Job stress and cardiovascular risk factors

Results from the BELSTRESS study

by

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Abstract

Research over the past 50 years has time and again supplied us with an overwhelming evidence of the associations between the occurrence of coronary heart disease (CHD) and risk factors such as age, male gender, smoking tobacco, arterial blood pressure, blood cholesterol, overweight and diabetes. Over the years, attention has gradually shifted to alternative explanations in which also a less tangible factor such as job stress has gained much attention. In this article, we focus on the relationship between job stress and conventional cardiovascular risk factors. Cross-sectional findings from the BELSTRESS study among 16,329 men and 5,090 women working in 25 large companies all over Belgium, are presented. Job stress was measured according to Karasek's expanded demand-control model, in which the most adverse health outcomes are expected in workers having 1) "high strain" jobs characterized by high job demands and low job control, and 2) low worksite social support.

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Our findings show that the job demands are positively associated with blood pressure and with total cholesterol in men, as well as with hypertension in women after adjustment for age and level of education. Job control shows an inverse adjusted association with the waist/hip ratio in men as well as with diabetes in both gender. Social support only shows a positive adjusted association with regular smoking in men. Job strain is found to be related only to regular smoking, in men and in women perceiving low worksite social support. A consistent relationship with biomarkers of inflammation is neither observed. Limitations related to the cross-sectional nature of this study are recognized.

Keywords

Introduction

Over the last 50 years epidemiological research has tried to explain differences in the occurrence of coronary heart disease (CHD) by time, by place and by personal characteristics. Nowadays variables such as age, male gender, smoking tobacco, arterial blood pressure, blood cholesterol, overweight and diabetes are accepted as major cardiovascular risk factors. These risk factors explain a large fraction of the within and the between population variance in CHD incidence; prevention efforts built on the knowledge about these risk factors have been quite effective in many countries.

However, these conventional risk factors, do not completely predict the differences in occurrence and in time trends of CHD. This was already observed in the seventies by M. Kornitzer et al. (1) in a prospective survey in 2 cohorts drawn from a private bank and from a semi-public saving bank. The 10-year incidence of CHD was 5% in the semi-public bank compared to 9% in the private bank; this difference was not explained by the classical risk factors. Results from a retrospective survey on job stress revealed, after adjustment for age and occupational class, a higher job stress score in the private bank employees compared to the semi-public bank.

Another frequently quoted illustration of this phenomenon comes from the Whitehall study (2). In this study the age-adjusted relative risk of dying

from CHD was calculated by professional class in the Whitehall Civil Servants. Compared to the highest class of administrators the relative risk doubled and even quadrupled in executives over clerical and other workers. Within each class the differences accounted for by cholesterol, smoking, blood pressure, body mass index, physical inactivity and height was limited. The conventional risk factors explained less than half of the social gradient in coronary risk between professional classes. This means that other risk factors play a role.

A number of psychosocial and occupational factors have been suspected for a long time. Some of these have been studied such as: poor social network, stressful life events, job stress, unemployment, work environment such as exposure to carbon disulphide or noise, depression and vital exhaustion. In this article the focus is on job stress but all the other factors may be of even or greater importance.

Differences in CHD by occupational characteristics have been observed for many years. In general, a shift of the social gradient with an increasingly strong inverse association of socio-economic status (SES) and cardiovascular disease risk and mortality is a prominent feature of the past decades (3-8). More particularly, higher incidences of cardiovascular diseases (CVD) have been found among shift workers (9), unskilled industrial workers, or bus-, tram-, truck- or taxi drivers (10-13), while otherwise low incidence has consistently been observed among academics and farmers (14-17).

Results from a large case-referent study in Sweden (18) based on almost 37,000 cases with 2 referents per case randomly selected from the study base, have shown that the incidence of acute myocardial infarction is very different between 173 occupational groups of men and 53 occupational groups of women. With few exceptions occupations with a low risk were characterised by a high level of education. There was a nine-fold difference between the extremes in men going from a relative risk of 0.3 in judges versus 2.8 in metal process workers and a five-fold difference in women going from 0.4 in teachers versus 2.0 in bench carpenters.

These and other results confirm that there are large differences in CVD between occupational groups. These may be explained by:

– differences in behaviour and living conditions;
– selection processes in or out of occupational groups;
– differences with regard to occupational CVD risk factors or combinations of these.

From the literature it seems that the magnitude of the difference can probably not be explained by differences in conventional risk factors. Occupation-related risk factors must be involved. Among the possible non-chemical occupational risk factors, one can identify stress, shift and night work, noise, heat and cold and physical activity. Cross-sectional studies in the sixties and seventies indicated that there may be a relationship between excessive over time work and CHD risk. Later in the seventies two different models were further developed.

The effort-reward imbalance model basically states that people who work hard but receive little reward are at increased risk of CVD. This model developed by Siegrist (19) is mainly supported by his own work and recently by results from the British Whitehall II study (20).

In the seventies Robert Karasek introduced the demand-control or job strain model (21). Originally the model operated with 2 dimensions: perceptions of job demands and job control. "Psychological job demands" relate to time pressure, work pace, deadlines. "Job control" or "decision latitude" has to do with influence over one owns work, possibilities for learning new things etc. Karasek's hypothesis was that workers with high demand and low control, will be in a high strain situation and at higher risk of CVD.

Demands and control have later been supplemented with a third dimension: "worksite social support". Using the expanded model, persons with high strain and low social support are at the highest risk (21, 22).

The job strain model has been tested in different studies. The popularity of the model is probably due to the fact that it is basically simple, that it has high face validity and that it has been found to be supported by a number of studies in the field of epidemiology, psychophysiology and organisation- and health psychology. Furthermore, it is not only directed at negative outcomes and sickness but also at productivity issues and it provides elegant starting points for stress management through job redesign.

The association between job stress and CHD has been studied in a large variety of studies including prospective cohort studies, case-reference studies and cross-sectional studies (22-38). In a majority of these studies an increased relative risk was found in the high job strain group regarding CHD mortality and morbidity. In prospective studies the predictive value of risk factors can be examined with more accuracy. In three studies no significant relation between the job stress scales and the inci-

dence of CHD events were found (26-28) while significant associations were found in five studies (22-25, 30). In another recent prospective study an association between job control and CHD was found but not between demand and CHD (29).

It is noteworthy that most of the early studies on the demand-control model were performed either in Sweden or in the U.S. More recent studies from Europe provide only partial support. It may be that certain national or cultural groups are more prone to be differentiated in their coronary risk by psychosocial work-related factors. On the other hand, homogeneity in exposure to job stress has been put forward as an explanation for the absence of a convincing relation between job strain and CHD. Large studies with heterogeneous job titles are needed.

Another limitation of some of the previous studies is that they used the imputation method. This method links risk weights of occupations found in another study to occupations in databases where no risks but only health outcomes are measured. The use of this method allows only between and not within occupational groups analysis. As a consequence, this method prohibits a proper disentanglement of socio-economic status and job stress risk. Moreover, not all prospective studies controlled for the conventional risk factors. So, the lack of coherence in the results of previous studies illustrates the need to study the relationship between job stress and CHD further, particularly in a prospective multinational, multicultural setting and taking into consideration the possible effects of other conventional risk factors. Furthermore, results should be analysed across and within occupational groups. This is precisely what is addressed in the JACE study (job stress, absenteeism and CHD in Europe). Preliminary results of JACE have been published (39). Final results addressing the association between job stress and CHD are not yet available.

But, if job stress is related to impaired health outcomes one may wonder through what mechanisms it acts. Hans Selye was one of the first to try to explain the process of stress-related illness with his general adaptation syndrome theory (40). Do we have good indicators of that syndrome, either bio-clinical or biochemical in nature or in the field of behavioural characteristics? Job strain may increase the risk through different physiological and behavioural changes. It is very difficult to study these causal networks empirically because many of these mechanisms may be working simultaneously and these factors are also influenced by factors outside the work environment. Nevertheless, it is important to know more on possible mechanisms because it has implications on the analysis of the model. If an association between job stress and the incidence of CHD

is observed, should one adjust for conventional risk factors? Yes, if these risk factors are not implicated in the model. No, if we accept that these risk factors mediate the risk disease association. And this could be the case for important conventional risk factors, such as the blood pressure, blood lipids, coagulation factors and behavioural pattern. Results on these questions of correlates of job stress, are presented from BELSTRESS. The design and the methodology of BELSTRESS, which is part of JACE, have been described in detail (41).

The main objectives of BELSTRESS are:

– To describe the prevalence of perceived job stress by gender, by age and by job title.
– To study the associations between perceived job stress and health status indicators, particularly regarding conventional cardiovascular risk factors.
– To study the association between perceived job stress and the incidence of sickness absence.
– To study the association between perceived job stress and the incidence of coronary heart disease.

The results presented here relate to the second objective. Conventional coronary risk factors relate to systolic and diastolic blood pressure, body mass index and waist over hip ratio, total cholesterol and HDL cholesterol levels, hypertension, diabetes and smoking behaviour.

Recently however, evidence has also been provided that inflammation plays a role in the development of CHD, but much less information is available on a possible association between the perceived job stress scales and biomarkers of chronic inflammation. In this, we will more particularly focus on the relationship between the perceived job stress scales and high-sensitivity C-reactive protein (CRP), for this factor was consistently observed to be a significant and independent discriminator between CHD-cases and matched controls (42-43).

Material and methods

The BELSTRESS-cohort

The BELSTRESS cohort consists of 21,419 subjects aged 35-59 years, 16,329 men (76%) and 5,090 women (24%). They were recruited in 25

large companies spread all over the country and build up 48% of the invited population. Screening took place in the plant departments of occupational medicine, between November 1994 and May 1998.

Job stress scales

Items designed to measure "psychological job demands" (9 items), "decision latitude" or "job control" (9 items) and "social support" (co-worker and supervisor support, 4 items each) are those that belong to the full recommended 1985-version of the Job Content Questionnaire (JCQ) (44). In case of one missing value per (sub)scale, the mean value calculated over the set of remaining valid scale-items for that particular respondent was imputed, picking up 5% more valid cases at most. All JCQ-scales have good or acceptable internal consistency (45). Dichotomies for these scales are defined by the median split yielding high and low values for each scale. "High job demands" refer to values strictly above the median, "low job control" and "low social support" refer to values strictly below the median in each gender. According to the model, "high job strain" refers to the gender-specific combination of high levels of job demands with low levels of job control. It is contrasted to the set of all other combinations of levels of job demands and job control (i.e. "else").

Biomedical examination

The classical coronary risk factors were measured by trained technicians using standardised methods. The blood pressure was measured twice and calculated means were used. Arterial hypertension was defined as a SBP ≥ 160 mmHg and/or DBP ≥ 95 mmHg and/or under drug therapy for hypertension. The smoking behaviour was surveyed in the questionnaire. Here, "smoking" refers to reported "regular smoking", i.e. the daily smoking of either cigarettes, cigars, pipes or some combination.

Statistical analysis

Associations between the job stress scales and conventional cardiovascular risk factors as outcomes were analysed by comparing mean CVD risk factor levels in tertiles of the respective job stress scales (job demands, job control and workplace social support). In this, T1 is denoting the lowest, T2 the middle and T3 the highest score tertile.

In the case of a continuous outcome variable, linear regression using GLM analysis of variance in SPSS 10.0 was used to estimate adjusted differences in subgroup means and standard errors. More particularly, the cardiovascular risk factor outcomes in the higher tertiles (T2 and T3, respectively) are compared to the baseline outcome in the lowest tertile (T1) for each of the job stress scales.

In the case of a categorical outcome variable, logistic regression using indicator dummy coding was applied to study adjusted associations. Quantification of the observed association was obtained through adjusted odds ratios by exponentiation of the estimated regression coefficients associated with the classification of the respective job stress scales in tertile groups, using the lowest tertile (T1) as the reference group. Adjusted odds ratios (OR) along with their 99% confidence intervals (99% CI) are presented. Statistical significance of the variables in the model was based upon the Wald chi-square statistic.

In all instances, adjustment was made for potential confounders such like age and educational level to ensure that possible associations between the exposure variable of interest (job stress scales classified in tertile groups) and measured outcomes cannot be attributed to heterogeneity in age or educational level between compared exposure groups in the model. To accommodate for the large sample size, the .01 significance level has been adopted. All analyses are stratified by gender.

CRP-study

The CRP levels have been measured by a fixed–time immuno-nephelometric method in a specific sample of 892 men from the BELSTRESS cohort which are free of antecedents of CHD (i.e. no account of previous hospitalisation for acute myocardial infarction, coronary angioplasty or bypass surgery and/or major ECG abnormalities suggestive of a myocardial scar) (43). The geometrical mean CRP values by tertile groups of the job stress scales are presented. Also, log transformed CRP distributions between tertile groups of the job stress scales are compared. More particularly, the estimated difference in means between the higher tertiles (T2, T3) of the job stress scales are compared to the baseline estimated mean in the lowest tertile (T1). Likewise, adjustment was made for age and educational level through linear regressions using GLM analysis of variance in SPSS 10.0. However, considering the smaller sample size, the level of statistical significance was set at $\alpha = 0.05$.

Results

Sample characteristics are presented in table 1 (a and b). The sex ratio is 3 to 1. Men compared to women have a somewhat older age profile (mean age: 45.9 versus 44.3 years) and are better represented in both the highest and lowest educational groups. The mean reference values and ranges for the job stress scales and for conventional CHD risk factors are also recorded for each gender.

The results from bivariate analysis are presented in tables 2a and 2b for men and women respectively. Regarding blood pressure and hypertension, the only significant – and indeed positive – associations were observed between either systolic (SBP) or diastolic blood pressure (DBP) and the job demands in men.

TABLE 1a

Sample characteristics for basic variables and dichotomous conventional cardiovascular risk factors

	MEN (n = 16,335)	WOMEN (n = 5,084)	p-value
Age (years)			
35-49	70.4	80.7	<.001
50-59	29.6	19.3	
	(n = 16,329)	(n = 5,090)	
Educational level			
Elementary & junior high (low)	43.5	39.4	<.001
High school & some graduate (medium)	28.5	37.3	
College & graduate school (high)	27.9	23.3	
	(n = 16,182)	(n = 5,036)	
Hypertension			
normal	78.4	83.4	<.001
hypertension	21.6	16.6	
	(n = 16,307)	(n = 5,085)	
Diabetes			
Yes	97.2	97.8	.016
No	2.8	2.2	
	(n = 16,137)	(n = 5,016)	
Current smoking			
Regular smoker	29.3	24.3	<.001
No regular smoker	70.7	75.7	
	(n = 16,062)	(n = 4,948)	

Notes:
n = number of observations.
P-value according to the Pearson Chi-square test.

TABLE 1b
*Sample characteristics for the job stress scales and for continuous conventional
cardiovascular risk factors*

		n	Mean	SD	Minimum	Maximum	p-value
Job demands	Men	15,911	23.5	4.17	9.0	36.0	.001
	Women	4,804	23.3	4.09	9.0	36.0	
Job Control	Men	16,055	69.7	12.08	24.0	96.0	<.001
	Women	4,905	63.9	12.35	24.0	96.0	
Worksite social support	Men	15,568	22.9	3.57	8.0	32.0	<.001
	Women	4,684	22.6	3.75	8.0	32.0	
Systolic blood pressure	Men	16,307	133.0	15.27	84.0	226.0	<.001
(mmHg)	Women	5,085	126.5	15.85	90.0	205.0	
Diastolic blood pressure	Men	16,307	84.6	10.23	10.0	140.0	<.001
(mmHg)	Women	5,085	79.6	10.29	10.0	132.0	
Body Mass Index	Men	16,305	26.4	3.59	14.7	49.2	<.001
(BMI, in kg/m^2)	Women	2,931	25.0	4.51	14.2	51.1	
Waist/Hip (ratio)	Men	15,979	0.94	0.068	0.59	2.05	<.001
	Women	5,064	0.81	0.077	0.61	1.78	
Total cholesterol (mg/dl)	Men	16,185	225.2	39.95	92.0	491.0	<.001
	Women	4,995	217.6	39.47	96.0	428.0	
HDL cholesterol (mg/dl)	Men	16,177	49.0	13.42	6.0	146.4	<.001
	Women	4,993	64.1	17.01	20.9	160.4	

Notes:
n = number of observations.
SD = standard deviation.
P-value according to the t-test.

The body mass index (BMI) and the waist/hip ratio (W/H) were inversely related to job demands and to job control and positively related to social support in men. In women, only the inverse relation with job control was also highly significant.

Total serum cholesterol was unrelated to any of the job stress scales in both gender.

HDL cholesterol was positively related to job demands and to job control in men and to job control in women.

Diabetes was more prevalent in the lowest tertile of job control in men and in women.

Regular smoking was inversely related to job demands and to job control and positively to social support in men. In women the inverse relation with job control was highly significant.

TABLE 2a

Association of conventional cardiovascular risk factors by tertiles of perceived job stress indicators, in men

		Job demands			Job control			Social support		
		T1	T2	T3	T1	T2	T3	T1	T2	T3
Systolic BP	M	**132.6**	**133.0**	**133.6**	132.9	133.4	132.9	133.0	133.3	132.7
(mmHg)	SD	15.13	15.43	15.17	15.44	15.31	15.01	14.92	15.53	15.34
	p	.005			.19			.27		
Diastolic BP	M	**84.2**	**84.5**	**85.1**	84.4	84.7	84.7	84.7	84.7	84.3
(mmHg)	SD	10.13	10.25	10.25	10.33	10.28	10.07	10.17	10.25	10.31
	p	<.001			.22			.18		
BMI	M	**26.6**	**26.4**	**26.2**	**26.6**	**26.3**	**26.3**	26.3	26.4	26.5
(kg/m²)	SD	3.63	3.56	3.57	3.70	3.55	3.49	3.56	3.56	3.66
	p	<.001			<.001			.014		
Waist/Hip	M	**0.95**	**0.94**	**0.94**	**0.95**	**0.94**	**0.94**	**0.94**	**0.94**	**0.95**
(ratio)	SD	0.066	0.067	0.070	0.066	0.067	0.070	0.069	0.066	0.069
	p	<.001			<.001			.003		
Total cholest	M	224.6	225.5	225.9	224.5	225.2	226.3	225.2	225.1	225.2
(mg/dl)	SD	39.18	40.40	40.06	40.37	39.33	39.85	39.76	40.11	39.87
	p	.18			.047			.97		
HDL cholest	M	**48.3**	**49.2**	**49.7**	**48.2**	**49.1**	**50.0**	48.8	49.2	49.3
(mg/dl)	SD	13.16	13.69	13.32	13.48	13.44	13.47	13.19	13.51	13.67
	p	<.001			<.001			.15		
Hypertension	%	21.5	21.2	22.2	21.9	22.7	20.4	21.9	21.7	21.3
	p	.43			.022			.79		
Diabetes	%	3.2	2.4	2.9	**3.5**	**2.4**	**2.4**	2.9	2.4	3.4
	p	.028			<.001			.023		
Smoker	%	**30.8**	**28.9**	**27.5**	**32.9**	**28.5**	**25.7**	**28.6**	**28.0**	**32.3**
(regular)	p	.001			<.001			<.001		

Notes:
M = mean, SD = standard deviation, p = p-value (ANOVA for differences in means / Chi-square test for differences in proportions).
T1 = lowest tertile, indicating the tertile with lowest job demands, lowest job control and lowest social support, respectively; T2 = middle tertile; T3 = highest tertile, indicating the tertile with highest job demands, highest job control and highest social support, respectively.
Associations which are significant at the .01-level are in bold.

TABLE 2b

Association of conventional cardiovascular risk factors by tertiles of perceived job stress indicators, in women

		Job demands			Job control			Social support		
		T1	T2	T3	T1	T2	T3	T1	T2	T3
Systolic BP	M	126.4	126.4	126.4	126.7	126.3	126.3	126.1	126.7	126.8
(mmHg)	SD	15.89	15.43	16.03	15.96	15.56	15.89	15.67	15.96	15.68
	p	.996			.73			.42		
Diastolic BP	M	79.4	79.5	79.9	79.5	79.6	79.7	79.6	79.5	79.7
(mmHg)	SD	10.23	10.28	10.26	10.32	10.11	10.43	10.13	10.21	10.38
	p	.36			.84			.96		
BMI	M	25.1	25.0	24.6	**25.4**	**24.7**	**24.7**	25.0	24.6	25.1
(kg/m^2)	SD	4.53	4.48	4.29	4.54	4.48	4.42	4.45	4.21	4.59
	p	.068			<.001			.012		
Waist/Hip	M	0.81	0.81	0.81	**0.82**	**0.81**	**0.80**	0.81	0.81	0.81
(ratio)	SD	0.079	0.079	0.073	0.080	0.075	0.076	0.073	0.076	0.084
	p	.055			<.001			.18		
Total cholest	M	218.4	216.6	216.7	218.4	216.9	216.3	217.5	215.9	218.8
(mg/dl)	SD	39.99	38.74	39.60	39.85	39.03	38.97	38.99	38.78	39.85
	p	.38			.30			.17		
HDL cholest	M	64.2	63.8	64.8	**63.2**	**64.4**	**65.3**	64.2	64.6	63.9
(mg/dl)	SD	16.50	17.30	17.24	16.70	17.90	18.14	17.62	16.57	16.59
	p	.29			.003			.49		
Hypertension	%	15.3	16.0	18.2	17.4	16.2	15.5	16.3	15.5	17.0
	p	.11			.31			.55		
Diabetes	%	2.4	1.6	2.6	**3.1**	**1.6**	**1.5**	2.4	1.8	1.8
	p	.11			.001			.32		
Smoker	%	23.5	24.7	25.3	**27.0**	**22.0**	**23.1**	24.9	22.7	25.6
(regular)	p	.51			.001			.17		

Notes:

M = mean, SD = standard deviation, p = p-value (ANOVA for differences in means / Chi-square test for differences in proportions).

T1 = lowest tertile, indicating the tertile with lowest job demands, lowest job control and lowest social support, respectively; T2 = middle tertile; T3 = highest tertile, indicating the tertile with highest job demands, highest job control and highest social support, respectively.

Associations which are significant at the .01-level are in bold.

In tables 3a and 3b results are presented from multivariate analysis. The associations between the job stress scales and the conventional risk factors are given, adjusted for age and educational level. For blood pressure the positive relation between SBP and DBP and job demands remain significant in men when the third tertile is compared with the first.

Most of the associations between BMI or W/H and the job stress scales disappear after adjustment for age and educational level. Only the inverse relationship between W/H and job control remains significant in men. In women no clear picture is found.

In contrast to the findings of the bivariate analysis, total serum cholesterol now displays a significant positive association with the job demands in men: men in the higher tertiles of job demands have on average a higher total cholesterol level if compared to males classified in the first tertile of job demands, after adjustment is being made for age and educational level. On the other hand, the bivariate associations between HDL-cholesterol and the job stress scales are fully explained by age and educational level.

The inverse association between diabetes and job control remains highly significant in both gender.

Smoking remains positively associated with social support in men; the inverse relationship with job control however has borderline significance. In women, the relationship between smoking and job control is no longer convincing after adjustment for age and educational level for it displays only borderline significance and has no clear pattern. Likewise, only a borderline significance is observed with respect to the "smoking – job demands" relationship.

In tables 4a and 4b the associations of conventional risk factors with job strain are presented, adjusted for age and educational level and stratified by worksite social support in respectively men and women. Both in men and in women, regular smoking is significantly more prevalent in the high job strain group of the lower social support stratum, independent of age and educational level. For the other risk factors, only borderline or no differences are observed.

Table 5 displays the associations between CRP levels and tertiles of the job stress scales in a sample of 892 men free from antecedents of CHD. No significant differences between the geometrical mean CRP values by testiles of the job stress scales were found. The Spearman

TABLE 3a

Association of conventional cardiovascular risk factors by tertiles of perceived job stress indicators, adjusted for age and educational level, in men

		Job demand		Job control		Social support	
		T2 vs.T1	T3 vs.T1	T2 vs.T1	T3 vs.T1	T2 vs.T1	T3 vs.T1
Systolic BP (mmHg)	B	0.36	1.16***	0.27	-0.17	0.25	-0.34
	99% CI	(-0.39, 1.11)	(0.35, 1.97)	(-0.49, 1.04)	(-0.96, 0.62)	(-0.47, 0.96)	(-1.16, 0.48)
	p	.001		.34		.19	
Diastolic BP (mmHg)	B	0.32	0.95***	0.13	0.03	0.04	-0.37
	99% CI	(-0.19, 0.83)	(0.41, 1.50)	(-0.38, 0.65)	(-0.50, 0.56)	(-0.44, 0.52)	(-0.92, 0.18)
	p	<.001		.78		.14	
BMI (kg/m^2)	B	0.03	0.03	-0.13	0.04	0.07	0.16*
	99% CI	(-0.14, 0.21)	(-0.15, 0.22)	(-0.30, 0.05)	(-0.15, 0.22)	(-0.10, 0.23)	(-0.03, 0.35)
	p	.86		.049		.084	
Waist/Hip (ratio)	B	0.001	0.001	-0.006***	-0.005***	0	0.003*
	99% CI	(-0.002, 0.004)	(-.003, .004)	(-.009, -.002)	(-.008, -.001)	(-.01, .003)	(0, .007)
	p	.81		<.001		.043	
Total cholest (mg/dl)	B	1.52*	2.59**	0.51	2.28**	-0.19	-0.19
	99% CI	(-0.46, 3.56)	(0.38, 4.64)	(-1.50, 2.51)	(0.15, 4.31)	(-2.07, 1.69)	(-2.35, 1.97)
	p	.009		.016		.96	
HDL cholest (mg/dl)	B	0.43	0.37	0.39	0.66*	0.40	0.48
	99% CI	(-0.23, 1.10)	(-0.35, 1.09)	(-0.28, 1.07)	(0.04, 1.36)	(-0.24, 1.03)	(-0.24, 1.21)
	p	.21		.049		.14	
Hypertension (yes/no)	OR	1.0	1.11	1.02	0.90*	0.98	0.94
	99% CI	(0.88, 1.13)	(0.97, 1.26)	(0.90, 1.15)	(0.79, 1.03)	(0.87, 1.10)	(0.82, 1.07)
	p	.059		.036		.50	
Diabetes (yes/no)	OR	0.78*	0.99	0.66***	0.68**	0.82	1.12
	99% CI	(0.57, 1.06)	(0.72, 1.36)	(0.49, 0.90)	(0.49, 0.93)	(0.61, 1.10)	(0.82, 1.53)
	p	.064		<.001		.042	
Smoking (yes/no)	OR	1.01	1.05	0.91*	0.88**	0.97	1.18***
	99% CI	(0.90, 1.13)	(0.94, 1.19)	(0.82, 1.02)	(0.78, 0.99)	(0.88, 1.08)	(1.04, 1.33)
	p	.048		.014		<.001	

Notes:
T1, T2, T3 = lowest, middle and highest tertile of job stress scales, respectively.
B = estimated difference in means (linear regression); OR = odds ratio (logistic regression).
CI = confidence interval.
p = p-value of differences in means among the 3 tertile groups (ANOVA) or of estimated odds ratio's (Wald test).
Significance: * .01 ≤ p < .05, ** .001 ≤ p < .01, *** p < .001.
Associations which are significant at the .01-level are in bold.

TABLE 3b

Association of conventional cardiovascular risk factors by tertiles of perceived job stress indicators, adjusted for age and educational level, in women

		Job demand		Job control		Social support	
		T2 vs.T1	T3 vs.T1	T2 vs.T1	T3 vs.T1	T2 vs.T1	T3 vs.T1
Systolic BP (mmHg)	B	0.46	0.87	0.15	0.63	0.55	0.44
	99% CI	(-0.88, 1.80)	(-0.57, 2.42)	(-1.17, 1.48)	(-0.86, 2.11)	(-0.76, 1.85)	(-1.08, 1.97)
	p	0.32		0.54		0.53	
Diastolic BP (mmHg)	B	0.38	0.97*	0.33	0.75*	-0.06	-0.11
	99% CI	(-0.51, 1.27)	(-0.01, 1.95)	(-0.55, 1.20)	(-0.23, 1.73)	(-0.92, 0.80)	(-1.11, 0.89)
	p	0.038		0.14		0.96	
BMI (kg/m^2)	B	0.16	-0.02	-0.40*	-0.08	-0.48**	-0.02
	99% CI	(-0.34, 0.66)	(-0.57, 0.53)	(-0.90, 0.10)	(-0.64, 0.47)	(-0.96, 0.0)	(-0.53, 0.57)
	p	0.60		0.097		0.015	
Waist/Hip (ratio)	B	0.004	0.0	-0.004	-0.006	0.0	0.004
	99% CI	(-0.002, 0.011)	(-0.007, 0.008)	(-0.011, 0.002)	(-0.013, 0.001)	(-0.007, 0.006)	(-0.004, 0.011)
	p	0.17		0.074		0.35	
Total cholest (mg/dl)	B	-0.59	0.59	-0.37	0.19	-1.46	0.81
	99% CI	(-3.96, 2.79)	(-3.13, 4.31)	(-3.69, 2.94)	(-3.52, 3.89)	(-4.71, 1.79)	(-2.99, 4.62)
	p	0.19		0.92		0.28	
HDL cholest (mg/dl)	B	-0.83	-0.21	0.82	1.12	0.45	-0.19
	99% CI	(-2.34, 0.68)	(-1.87, 1.46)	(-0.67, 2.30)	(0.54, 2.79)	(-1.01, 1.92)	(-2.02, 1.41)
	p	0.33		0.17		0.51	
Hypertension (yes/no)	OR	1.13	1.43***	0.97	0.97	0.94	1.02
	99% CI	(0.88, 1.44)	(1.08, 1.84)	(0.77, 1.23)	(0.74, 1.27)	(0.74, 1.20)	(0.78, 1.34)
	p	0.004		0.94		0.71	
Diabetes (yes/no)	OR	0.68	1.17	**0.52****	**0.47****	0.75	0.74
	99% CI	(0.36, 1.31)	(0.62, 2.21)	(0.28, 0.96)	(0.23, 0.97)	(0.41, 1.39)	(0.36, 1.52)
	p	0.11		0.004		0.38	
Smoking (yes/no)	OR	1.17	1.28**	0.81**	0.97	0.89	1.03
	99% CI	(0.95, 1.44)	(1.01, 1.61)	(0.66, 1.0)	(0.77, 1.23)	(0.72, 1.09)	(0.81, 1.30)
	p	0.018		0.023		0.18	

Notes:
T1, T2, T3 = lowest, middle and highest tertile of job stress scales, respectively.
B = estimated difference in means (linear regression); OR = odds ratio (logistic regression).
CI = confidence interval.
p = *p*-value of differences in means among the 3 tertile groups (ANOVA) or of estimated odds ratio's (Wald test).
Significance: * .01 ≤ p < .05, ** .001 ≤ p < .01, *** p < .001.
Associations which are significant at the .01-level are in bold.

TABLE 4a

Association of conventional cardiovascular risk factors with "job strain" (high/else), adjusted for age and educational level and stratified by social support, in men

	Low social support			High social support		
	B	99% CI	p	B	99% CI	p
Systolic BP (mmHg)	-0.07	(-1.16, 1.02)	0.87	0.73	(-0.63, 2.09)	0.17
Diastolic BP (mmHg)	0.34	(-0.41, 1.08)	0.24	0.74	(-0.17, 1.65)	0.036
BMI (kg/m²)	0.03	(-0.23, 0.29)	0.77	0.10	(-0.21, 0.41)	0.41
Waist/Hip (ratio)	0.003	(-0.001, 0.008)	0.072	0.004	(-0.002, 0.010)	0.064
Total cholesterol (mg/dl)	-0.58	(-3.52, 2.36)	0.61	-1.0	(-4.52, 2.52)	0.46
HDL cholesterol (mg/dl)	-0.51	(-1.48, 0.47)	0.18	-0.78	(-1.97, 0.42)	0.095
	OR	99% CI	p	OR	99% CI	p
Hypertension (yes/no)	1.07	(0.89, 1.28)	0.33	1.20	(0.97, 1.48)	0.026
Diabetes (yes/no)	0.97	(0.62, 1.52)	0.86	1.40	(0.86, 2.27)	0.078
Smoking (yes/no)	**1.20**	(1.02, 1.41)	0.003	1.15	(0.95, 1.39)	0.058

Notes::

"High" job strain is the combination of a high level of job demands with a low level of job control, according to the gender-specific median split. It is contrasted to the set of all other combinations of levels of job demands and job control ("else").

B = estimated difference in means between "strain" group and "else" (linear regression).

OR = odds ratio of "strain" group versus "else" (logistic regression).

CI = confidence interval.

p = p-value of differences in means (ANOVA) or of estimated odds ratio's (Wald test).

Associations which are significant at the .01-level are in bold.

TABLE 4b

Association of conventional cardiovascular risk factors with "job strain" (high/else), adjusted for age and educational level and stratified by social support, in women

	Low social support			High social support		
	B	99% CI	p	B	99% CI	p
Systolic BP (mmHg)	0.09	(-1.97, 2.14)	0.91	-1.46	(-4.0, 1.08)	0.14
Diastolic BP (mmHg)	-0.01	(-1.34, 1.35)	0.99	-0.77	(-2.46, 0.91)	0.24
BMI (kg/m^2)	-0.36	(-1.13, 0.41)	0.23	0.14	(-0.76, 1.04)	0.69
Waist/Hip (ratio)	0.003	(-0.007, -0.013)	0.47	0.004	(-0.009, 0.017)	0.42
Total cholesterol (mg/dl)	-0.75	(-5.89, 4.39)	0.71	-3.19	(-9.56, 3.17)	0.20
HDL cholesterol (mg/dl)	0.21	(-2.21, 2.63)	0.82	-1.77	(-4.54, 0.99)	0.098
	OR	99% CI	p	OR	99% CI	p
Hypertension (yes/no)	0.96	(0.66, 1.40)	0.80	1.01	(0.64, 1.60)	0.96
Diabetes (yes/no)	1.85	(0.84, 4.11)	0.045	1.10	(0.32, 3.81)	0.84
Smoking (yes/no)	**1.40**	(1.03, 1.91)	0.005	1.26	(0.86, 1.84)	0.12

Notes:

"High" job strain is the combination of a high level of job demands with a low level of job control, according to the gender-specific median split. It is contrasted to the set of all other combinations of levels of job demands and job control ("else").

B = estimated difference in means between "strain" group and "else" (linear regression).

OR = odds ratio of "strain" group versus "else" (logistic regression).

CI = confidence interval.

p = p-value of differences in means (ANOVA) or of estimated odds ratio's (Wald test).

Associations which are significant at the .01-level are in bold.

TABLE 5

Association between CRP values (mg/l) and tertiles of job stress scales in 892 men free of CHD from the BELSTRESS cohort

		Unadjusted		Adjusted for age and educational level		
		Geometric mean	p	B	95% CI	p
Job demand	T1	1.002	0.20	0		
	T2	0.995		0.077	(-0.112, 0.266)	0.43
	T3	0.850		-0.026	(-0.231, 0.180)	0.81
Job control	T1	1.001	0.55	0		
	T2	0.932		0.011	(-0.187, 0.208)	0.92
	T3	0.902		0.047	(-0.155, 0.250)	0.65
Social support	T1	0.886	0.31	0		
	T2	0.972		0.099	(-0.086, 0.284)	0.29
	T3	1.036		0.159	(-0.047, 0.366)	0.13

Notes:
T1, T2, T3 = tertiles of perceived job stress scales;
B = estimated difference in means = regression coefficient of T2 vs.T1 and T3 vs. T1;
P-values and contrast estimated differences are evaluated for log transformed CRP-values using ANOVA.

correlation coefficients between the job stress scales and CRP were also non significant (job demand: $r_s = -.052$, $p = .14$; job control: $r_s = -.028$, $p = .42$; social support: $r_s = .047$, $p = .18$). In a multivariate analysis controlling for age and educational level, the estimated differences in log transformed CRP means contrasting the upper and middle tertiles to the first tertile on the different job stress scales, did neither produce any significant association.

Discussion

How do these findings fit with the literature? A review of this subject (46), revealed that the association with arterial blood pressure is more convincing if one uses more sophisticated measurement techniques such as ambulatory blood pressure recordings. The international literature on the correlation between job stress and blood lipids is less consistent.

Some researchers have suggested an association between stress and the development of excess abdominal obesity. Bjorntorp found in the Göteborg population study an association between the waist/hip ratio and symptoms consistent with diagnosis of stress in men and women (47). This notion has also a plausible biological basis. Gluco-corticoids are elevated in stress; they may block the regulatory action of sex steroids on fat depots.

In the BELSTRESS cross-sectional survey, the job stress scales are not or not very strongly related to the conventional cardiovascular risk factors. Even the rather scarce significant differences show little variation, the clinical relevance of which might be questioned. Nonetheless, it should be kept in mind that even small variations in population means of risk factors may indeed have a major impact on population health outcomes. For instance, data from overviews of observational studies and randomised trials in U.S. white men and women aged 35 to 64 years, suggest that a 2-mmHg reduction in DBP in the mean of the populations distribution, could have a great health impact on the number of CHD and stroke events prevented. A 17% decrease in the prevalence of hypertension as well as a 6% reduction in the risk of CHD and a 15% reduction in risk of stroke and transient ischemic attacks were estimated. (48).

Certainly, we should also point to the major limitations of a cross-sectional analysis. First, an explanation in terms of cause and effect is obviously beyond its scope, mainly because the information of the time-sequence of related events is lacking.

Secondly, a cross-sectional design cannot properly account for time-lag effects. If it needs a certain time until adverse health effects of job stress become apparent, it will be clear that respondents scoring only incidentally high on the job stress scales will rather tend to attenuate the associations between perceived job stress and health indicators. A far better approach would be a longitudinal study design. Consecutive screening rounds in the same subjects may then enable us to discriminate between those workers scoring consistently high on the job stress scales from those scoring only incidentally high, and see how these consecutive scores are related to well-known cardiovascular risk factors over time. By the same token, this approach would enlarge the variation in perceived job stress over time, which may add to the detecting of health effects.

A related issue points to the "healthy worker effect", which tends to create a bias towards the null, attenuating associations as well, in that the more severe cases that possibly suffered from job stress may have left the workplace. (49-50). This will all be the more so if perceptions of high job demands and low job control persist over time and effects are chronic, so that they might not become apparent until older ages and perhaps not until after workers have left the workplace. It is therefore recommended to continue observations of health outcomes among subjects that have left the workplace.

However, the absence of a clear relationship between the job stress concept and conventional cardiovascular risk factors does by no means rule out the role of job stress in the development of CVD; it may else operate in a more direct way or through other mediators. One alternative factor that has been explored in the literature is chronic inflammation, of which elevated CRP-concentrations or higher levels of plasma fibrinogen serve as biomarkers. With respect to CRP-concentrations, the cross-sectional findings from BELSTRESS presented here do not reveal evidence that may support the hypothesis that effects of job stress on CHD may operate through elevated CRP-concentrations.

Fibrinogen on the other hand is involved in platelet aggregation and in the maintenance of blood viscosity. Increased levels of plasma fibrinogen have been associated with CHD risk in different prospective studies. Plasma fibrinogen increases with virtually every stress ever measured in humans. Regarding fibrinogen and job stress, the Whitehall and Goteborg studies found significant lower levels of fibrinogen in workers from a higher socio-economic status compared to lower socio-economic classes (51-52). Preliminary results from BELSTRESS show higher fibrinogen levels in the job strain group in men, not in women. In multivariate analysis job strain

remained associated with plasma fibrinogen, independent of age, BMI, smoking, alcohol consumption and physical activity (53).

Innovative research certainly has identified a number of risk factors for CHD. However, our understanding of the epidemic of CHD generally still remains rather limited, if not to point to the rather limited abilities to manage the epidemic. A social epidemiologic paradigm suggests that hypertension and CVD are diseases of the modern industrialised society (54). It could well be that the epidemic of CHD follows the fate of previous ones of which one of the pioneers from biomedical science, Rudolf Virchow ever said: *"Epidemics appear and often disappear without traces after a new culture period has started. The history of epidemics is therefore the history of disturbances of human culture"*.

Conclusion

These preliminary results from the BELSTRESS study show that the perception of job stress is not strongly related to conventional risk factors and do not support a strong or consistent association with mechanisms that relate to inflammation. More observations and a more detailed analysis are however needed.

The job strain model has mainly been used in studies of CHD but it has now also been tested in studies with other endpoints such as sickness absence, exhaustion, depression, musculo-skeletal symptoms and even traffic accidents, cancer and reproductive behaviour. For most of these outcomes the literature indicates that job strain has unfavourably effects on health and quality of life. The demand-control model has inspired research efforts in the field of psychosocial and environmental health. The quality of that research has increased and intervention studies are now ongoing. At this moment in time it is difficult to draw for conclusions or to recommend preventive strategies.

Acknowledgements

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