prevention Study (PPS) is a population-based cohort study from Gothenburg, Sweden. It was established in 1970 as previously described (13). The source population comprised all men living in Gothenburg born between 1915 and 1925. The initial study population was a random sample of 10 000 men, and 7494 men (75% of the sample) participated in screening examinations between January 1970 and March 1973 (14, 15). Three years later, **1974-1977**, a clinical follow-up investigation was performed where 7 133 men participated. In the present study we are using data from the first follow-up investigation, because in that round there were complete occupational data. All participants gave their informed consent to participate in the study and it was approved by the Ethics Committee for Medical Research at Gothenburg University.

The current occupation at baseline **(1974-1977)** was classified at three-digit level according to the Nordic Classification of Occupations, NYK-74 (16). For assessing the psychosocial workplace exposure we used a previously published job-exposure matrix (17, 18). This JEM was developed in late 1970s based on information from large Swedish population surveys where around 12 000 randomly selected subjects aged 25 to 74 years were classified for psychological demands and decision latitude. The JEM gives separate estimates of demand and control for 261 occupations separated into gender and age (25-44 and 45 to 74). Socioeconomic status, high or low, was obtained based on one-digit level of occupations, i e blue-collar vs. white-collar workers

Psychological job demands and decision latitude were explored with four items each. All items were scored using a scale (1-10), with a score of 10 indicating high psychological demands or high decision latitude. Each subject was assigned a certain score based on occupation and age. The scores were then dichotomized into high and low, using the median of the distribution as cut-off. Combining demand and control with the median cut-offs divides the participants into four categorical quadrants; high strain (high demand-low control), active (high demand-high control), passive (low demand-low control) and low-strain (low demand-high control).

In the present study there was information at baseline about age, country of birth (Sweden/other), body mass index (BMI), serum cholesterol (s-cholesterol) level, systolic blood pressure, diastolic blood pressure, use of antihypertensive medication (yes/no), history of diabetes (yes/no), coronary heart disease (yes/no), hypertension (yes/no) or stroke (yes/no) at baseline and smoking as previously described (19).

Subjects with coronary heart disease or stroke at baseline **(1974-1977)** were excluded resulting in a study population of 6 070 subjects (Table 1). Based on unique personal identification numbers, participants were followed from the date of their baseline examination until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register. The hospital discharge register has operated on a nationwide basis since 1987, but all discharges from Gothenburg hospitals have been entered in the national register since 1970 (except for 1976, because of a legislative change for that year). Additional data from the Gothenburg stroke register were used to identify strokes from the start of the study until 1983. The International Classification of Disease (ICD) codes listed in the registries were used to identify stroke events (both non-fatal and fatal events) and coronary heart disease during the entire follow-up period. The eighth version of the ICD code was used until 1986, ICD-9 was used from 1987 to 1996, and ICD-10 was used from 1997 onwards. Ischemic stroke was defined as ICD codes 431-438 and I61-I69. Non-fatal CHD was defined as 410 and I21. Fatal CHD was defined as 410-414 and I20-I25. **Each type of event was treated separately and only the first event of each type was used in the analysis.**

Statistical analysis

Descriptive statistics are presented as percentages or mean values with standard deviations (SD). All analyses were performed using the SAS statistical package (version 9.3) and R (version 3.0.1). The material were analysed with Cox regression models using SAS (the PHREG procedure). The proportional hazards assumptions were investigated using tests and plots based on weighted residuals (20) using the R package Survival. All assumptions were found reasonable except for the analysis **of** baseline diabetes. Hospital care or mortality (whatever came first) from stroke or coronary heart disease were events and time were measured as months since baseline. The observation period stopped at the age of 75. In the crude model hazard ratios were calculated using the job-demand-control model and age as explanatory variables. The low strain group was used as reference group. There were also models using high strain vs. all other subjects as an independent variable. There were also separate models stratifying for ever-smoking and never-smoking, adiposity (body mass index ≥30) or not, hypertension or not at baseline and diabetes or not, **self-reported stress or not at baseline and finally status as white-collar worker or blue-collar worker at baseline.** There was also one model with five years latency time, i.e excluding subject with any event occurring during the five first year during the follow-up.

Results

For the follow-up period there were 1 052 events due to coronary heart disease. The Cox regression models adjusted for age showed an increased risk (HR) for coronary heart disease in relation to high job strain, HR 1.31, 95% CI 1.01-1.70 (Table 2). In the stratified analysis high strain was associated with an even slightly higher risk for coronary heart disease among ever-smokers, (HR 1.37, 95% CI 1.02-1.83) and among blue-collar-workers (HR 1.36, 95% CI 1.01-1.84). Among obese subjects there was an indication of increased risk in relation to high-strain (HR 2.05, 95% CI 0.93-4.81) but with wide confidence intervals. In other strata there was an increased risk for coronary heart disease in the active group among those with hypertension (HR 1.50, 95% CI 1.00-2.33) (Table 2).

For the follow-up period there were 549 events due to stroke. In the total population there was no increased risk for stroke in any of the job-demand-control categories. In the stratified analyses those with self-reported stress at baseline seem to have increased risk, both in the active group (HR 1.98, 95% CI 1.09-4.05) and in the passive group as well (HR 2.15, 95% CI 1.17-4.44) (Table 2).

In the additional analyses subjects with five years latency time the results were similar. The risk for coronary heart disease among subjects with high strain was slightly higher (HR 1.34, 95% CI 1.00-1.80) (Table 3). In the final full model, adjusted age, adiposity, diabetes, smoking and hypertension, there was an indication of increased risk of CHD in relation to high strain (HR 1.29, 95% CI 0.97-1.72). There were no increased risks for stroke.

Further additional analyses explored the relations between low control and high demands, respectively. There was a clear relation between low control and increased risk for coronary heart disease (Table 4). This was found among all subjects, but also among smokers and in subjects without hypertension, without diabetes, without self-reported stress or with BMI<30. There were no clear signals regarding high demands and risk for coronary heart disease. There were no significant relations between low control or high demands and the risk for stroke (Table 4).

Discussion

Principal findings

In line with the other studies an increased risk for coronary heart disease was found in relation to high strain, job-strain. Of interest is that job strain risks increased further among ever-smokers, obese subjects and among subjects with low socioeconomic status. Active subjects with hypertension also ran an increased risk for coronary heart disease. **There was also a clear association between low control and increased risk for coronary heart disease.** Of interest, even if it is a negative report, is that there was no increased risk for stroke in most of the job-demand control groups. In the strata with high levels of self-reported stress there was an increased risk for stroke in all job-demand categories.

Methodological considerations

This study has several strengths, a general-population sample with a long period of follow-up and use of a national mortality register and hospital discharge register with high coverage. The assessment of psycho-social stress is based on occupations, which probably is less biased than self-reports of demand and control. Further, the population was in their fifties at baseline, meaning that they are quite stable in their occupations. Finally, the study comprises only men which limit the external validity.

The regression models have been adjusted for age. The study population comprises only men. In the literature it has been discussed that further adjustments for different lifestyle factors marginally decreased the risk estimates, which is in line with the findings from a large metaanalyses (3). There is also a possibility that that smoking, adiposity and hypertension can be part of the causal chain act and hence stratifications are to prefer. Further, there were no separate adjustments for socioeconomic position. The reason is that the exposure for psychosocial stress is based on occupational titles and the socioeconomic position is part of the occupational classification. However, in the stratified analysis, the risk for CHD was increased among blue-collar workers (low SES), but not among the white-collar works (high SES). In the literature, the job-demand-control model mostly predicts to ill-health associations among blue-collar workers, often men (2, 17, 21, 22, 23, 24). One plausible explanation is that the development of the JDC model was mainly conducted among male blue-collar jobs, and is consequently adjusted to such

job characteristics. When broadening study populations, more conflicting findings emerge. For example, little support has been found for female high-strain related ill-health (25).

The effect of psycho-social stress

It is evident from this study that both high strain and the passive dimension increase the risk for coronary heart disease. It is of interest that low control, the common denominator for job-strain and the passive dimension, was clearly related to increased risk for coronary heart disease.

The results from the present study indicate that exposure to occupational psycho-social stress is not increasing the risk for stroke. The study is rather large, 549 stroke events, and there was no increased risks in different lifestyle strata. Previously the association with job-strain has been unclear with both positive **(9, 10, 12)** and negative studies (11). There is probably a publication bias as studies with no or weak associations may not be published, as it has been shown for job strain and coronary heart disease (3). Hypertension has been associated with occupational psycho-social stress, especially among men (26). However, job strain was not associated with stroke among men with hypertension at baseline. Hence, the present study indicates that stroke has a different pattern of risk factors compared to coronary heart disease.

Self-reported stress has been associated with stroke, both in cohort studies (5, 27, 28) and in case-control studies (6, 29). Self-reported stress is a global composite item reflecting both occupational and non-occupational exposure. In the present study, increased risks for stroke was among subjects reporting stress at baseline and belonging to either the active, high strain or passive strata (compared to low strain). This may indicate an interaction between occupational and non-occupational stress in relation to stroke.

One limitation of our study is that there was only one assessment of the exposure the occupational psychosocial stress. There are indications in the literature that psychosocial stress occurs late in the causal chain for stroke as indicated by the observation that studies with short period of follow-up have higher risks of stroke in relation to psychosocial stress (8, 9). We have a rather long observation period, which may result in low risk estimates due to misclassification of the exposure.

Another limitation of this study is that the sample consisted only of men. Previous studies have indicated that health outcomes differ between men and women when exposed to Job demand-control (8, 9, 10, 11, 22, 25). Since the cohort was established with only men it was not possible to include women in our study, but we recommend that future similar analyzes include women as to investigate gender differences

The study confirms the previous findings of an association with job strain and risk for coronary heart disease. Compared to some other studies the risk levels were quite modest, which may reflect non-differential misclassification of the exposure assessment or may reflect the true underlying risk (3, 30). There was a slight interaction with lifestyle factors, especially smoking and to some extent also obesity, as the risks were further increased among smoking subjects and obese subjects. Positive interaction with both smoking and obesity was recently shown in a meta-analysis (4). A finding that needs to be replicated is that active subjects with hypertension had a high risk for coronary heart disease.

Conclusions

Exposure to occupational psycho-social stress defined as job strain increased the risk for CHD, especially among smokers and blue-collar workers. **Low control was also related to increased risk for CHD.** There was no increased risk for stroke in any of the job-demand-control categories.

Acknowledgements

The study was funded by the Swedish Research Council (VR), the Swedish Research Council for Health, Working Life and Welfare (FORTE) and the Swedish Heart and Lung Foundation

Strengths and limitations of the paper;

Job strain increase the risk for coronary heart disease but the relation to stroke is uncertain. There is a need for longitudinal general-population based studies in this field. This study confirms that job strain increase the risk for coronary heart disease, but the risk seems to be limited to blue-collar workers. There was no clear relation between job strain and risk for stroke.

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Table 1. Baseline characteristics of a general population study of 6 070 Swedish men.

	Active N=2357	High strain N=671	Low strain N=679	Passive N=2363	Overall N=6070
Age, yrs (SD)	55.2 (2.1)	55.3 (2)	55.2 (2)	55.4 (2)	55.3 (2.1)
Cholesterol, mmol/L (SD)	6.37 (1.05)	6.45 (1.1)	6.37 (0.99)	6.43 (1.05)	6.4 (1.05)
SBP, mm Hg (SD)	145.1(19.5)	147.2 (20.5)	145.2 (18.8)	146.8 (19.7)	146 (19.6)
BMI, kg/m^2 (SD)	25.5 (3.1)	25.6 (3.4)	25.8 (3.2)	25.8 (3.4)	25.6 (3.3)
Diabetes, % (N)	2.8 (65)	3.6 (24)	2.5 (17)	2.7 (64)	2.8 (170)
Hypertension, % (N)	21.8 (512)	23.9 (160)	22.5 (152)	21.9 (517)	22.1 (1341)
Hypertensive medication, % (N)	15.2 (358)	16.5 (111)	14.6 (99)	13.9 (328)	14.8 (896)
Smoking status					
Never % (N) N=1437	25.8 (607)	21 (141)	25.2 (171)	21.9 (518)	23.7 (1437)
Current % (N) N=2460	37.3 (879)	47.4 (318)	39.0 (265)	42.2 (998)	40.5 (2460)
Former % (N) N=1890	32.7 (771)	27 (181)	31.4 (213)	30.7 (725)	31.1 (1890)
Unknown % (N) N=283	4.2 (100)	4.6 (31)	4.4 (30)	5.2 (122)	4.7 (283)
Number of events (mean age, yrs, at event)					
Coronary heart disease	384 (66.2)	131 (66.4)	104 (65.9)	433 (65.9)	1052 (66.0)
Stroke	208	64	65	212	549
Mean follow-up time, months					
Coronary heart disease	200	193	199	192	196
Stroke	204	195	203	197	200

Table 2. Cox Regression models 6070 men followed from 1974-1977 until event or until 75 years of age. All models are adjusted for age. Low strain group is used as the reference group in all analyses.

Strain group	Coronary heart disease		Stroke	
	N (N Events)	Hazard ratio (95% CI)	N (N Events)	Hazard ratio (95% CI)
All	6070 (1052)		6070 (549)	
Active	2357 (384)	1.06 (0.85-1.32)	2357 (208)	0.91 (0.70-1.22)
High strain	671 (131)	1.31 (1.01-1.70)	671 (64)	1.05 (0.74-1.48)
Passive	2363 (433)	1.23 (1.00-1.53)	2363 (212)	0.96 (0.74-1.28)
Ever-smokers	4350 (826)		4350 (406)	
Active	1650 (277)	1.00 (0.78-1.29)	1650 (152)	0.87 (0.64-1.20)
High strain	499 (109)	1.37 (1.02-1.83)	499 (46)	0.92 (0.62-1.38)
Passive	1723 (361)	1.31 (1.03-1.68)	1723 (158)	0.90 (0.66-1.25)
Never-smokers	1437 (184)		1437 (113)	
Active	607 (88)	1.21 (0.76-1.99)	607 (46)	1.11 (0.61-2.18)
High strain	141 (18)	1.04 (0.55-1.96)	141 (13)	1.39 (0.63-3.08)
Passive	518 (57)	0.90 (0.55-1.52)	518 (42)	1.18 (0.64-2.35)
Blue-collar	3020 (555)		3020 (279)	
Active	41 (7)	1.04 (0.44-2.11)	41 (5)	1.30 (0.45-2.906)
High strain	492 (101)	1.36 (1.01-184)	53 (492)	1.22 (0.82-1.82)
Passive	2008 (372)	1.20 (0.94-1.55)	2008 (75)	0.93 (0.68-1.30)
White-collar	3050 (497)		3050 (270)	
Active	2316 (377)	1.14 (0.80-1.71)	2316 (203)	0.93 (0.60-1.54)
High strain	179 (30)	1.15 (0.69-1.92)	179 (11)	0.63 (0.29-1.30)
Passive	355 (612)	1.24 (0.80-1.95)	355 (37)	1.16 (0.68-2.06)
Self-reported stress at baseline	2177 (381)		2177 (201)	
Active	1014 (170)	1.01 (0.70-1.49)	1014 (98)	1.98 (1.09-4.05)
High strain	236 (47)	1.28 (0.82-2.02)	236 (20)	1.92 (0.92-4.28)

Passive	722 (131)	1.13 (0.78-1.69)	722 (73)	2.15 (1.17-4.44)
No self-reported stress at baseline	3742 (381)		3742 (330)	
Active	1304 (203)	1.00 (0.77-1.32)	1304 (105)	0.67 (0.49-0.94)
High strain	411 (77)	1.23 (0.89-1.70)	411 (40)	0.84 (0.56-1.26)
Passive	1568 (635)	1.21 (0.94-1.58)	1568 (131)	0.72 (0.53-1.00)
Hypertension at baseline	1341 (314)		1341 (201)	
Active	512 (129)	1.50 (1.00-2.33)	512 (78)	0.86 (0.56-1.35)
High strain	160 (37)	1.37 (0.84-2.29)	160 (22)	0.79 (0.45-1.38)
Passive	517 (122)	1.41 (0.94-2.20)	517 (74)	0.81 (0.53-1.29)
No hypertension at baseline	4715 (736)		4715 (347)	
Active	1840 (254)	0.93 (0.72-1.21)	1840 (129)	0.96 (0.68-1.39)
High strain	509 (94)	1.30 (0.96-1.76)	509 (42)	1.21 (0.78-1.88)
Passive	1842 (311)	1.18 (0.93-1.53)	1842 (138)	1.07 (0.76-1.55)
Body mass index<30	5544 (938)		5544 (499)	
Active	2188 (343)	0.99 (0.79-1.25)	2188 (196)	0.97 (0.72-1.31)
High strain	598 (113)	1.23 (0.94-1.62)	598 (57)	1.08 (0.75-1.57)
Passive	2150 (387)	1.18 (0.95-1.48)	2150 (190)	0.99 (0.74-1.34)
Body mass index ≥30	516 (113)		516 (50)	
Active	167 (41)	1.92 (0.98-4.21)	167 (12)	0.54 (0.23-1.33)
High strain	70 (17)	2.05 (0.93-4.81)	70 (7)	0.88 (0.31-2.35)
Passive	209 (46)	1.76 (0.90-3.84)	209 (22)	0.83 (0.40-1.91)
No Diabetes at baseline	5900 (989)		5900 (515)	
Active	2292 (357)	1.04 (0.84-1.31)	2292 (194)	0.91 (0.69-1.22)
High strain	647 (123)	1.31 (1.01-1.72)	647 (60)	1.05 (0.74-1.50)

Passive	2299 (411)	1.24 (1.00-1.55)	2299 (200)	0.97 (0.73-1.30)
Diabetes at baseline	170 (63)		170 (34)	
Active	65 (27)	1.26 (0.56-3.39)	65 (14)	1.02 (0.36-3.59)
High strain	24 (8)	1.08 (0.37-3.28)	24 (4)	0.96 (0.23-4.09)
Passive	64 (22)	1.00 (0.43-2.73)	64 (12)	0.96 (0.33-3.43)

Table 3. Cox Regression models 6070 men followed from 1974-1977 until event or until 75 years of age. Subjects with events the first five years after baseline are excluded. Models adjusted for age, adiposity, diabetes, smoking and hypertension.

Strain group	Coronary heart disease		Stroke	
	N (N Events)	Hazard ratio (95% CI)	N (N Events)	Hazard ratio (95% CI)
Low strain	642 (85)	1.00	642 (60)	1.00
Active	2247 (312)	1.08 (0.85-1.38)	2275 (189)	0.93 (0.70-1.25)
High strain	630 (109)	1.29 (0.97-1.72)	640 (54)	0.91 (0.63-1.32)
Passive	2208 (351)	1.22 (0.97-1.56)	2248 (190)	0.94 (0.70-1.26)

Table 4. Cox regression models of 6070 men followed from 1974-1977 until event or until 75 years of age showing hazard ratios (HR) for low control and high demands in relation to coronary heart disease and stroke for different subgroups. All models are adjusted for age.

Subgroup	Coronary heart disease		Stroke	
	Low Control vs. high control	HR High Demands vs. low demands	HR Low Control vs. high control	HR High Demands vs. low demands
All	1.19 (1.06-1.35)	0.94 (0.84-1.07)	1.05 (0.89-1.24)	0.97 (0.82-1.15)
Never smokers	0.80 (0.60-1.07)	1.27 (0.95-1.71)	1.13 (0.78-1.64)	1.02 (0.70-1.48)
Ever smokers	1.32 (1.15-1.52)	0.87 (0.76-1.00)	1.01 (0.83-1.23)	0.95 (0.79-1.16)
No hypertension	1.28 (1.11-1.48)	0.88 (0.76-1.02)	1.14 (0.92-1.40)	0.96 (0.78-1.18)
Hypertension	1.02 (0.81-1.27)	1.12 (0.89-1.39)	0.91 (0.69-1.20)	0.98 (0.74-1.30)
BMI<30	1.20 (1.05-1.36)	0.92 (0.81-1.04)	1.03 (0.87-1.23)	1.00 (0.84-1.19)
BMI>=30	1.11 (0.77-1.61)	1.25 (0.86-1.81)	1.25 (0.72-2.22)	0.72 (0.40-1.26)
No diabetes	1.22 (1.07-1.38)	0.93 (0.82-1.05)	1.06 (0.89-1.26)	0.96 (0.81-1.14)
Diabetes	0.85 (0.51-1.40)	1.21 (0.74-2.01)	0.95 (0.47-1.87)	1.04 (0.52-2.07)
No stress	1.21 (1.04-1.42)	0.91 (0.78-1.06)	0.99 (0.80-1.23)	0.90 (0.73-1.12)
Self reported stress	1.16 (0.95-1.42)	0.96 (0.78-1.17)	1.15 (0.87-1.52)	1.04 (0.79-1.39)
Blue Collar	1.23 (0.98-1.56)	1.15 (0.93-1.41)	0.96 (0.72-1.31)	1.31 (0.97-1.73)
White collar	1.06 (0.84-1.33)	1.00 (0.80-1.26)	1.04 (0.75-1.40)	0.83 (0.62-1.12)

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Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004355.R2
Article Type:	Research
Date Submitted by the Author:	07-Feb-2014
Complete List of Authors:	Torén, Kjell; Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden, Section of Occupational and Environmental Medicine Schiöler, Linus; Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden, Section of Occupational and Environmental Medicine Kok, Wai; Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden, Department of Molecular and Clinical Medicine Novak, Masuma; Medicine, ; Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden, Department of Molecular and Clinical Medicine Söderberg, Mia; Medicine, Occupational and environmental medicine; Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden, Section of Occupational and Environmental Medicine Rosengren, Annika; Medicine, ; Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden, Department of Molecular and Clinical Medicine
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Cardiovascular medicine, Epidemiology
Keywords:	STROKE MEDICINE, PUBLIC HEALTH, OCCUPATIONAL & INDUSTRIAL MEDICINE

A longitudinal general-population based study of job strain and risk for coronary heart disease and stroke in Swedish men.

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The authors declare no conflicts of interest

Word count (body of test); 2 623

Keywords

Epidemiology, job strain, longitudinal, cerebrovascular disease

Abstract

Objectives

The aim was to investigate whether psycho-social stress based on the job-demand-control model increased the risk for coronary heart disease (CHD) and stroke.

Setting

Swedish men

Participants

The Primary Prevention Study comprise 6 070 men born between 1915 and 1925 free from previous history of coronary heart disease and stroke at baseline (1974-1977). Psychosocial workplace exposure was assessed using a job-exposure matrix for the job-demand-control model based on occupation at baseline. The participants were followed from baseline examination, until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register for non-fatal and fatal stroke and CHD events. Cox regression models were used with stroke or CHD as the outcome using job-demand-control model and age as explanatory variables, as well as stratified models with regard to smoking, self-reported stress, socio-economic status, obesity, hypertension, and diabetes.

Primary and secondary outcome measures

Risk for stroke and coronary heart disease

Results

There was an increased risk (HR) for CHD in relation to high strain, HR 1.31, 95% CI 1.01-1.70. The risk was further increased among ever-smokers and among blue-collar workers. There was a relation between low control and increased risk for CHD, HR 1.19, 95% CI 1.06-1.35. There was no increased risk for stroke in any of the job-demand-control categories.

Conclusions

Exposure to occupational psycho-social stress defined as job strain or low control increased the risk for CHD, especially among smokers and blue-collar workers. There was no increased risk for stroke in any of the job-demand-control categories.

Strengths and limitations of the paper;

Job strain increase the risk for coronary heart disease but the relation to stroke is uncertain. There is a need for longitudinal general-population based studies in this field. This study confirms that job strain increase the risk for coronary heart disease, but the risk seems to be limited to blue-collar workers. There was no clear relation between job strain and risk for stroke.

Introduction

During the last decades a growing body of evidence have accumulated showing that psychosocial stress is associated with adverse health outcomes, especially coronary heart disease (CHD) (1). Psycho-social stress as a risk factor has been studied both as a general factor and linked to the work-place. The most studied definition of work-place related stress has been the job-demand-control model (2). According to Karasek the job demand variable constitutes volume and intensity of workload and job control referred to the working individual's potential control over pace and content of their tasks (2). In this model it is postulated that the combination of high demands and low decision latitude at work results in high strain (job-strain) which increase the risk of cardiovascular diseases. There are studies showing that high strain is associated with a doubled risk of coronary heart disease. However, in a recent meta-analysis of 13 studies the association was rather modest, hazard ratio 1.23. The used models were adjusted for gender and age, and in some cases also for socioeconomic status. The authors concluded that adjustments for life style factors did not substantially affect the association (3). However, in an additional paper from the previous meta-analysis it was found that the risk of coronary heart disease was further increased among subjects with job-strain in combination with current smoking, being obese or reporting low physical activity (4). Hence, it seems to clear that job strain is associated with an increased risk for coronary heart disease, and there may also exist interactions with life-style factors.

There are studies indicating that self-reported psychosocial stress increase the risk for stroke (5, 6). However, the evidence between occupational exposure to psycho-social stress and stroke is less clear. There are a two longitudinal studies showing slightly increased risk for stroke associated with low control (7, 8). One study showed an increased risk in working Finnish men (7) and in one study based on the Swedish working population there was an increased risk among women, but not among men (8). The association with job-strain is also unclear, two studies in women show an association (9, 10) and one study in the general population did not find any association, either among women or among men (11). In a prospective general-population based study from Japan it was found that men, but not women, with high-strain job had an increased

risk for stroke, with more than doubled risks among those with active, passive or high-strain jobs (12).

The aim of the present study was to investigate whether psycho-social stress based on the job-demand-control model increased the risk for coronary heart disease and stroke. The study base is a longitudinal general population study of 6 070 Swedish men followed from baseline examination (1974-1977), until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register.

Methods

Study population

The Primary Prevention Study (PPS) is a population-based cohort study from Gothenburg, Sweden. It was established in 1970 as previously described (13). The source population comprised all men living in Gothenburg born between 1915 and 1925. The initial study population was a random sample of 10 000 men, and 7494 men (75% of the sample) participated in screening examinations between January 1970 and March 1973 (14, 15). Three years later, 1974-1977, a clinical follow-up investigation was performed where 7 133 men participated. In the present study we are using data from the first follow-up investigation, because in that round there were complete occupational data. All participants gave their informed consent to participate in the study and it was approved by the Ethics Committee for Medical Research at Gothenburg University.

The current occupation at baseline (1974-1977) was classified at three-digit level according to the Nordic Classification of Occupations, NYK-74 (16). For assessing the psychosocial workplace exposure we used a previously published job-exposure matrix (17, 18). This JEM was developed in late 1970s based on information from large Swedish population surveys where around 12 000 randomly selected subjects aged 25 to 74 years were classified for psychological demands and decision latitude. The JEM gives separate estimates of demand and control for 261 occupations separated into gender and age (25-44 and 45 to 74). Socioeconomic status, high or low, was obtained based on one-digit level of occupations, i e blue-collar vs. white-collar workers

Psychological job demands and decision latitude were explored with four items each. All items were scored using a scale (1-10), with a score of 10 indicating high psychological demands or high decision latitude. Each subject was assigned a certain score based on occupation and age. The scores were then dichotomized into high and low, using the median of the distribution as cut-off. Combining demand and control with the median cut-offs divides the participants into four categorical quadrants; high strain (high demand-low control), active (high demand-high control), passive (low demand-low control) and low-strain (low demand-high control).

In the present study there was information at baseline about age, country of birth (Sweden/other), body mass index (BMI), serum cholesterol (s-cholesterol) level, systolic blood pressure, diastolic blood pressure, use of antihypertensive medication (yes/no), history of diabetes (yes/no), coronary heart disease (yes/no), hypertension (yes/no) or stroke (yes/no) at baseline, self-reported stress and smoking as previously described (19).

Subjects with coronary heart disease or stroke at baseline (1974-1977) were excluded resulting in a study population of 6 070 subjects (Table 1). Based on unique personal identification numbers, participants were followed from the date of their baseline examination until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register. The hospital discharge register has operated on a nationwide basis since 1987, but all discharges from Gothenburg hospitals have been entered in the national register since 1970 (except for 1976, because of a legislative change for that year). Additional data from the Gothenburg stroke register were used to identify strokes from the start of the study until 1983. The International Classification of Disease (ICD) codes listed in the registries were used to identify stroke events (both non-fatal and fatal events) and coronary heart disease during the entire follow-up period. The eighth version of the ICD code was used until 1986, ICD-9 was used from 1987 to 1996, and ICD-10 was used from 1997 onwards. Ischemic stroke was defined as ICD codes 431-438 and I61-I69. Non-fatal CHD was defined as 410 and I21. Fatal CHD was defined as 410-414 and I20-I25. Each type of event was treated separately and only the first event of each type was used in the analysis.

Statistical analysis

Descriptive statistics are presented as percentages or mean values with standard deviations (SD). All analyses were performed using the SAS statistical package (version 9.3) and R (version 3.0.1). The material were analysed with Cox regression models using SAS (the PHREG procedure). The proportional hazards assumptions were investigated using tests and plots based on weighted residuals (20) using the R package Survival. All assumptions were found reasonable except for the analysis of baseline diabetes. Hospital care or mortality (whatever came first) from stroke or coronary heart disease were events and time were measured as months since baseline. The observation period stopped at the age of 75. In the crude model hazard ratios were calculated using the job-demand-control model and age as explanatory variables. The low strain group was used as reference group. There were also models using high strain vs. all other subjects as an independent variable. There were also separate models stratifying for ever-smoking and never-smoking, adiposity (body mass index ≥30) or not, hypertension or not at baseline and diabetes or not, self-reported stress or not at baseline and finally status as white-collar worker or blue-collar worker at baseline. There was also one model with five years latency time, i.e excluding subject with any event occurring during the five first year during the follow-up.

Results

For the follow-up period there were 1 052 events due to coronary heart disease. The Cox regression models adjusted for age showed an increased risk (HR) for coronary heart disease in relation to high job strain, HR 1.31, 95% CI 1.01-1.70 (Table 2). In the stratified analysis high strain was associated with an even slightly higher risk for coronary heart disease among ever-smokers, (HR 1.37, 95% CI 1.02-1.83) and among blue-collar-workers (HR 1.36, 95% CI 1.01-1.84). Among obese subjects there was an indication of increased risk in relation to high-strain (HR 2.05, 95% CI 0.93-4.81) but with wide confidence intervals. In other strata there was an increased risk for coronary heart disease in the active group among those with hypertension (HR 1.50, 95% CI 1.00-2.33) (Table 2).

For the follow-up period there were 549 events due to stroke. In the total population there was no increased risk for stroke in any of the job-demand-control categories. In the stratified analyses those with self-reported stress at baseline seem to have increased risk, both in the active group (HR 1.98, 95% CI 1.09-4.05) and in the passive group as well (HR 2.15, 95% CI 1.17-4.44) (Table 2).

In the additional analyses subjects with five years latency time the results were similar. The risk for coronary heart disease among subjects with high strain was slightly higher (HR 1.34, 95% CI 1.00-1.80) (Table 3). In the final full model, adjusted age, adiposity, diabetes, smoking and hypertension, there was an indication of increased risk of CHD in relation to high strain (HR 1.29, 95% CI 0.97-1.72). There were no increased risks for stroke.

Further additional analyses explored the relations between low control and high demands, respectively. There was a clear relation between low control and increased risk for coronary heart disease (Table 4). This was found among all subjects, but also among smokers and in subjects without hypertension, without diabetes, without self-reported stress or with BMI<30. There were no clear signals regarding high demands and risk for coronary heart disease. There were no significant relations between low control or high demands and the risk for stroke (Table 4).

Discussion

Principal findings

In line with the other studies an increased risk for coronary heart disease was found in relation to high strain, job-strain. Of interest is that job strain risks increased further among ever-smokers, obese subjects and among subjects with low socioeconomic status. Active subjects with hypertension also ran an increased risk for coronary heart disease. There was also a clear association between low control and increased risk for coronary heart disease. Of interest, even if it is a negative report, is that there was no increased risk for stroke in most of the job-demand control groups. In the strata with high levels of self-reported stress there was an increased risk for stroke in all job-demand categories.

Methodological considerations

This study has several strengths, a general-population sample with a long period of follow-up and use of a national mortality register and hospital discharge register with high coverage. The assessment of psycho-social stress is based on occupations, which probably is less biased than self-reports of demand and control. Further, the population was in their fifties at baseline, meaning that they are quite stable in their occupations. Finally, the study comprises only men which limit the external validity.

The regression models have been adjusted for age. The study population comprises only men. In the literature it has been discussed that further adjustments for different lifestyle factors marginally decreased the risk estimates, which is in line with the findings from a large metaanalyses (3). There is also a possibility that that smoking, adiposity and hypertension can be part of the causal chain act and hence stratifications are to prefer. Further, there were no separate adjustments for socioeconomic position. The reason is that the exposure for psychosocial stress is based on occupational titles and the socioeconomic position is part of the occupational classification. However, in the stratified analysis, the risk for CHD was increased among blue-collar workers (low SES), but not among the white-collar works (high SES). In the literature, the job-demand-control model mostly predicts to ill-health associations among blue-collar workers, often men (2, 17, 21, 22, 23, 24). One plausible explanation is that the development of the JDC model was mainly conducted among male blue-collar jobs, and is consequently adjusted to such

job characteristics. When broadening study populations, more conflicting findings emerge. For example, little support has been found for female high-strain related ill-health (25).

The effect of psycho-social stress

It is evident from this study that both high strain and the passive dimension increase the risk for coronary heart disease. It is of interest that low control, the common denominator for job-strain and the passive dimension, was clearly related to increased risk for coronary heart disease.

The results from the present study indicate that exposure to occupational psycho-social stress is not increasing the risk for stroke. The study is rather large, 549 stroke events, and there was no increased risks in different lifestyle strata. Previously the association with job-strain has been unclear with both positive (9, 10, 12) and negative studies (11). There is probably a publication bias as studies with no or weak associations may not be published, as it has been shown for job strain and coronary heart disease (3). Hypertension has been associated with occupational psycho-social stress, especially among men (26). However, job strain was not associated with stroke among men with hypertension at baseline. Hence, the present study indicates that stroke has a different pattern of risk factors compared to coronary heart disease.

Self-reported stress has been associated with stroke, both in cohort studies (5, 27, 28) and in case-control studies (6, 29). Self-reported stress is a global composite item reflecting both occupational and non-occupational exposure. In the present study, increased risks for stroke was among subjects reporting stress at baseline and belonging to either the active, high strain or passive strata (compared to low strain). This may indicate an interaction between occupational and non-occupational stress in relation to stroke.

One limitation of our study is that there was only one assessment of the exposure the occupational psychosocial stress. There are indications in the literature that psychosocial stress occurs late in the causal chain for stroke as indicated by the observation that studies with short period of follow-up have higher risks of stroke in relation to psychosocial stress (8, 9). We have a rather long observation period, which may result in low risk estimates due to misclassification of the exposure.

Another limitation of this study is that the sample consisted only of men. Previous studies have indicated that health outcomes differ between men and women when exposed to Job demand-control (8, 9, 10, 11, 22, 25). Since the cohort was established with only men it was not possible to include women in our study, but we recommend that future similar analyzes include women as to investigate gender differences

The study confirms the previous findings of an association with job strain and risk for coronary heart disease. Compared to some other studies the risk levels were quite modest, which may reflect non-differential misclassification of the exposure assessment or may reflect the true underlying risk (3, 30). There was a slight interaction with lifestyle factors, especially smoking and to some extent also obesity, as the risks were further increased among smoking subjects and obese subjects. Positive interaction with both smoking and obesity was recently shown in a meta-analysis (4). A finding that needs to be replicated is that active subjects with hypertension had a high risk for coronary heart disease.

Conclusions

Exposure to occupational psycho-social stress defined as job strain increased the risk for CHD, especially among smokers and blue-collar workers. Low control was also related to increased risk for CHD. There was no increased risk for stroke in any of the job-demand-control categories.

Acknowledgements

The study was funded by the Swedish Research Council (VR), the Swedish Research Council for Health, Working Life and Welfare (FORTE) and the Swedish Heart and Lung Foundation

Contributorship Statement

Alla authors was responsible for the design, drafting of the manuscript and for the final approvement of the mansucript. In addition, Linus Schiöler performed the statistical analyses.

Competing interests

None

Data Sharing Statement

This is a large general population study which ahve been followed for decades. There are a lot of unpublished data in the data set. Scientific cooperation around this study is possible.

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Table 1. Baseline characteristics of a general population study of 6 070 Swedish men.

	Active N=2357	High strain N=671	Low strain N=679	Passive N=2363	Overall N=6070
Age, yrs (SD)	55.2 (2.1)	55.3 (2)	55.2 (2)	55.4 (2)	55.3 (2.1)
Cholesterol, mmol/L (SD)	6.37 (1.05)	6.45 (1.1)	6.37 (0.99)	6.43 (1.05)	6.4 (1.05)
SBP, mm Hg (SD)	145.1(19.5)	147.2 (20.5)	145.2 (18.8)	146.8 (19.7)	146 (19.6)
BMI, kg/m^2 (SD)	25.5 (3.1)	25.6 (3.4)	25.8 (3.2)	25.8 (3.4)	25.6 (3.3)
Diabetes, % (N)	2.8 (65)	3.6 (24)	2.5 (17)	2.7 (64)	2.8 (170)
Hypertension, % (N)	21.8 (512)	23.9 (160)	22.5 (152)	21.9 (517)	22.1 (1341)
Hypertensive medication, % (N)	15.2 (358)	16.5 (111)	14.6 (99)	13.9 (328)	14.8 (896)
White collar Job, % (N)	98.3 (2316)	26.7 (179)	29.5 (200)	15.0 (355)	36.8 (2177)
Self-reported stress at baseline, % (N)	43.7 (1014)	36.5 (236)	30.9 (205)	31.5 (722)	36.8 (2177)
Smoking status					
Never % (N) N=1437	25.8 (607)	21 (141)	25.2 (171)	21.9 (518)	23.7 (1437)
Current % (N) N=2460	37.3 (879)	47.4 (318)	39.0 (265)	42.2 (998)	40.5 (2460)
Former % (N) N=1890	32.7 (771)	27 (181)	31.4 (213)	30.7 (725)	31.1 (1890)
Unknown % (N) N=283	4.2 (100)	4.6 (31)	4.4 (30)	5.2 (122)	4.7 (283)
Number of events (mean age, yrs, at event)					
Coronary heart disease	384 (66.2)	131 (66.4)	104 (65.9)	433 (65.9)	1052 (66.0)
Stroke	208	64	65	212	549

Mean follow-up time, months					
Coronary heart disease	200	193	199	192	196
Stroke	204	195	203	197	200

Table 2. Cox Regression models 6070 men followed from 1974-1977 until event or until 75 years of age. All models are adjusted for age. Low strain group is used as the reference group in all analyses.

Strain group	Coronary heart disease		Stroke	
	N (N Events)	Hazard ratio (95% CI)	N (N Events)	Hazard ratio (95% CI)
All	6070 (1052)		6070 (549)	
Active	2357 (384)	1.06 (0.85-1.32)	2357 (208)	0.91 (0.70-1.22)
High strain	671 (131)	1.31 (1.01-1.70)	671 (64)	1.05 (0.74-1.48)
Passive	2363 (433)	1.23 (1.00-1.53)	2363 (212)	0.96 (0.74-1.28)
Ever-smokers	4350 (826)		4350 (406)	
Active	1650 (277)	1.00 (0.78-1.29)	1650 (152)	0.87 (0.64-1.20)
High strain	499 (109)	1.37 (1.02-1.83)	499 (46)	0.92 (0.62-1.38)
Passive	1723 (361)	1.31 (1.03-1.68)	1723 (158)	0.90 (0.66-1.25)
Never-smokers	1437 (184)		1437 (113)	
Active	607 (88)	1.21 (0.76-1.99)	607 (46)	1.11 (0.61-2.18)
High strain	141 (18)	1.04 (0.55-1.96)	141 (13)	1.39 (0.63-3.08)
Passive	518 (57)	0.90 (0.55-1.52)	518 (42)	1.18 (0.64-2.35)
Blue-collar	3020 (555)		3020 (279)	
Active	41 (7)	1.04 (0.44-2.11)	41 (5)	1.30 (0.45-2.906)
High strain	492 (101)	1.36 (1.01-184)	53 (492)	1.22 (0.82-1.82)
Passive	2008 (372)	1.20 (0.94-1.55)	2008 (75)	0.93 (0.68-1.30)
White-collar	3050 (497)		3050 (270)	
Active	2316 (377)	1.14 (0.80-1.71)	2316 (203)	0.93 (0.60-1.54)
High strain	179 (30)	1.15 (0.69-1.92)	179 (11)	0.63 (0.29-1.30)
Passive	355 (612)	1.24 (0.80-1.95)	355 (37)	1.16 (0.68-2.06)
Self-reported stress at baseline	2177 (381)		2177 (201)	
Active	1014 (170)	1.01 (0.70-1.49)	1014 (98)	1.98 (1.09-4.05)
High strain	236 (47)	1.28 (0.82-2.02)	236 (20)	1.92 (0.92-4.28)

Passive	722 (131)	1.13 (0.78-1.69)	722 (73)	2.15 (1.17-4.44)
No self-reported stress at baseline	3742 (381)		3742 (330)	
Active	1304 (203)	1.00 (0.77-1.32)	1304 (105)	0.67 (0.49-0.94)
High strain	411 (77)	1.23 (0.89-1.70)	411 (40)	0.84 (0.56-1.26)
Passive	1568 (635)	1.21 (0.94-1.58)	1568 (131)	0.72 (0.53-1.00)
Hypertension at baseline	1341 (314)		1341 (201)	
Active	512 (129)	1.50 (1.00-2.33)	512 (78)	0.86 (0.56-1.35)
High strain	160 (37)	1.37 (0.84-2.29)	160 (22)	0.79 (0.45-1.38)
Passive	517 (122)	1.41 (0.94-2.20)	517 (74)	0.81 (0.53-1.29)
No hypertension at baseline	4715 (736)		4715 (347)	
Active	1840 (254)	0.93 (0.72-1.21)	1840 (129)	0.96 (0.68-1.39)
High strain	509 (94)	1.30 (0.96-1.76)	509 (42)	1.21 (0.78-1.88)
Passive	1842 (311)	1.18 (0.93-1.53)	1842 (138)	1.07 (0.76-1.55)
Body mass index<30	5544 (938)		5544 (499)	
Active	2188 (343)	0.99 (0.79-1.25)	2188 (196)	0.97 (0.72-1.31)
High strain	598 (113)	1.23 (0.94-1.62)	598 (57)	1.08 (0.75-1.57)
Passive	2150 (387)	1.18 (0.95-1.48)	2150 (190)	0.99 (0.74-1.34)
Body mass index ≥30	516 (113)		516 (50)	
Active	167 (41)	1.92 (0.98-4.21)	167 (12)	0.54 (0.23-1.33)
High strain	70 (17)	2.05 (0.93-4.81)	70 (7)	0.88 (0.31-2.35)
Passive	209 (46)	1.76 (0.90-3.84)	209 (22)	0.83 (0.40-1.91)
No Diabetes at baseline	5900 (989)		5900 (515)	
Active	2292 (357)	1.04 (0.84-1.31)	2292 (194)	0.91 (0.69-1.22)
High strain	647 (123)	1.31 (1.01-1.72)	647 (60)	1.05 (0.74-1.50)

Passive	2299 (411)	1.24 (1.00-1.55)	2299 (200)	0.97 (0.73-1.30)
Diabetes at baseline	170 (63)		170 (34)	
Active	65 (27)	1.26 (0.56-3.39)	65 (14)	1.02 (0.36-3.59)
High strain	24 (8)	1.08 (0.37-3.28)	24 (4)	0.96 (0.23-4.09)
Passive	64 (22)	1.00 (0.43-2.73)	64 (12)	0.96 (0.33-3.43)

Table 3. Cox Regression models 6070 men followed from 1974-1977 until event or until 75 years of age. Subjects with events the first five years after baseline are excluded. Models adjusted for age, adiposity, diabetes, smoking and hypertension.

Strain group	Coronary heart disease		Stroke	
	N (N Events)	Hazard ratio (95% CI)	N (N Events)	Hazard ratio (95% CI)
Low strain	642 (85)	1.00	642 (60)	1.00
Active	2247 (312)	1.08 (0.85-1.38)	2275 (189)	0.93 (0.70-1.25)
High strain	630 (109)	1.29 (0.97-1.72)	640 (54)	0.91 (0.63-1.32)
Passive	2208 (351)	1.22 (0.97-1.56)	2248 (190)	0.94 (0.70-1.26)

Table 4. Cox regression models of 6070 men followed from 1974-1977 until event or until 75 years of age showing hazard ratios (HR) for low control and high demands in relation to coronary heart disease and stroke for different subgroups. All models are adjusted for age.

Subgroup	Coronary heart disease		Stroke	
	Low Control vs. high control	HR High Demands vs. low demands	HR Low Control vs. high control	HR High Demands vs. low demands
All	1.19 (1.06-1.35)	0.94 (0.84-1.07)	1.05 (0.89-1.24)	0.97 (0.82-1.15)
Never smokers	0.80 (0.60-1.07)	1.27 (0.95-1.71)	1.13 (0.78-1.64)	1.02 (0.70-1.48)
Ever smokers	1.32 (1.15-1.52)	0.87 (0.76-1.00)	1.01 (0.83-1.23)	0.95 (0.79-1.16)
No hypertension	1.28 (1.11-1.48)	0.88 (0.76-1.02)	1.14 (0.92-1.40)	0.96 (0.78-1.18)
Hypertension	1.02 (0.81-1.27)	1.12 (0.89-1.39)	0.91 (0.69-1.20)	0.98 (0.74-1.30)
BMI<30	1.20 (1.05-1.36)	0.92 (0.81-1.04)	1.03 (0.87-1.23)	1.00 (0.84-1.19)
BMI>=30	1.11 (0.77-1.61)	1.25 (0.86-1.81)	1.25 (0.72-2.22)	0.72 (0.40-1.26)
No diabetes	1.22 (1.07-1.38)	0.93 (0.82-1.05)	1.06 (0.89-1.26)	0.96 (0.81-1.14)
Diabetes	0.85 (0.51-1.40)	1.21 (0.74-2.01)	0.95 (0.47-1.87)	1.04 (0.52-2.07)
No stress	1.21 (1.04-1.42)	0.91 (0.78-1.06)	0.99 (0.80-1.23)	0.90 (0.73-1.12)
Self reported stress	1.16 (0.95-1.42)	0.96 (0.78-1.17)	1.15 (0.87-1.52)	1.04 (0.79-1.39)
Blue Collar	1.23 (0.98-1.56)	1.15 (0.93-1.41)	0.96 (0.72-1.31)	1.31 (0.97-1.73)
White collar	1.06 (0.84-1.33)	1.00 (0.80-1.26)	1.04 (0.75-1.40)	0.83 (0.62-1.12)

A longitudinal general-population based study of job strain and risk for coronary heart disease and stroke in Swedish men.

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The authors declare no conflicts of interest

Word count (body of test); 2 623

Keywords

Epidemiology, job strain, longitudinal, cerebrovascular disease

Abstract

Objectives

The aim was to investigate whether psycho-social stress based on the job-demand-control model increased the risk for coronary heart disease (CHD) and stroke.

Setting

Swedish men

Participants

The Primary Prevention Study comprise 6 070 men born between 1915 and 1925 free from previous history of coronary heart disease and stroke at baseline (1974-1977). Psychosocial workplace exposure was assessed using a job-exposure matrix for the job-demand-control model based on occupation at baseline. The participants were followed from baseline examination, until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register for non-fatal and fatal stroke and CHD events. Cox regression models were used with stroke or CHD as the outcome using job-demand-control model and age as explanatory variables, as well as stratified models with regard to smoking, self-reported stress, socio-economic status, obesity, hypertension, and diabetes.

Primary and secondary outcome measures

Risk for stroke and coronary heart disease

Results

There was an increased risk (HR) for CHD in relation to high strain, HR 1.31, 95% CI 1.01-1.70. The risk was further increased among ever-smokers and among blue-collar workers. There was a relation between low control and increased risk for CHD, HR 1.19, 95% CI 1.06-1.35. There was no increased risk for stroke in any of the job-demand-control categories.

Conclusions

Exposure to occupational psycho-social stress defined as job strain or low control increased the risk for CHD, especially among smokers and blue-collar workers. There was no increased risk for stroke in any of the job-demand-control categories.

Introduction

During the last decades a growing body of evidence have accumulated showing that psychosocial stress is associated with adverse health outcomes, especially coronary heart disease (CHD) (1). Psycho-social stress as a risk factor has been studied both as a general factor and linked to the work-place. The most studied definition of work-place related stress has been the job-demand-control model (2). According to Karasek the job demand variable constitutes volume and intensity of workload and job control referred to the working individual's potential control over pace and content of their tasks (2). In this model it is postulated that the combination of high demands and low decision latitude at work results in high strain (job-strain) which increase the risk of cardiovascular diseases. There are studies showing that high strain is associated with a doubled risk of coronary heart disease. However, in a recent meta-analysis of 13 studies the association was rather modest, hazard ratio 1.23. The used models were adjusted for gender and age, and in some cases also for socioeconomic status. The authors concluded that adjustments for life style factors did not substantially affect the association (3). However, in an additional paper from the previous meta-analysis it was found that the risk of coronary heart disease was further increased among subjects with job-strain in combination with current smoking, being obese or reporting low physical activity (4). Hence, it seems to clear that job strain is associated with an increased risk for coronary heart disease, and there may also exist interactions with life-style factors.

There are studies indicating that self-reported psychosocial stress increase the risk for stroke (5, 6). However, the evidence between occupational exposure to psycho-social stress and stroke is less clear. There are a two longitudinal studies showing slightly increased risk for stroke associated with low control (7, 8). One study showed an increased risk in working Finnish men (7) and in one study based on the Swedish working population there was an increased risk among women, but not among men (8). The association with job-strain is also unclear, two studies in women show an association (9, 10) and one study in the general population did not find any association, either among women or among men (11). In a prospective general-population based study from Japan it was found that men, but not women, with high-strain job had an increased

risk for stroke, with more than doubled risks among those with active, passive or high-strain jobs (12).

The aim of the present study was to investigate whether psycho-social stress based on the job-demand-control model increased the risk for coronary heart disease and stroke. The study base is a longitudinal general population study of 6 070 Swedish men followed from baseline examination (1974-1977), until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register.

Methods

Study population

The Primary Prevention Study (PPS) is a population-based cohort study from Gothenburg, Sweden. It was established in 1970 as previously described (13). The source population comprised all men living in Gothenburg born between 1915 and 1925. The initial study population was a random sample of 10 000 men, and 7494 men (75% of the sample) participated in screening examinations between January 1970 and March 1973 (14, 15). Three years later, 1974-1977, a clinical follow-up investigation was performed where 7 133 men participated. In the present study we are using data from the first follow-up investigation, because in that round there were complete occupational data. All participants gave their informed consent to participate in the study and it was approved by the Ethics Committee for Medical Research at Gothenburg University.

The current occupation at baseline (1974-1977) was classified at three-digit level according to the Nordic Classification of Occupations, NYK-74 (16). For assessing the psychosocial workplace exposure we used a previously published job-exposure matrix (17, 18). This JEM was developed in late 1970s based on information from large Swedish population surveys where around 12 000 randomly selected subjects aged 25 to 74 years were classified for psychological demands and decision latitude. The JEM gives separate estimates of demand and control for 261 occupations separated into gender and age (25-44 and 45 to 74). Socioeconomic status, high or low, was obtained based on one-digit level of occupations, i e blue-collar vs. white-collar workers

Psychological job demands and decision latitude were explored with four items each. All items were scored using a scale (1-10), with a score of 10 indicating high psychological demands or high decision latitude. Each subject was assigned a certain score based on occupation and age. The scores were then dichotomized into high and low, using the median of the distribution as cut-off. Combining demand and control with the median cut-offs divides the participants into four categorical quadrants; high strain (high demand-low control), active (high demand-high control), passive (low demand-low control) and low-strain (low demand-high control).

In the present study there was information at baseline about age, country of birth (Sweden/other), body mass index (BMI), serum cholesterol (s-cholesterol) level, systolic blood pressure, diastolic blood pressure, use of antihypertensive medication (yes/no), history of diabetes (yes/no), coronary heart disease (yes/no), hypertension (yes/no) or stroke (yes/no) at baseline, **self-reported stress** and smoking as previously described (19).

Subjects with coronary heart disease or stroke at baseline (1974-1977) were excluded resulting in a study population of 6 070 subjects (Table 1). Based on unique personal identification numbers, participants were followed from the date of their baseline examination until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register. The hospital discharge register has operated on a nationwide basis since 1987, but all discharges from Gothenburg hospitals have been entered in the national register since 1970 (except for 1976, because of a legislative change for that year). Additional data from the Gothenburg stroke register were used to identify strokes from the start of the study until 1983. The International Classification of Disease (ICD) codes listed in the registries were used to identify stroke events (both non-fatal and fatal events) and coronary heart disease during the entire follow-up period. The eighth version of the ICD code was used until 1986, ICD-9 was used from 1987 to 1996, and ICD-10 was used from 1997 onwards. Ischemic stroke was defined as ICD codes 431-438 and I61-I69. Non-fatal CHD was defined as 410 and I21. Fatal CHD was defined as 410-414 and I20-I25. Each type of event was treated separately and only the first event of each type was used in the analysis.

Statistical analysis

Descriptive statistics are presented as percentages or mean values with standard deviations (SD). All analyses were performed using the SAS statistical package (version 9.3) and R (version 3.0.1). The material were analysed with Cox regression models using SAS (the PHREG procedure). The proportional hazards assumptions were investigated using tests and plots based on weighted residuals (20) using the R package Survival. All assumptions were found reasonable except for the analysis of baseline diabetes. Hospital care or mortality (whatever came first) from stroke or coronary heart disease were events and time were measured as months since baseline. The observation period stopped at the age of 75. In the crude model hazard ratios were calculated using the job-demand-control model and age as explanatory variables. The low strain group was used as reference group. There were also models using high strain vs. all other subjects as an independent variable. There were also separate models stratifying for ever-smoking and never-smoking, adiposity (body mass index ≥30) or not, hypertension or not at baseline and diabetes or not, self-reported stress or not at baseline and finally status as white-collar worker or blue-collar worker at baseline. There was also one model with five years latency time, i.e excluding subject with any event occurring during the five first year during the follow-up.

Results

For the follow-up period there were 1 052 events due to coronary heart disease. The Cox regression models adjusted for age showed an increased risk (HR) for coronary heart disease in relation to high job strain, HR 1.31, 95% CI 1.01-1.70 (Table 2). In the stratified analysis high strain was associated with an even slightly higher risk for coronary heart disease among ever-smokers, (HR 1.37, 95% CI 1.02-1.83) and among blue-collar-workers (HR 1.36, 95% CI 1.01-1.84). Among obese subjects there was an indication of increased risk in relation to high-strain (HR 2.05, 95% CI 0.93-4.81) but with wide confidence intervals. In other strata there was an increased risk for coronary heart disease in the active group among those with hypertension (HR 1.50, 95% CI 1.00-2.33) (Table 2).

For the follow-up period there were 549 events due to stroke. In the total population there was no increased risk for stroke in any of the job-demand-control categories. In the stratified analyses those with self-reported stress at baseline seem to have increased risk, both in the active group (HR 1.98, 95% CI 1.09-4.05) and in the passive group as well (HR 2.15, 95% CI 1.17-4.44) (Table 2).

In the additional analyses subjects with five years latency time the results were similar. The risk for coronary heart disease among subjects with high strain was slightly higher (HR 1.34, 95% CI 1.00-1.80) (Table 3). In the final full model, adjusted age, adiposity, diabetes, smoking and hypertension, there was an indication of increased risk of CHD in relation to high strain (HR 1.29, 95% CI 0.97-1.72). There were no increased risks for stroke.

Further additional analyses explored the relations between low control and high demands, respectively. There was a clear relation between low control and increased risk for coronary heart disease (Table 4). This was found among all subjects, but also among smokers and in subjects without hypertension, without diabetes, without self-reported stress or with BMI<30. There were no clear signals regarding high demands and risk for coronary heart disease. There were no significant relations between low control or high demands and the risk for stroke (Table 4).

Discussion

Principal findings

In line with the other studies an increased risk for coronary heart disease was found in relation to high strain, job-strain. Of interest is that job strain risks increased further among ever-smokers, obese subjects and among subjects with low socioeconomic status. Active subjects with hypertension also ran an increased risk for coronary heart disease. There was also a clear association between low control and increased risk for coronary heart disease. Of interest, even if it is a negative report, is that there was no increased risk for stroke in most of the job-demand control groups. In the strata with high levels of self-reported stress there was an increased risk for stroke in all job-demand categories.

Methodological considerations

This study has several strengths, a general-population sample with a long period of follow-up and use of a national mortality register and hospital discharge register with high coverage. The assessment of psycho-social stress is based on occupations, which probably is less biased than self-reports of demand and control. Further, the population was in their fifties at baseline, meaning that they are quite stable in their occupations. Finally, the study comprises only men which limit the external validity.

The regression models have been adjusted for age. The study population comprises only men. In the literature it has been discussed that further adjustments for different lifestyle factors marginally decreased the risk estimates, which is in line with the findings from a large metaanalyses (3). There is also a possibility that that smoking, adiposity and hypertension can be part of the causal chain act and hence stratifications are to prefer. Further, there were no separate adjustments for socioeconomic position. The reason is that the exposure for psychosocial stress is based on occupational titles and the socioeconomic position is part of the occupational classification. However, in the stratified analysis, the risk for CHD was increased among blue-collar workers (low SES), but not among the white-collar works (high SES). In the literature, the job-demand-control model mostly predicts to ill-health associations among blue-collar workers, often men (2, 17, 21, 22, 23, 24). One plausible explanation is that the development of the JDC model was mainly conducted among male blue-collar jobs, and is consequently adjusted to such

job characteristics. When broadening study populations, more conflicting findings emerge. For example, little support has been found for female high-strain related ill-health (25).

The effect of psycho-social stress

It is evident from this study that both high strain and the passive dimension increase the risk for coronary heart disease. It is of interest that low control, the common denominator for job-strain and the passive dimension, was clearly related to increased risk for coronary heart disease.

The results from the present study indicate that exposure to occupational psycho-social stress is not increasing the risk for stroke. The study is rather large, 549 stroke events, and there was no increased risks in different lifestyle strata. Previously the association with job-strain has been unclear with both positive (9, 10, 12) and negative studies (11). There is probably a publication bias as studies with no or weak associations may not be published, as it has been shown for job strain and coronary heart disease (3). Hypertension has been associated with occupational psycho-social stress, especially among men (26). However, job strain was not associated with stroke among men with hypertension at baseline. Hence, the present study indicates that stroke has a different pattern of risk factors compared to coronary heart disease.

Self-reported stress has been associated with stroke, both in cohort studies (5, 27, 28) and in case-control studies (6, 29). Self-reported stress is a global composite item reflecting both occupational and non-occupational exposure. In the present study, increased risks for stroke was among subjects reporting stress at baseline and belonging to either the active, high strain or passive strata (compared to low strain). This may indicate an interaction between occupational and non-occupational stress in relation to stroke.

One limitation of our study is that there was only one assessment of the exposure the occupational psychosocial stress. There are indications in the literature that psychosocial stress occurs late in the causal chain for stroke as indicated by the observation that studies with short period of follow-up have higher risks of stroke in relation to psychosocial stress (8, 9). We have a rather long observation period, which may result in low risk estimates due to misclassification of the exposure.

Another limitation of this study is that the sample consisted only of men. Previous studies have indicated that health outcomes differ between men and women when exposed to Job demand-control (8, 9, 10, 11, 22, 25). Since the cohort was established with only men it was not possible to include women in our study, but we recommend that future similar analyzes include women as to investigate gender differences

The study confirms the previous findings of an association with job strain and risk for coronary heart disease. Compared to some other studies the risk levels were quite modest, which may reflect non-differential misclassification of the exposure assessment or may reflect the true underlying risk (3, 30). There was a slight interaction with lifestyle factors, especially smoking and to some extent also obesity, as the risks were further increased among smoking subjects and obese subjects. Positive interaction with both smoking and obesity was recently shown in a meta-analysis (4). A finding that needs to be replicated is that active subjects with hypertension had a high risk for coronary heart disease.

Conclusions

Exposure to occupational psycho-social stress defined as job strain increased the risk for CHD, especially among smokers and blue-collar workers. Low control was also related to increased risk for CHD. There was no increased risk for stroke in any of the job-demand-control categories.

Acknowledgements

The study was funded by the Swedish Research Council (VR), the Swedish Research Council for Health, Working Life and Welfare (FORTE) and the Swedish Heart and Lung Foundation

Strengths and limitations of the paper;

Job strain increase the risk for coronary heart disease but the relation to stroke is uncertain. There is a need for longitudinal general-population based studies in this field. This study confirms that job strain increase the risk for coronary heart disease, but the risk seems to be limited to blue-collar workers. There was no clear relation between job strain and risk for stroke.

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Table 1. Baseline characteristics of a general population study of 6 070 Swedish men.

	Active N=2357	High strain N=671	Low strain N=679	Passive N=2363	Overall N=6070
Age, yrs (SD)	55.2 (2.1)	55.3 (2)	55.2 (2)	55.4 (2)	55.3 (2.1)
Cholesterol, mmol/L (SD)	6.37 (1.05)	6.45 (1.1)	6.37 (0.99)	6.43 (1.05)	6.4 (1.05)
SBP, mm Hg (SD)	145.1(19.5)	147.2 (20.5)	145.2 (18.8)	146.8 (19.7)	146 (19.6)
BMI, kg/m^2 (SD)	25.5 (3.1)	25.6 (3.4)	25.8 (3.2)	25.8 (3.4)	25.6 (3.3)
Diabetes, % (N)	2.8 (65)	3.6 (24)	2.5 (17)	2.7 (64)	2.8 (170)
Hypertension, % (N)	21.8 (512)	23.9 (160)	22.5 (152)	21.9 (517)	22.1 (1341)
Hypertensive medication, % (N)	15.2 (358)	16.5 (111)	14.6 (99)	13.9 (328)	14.8 (896)
White collar Job, % (N)	**98.3 (2316)**	**26.7 (179)**	**29.5 (200)**	**15.0 (355)**	**36.8 (2177)**
Self-reported stress at baseline, % (N)	**43.7 (1014)**	**36.5 (236)**	**30.9 (205)**	**31.5 (722)**	**36.8 (2177)**
Smoking status					
Never % (N) N=1437	25.8 (607)	21 (141)	25.2 (171)	21.9 (518)	23.7 (1437)
Current % (N) N=2460	37.3 (879)	47.4 (318)	39.0 (265)	42.2 (998)	40.5 (2460)
Former % (N) N=1890	32.7 (771)	27 (181)	31.4 (213)	30.7 (725)	31.1 (1890)
Unknown % (N) N=283	4.2 (100)	4.6 (31)	4.4 (30)	5.2 (122)	4.7 (283)
Number of events (mean age, yrs, at event)					
Coronary heart disease	384 (66.2)	131 (66.4)	104 (65.9)	433 (65.9)	1052 (66.0)
Stroke	208	64	65	212	549

Mean follow-up time, months					
Coronary heart disease	200	193	199	192	196
Stroke	204	195	203	197	200

Table 2. Cox Regression models 6070 men followed from 1974-1977 until event or until 75 years of age. All models are adjusted for age. Low strain group is used as the reference group in all analyses.

Strain group	Coronary heart disease		Stroke	
	N (N Events)	Hazard ratio (95% CI)	N (N Events)	Hazard ratio (95% CI)
All	6070 (1052)		6070 (549)	
Active	2357 (384)	1.06 (0.85-1.32)	2357 (208)	0.91 (0.70-1.22)
High strain	671 (131)	1.31 (1.01-1.70)	671 (64)	1.05 (0.74-1.48)
Passive	2363 (433)	1.23 (1.00-1.53)	2363 (212)	0.96 (0.74-1.28)
Ever-smokers	4350 (826)		4350 (406)	
Active	1650 (277)	1.00 (0.78-1.29)	1650 (152)	0.87 (0.64-1.20)
High strain	499 (109)	1.37 (1.02-1.83)	499 (46)	0.92 (0.62-1.38)
Passive	1723 (361)	1.31 (1.03-1.68)	1723 (158)	0.90 (0.66-1.25)
Never-smokers	1437 (184)		1437 (113)	
Active	607 (88)	1.21 (0.76-1.99)	607 (46)	1.11 (0.61-2.18)
High strain	141 (18)	1.04 (0.55-1.96)	141 (13)	1.39 (0.63-3.08)
Passive	518 (57)	0.90 (0.55-1.52)	518 (42)	1.18 (0.64-2.35)
Blue-collar	3020 (555)		3020 (279)	
Active	41 (7)	1.04 (0.44-2.11)	41 (5)	1.30 (0.45-2.906)
High strain	492 (101)	1.36 (1.01-184)	53 (492)	1.22 (0.82-1.82)
Passive	2008 (372)	1.20 (0.94-1.55)	2008 (75)	0.93 (0.68-1.30)
White-collar	3050 (497)		3050 (270)	
Active	2316 (377)	1.14 (0.80-1.71)	2316 (203)	0.93 (0.60-1.54)
High strain	179 (30)	1.15 (0.69-1.92)	179 (11)	0.63 (0.29-1.30)
Passive	355 (612)	1.24 (0.80-1.95)	355 (37)	1.16 (0.68-2.06)
Self-reported stress at baseline	2177 (381)		2177 (201)	
Active	1014 (170)	1.01 (0.70-1.49)	1014 (98)	1.98 (1.09-4.05)
High strain	236 (47)	1.28 (0.82-2.02)	236 (20)	1.92 (0.92-4.28)

Passive	722 (131)	1.13 (0.78-1.69)	722 (73)	2.15 (1.17-4.44)
No self-reported stress at baseline	3742 (381)		3742 (330)	
Active	1304 (203)	1.00 (0.77-1.32)	1304 (105)	0.67 (0.49-0.94)
High strain	411 (77)	1.23 (0.89-1.70)	411 (40)	0.84 (0.56-1.26)
Passive	1568 (635)	1.21 (0.94-1.58)	1568 (131)	0.72 (0.53-1.00)
Hypertension at baseline	1341 (314)		1341 (201)	
Active	512 (129)	1.50 (1.00-2.33)	512 (78)	0.86 (0.56-1.35)
High strain	160 (37)	1.37 (0.84-2.29)	160 (22)	0.79 (0.45-1.38)
Passive	517 (122)	1.41 (0.94-2.20)	517 (74)	0.81 (0.53-1.29)
No hypertension at baseline	4715 (736)		4715 (347)	
Active	1840 (254)	0.93 (0.72-1.21)	1840 (129)	0.96 (0.68-1.39)
High strain	509 (94)	1.30 (0.96-1.76)	509 (42)	1.21 (0.78-1.88)
Passive	1842 (311)	1.18 (0.93-1.53)	1842 (138)	1.07 (0.76-1.55)
Body mass index<30	5544 (938)		5544 (499)	
Active	2188 (343)	0.99 (0.79-1.25)	2188 (196)	0.97 (0.72-1.31)
High strain	598 (113)	1.23 (0.94-1.62)	598 (57)	1.08 (0.75-1.57)
Passive	2150 (387)	1.18 (0.95-1.48)	2150 (190)	0.99 (0.74-1.34)
Body mass index ≥30	516 (113)		516 (50)	
Active	167 (41)	1.92 (0.98-4.21)	167 (12)	0.54 (0.23-1.33)
High strain	70 (17)	2.05 (0.93-4.81)	70 (7)	0.88 (0.31-2.35)
Passive	209 (46)	1.76 (0.90-3.84)	209 (22)	0.83 (0.40-1.91)
No Diabetes at baseline	5900 (989)		5900 (515)	
Active	2292 (357)	1.04 (0.84-1.31)	2292 (194)	0.91 (0.69-1.22)
High strain	647 (123)	1.31 (1.01-1.72)	647 (60)	1.05 (0.74-1.50)

Passive	2299 (411)	1.24 (1.00-1.55)	2299 (200)	0.97 (0.73-1.30)
Diabetes at baseline	170 (63)		170 (34)	
Active	65 (27)	1.26 (0.56-3.39)	65 (14)	1.02 (0.36-3.59)
High strain	24 (8)	1.08 (0.37-3.28)	24 (4)	0.96 (0.23-4.09)
Passive	64 (22)	1.00 (0.43-2.73)	64 (12)	0.96 (0.33-3.43)

Table 3. Cox Regression models 6070 men followed from 1974-1977 until event or until 75 years of age. Subjects with events the first five years after baseline are excluded. Models adjusted for age, adiposity, diabetes, smoking and hypertension.

Strain group	Coronary heart disease		Stroke	
	N (N Events)	Hazard ratio (95% CI)	N (N Events)	Hazard ratio (95% CI)
Low strain	642 (85)	1.00	642 (60)	1.00
Active	2247 (312)	1.08 (0.85-1.38)	2275 (189)	0.93 (0.70-1.25)
High strain	630 (109)	1.29 (0.97-1.72)	640 (54)	0.91 (0.63-1.32)
Passive	2208 (351)	1.22 (0.97-1.56)	2248 (190)	0.94 (0.70-1.26)

Table 4. Cox regression models of 6070 men followed from 1974-1977 until event or until 75 years of age showing hazard ratios (HR) for low control and high demands in relation to coronary heart disease and stroke for different subgroups. All models are adjusted for age.

Subgroup	Coronary heart disease		Stroke	
	Low Control vs. high control	HR High Demands vs. low demands	HR Low Control vs. high control	HR High Demands vs. low demands
All	1.19 (1.06-1.35)	0.94 (0.84-1.07)	1.05 (0.89-1.24)	0.97 (0.82-1.15)
Never smokers	0.80 (0.60-1.07)	1.27 (0.95-1.71)	1.13 (0.78-1.64)	1.02 (0.70-1.48)
Ever smokers	1.32 (1.15-1.52)	0.87 (0.76-1.00)	1.01 (0.83-1.23)	0.95 (0.79-1.16)
No hypertension	1.28 (1.11-1.48)	0.88 (0.76-1.02)	1.14 (0.92-1.40)	0.96 (0.78-1.18)
Hypertension	1.02 (0.81-1.27)	1.12 (0.89-1.39)	0.91 (0.69-1.20)	0.98 (0.74-1.30)
BMI<30	1.20 (1.05-1.36)	0.92 (0.81-1.04)	1.03 (0.87-1.23)	1.00 (0.84-1.19)
BMI>=30	1.11 (0.77-1.61)	1.25 (0.86-1.81)	1.25 (0.72-2.22)	0.72 (0.40-1.26)
No diabetes	1.22 (1.07-1.38)	0.93 (0.82-1.05)	1.06 (0.89-1.26)	0.96 (0.81-1.14)
Diabetes	0.85 (0.51-1.40)	1.21 (0.74-2.01)	0.95 (0.47-1.87)	1.04 (0.52-2.07)
No stress	1.21 (1.04-1.42)	0.91 (0.78-1.06)	0.99 (0.80-1.23)	0.90 (0.73-1.12)
Self reported stress	1.16 (0.95-1.42)	0.96 (0.78-1.17)	1.15 (0.87-1.52)	1.04 (0.79-1.39)
Blue Collar	1.23 (0.98-1.56)	1.15 (0.93-1.41)	0.96 (0.72-1.31)	1.31 (0.97-1.73)
White collar	1.06 (0.84-1.33)	1.00 (0.80-1.26)	1.04 (0.75-1.40)	0.83 (0.62-1.12)