Work-Related Psychosocial Factors and the Development of Ischemic Heart Disease

A Systematic Review

Nanna H. Eller, MD, Bo Netterstrøm, MD, DMSc,* Finn Gyntelberg, MD, DMSc,† Tage S. Kristensen, DMSc,‡ Finn Nielsen, MD, DMSc,§ Andrew Steptoe, MA, DPhil, DSc,¶ and Töres Theorell, MD, DMSc‖*

Abstract: The literature on the relationship between work-related psychosocial factors and the development of ischemic heart disease (IHD) was systematically reviewed: 33 articles presented 51 analyses of studies involving male participants, 18 analyses involving female participants, and 8 analyses with both genders. Twenty of the studies originated in the Nordic countries, and the major dimensions of the Demand-Control Model were the focus of 23 articles. A balanced evaluation of the studies indicates moderate evidence that high psychologic demands, lack of social support, and iso-strain are risk factors for IHD among men. Studies performed during recent years have not shown evidence for lack of control as a risk factor for IHD. Several studies have shown that job strain is a risk factor, but in the more recent ones, these associations can be fully explained by the association between demands and disease risk. Insufficient evidence was found for a relationship between IHD and effort-reward imbalance, injustice, job insecurity, or long working hours. Studies involving women are too few to draw any conclusion concerning women, work stress, and IHD.

Key Words: ischemic heart disease, psychosocial factors, work, epidemiology

(*Cardiology in Review* 2009;17: 83–97)

During the past several decades, evidence has emerged suggesting that psychosocial factors in the workplace are independent risk factors for atherosclerosis and ischemic heart disease (IHD). The pathophysiological mechanisms through which the physiological stress response increases atherosclerosis may be manifold and varies across individuals, including increased vascular inflammation[1] and a malfunctioning of the hypothalamic-pituitary adrenocortical axis, because flattened cortisol secretion patterns have been found to be associated with an increased risk for the metabolic syndrome.[2–4] Additionally, the activation of the sympathetic-adrenal-medullary system increases cardiovascular risk, for example, by activating the renin-angiotensin system[5] and by leading to vagal withdrawal.[6,7]

Psychologic stressors can be evaluated objectively (eg, the number of hours at work) and subjectively in the form of self-report data. Further, the so-called ecological method uses reports from people with particular types of jobs to describe their exposure to psychosocial factors in those types of jobs (aggregate data). This method prevents individual experience and strain from influencing the measure of exposure. Often theoretical stress models are used as the basis for questionnaires, ie, the Demand-Control Model,[8] the Effort-Reward Model,[9] and the Organizational Injustice Model.[10] Additionally, job insecurity might be measured based on uncertainty concerning the closure of a workplace.[11]

The current article provides a systematic review of the literature on work-related psychosocial factors and manifest IHD; the goal is to present the factors that may increase risk, as well as to suggest directions for future research. The review is based on a report (submitted in September 2007 for the Danish Working Environment Research Fund) that describes the relationship between work-related stressors and the development of IHD. The report, requested by the Danish National Board of Industrial Injuries and its associated work-related illnesses committee, provides scientific evidence for the ongoing negotiations concerning which disorders should be included in the Danish directory of occupational diseases.

METHODS

We conducted a Medline search using the limits "human" and "English." The MeSH terms ischemic heart disease, coronary heart disease, and myocardial infarction were used in combination with "measures of exposure" (Table 1). In addition, the bibliographies of recent reviews[12–16] and the authors' personal holdings were checked to ensure that all relevant articles were identified. Inclusion criteria were: (1) prospective study or case-control study if exposure assessment was not self-reported, (2) definite IHD, and (3) exposure assessed as a work-related psychosocial factor.

We excluded articles in which the exposure was associated with the following: shift work or night work, unemployment, trauma, violence or accidents at work, social capital, social network outside the workplace, personality, coping, over-commitment, burnout, perceived stress, or life course perspective. We also excluded articles in which the following designs were used: prognostic studies, exclusive evaluation of self-report symptoms or disease, and studies on total mortality. In cases of duplicate publications, the article with the more specific description of exposure and effect estimates was chosen.

In total, 33 articles were included in the current review. Study quality was evaluated using the criteria shown in Table 2, with a maximum score of 11 points. The scale was constructed for the purpose of the current review.

RESULTS

An overview of the articles included in the review is shown in Table 3. Twenty of the studies originated in the Nordic countries, 7 were conducted in the United States and 2 were conducted in England. Germany, Belgium, and Japan were represented by 1 study each, and 1 study was an international study including data from Belgium, France, Spain, and Sweden. The primary dimensions of

From the *Clinic of Occupational Medicine, Hillerød Hospital, Hillerød, Denmark; †Clinic of Occupational and Environmental Medicine, Bispebjerg Hospital, Copenhagen, Denmark; ‡Task-Consult, Gilleleje, Denmark; §Department of Cardiology, Herlev Hospital, Herlev, Denmark; ¶Department of Epidemiology and Public Health, University College London, London, England; and ‖Institute of Stress Research, Karolinska Institute, Stockholm, Sweden.

Correspondence: Nanna H. Eller, MD, Clinic of Occupational Medicine, Hillerød Hospital, Helsevej 2, DK 3400 Hillerød, Denmark. E-mail: nael@noh.regionh.dk.

ISSN: 1061-5377/09/1702-0083
DOI: 10.1097/CRD.0b013e318198c8e9

TABLE 1. Measures of Exposure Used as Search Terms (ie, Included Psychosocial Factors)

Work
Working hours, overtime work, part-time work
Downsizing, threats to employment security, job insecurity, loss of employment
Demand control model, demands, control, social support, strain, iso-strain
Effort-reward model, effort, reward, effort-reward imbalance, ERI
Organizational justice, injustice
Competition at work
Bullying at work
Salary, wages, esteem, status inconsistency

the Demand-Control Model are the focus of 23 of the articles. Four articles refer to the dimensions of the Effort-Reward Model, and only 2 articles include both models. The remainder of the articles include exposures that can be grouped as work load (traffic intensity, working hours), job insecurity (downsizing, threat to employment, work-related life events, closure of work place), and work-related injustices.

Three articles presenting prospective data[17–19] and 1 case-control study[20] presented multivariate-adjusted results separately for men and women. Three of the studies included only female participants.[21–23] However, the majority of the studies reported on in these articles included only male participants.

Many of the articles included in the current study present results of analyses using a variety of exposures as independent variables, but with the same end point, ie, analyses of the associations of demands and control with IHD; thus, 2 articles appear several times in the table.[10,24] The term "analysis" is used to indicate the results of an analysis of the statistical association between a given exposure and IHD. In this way, 1 article presents the results of several analyses. All analyses are presented in Table 3.

The studies conducted in the Nordic countries represent 73% of the analyses with significant positive associations for men between an exposure (eg, demands, lack of control, etc.) and an incidence of HD. In the 7 articles from the United States, only 3 (14%) report a significant association between a psychosocial work factor and IHD.[19,25,26] In the following section, results referring to the stress models are presented.

The Demand-Control Model

The Demand-Control Model describes 2 main dimensions: demands and control (decision latitude). The latter dimension consists of 2 subdimensions: decision authority and skill discretion. The model is based on the notion that demands per se are not stressful if they are coupled with adequate control over work and the work environment. By combining the 2 main dimensions, 4 working conditions are possible: jobs with high demands and high control are termed "active" (eg, lawyers and general practitioners), jobs combining high demands and low control are termed "strained" (eg, assembly line workers and bus drivers), jobs with low demands and high control are termed "relaxed" (eg, craftsmen), and jobs with both low demands and low control are termed "passive" (eg, attendants). According to the Demand-Control Model, individuals working under job conditions characterized as "strained" have a greater risk of developing stress-related diseases.[8,27]

Demands by any definition (eg, intense work without breaks, extreme work load) were referred to in 18 articles. For men, demands were significantly positively associated with IHD in 6 of 16 analyses. One analysis demonstrated a significant negative association.[28] For women, demands were evaluated in 5 analyses, of which only 1 study demonstrated a significant positive association with risk of IHD.

TABLE 2. Criteria used to Assess Quality of the Articles

Issue Evaluated	Scoring
A. Exposure assessment valid and reproducible?	0 (exposure assessed by questionnaires not published) 1 (exposure assessed by published questionnaires) 2 (exposure assessed by published and validated questionnaires)
B. Endpoint assessment?	0 (endpoint assessment not described) 1 (cause of death from register) 2 (endpoint assessment from clinical examination, hospital records, register of cause of admission to hospital)
C. Exclusion of prevalent cases	0 (no exclusion or not described) 1 (exclusion of prevalent cases)
D. Population	0 (population restricted to occupation or firm) 1 (general population)
E. Age of population	0 (mean age >55 yr, upper range >65) 1 (mean age ≤55 yr, upper range <65)
F. Follow-up period	0 (>10 yr) 1 (≤10 yr)
G. Gender separated	0 (studies using gender as a covariate) 1 (studies including only 1 gender or using gender separated analyses)
H. Adjustment for confounding variables (age, socio-economic status, smoking, physical activity, BMI, lipids, diabetes, blood pressure)	0 (only adjustment for confounders in 1 or 2 groups) 1 (adjustment for confounders describing socioeconomic status, behaviour, and physiological status) 2 (adjustment for all mentioned confounders)

BMI indicates body mass index.

TABLE 3. Characteristics of Articles Included in the Review

First Author/Year (Ref. No.)	Exposures (Quality Score A)	Outcome (Quality Score B)	Population (Quality Scores C, D, E)	Cases/Follow-up (Quality Score F)	Risk-Estimate, Males or Both Genders (95% Confidence Interval) (Quality Score G)	Risk-Estimate, Females (95% Confidence Interval)	Confounders (Quality Score H)	Quality Score (Total Sum of A–H, Max. 11)
				Aggregated Exposure				
The Demand Control Model								
Alfredsson 1985[17]	Early job strain: hectic and monotonous work, hectic work with little opportunity to learn new things, hectic and little influence over work tempo (1)	Myocardial infarction, hospitalization data (2)	Sweden, 958,096 citizens (20–64 yr) (0, 1, 1)	1201/1 yr (1)	Age 20–64 yr: Standardized morbidity ratio: Hectic and monotonous work: 1.18 (1.02–1.35). Hectic work with little opportunity to learn new things: 1.28 (1.09–1.48). Age 20–54 yr: Hectic and monotonous work: 1.53 (1.23–1.87). Hectic work with little opportunity to learn new things: 1.57 (1.25–1.94) (1)	Age 20–64 yr: Standardized morbidity ratio: Hectic and monotonous work: 1.64 (1.12–2.33)	Univariate analysis (0)	7
	Strengths: inclusion of nearly 1 million citizens, short follow-up. Limitations: only univariate adjustments, different kinds of exposure are included in the measures used (ie, hectic and monotonous work). Comments: the exposure is measured in a form which hides the meaning of the single terms included. As development of IHD takes place over several years, the short follow-up period may be a problem. Notice increased risk in the younger stratus.							
Reed 1989[28]	Demands, decision latitude, strain (1)	Non-fatal and fatal CHD, register-based and clinical records (2)	USA, Honolulu, 4737 men of Japanese origin (45–65 yr) (1, 1, 0)	359/18 yr (0)	Age-adjusted relative incidence for high/low demands 0.86, high/low decision latitude 1, strain 0.94 (calculated by author) (1)		Age, smoking, blood pressure, cholesterol, glucose, exercise (0)	6
	Strengths: A rather large cohort, use of clinical records to insure the diagnoses are correct. Limitations: Very long follow-up period. Exposure estimated on the basis of data from a white population. Comments: As the included sample is of Japanese origin, there is a risk of misclassification. The long follow-up increases the risk of change in exposure.							
Johnson 1989[39]	Iso-strain (low social support, high demands, low control) (1)	Fatal CVD, register-based (1)	Sweden, 7219 employed men (1, 1, 0)	193/9 yr (1)	Iso-strain RR: All: 1.92 (1.15–3.21) Blue-collar: 2.58 (1.06–6.28) White-collar: 1.31 (0.58–2.98) (1)		Age, stratification on social status (0)	6
	Strengths: large sample, relatively short follow-up. Limitations: use of cardiovascular death as the endpoint, as this includes coronary deaths, death due to stroke, etc. Comments: the data are only analyzed according to iso-strain and mostly in figures. This is a problem when one wants to compare results.							
Alterman 1994[30]	Decision latitude, demand, strain (1)	CHD (clinical data) (2)	USA, 1683 men (38–56 yr) (1, 0, 1)	115 CHD/10 yr (1)	Low decision latitude 0.87 (0.57–1.31), high demands 1.07 (0.54–2.12), job strain 1.5 (0.85–2.80) (1)		Age, smoking, blood pressure, cholesterol, alcohol, family history of CVD, education (1)	8
	Strengths: use of clinical data to insure reliable diagnosis. Relatively short follow-up. Limitations: a rather large proportion of the sample had to be excluded as job titles could not be linked to exposure data (338 of 2107 men). Comments: the nonsignificant result may originate in a lack of variation in exposure.							

(*Continued*)

TABLE 3. (*Continued*)

First Author/Year (Ref. No.)	Exposures (Quality Score A)	Outcome (Quality Score B)	Population (Quality Scores C, D, E)	Cases/Follow-up (Quality Score F)	Risk-Estimate, Males or Both Genders (95% Confidence Interval) (Quality Score G)	Risk-Estimate, Females (95% Confidence Interval)	Confounders (Quality Score H)	Quality Score (Total Sum of A–H, Max. 11)
Aggregated Exposure								
Steenland 1997[26]	Control, demands, strain (1)	Incident CHD, hospital admission data and death certificates (23%) (1)	USA, 3575 men (25–74 yr) (1, 1, 0)	519/12–16 yr (0)	Low control 1.41 (1.07–1.85), high demands 0.81 (0.61–1.09), high demands/low control 1.08 (0.81–1.49). Blue-collar: high demands/low control 1.14 (0.80–1.63) White-collar: high demands/low control 1.05 (0.63–1.77) (1)		Age, blood pressure, education, body mass index, cholesterol, smoking, self-reported diabetes (1)	7
	Strengths: large cohort, many incident cases. Limitations: long follow-up, inclusion of older participants. Comments: though the participants were all working, the sample includes very old men, whose age itself comprises a large increase in risk.							
Andersen 2004[47]	Decision authority, skill discretion (1)	Register-based fatal (35%) and non-fatal MI (1)	Denmark, 16,216 (44% women) (20–75 yr), data from several population-studies (0, 1, 0)	610 male, 121 female cases/ different follow-up (0)	Low decision authority and low SES 1.47 (0.93–2.31), low skill discretion and low SES 1.07 (0.72–1.60) (0)		Cohort of investigation, age, gender, cohabitation, smoking, alcohol, exercise, BMI, blood pressure, cholesterol, socio-economic status (1)	4
	Strengths: a very large sample including women. Limitations: very old participants, use of gender as confounder. Comments: the combination of data from several cohorts carries a risk of uneven exposure-assessment and it is difficult to know what the study adds.							
Eaker 2004[19]	Decision latitude, demands, strain (1)	CHD morbidity (2)	USA, 3,039 (1711 men and 1328 women) (18–77 yr) (1, 1, 0)	149 incident CHD/ 10 yr (1)	Low decision latitude 0.99 (0.98–1.02), high demands 1.00 (0.97–1.04). High strain 1.18 (0.69–2.0) (calculated by author) (1)	Low decision latitude 1.98 (1.26–3.10), high demands 0.99 (0.93–1.06). High strain 0.61 (0.21–1.75) (calculated by author)	Blood pressure, body mass index, cigarette smoking, diabetes, total cholesterol/HDL-cholesterol (1)	8
	Strengths: a large sample including women, rather short follow-up. Limitations: inclusion of very old people, use of aggregated data from 1980 to estimate exposure in 1984 to 1987. Comments: it is a problem to include participants who are old. Their exposures have changed during their lifetime and age itself constitutes a high risk.							
Downsizing								
Vahtera 2004[46]	Downsizing (0)	CHD mortality, register-based (1)	Finland, 5909 men and 16,521 women (19–62 yr) (0, 1, 0)	79 CHD death/ 7.5 yr (1)	2.00 (1.02–3.92) (0)		Age, gender, socioeconomic status and type of employment (0)	3
	Strengths: large cohort, short follow-up. Limitations: few cases, gender used as confounder. Comments: the authors used a rough measure of exposure (ie, % reduction in different occupational groups).							

(*Continued*)

TABLE 3. (*Continued*)

First Author/Year (Ref. No.)	Exposures (Quality Score A)	Outcome (Quality Score B)	Population (Quality Scores C, D, E)	Cases/Follow-up (Quality Score F)	Risk-Estimate, Males or Both Genders (95% Confidence Interval) (Quality Score G)	Risk-Estimate, Females (95% Confidence Interval)	Confounders (Quality Score H)	Quality Score (Total Sum of A–H, Max. 11)
Self-Reported Exposure								
The Demand-Control Model								
Theorell 1977[36]	Workload index (eg, extra job, change of work hours, change in responsibility, problems with superiors) (1)	Fatal or non-fatal myocardial infarction, hospital records (2)	Sweden, 5187 building construction workers (all males, 41–61 yr) (1, 0, 1)	51/2 yr (1)	RR, work load: 1.98 ($P < 0.01$) (1)		Age (0)	7
	Strengths: a large sample and short follow-up. Limitations: 1 occupational group, no adjustments except for age, exposure assessed as an index of different work-associated problems. Comments: the study includes rather few cases.							
Haan 1988[31]	Job strain scale composed of 3 subscales: physical strain, variety, control (0)	Non-fatal and fatal CHD, register-based (1)	Finland, 902 employees of a metal company (33% women, 17–65 yr) (1, 0, 0)	60/10 yr (1)	The summed job strain, OR: 4.95 ($P = 0.03$) (0)		Age, gender, smoking, alcohol, relative weight, cholesterol, systolic blood pressure (0)	3
	Strengths: inclusion of both women and men. Relatively short follow-up. Limitations: the used job strain scale includes both physical and psychological factors. Gender used as covariate. Comments: the design of the study makes the results difficult to interpret.							
Suadicani 1993[38]	Job influence, work pace, monotony (1)	Nonfatal and fatal CHD (24%), register-based (2)	Denmark, 1638 men (55–74 yr) (1, 1, 0)	46/4 yr (1)	Job influence 0.93 (ns*) Work pace 1.25 (ns*) Monotony 0.91 (ns*) * calculated by author (1)		Social status, tobacco, alcohol, exercise, blood pressure, BMI, lipids (1)	8
	Strengths: a rather large sample and short follow-up. Limitations: inclusion of rather old participants as age in itself increases the risk of IHD significantly. Comments: the article focused on the finding of significantly increased risk in those participants who were not able to relax after work.							
Kivimäki 2002[24]	Demand, control, job strain effort, reward, effort-reward imbalance (ERI) (1)	Register-based CVD mortality (1)	Finland, 545 men and 267 women (1, 0, 0)	73/mean 25.6 yr (0)	Adjustment only for age and gender: High demands 1.35 (0.77–2.36). High effort 1.63 (0.90–2.96). Low reward 2.04 (1.21–3.43). Multivariate adjustment: Low control 1.42 (0.72–2.82), strain 2.22 (1.04–4.73), ERI 2.42 (1.02–5.73) (0)		Age, gender, occupational group, smoking, exercise, blood pressure, cholesterol, body mass index (1)	4
	Strengths: inclusion of both men and women. Limitations: very long follow-up, use of cardiovascular register-based mortality as endpoint. Use of gender as covariate. Comments: the authors discuss the problem of exposure assessment one or more times. The association between exposure and IHD was stronger for those having the same job 5 years after exposure assessment.							

(*Continued*)

TABLE 3. (*Continued*)

Self-Reported Exposure								
First Author/Year (Ref. No.)	**Exposures (Quality Score A)**	**Outcome (Quality Score B)**	**Population (Quality Scores C, D, E)**	**Cases/Follow-up (Quality Score F)**	**Risk-Estimate, Males or Both Genders (95% Confidence Interval) (Quality Score G)**	**Risk-Estimate, Females (95% Confidence Interval)**	**Confounders (Quality Score H)**	**Quality Score (Total Sum of A–H, Max. 11)**
Lee 2002[22]	Demands, control, support, strain (1)	Nonfatal myocardial infarction (medical records) and fatal CHD (26%) (2)	USA, 35,038 women (30–55 yr) (1, 0, 1)	146/4 yr (1)	(1)	Low strain 1.00, passive 1.12 (0.67–1.84), active 0.75 (0.40–1.42), high strain 0.63 (0.34–1.17). High demands 0.80 (0.52–1.24), low control 0.97 (0.65–1.45), low support 1.15 (0.80–1.64)	Age, smoking, alcohol, BMI, history of hypertension, diabetes or hypercholesterolemia, menopausal status, education (1)	8
	Strengths: a very large middle-aged sample and short follow-up. Diagnosis very certain. Limitations: only nurses included. Comments: when only 1 occupational group is included in a study there is a risk of too small variation in exposure. This may be a reason for no significant associations. Furthermore, among nurses, the demand of hiding feelings or the like may be a more relevant exposure to be assessed.							
De Bacquer 2005[40]	Demands, control, support, strain, iso-strain model (2)	Fatal (23%) and nonfatal AMI, clinical records (2)	Belgium, 14,987 men (35–59 yr) (1, 1, 1)	87/mean 3.15 yr (1)	High demands 1.43 (0.80–2.57), low decision latitude 0.83 (0.48–1.43), low social support 2.36 (1.38–4.01), strain 1.26 (0.66–2.41), iso-strain 1.92 (1.05–3.54) (1)		Age, education, BMI, smoking, diabetes, systolic blood pressure, serum total cholesterol, international standard classification of occupations code and company (2)	11
	Strengths: reliable diagnoses, large sample, short follow-up. Full adjustment for confounders. Limitations: other psychosocial factors may have been included. Comments: a well-designed study.							
Kivimäki 2005[10]	Effort-reward imbalance (ERI), job strain, justice at work (2)	Register-based CHD-death, non-fatal CHD (clinical records) (1)	England, 6442 men (35–55 yr) (1, 1, 0)	250/8.7 yr (1)	Job strain 1.44 (1.01–2.05), ERI 0.95 (0.65–1.40), high justice 0.69 (0.49–0.98) (1)		Age, employment grade, and strain, ERI, justice (0)	7
	Strengths: large cohort and fairly short follow-up. Limitations: only few adjustments. Comments: Whitehall II study. For some participants exposure was assessed at both phase 1 and 2, for others only at 1 occasion.							
Kornitzer 2006[32]	Demands, control, job strain (2)	Fatal and nonfatal MI, register-based or clinical records (1)	Belgium, France, Spain, Sweden, 20,435 male (35–59 yr) (0, 1, 1)	180/40 mo (1)	High demands 1.46 (1.08–1.97), low control 1.00 (0.74–1.34), job strain 1.47 (0.96–2.25) (1)		Age, smoking, blood pressure (0)	7
	Strengths: large cohort, short follow-up. Limitations: inclusion of participants from different cultures, few adjustments, exposure assessed by different questionnaires. Comments: the results should have been stratified by country.							

(*Continued*)

TABLE 3. (*Continued*)

	Self-Reported Exposure							
First Author/Year (Ref. No.)	**Exposures (Quality Score A)**	**Outcome (Quality Score B)**	**Population (Quality Scores C, D, E)**	**Cases/Follow-up (Quality Score F)**	**Risk-Estimate, Males or Both Genders (95% Confidence Interval) (Quality Score G)**	**Risk-Estimate, Females (95% Confidence Interval)**	**Confounders (Quality Score H)**	**Quality Score (Total Sum of A–H, Max. 11)**
Kuper 2006[21]	Demands, control, job strain, support (1)	Incident fatal (10%) and non-fatal CHD, register-based (2)	Sweden, 19,565 women (30–50 yr) (1, 1, 1)	89/135 mo (0)	(1)	Low control 0.7 (0.4–1.2), high demands 1.4 (0.8–2.3), job strain 1.0 (0.5–1.9), low support 1.2 (0.7–2.1)	Age, socio economic status, body mass index, alcohol, cigarettes, diabetes, high blood pressure, exercise (1)	8
	Strengths: reliable endpoints, large cohort, short follow-up, analyses stratified by full-time and part-time workers. Limitations: a minor flaw is the lack of adjustment for lipids. Other psychosocial factors might have been included. Comments: a reliable study.							
Netterstrom 2006[34]	Demands, decision latitude, strain (2)	Incident fatal and nonfatal CHD, register-based (2)	Denmark, 659 men (mean age 44.3 yr) (1, 1, 0)	47/14 yr (0)	High demands 1.4 (1.1–1.6), decision latitude 1.0 (0.9–1.2), job strain 2.4 (1.0–5.7) (1)		Age, social status, exercise, alcohol, lipids, blood pressure, smoking (1)	8
	Strengths: reliable exposure assessment according to the Demand Control Model. Limitations: long follow-up. Comments: the study included an objective assessment of job strain, which did not support the Demand Control Model.							
André-Petersson 2007[18]	Social support, job strain (2)	First time myocardial infarction (2)	Sweden, 4740 women (54.2 yr) and 3,063 men (55.5 yr) (1, 1, 1)	205/7.8–9 yr (1)	Unadjusted: Low support 1.00 (0.69–1.45), job strain 1.17 (0.67–2.06). No results from multivariate analyses (1)	Unadjusted: strain 1.29 (0.44–3.85). Multivariate adjusted: Low support 2.72 (1.42–5.22)	Age, blood pressure, use of antihypertensive drugs, prevalent diabetes, BMI, treatment for hyperlipidemia, alcohol, smoking, education and occupation (1)	10
	Strengths: reliable diagnoses, large cohort, short follow-up, inclusion of both men and women. Limitations: no male results from multivariate analyses. Comments: very reliable study.							
Kivimäki 2008[63]	Job strain (2)	Incident fatal (23%) or non-fatal CVD, hospital records and register-based (2)	Sweden, 3160 men (19–65 yr) (1, 1, 1)	93/9.7 yr (1)	Job strain, Men aged 19–65, 1.24 (0.73–2.10) Men aged 19–55, 1.70 (0.96–3.01) (1)		Age (0)	9
	Strengths: large cohort and relatively short follow-up. Reliable exposure assessment and endpoint. Limitations: few adjustments, inclusion of older participants. Comments: notice an increased relative risk when the sample is restricted to those aged 19–55.							

(*Continued*)

TABLE 3. (*Continued*)

First Author/Year (Ref. No.)	Exposures (Quality Score A)	Outcome (Quality Score B)	Population (Quality Scores C, D, E)	Cases/Follow-up (Quality Score F)	Risk-Estimate, Males or Both Genders (95% Confidence Interval) (Quality Score G)	Risk-Estimate, Females (95% Confidence Interval)	Confounders (Quality Score H)	Quality Score (Total Sum of A–H, Max. 11)
			Self-Reported Exposure					
The Effort-Reward Model								
Siegrist 1992[42]	Reward (status consistency) and intrinsic effort (1)	Non-fatal and fatal CHD, register-based, clinical records (1)	Germany, 323 blue-collar workers, men (25–55 yr) (1, 0, 1)	27/6.5 yr (1)	Status inconsistency 2.9 (1–8) High intrinsic effort 3.6 (1.2–10.5) (1)		Age, BMI, blood pressure, lipids, exercise, smoking (1)	7
	Strengths: middle-aged participants, short follow-up. Limitations: as the study introduces a new stress model and questionnaire, the sample is rather small. Comments: the study must be seen as one introducing a new stress model, and therefore the results have to be confirmed in other settings.							
Lynch 1997[43]	Demands, resources, income (1)	Non-fatal and fatal CHD, register-based (acute myocardial infarction register) (2)	Finland, 1727 men (42, 48, 54, and 60 yr at inclusion) (1, 1, 0)	89 cases/8.1 yr (1)	High demands, low resources, low income, RR: 1.57 (0.78–3.18) (1)		Age, lipids, exercise, blood pressure, BMI, alcohol, tobacco, prevalent disease incl. diabetes, marital status (2)	9
	Strengths: rather large, middle-aged sample and short follow-up. Reliable endpoint. Limitations: the measure used to estimate exposure is mixed and describes conditions other than work. Comments: the exposure assessment may be better used in a "life course" perspective.							
Kivimäki 2002[24]	Demands, control, job strain effort, reward, effort-reward ratio (ERI) (1)	Register-based CVD mortality (1)	Finland, 545 men and 267 women (1, 0, 0)	73/mean 25.6 yr (0)	Low control 1.42 (0.72–2.82), job strain 2.22 (1.04–4.73), ERI 2.42 (1.02–5.73) (0)		Occupational group, smoking, exercise, systolic blood pressure, cholesterol, BMI (1)	4
	Strengths: inclusion of both men and women. Limitations: proxy measures for effort and reward were constructed on the basis of questionnaires from 1973, but the included items were not exemplified. Very long follow-up, use of cardiovascular register-based mortality as endpoint. Use of gender as covariate. Comments: the authors discuss the problem of exposure assessment one or more times. The association between exposure and IHD was stronger in those having the same job 5 years after exposure assessment.							
Kivimäki 2005[10]	Effort-reward imbalance (ERI) (proxy measures), job strain, justice at work (1)	Register-based CHD-death, non-fatal cases (clinical records) (1)	England, 6,442 men (35–55 yr) (1, 1, 0)	250/8.7 yr (1)	Job strain 1.44 (1.01–2.05), ERI 0.95 (0.65–1.40), injustice 1.45 (1.02–2.04) (1)		Age, employment grade, and job strain, ERI, justice (0)	6
	Strengths: large cohort and fairly short follow-up. Limitations: only a few adjustments. Exposure assessment in the form of proxy measures for effort and reward were constructed on the basis of items, which merely mirrored demands and social support/job satisfaction, respectively (questionnaire in Kuper et al, 2002). Comments: Whitehall II study. For some participants exposure was assessed at both phase 1 and 2, for others only at 1 occasion.							

(*Continued*)

TABLE 3. (*Continued*)

First Author/Year (Ref. No.)	Exposures (Quality Score A)	Outcome (Quality Score B)	Population (Quality Scores C, D, E)	Cases/Follow-up (Quality Score F)	Risk-Estimate, Males or Both Genders (95% Confidence Interval) (Quality Score G)	Risk-Estimate, Females (95% Confidence Interval)	Confounders (Quality Score H)	Quality Score (Total Sum of A–H, Max. 11)
Self-Reported Exposure								
Justice at Work								
Kivimäki 2005[10]	Effort-reward imbalance (ERI), job strain, justice at work (2)	Register-based CHD-death, non-fatal CHD (clinical records) (1)	England, 6442 men (35–55 yr) (1, 1,0)	250/8.7 yr (1)	Job strain 1.44 (1.01–2.05), ERI 0.95 (0.65–1.40), injustice 1.45 (1.02–2.04) (1)		Age, employment grade, and job strain, ERI, justice (0)	7
	Strengths: large cohort and fairly short follow-up. Limitations: few adjustments. It is unclear what "justice" is, as the concept included level of information, willingness of the superior to listen to problems and appraisal. Comments: Whitehall II study. For some participants exposure was assessed at both phase 1 and 2, for others only at 1 occasion. The demonstrated association may not be describing justice but something about support and predictability.							
Elovainio 2006[44]	Justice at work (1)	Register-based CVD-mortality (1)	Finland, 804 engineering-industry employees (33% women) (17–65 yr) (1, 0, 0)	73/25.6 yr	High justice 0.61 (0.36–1.00) (0)		Gender, age, occupational group, smoking, physical activity, systolic blood pressure, cholesterol, BMI, job strain, effort-reward imbalance (1)	4
	Strengths: justice measured by the use of one relevant question. Limitations: use of CVD-deaths as endpoint. Long follow-up, use of gender as covariate. Comments: a weak study.							
Various Exposures								
Netterstrom 1988[33]	Work load (objective: traffic intensity. Subjective: work pace too high, work pace higher than 5 yr ago), social contact in spare time (1)	Nonfatal and fatal CHD (34%), register-based (1)	Denmark, 2045 male bus drivers (20–64 yr) (1, 0, 0)	62 cases, 50 without symptoms at inclusion/6 yr (1)	High traffic intensity 4.4 (1.2–16.4) Higher work pace than 5 yr ago 2.7 (1.1–7.1) No social contact 2.0 (1.0–3.8) (1)		Smoking, age (0)	5
	Strengths: rather large sample, short follow-up. Work load assessed both as an objective and subjective measure. Limitations: few adjustments. Comments: the association between traffic intensity and IHD may originate in pollution.							
Matthews 2002[25]	Work stress measure containing 7 work-related life events (eg, change to a new job, demotion, business failure) Marital stress (eg, separation) (1)	Register-based CHD mortality (1)	USA, Multiple Risk Factor Intervention Trial: 6,428 in intervention group and 6,438 in control group, men (35–57 yr) (0, 1, 1)	771/9 yr (1)	CHD: More than 2 work events, RR 1.35 (1.03–1.76) (1)		Age, study group, education, non-fatal CHD event, smoking, diastolic blood pressure, alcohol, cholesterol (1)	7
	Strengths: large sample, short follow-up. Limitations: the combined measure of exposure as this does not describe work environment but merely employment status, etc. Comments: a study that demonstrates the significance of both job and family.							

(*Continued*)

TABLE 3. (*Continued*)

Self-Reported Exposure

First Author/Year (Ref. No.)	Exposures (Quality Score A)	Outcome (Quality Score B)	Population (Quality Scores C, D, E)	Cases/Follow-up (Quality Score F)	Risk-Estimate, Males or Both Genders (95% Confidence Interval) (Quality Score G)	Risk-Estimate, Females (95% Confidence Interval)	Confounders (Quality Score H)	Quality Score (Total Sum of A–H, Max. 11)
Lee 2004[23]	Job insecurity (1)	CHD (clinical records) (2)	USA, 36,910 women (46–71 yr) (1, 0, 0)	154/4 yr (1)	(1)	Nonfatal MI, 1.28 (0.82–2.00)	Age, follow up period, smoking, alcohol, BMI, history of hypertension, diabetes and hypercholesterolemia, menopausal status, exercise, education (1)	7
	Strengths: large cohort, short follow-up, reliable endpoint. Limitations: inclusion of old participants as age is a significant risk factor in itself. Comments: job insecurity may be seen as an example of universal lack of control.							

Case-Control Studies

First Author/Year (Ref. No.)	Exposures (Quality Score A)	Outcome (Quality Score B)	Population (Quality Scores C, D, E)	Cases/Follow-up (Quality Score F—Left Out)	Risk-Estimate, Males or Both Genders (95% Confidence Interval) (Quality Score G)	Risk-Estimate, Females (95% Confidence Interval)	Confounders (Quality Score H)	Quality Score (Total Sum, Max. 10)
Various Exposures								
Alfredsson 1982[29]	Aggregated data, hectic work, monotony, low influence (1)	Fatal/nonfatal AMI (1)	Sweden, 882 controls, men (1, 1, 1)	334	Low influence, hectic work 1.35 (1.01–1.81). Not learning new things, hectic 1.45 (1.02–2.04) (1)		Age (0)	6
	Strengths: large case-control study. Limitations: only adjustment for age. The use of aggregated data and no information on job title of the individual make the exposure assessment rather uncertain. Comments: as social status has significant meaning this should have been included as confounder.							
Iversen 1989[11]	Aggregated data, closure of a shipyard (1)	Hospital admission, disease of circulatory system (1)	Denmark, 441 controls, men (1, 0, 0)	887	1.60 (0.78–3.25) (1)		Age (0)	4
	Strengths: a "natural experiment." Limitations: use of hospital admission due to CVD disease as endpoint. Only adjustment for age. Comments: the study describes the significance of closure of a workplace to the health of the employees.							
Johnson 1996[37]	Aggregated data, control, demands, support (1)	CVD-death (1)	Sweden, 2422 controls, men (24–74 yr) (1, 1, 0)	521	RR (10 yr employment): Low control 1.83 (1.19–2.82), high demands 0.93 (0.71–1.22), low support 1.09 (0.81–1.46) (1)		Age, yr last worked, survey yr, smoking, exercise, education, social class, and nationality (0)	5
	Strengths: report of results according to exposure duration, 5, 10, 15, 20, 25, and 26+ yrs. Limitations: use of CVD death as endpoint, inclusion of older participants. Comments: the study aims to answer the question: "how long do you have to suffer from a psychosocial factor at work to have an increased risk for IHD?" Low risk after 25 years of exposure may be due to a "healthy worker" effect.							

(*Continued*)

TABLE 3. (*Continued*)

Case-Control Studies								
First Author/Year (Ref. No.)	**Exposures (Quality Score A)**	**Outcome (Quality Score B)**	**Population (Quality Scores C, D, E)**	**Cases/Follow-up (Quality Score F—Left Out)**	**Risk-Estimate, Males or Both Genders (95% Confidence Interval) (Quality Score G)**	**Risk-Estimate, Females (95% Confidence Interval)**	**Confounders (Quality Score H)**	**Quality Score (Total Sum, Max. 10)**
Ferrie 1998[45]	Aggregated data on threat to employment (1)	Diagnosed cardiac ischemia (2)	England, 5347 men and 2477 women with stable employment (1, 1, 1)	513 men and 153 women, department sold	1.40 (0.9–2.2) (1)	1.69 (0.8–3.3)	Age and grade (0)	7
	Strengths: inclusion of both men and women, natural experiment. Limitations: few adjustments. Comments: Whitehall II study. Participants were employees at a department which was outsourced.							
Hammar 1998[20]	Aggregated data, demands, decision latitude, support, job strain, iso-strain (1)	Fatal/non-fatal AMI, hospital discharge register and death register (1)	Sweden, controls 24,913 men and 3553 women (30–64 yr) (1, 1, 1)	8833 men, 1175 women	Low decision latitude 1.37 (1.25–1.50), high demands 0.93 (0.89–1.02), low social support 1.28 (1.17–1.41), iso-strain 1.35 (1.16–1.58) (1)	Low decision latitude 1.12 (1.05–1.19), high demands 0.95 (0.89–1.01), low social support 1.10 (0.99–1.17), iso-strain 1.31 (0.99–1.73)	Age, county of residence, and calendar yr (0)	6
	Strengths: inclusion of many cases and both genders. Limitations: few adjustments. Comments: though the diagnoses originated from the hospital discharge register the study is seen as reliable.							
Theorell 1998[54]	Aggregated data, Inferred decision latitude (1)	Fatal (23%) and non-fatal AMI, hospital discharge register and death register (2)	Sweden, controls 300, men (45–64 yr) (1, 1, 1)	1047	Low decision latitude OR, 1.2 (0.8–2.0). Negative change in decision latitude OR 1.4 (1.0–2.0) (1)		Age, hospital catchment area, smoking, LDL-HDL ratio, social class, history of hypertension, and chest pain (1)	8
	Strengths: inclusion of many cases. Limitations: aggregated data. Comments: reliable study.							
Sokejima 1998[35]	Self-report (information from table of salary) working hours (1)	First time AMI, hospital admission (2)	Japan, controls 331, men (30–69 yr) (1, 1, 0)	195	Daily working hours last month before infarction: ≤7 h 2.0 (1.52–5.28), 7–11 h 0.96 (0.58–1.60) ≥11 h 2.94 (1.39–6.25). Increase in working hours ≥3 h 2.49 (1.24–4.99) (1)		Age, occupation category, hypertension, hypercholesterolemia, diabetes, BMI, smoking habits, proportion of sedentary work, and burn out index (1)	7
	Strengths: working hours are an objective measure of workload. Limitations: risk of bias as the data from the table of salary were reported by the participant. Comments: exposure was reported by the use of table of salary and was seen as "objective."							

Risk estimates are fully adjusted with the confounders mentioned, if nothing else is stated.

AMI indicates acute myocardial infarction; BMI, body mass index; CHD, coronary heart disease; CVD, cardiovascular disease; ERI, effort reward imbalance; HDL, high density cholesterol; MI, myocardial infarction; OR, odds ratio; RR, risk ratio; SES, socioeconomic status.

Studies using aggregated data regarding demands did not find significant associations between demands and risk of IHD.[17,19,26,28–30] This is contrary to findings from studies using self-report data.[31–36]

Control or decision latitude was evaluated in 15 articles. For men, control was assessed in 13 analyses, of which 3 demonstrated significant positive associations between lack of control and an increased risk of IHD. For women, control was assessed in 4 analyses, of which 2 demonstrated significant positive associations between lack of control and increased risk of IHD. Studies analyzing aggregated data (as opposed to self-report data) on control were significantly associated with risk of IHD.[19–22,26,32,37,38]

Associations between job strain and incidence of IHD were examined in 13 articles. For men, job strain was evaluated in 11 analyses, of which 4 revealed a significant positive association between job strain and an increased risk of IHD.[10,24,31,34] For women, associations between job strain and incidence of HD were evaluated in 4 analyses, all of which found trends toward associations between job strain and increased risk of IHD.[18,19,21,22]

Social Support

Social support at work and/or during spare time has been shown to modify the strain that might lead to stress, and in some studies, social support therefore is used together with the Demand-Control Model.[39] In this context, determining whether a social network provides support in the handling of psychosocial strain is decisive in the development of illness. Working conditions that include both strain and low social support, iso-strain, are the worst.

Lack of social support was examined in 7 articles. For men, the effect of social support was analyzed in 5 studies, of which 3 found significantly increased risk of IHD among participants lacking social support,[20,33,40] while 2 analyses reported trends toward increased risk of IHD.[18,37] For women, 1 study reported a significantly increased risk of IHD for participants who lacked social support[18] while 3 indicated trends toward increased risk of IHD.[20–22]

Iso-Strain

The experience of iso-strain (strain and no support) for men was significantly and positively associated with the risk of IHD in 3 analyses for aggregated data[20,39] and self-report data.[40] For women, 1 study demonstrated a significantly increased risk of IHD in relation to iso-strain.[20]

The Effort-Reward Model

The Effort-Reward Model refers to the individual's experience of the balance between the effort made and the reward received.[9,41] According to the Effort-Reward Model, the most stressful condition occurs when the effort made is not followed by sufficient reward. Reward is not only a financial matter, but also includes the esteem associated with the work, as well as the security of the work and future prospects. An effort-reward imbalance, according to the model, will lead to stress. People with personalities characterized by over-commitment are more likely to accept such an imbalance, and face greater risk of becoming stressed.[41]

The Effort-Reward Model was used in only 4 articles, none including women. The study by Siegrist et al examined status inconsistency and intrinsic effort.[42] The coexistence of high effort and low reward was significantly and positively associated with an increased risk of IHD in 1 study using proxy measures for effort and reward.[24] Lynch et al demonstrated a nonsignificant trend towards a positive association between a measure of effort-reward imbalance in a life course perspective and the risk of IHD,[43] while 1 study using proxy measures from the Whitehall II study showed no association.[10]

Other

The Organizational Injustice Model, a more recent model, claims that stress-related disease occurs if an individual does not feel that he/she is treated fairly in the organization.[10] A feeling of injustice was significantly associated with the risk of IHD in 2 analyses with male participants.[10,44]

Five articles analyzed the association between job insecurity and IHD.[11,23,25,45,46] Of these, 2 analyses reported significant positive associations,[25,46] both analyses including only male participants.

DISCUSSION

This systematic review included 33 articles presenting 51 analyses with male participants, 18 analyses with female participants, and 8 analyses with both genders. Of the 69 analyses including only men or women, 24 indicated a significant positive association between an undesirable psychosocial factor at work and an increased risk of IHD. The review revealed many nonsignificant trends toward associations and demonstrated a large variation in the measurements of exposure and study designs.

A meta-analysis was not conducted because the measurements of exposure were too varied, several of the exposures were included in only one or few studies, and the studies were hard to compare, especially culturally, and in reference to gender and age.

Generally, the articles included in the review were of good quality. However, construction of a quality score is difficult and is associated with the danger of "automatic rating." Furthermore, as is apparent in Table 3, some articles were assigned rather high quality scores despite serious limitations. Several studies[19,24,28,30,32,47] have limitations to such a great degree that their lack of significant results can not be taken as evidence of no association. The prevailing problem is not confounding variables, but rather selection bias and problems related to exposure assessment (as mentioned later). The inclusion of older participants increases the risk of the "healthy worker effect" and dilutes exposure assessment in several ways: people who work into their old age presumably work in professions in which they are not exposed to psychosocial loads, or they are especially dedicated to their work. The population studied has to vary sufficiently in terms of exposure, ie, inclusion of only 1 occupational group may be a problem. At the same time, however, the participants have to belong to the same culture, as the interpretation of stressors has to be comparable. Several articles included relatively few cases and therefore do not have the statistical power necessary to demonstrate significant associations.

Validity of Measures of Exposure

The variation in how exposure is measured mirrors the fact that psychosocial factors acting as stressors in daily work life are multifarious. The range of exposures originates in various working environments and cultures. Other exposure measures, like bullying at work, may exist.[48] The use of theoretically-based stress models may be a strength of a design, but at the same time it is important that the models do not rule out the exploration of other stressors. During the last 10 to 20 years, the labor market has changed and fewer people are employed in production (eg, industry and farming), while more people are employed in education, administration, health care, and knowledge production. This means that the stress models used in the 1980s might have to be further developed to be used today. In the 1970s, when the Demand-Control Model was developed, job strain showed stronger association with disease than did demands and control separately. However, the level of decision authority has generally increased, though it is still different between groups. Furthermore, skill discretion increased in Western society during the 1980s. The working populations increased education

level, as well as increased demands on the labor market, necessitate adjustments to the way we measure exposure.

One important issue that should be addressed is the validity of the measures; that is, are the researchers measuring the stressors they intended to measure? Steenland et al argue, in relation to the lack of an association between demands and risk of IHD, that they might not have measured what they had intended to measure.[26] Different occupations have different kinds of psychologic demands, and higher status occupations tend to be associated with higher psychologic demands.[49] This methodological challenge is discussed by Kristensen et al, who suggest that researchers in the field should distinguish between intensification (faster work pace, mostly relevant for blue-collar workers) and extensification (longer working hours and deadlines, mostly relevant for white collar workers) of demands.[50] The Demand-Control Model is the most prevalent stress model, but the dimensions of the model need to be further elucidated.[50,51]

Precise descriptions of exposures, which can be compared across studies, require several methodological considerations to be taken into account. Use of the same stress model and questionnaire are obvious necessities for comparing studies, but it is also necessary for the studies to be comparable with regard to culture. Cultural differences may be the reason for nonsignificant results reported in studies from the United States, in contrast to the many significant findings of the Nordic studies. Comparing results between cultures reveals information about differences and similarities between the cultures, but does not determine whether a certain psychosocial factor related to a job is associated with an increased risk of disease. Seen from this perspective, the Nordic studies present evidence of an increased risk of IHD when people are exposed to hectic work environments, high workload or demands, and iso-strain. For example, of the studies that originated in the Nordic countries, 4 studies[17,33,34,36] reported significantly increased risk for IHD in men with high workloads and 2 studies[20,39] indicated significantly increased risk for IHD in men experiencing iso-strain.

However, if one concludes that a certain psychosocial factor at work indicates an increased risk of disease in a specific culture, this psychosocial factor has to be clearly defined and the relevant length of exposure to this factor has to be stated. As an example, one might hypothesize that high psychologic demands are associated with an increased risk of IHD. A study examining this association would require a clear and unequivocal definition of "demands," a culture in which the defined type of demand is unwanted, and a population in which a sufficient exposure contrast is present. Furthermore, a precondition for developing IHD due to atherosclerosis is that the exposure is prolonged, ie, years in length. So, if the demands are not clearly defined, if the demands are a preferred condition, if no exposure contrasts are present, or if the exposure is of a short duration, a significant association would not be expected. Studies exhibiting these methodological problems include Alfredsson et al,[17] Reed et al,[28] and Lee et al.[22] For example, Alfredsson et al[17] included nearly 1 million residents of Stockholm (high exposure contrast) and the exposure was clearly defined ("hectic work" in a culturally homogenous population). The follow-up period was only 1 year. This is a rather short duration for developing atherosclerotic disease, but sufficient, as the extremely large sample includes people who vary to a great extent concerning predisposition and stages of atherosclerosis. In addition, psychophysiological mechanisms triggering a myocardial infarction via metabolic and immunologic pathways could certainly play an important role during short periods of time (eg, weeks or months). On the other hand, Reed et al[28] used aggregated data concerning a group of Japanese-Americans living in Honolulu. As few as 359 men were followed for 18 years. The measurement of exposure presumably did not fit the culture of the population, and the follow-up was far too long (exposure may have changed several times). In the study by Lee et al,[22] the participants consisted of female registered nurses in the United States. As the Demand-Control Model describes demands and control among assembly line workers rather than among nurses, this model may not be useful for understanding the demands perceived by nurses in the United States. A questionnaire addressing hiding one's feelings, being responsible for other people's lives, or problems originating from being both a mother and a nurse (double exposure[52,53]) might have been more relevant.

Most of the studies measure exposure solely at baseline. In large population studies, this is the most feasible design. However, as in the study by Reed et al,[28] exposure may change during a long follow-up. A negative change can be important as demonstrated by Theorell et al[54] For workers experiencing the same level of work stress during the follow-up period, exposure measured at one point in time may be sufficient.[55] This could be evaluated by stratifying participants according to whether they maintained the same job during the follow-up period. Using this design, Kivimäki et al[24] found a stronger association among those whose occupational group was unchanged. A significant change in exposure occurs when individuals retire. Therefore, follow-up beyond the age at which most people in the specific population retire is inexpedient.

Use of aggregated data instead of self-report data may allow the inclusion of a large sample of the population at the expense of specificity of exposure. The studies using aggregated data found no associations between demands and IHD, while control and IHD more consistently were associated. This may point to a distinction between the 2 dimensions: the items included in the demands dimension address the feeling of having enough time to do the job etc. This is clearly an individual feeling. The control dimension includes items concerning who tells you what to do at work and how to do it, ie, structural factors at work. Originally, the Demand-Control Model did not state that demands per se are stressful if coupled with sufficient control.[56] The results of the studies using aggregated data support this. The fact that self-reported demands are associated with an increased risk of IHD may indicate that people who state they experience high demands do not feel in control. Self-reported control seems not to be associated with IHD. According to the discussion on the cultural aspects of stress, this may be caused by the fact that the degree of control over one's work situation is very high in the Nordic countries (ie, exposure contrast is low).

Job strain is significantly associated with risk of IHD in several studies. An interaction between demands and control was found in only 1 study,[34] and was not demonstrated in others.[18,32,57] It is preferable to present results on single dimensions rather than the combined dimension (ie, demands and control instead of strain).

Results reported for the iso-strain theory[20,32,40] indicated consistent significant, increased risk for IHD. This may be due to the strong effect of support.[20,40]

The Effort-Reward Model and the Organizational Injustice Model are examples of new theories that have to be evaluated in future studies before it is possible to determine the effect of the included dimensions. This also applies to job insecurity. The results till now point to the significance of all 3, but standard questionnaires were not used in studies included in this review.

Validity of the Endpoints

The use of IHD as the end point should be addressed. One of the inclusion criteria was "definite coronary heart disease." The endpoints used were angina pectoris (objectively assessed), acute myocardial infarction, cardiovascular or coronary death, or sudden death. These endpoints were chosen as they are "hard" endpoints. It should be noted that the presentation of acute coronary syndromes differs between the 2 genders.[58–61] This may be 1 reason for the lack of female participants in some population studies, leading to the

exclusion of women.[32,34] The validity of self-reported disease may be questionable, as symptoms tend to be felt more strongly when one has difficulties at the job, than otherwise. Therefore, results for self-reported angina pectoris were not included in this review.

Bias in the form of misclassification may occur in countries in which health care is not free, as is the case in the United States. IHD may not be found if the individual experiencing symptoms does not have the financial resources necessary for hospitalization or treatment. At the same time, more prosperous people may be examined more carefully. This may lead to misclassification, ie, overrepresentation of people with higher socioeconomic status and underrepresentation of lower socioeconomic status, which again may lead to nonsignificant findings.

Sudden death is included as an end point in some studies. The reason for sudden death may not only be myocardial infarction. Among other reasons, arrhythmia may very well be caused by the same conditions as IHD on the basis of atherosclerosis; however the time from exposure to end point may be considerably shorter.[62]

Length of Exposure

The literature included in this review is not sufficient to determine any dose response relationship between exposure to a psychosocial factor at work and incidence of IHD. One study by Johnson et al, tries to establish a dose response relationship between the dimensions of the Demand-Control Model and cardiovascular mortality. The study demonstrates an increasing risk till 10 to 15 years of exposure, but a decreasing risk thereafter.[37] This is to be expected, as the exposure has to be present a considerable length of time until it can be demonstrated that the atherosclerotic condition progresses with a higher rate than otherwise. Those who are diseased leave the work place, and the people still working after 15 or 20 years are believed to have a genetic constitution not prone to developing IHD.

With regard to the length of exposure, the age of the population included in the study is important. As argued before, a long follow-up is accompanied with a risk of change in exposure, especially change due to retirement. The effect of work stress seems most pronounced in the younger age groups,[17,20,54,63] presumably because the effect of other risk factors takes over during aging, or the stressors are perceived as more uncontrollable by younger individuals.

Analytical Strategy

In this review, we decided to present risk estimates with multivariate adjustments. This may be an over-adjustment. However, the multivariate adjustments did not change the results much. On the other hand, it is important to realize that among the most frequent factors predisposing to IHD, several factors may in fact be caused by the physiological stress response. Psychosocial factors might be associated with hypertension itself,[64,65] as well as choice of diet and development of obesity[66,67] and smoking.[68]

Because the stress response as well as the perception of stressors is different across gender, it is of paramount importance that researchers evaluate stressors and data accordingly by the use of gender-separated analyses. Alfredsson et al found hectic and monotonous work associated with an increased risk of IHD in both genders(ie, relative risk 1.18 for men and 1.64 for women).[17]

CONCLUSIONS

A balanced evaluation of the studies indicates moderate evidence that high psychologic demands, lack of social support, and iso-strain are risk factors for IHD among men. Studies performed during recent years have not shown evidence for lack of control as a risk factor for IHD. Several studies have shown that job strain is a risk factor, but in the more recent ones, these associations can be fully explained by the association between demands and disease risk. There was insufficient evidence for effort-reward imbalance, injustice, job insecurity or long working hours among men. Furthermore, there was insufficient evidence for any effects concerning women. Several of the published studies had insufficient statistical power. Future research should focus on refining measures of exposure, and on the assessment of the significance of psychosocial factors at work for women.

It is further suggested that future research focus on refinement of exposure measures, including evaluation of intensity and duration of exposure, concerning conditions in women and gender differences.

REFERENCES

1. Black PH. The inflammatory response is an integral part of the stress response: implications for atherosclerosis, insulin resistance, type II diabetes, and metabolic syndrome X. *Brain Behav Immun*. 2003;17:350–364.
2. Bjorntorp P, Rosmond R. Neuroendocrine abnormalities in visceral obesity. *Int. J Obes Relat Metab Disord*. 2000;24(Suppl 2):S80–S85.
3. Rabin B. Stress: a system of the whole. In: Ader R, ed. *Psychoneuroimmunology.* Elsevier Academic Press; 2007;709–722.
4. Rosmond R, Wallerius S, Wanger P, et al. A 5-year follow-up study of disease incidence in men with an abnormal hormone pattern. *J Intern Med*. 2003;254:386–390.
5. Remme WJ. The sympathetic nervous system and ischaemic heart disease. *Eur Heart J*. 1998;19(Suppl F):F62–F71.
6. Cohen S, Janicki-Deverts D, Miller GE. Psychological stress and disease. *JAMA*. 2007;298:1685–1687.
7. Lahiri MK, Kannankeril PJ, Goldberger JJ. Assessment of autonomic function in cardiovascular disease: physiological basis and prognostic implications. *J Am Coll Cardiol*. 2008;51:1725–1733.
8. Karasek R, Theorell T. *Healthy Work—Stress, Productivity, and the Reconstruction of Working Life.* New York, NY: Basic Books Inc; 1990.
9. Siegrist J, Starke D, Chandola T, et al. The measurement of effort-reward imbalance at work: European comparisons. *Soc Sci Med*. 2004;58:1483–1499.
10. Kivimaki M, Ferrie JE, Brunner E, et al. Justice at work and reduced risk of coronary heart disease among employees: the Whitehall II Study. *Arch Intern Med*. 2005;165:2245–2251.
11. Iversen L, Sabroe S, Damsgaard MT. Hospital admissions before and after shipyard closure. *BMJ*. 1989;299:1073–1076.
12. Belkic KL, Landsbergis PA, Schnall PL, et al. Is job strain a major source of cardiovascular dis ease risk? *Scand J Work Environ Health*. 2004;30:85–128.
13. Kivimaki M, Virtanen M, Elovainio M, et al. Work stress in the etiology of coronary heart disease–a meta-analysis. *Scand J Work Environ Health*. 2006;32:431–442.
14. Kuper H, Marmot M, Hemingway H. Systematic review of prospective cohort studies of psycho social factors in the etiology and prognosis of coronary heart disease. *Semin Vasc Med*. 2002;2:267–314.
15. Tsutsumi A, Kawakami N. A review of empirical studies on the model of effort-reward imbalance at work: reducing occupational stress by implementing a new theory. *Soc Sci Med*. 2004;59:2335–2359.
16. van Vegchel N, de Jonge J, Bosma H, et al. Reviewing the effort-reward imbalance model: drawing up the balance of 45 empirical studies. *Soc Sci Med*. 2005;60:1117–1131.
17. Alfredsson L, Spetz CL, Theorell T. Type of occupation and near-future hospitalization for myocardial infarction and some other diagnoses. *Int J Epidemiol*. 1985;14:378–388.
18. Andre-Petersson L, Engstrom G, Hedblad B, et al. Social support at work and the risk of myocardial infarction and stroke in women and men. *Soc Sci Med*. 2007;64:830–841.
19. Eaker ED, Sullivan LM, Kelly-Hayes M, et al. Does job strain increase the risk for coronary heart disease or death in men and women? The Framingham Offspring Study. *Am J Epidemiol*. 2004;159:950–958.
20. Hammar N, Alfredsson L, Johnson JV. Job strain, social support at work, and incidence of myocardial infarction. *Occup Environ Med*. 1998;55:548–553.
21. Kuper H, Adami HO, Theorell T, et al. Psychosocial determinants of coronary heart disease in middle-aged women: a prospective study in Sweden. *Am J Epidemiol*. 2006;164:349–357.
22. Lee S, Colditz G, Berkman L, et al. A prospective study of job strain and coronary heart disease in US women. *Int J Epidemiol*. 2002;31:1147–1153.
23. Lee S, Colditz GA, Berkman LF, et al. Prospective study of job insecurity and coronary heart disease in US women. *Ann Epidemiol*. 2004;14:24–30.

24. Kivimaki M, Leino-Arjas P, Luukkonen R, et al. Work stress and risk of cardiovascular mortality: prospective cohort study of industrial employees. *BMJ*. 2002;325:857.
25. Matthews KA, Gump BB. Chronic work stress and marital dissolution increase risk of posttrial mortality in men from the Multiple Risk Factor Intervention Trial. *Arch Intern Med*. 2002;162:309–315.
26. Steenland K, Johnson J, Nowlin S. A follow-up study of job strain and heart disease among males in the NHANES1 population. *Am J Ind Med*. 1997;31: 256–260.
27. Karasek RA, Theorell T, Schwartz JE, et al. Job characteristics in relation to the prevalence of myocardial infarction in the US Health Examination Survey (HES) and the Health and Nutrition Examination Survey (HANES). *Am J Public Health*. 1988;78:910–918.
28. Reed DM, LaCroix AZ, Karasek RA, et al. Occupational strain and the incidence of coronary heart disease. *Am J Epidemiol*. 1989;129:495–502.
29. Alfredsson L, Karasek R, Theorell T. Myocardial infarction risk and the psychosocial work environment: an analysis of the male Swedish working force. *Soc Sci Med*. 1982;16:463–467.
30. Alterman T, Shekelle RB, Vernon SW, et al. Decision latitude, psychologic demand, job strain, and coronary heart disease in the Western Electric Study. *Am J Epidemiol*. 1994;139:620–627.
31. Haan MN. Job strain and ischaemic heart disease: an epidemiologic study of metal workers. *Ann Clin Res*. 1988;20:143–145.
32. Kornitzer M, deSmet P, Sans S, et al. Job stress and major coronary events: results from the job stress, absenteeism, and coronary heart disease in Europe study. *Eur J Cardiovasc Prev Rehabil*. 2006;13:695–704.
33. Netterstrom B, Juel K. Impact of work-related and psychosocial factors on the development of ischemic heart disease among urban bus drivers in Denmark. *Scand J Work Environ Health*. 1988;14:231–238.
34. Netterstrom B, Kristensen TS, Sjol A. Psychological job demands increase the risk of ischaemic heart disease: a 14-year cohort study of employed Danish men. *Eur J Cardiovasc Prev Rehabil*. 2006;13:414–420.
35. Sokejima S, Kagamimori S. Working hours as a risk factor for acute myocardial infarction in Japan: case-control study. *BMJ*. 1998;317:775–780.
36. Theorell T, Floderus-Myrhed B. "Workload" and risk of myocardial infarction–a prospective psychosocial analysis. *Int J Epidemiol*. 1977;6:17–21.
37. Johnson JV, Stewart W, Hall EM, et al. Long-term psychosocial work environment and cardiovascular mortality among Swedish men. *Am J Public Health*. 1996;86:324–331.
38. Suadicani P, Hein HO, Gyntelberg F. Are social inequalities as associated with the risk of ischaemic heart disease a result of psychosocial working conditions? *Atherosclerosis*. 1993;101:165–175.
39. Johnson JV, Hall EM, Theorell T. Combined effects of job strain and social isolation on cardiovascular disease morbidity and mortality in a random sample of the Swedish male working population. *Scand J Work Environ Health*. 1989;15:271–279.
40. de Bacquer D, Pelfrene E, Clays E, et al. Perceived job stress and incidence of coronary events: 3-year follow-up of the Belgian Job Stress Project cohort. *Am J Epidemiol*. 2005;161:434–441.
41. Siegrist J. Adverse health effects of high-effort/low-reward conditions. *J Occup Health Psychol*. 1996;1:27–41.
42. Siegrist J, Peter R, Motz W, et al. The role of hypertension, left ventricular hypertrophy, and psychosocial risks in cardiovascular disease: prospective evidence from blue-collar men. *Eur Heart J*. 1992;13(suppl D):89–95.
43. Lynch J, Krause N, Kaplan GA, et al. Workplace conditions, socioeconomic status, and the risk of mortality and acute myocardial infarction: the Kuopio Ischemic Heart Disease Risk Factor Study. *Am J Public Health*. 1997;87: 617–622.
44. Elovainio M, Leino-Arjas P, Vahtera J, et al. Justice at work and cardiovascular mortality: a prospective cohort study. *J Psychosom Res*. 2006;61:271–274.
45. Ferrie JE, Shipley MJ, Marmot MG, et al. The health effects of major organisational change and job insecurity. *Soc Sci Med*. 1998;46:243–254.
46. Vahtera J, Kivimaki M, Pentti J, et al. Organisational downsizing, sickness absence, and mortality: 10-town prospective cohort study. *BMJ*. 2004;328: 555.
47. Andersen I, Burr H, Kristensen TS, et al. Do factors in the psychosocial work environment mediate the effect of socioeconomic position on the risk of myocardial infarction? Study from the Copenhagen Centre for Prospective Population Studies. *Occup Environ Med*. 2004;61:886–892.
48. Kivimaki M, Virtanen M, Vartia M, et al. Workplace bullying and the risk of cardiovascular disease and depression. *Occup Environ Med*. 2003;60:779–783.
49. Marmot MG, Bosma H, Hemingway H, et al. Contribution of job control and other risk factors to social variations in coronary heart disease incidence. *Lancet*. 1997;350:235–239.
50. Kristensen TS, Bjorner JB, Christensen KB, et al. The distinction between work pace and working hours in the measurement of quantitative demands at work. *Work Stress*. 2004;18:305–322.
51. Kristensen TS. Job stress and cardiovascular disease: a theoretic critical review. *J Occup Health Psychol*. 1996;1:246–260.
52. Lundberg U, Frankenhaeuser M. Stress and workload of men and women in high-ranking positions. *J Occup Health Psychol*. 1999;4:142–151.
53. Tobe SW, Kiss A, Szalai JP, et al. Impact of job and marital strain on ambulatory blood pressure results from the double exposure study. *Am J Hypertens*. 2005;18:1046–1051.
54. Theorell T, Tsutsumi A, Hallquist J, et al. Decision latitude, job strain, and myocardial infarction: a study of working men in Stockholm. The SHEEP Study Group. Stockholm Heart epidemiology Program. *Am J Public Health*. 1998;88:382–388.
55. Kivimaki M, Head J, Ferrie JE, et al. Why is evidence on job strain and coronary heart disease mixed? An illustration of measurement challenges in the Whitehall II study. *Psychosom Med*. 2006;68:398–401.
56. Karasek R, Baker D, Marxer F, et al. Job decision latitude, job demands, and cardiovascular disease: a prospective study of Swedish men. *Am J Public Health*. 1981;71:694–705.
57. De Backer G, Ambrosioni E, Borch-Johnsen K, et al. European guidelines on cardiovascular disease prevention in clinical practice: third joint task force of European and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of eight societies and by invited experts). *Eur J Cardiovasc Prev Rehabil*. 2003;10:S1–S10.
58. Elsaesser A, Hamm CW. Acute coronary syndrome: the risk of being female. *Circulation*. 2004;109:565–567.
59. Pilote L, Dasgupta K, Guru V, et al. A comprehensive view of sex-specific issues related to cardiovascular disease. *CMAJ*. 2007;176:S1–S44.
60. Schenck-Gustafsson K. Are the symptoms of myocardial infarction different in men and women, if so, will there be any consequences? *Scand Cardiovasc J*. 2006;40:325–326.
61. Stramba-Badiale M, Fox KM, Priori SG, et al. Cardiovascular diseases in women: a statement from the policy conference of the European Society of Cardiology. *Eur Heart J*. 2006;27:994–1005.
62. Hemingway H. Social and psychosocial influences on sudden cardiac death, ventricular arrhythmia, and cardiac autonomic function. In: Stansfeld S, Marmot M, eds. *Stress and the Heart: Psychosocial Pathways to Coronary Heart Disease.* London, UK: BMJ Publishing Group; 2002;221–255.
63. Kivimäki M, Theorell T, Westerlund H, et al. Job strain and ischemic heart disease: does the inclusion of older employees in the cohort dilute the association? The WOLF Stockholm Study. *J Epidemiol Community Health*. 2008;62:372–374.
64. Steffen PR, Smith TB, Larson M, et al. Acculturation to Western society as a risk factor for high blood pressure: a meta-analytic review. *Psychosom Med*. 2006;68:386–397.
65. Yan LL, Liu K, Matthews KA, et al. Psychosocial factors and risk of hypertension: the Coronary Artery Risk Development in Young Adults (CARDIA) study. *JAMA*. 2003;290:2138–2148.
66. Alonso-Alonso M, Pascual-Leone A. The right brain hypothesis for obesity. *JAMA*. 2007;297:1819–1822.
67. Anthony K, Reed LJ, Dunn JT, et al. Attenuation of insulin-evoked responses in brain networks controlling appetite and reward in insulin resistance: the cerebral basis for impaired control of food intake in metabolic syndrome? *Diabetes*. 2006;55:2986–2992.
68. Jarvis M. Smoking and stress. In: Stansfeld S, Marmot M, eds. *Stress and the Heart: Psychosocial Pathways to Coronary Heart Disease*. London, UK: BMJ Publishing Group; 2002:150–157.

