RESEARCH FINDINGS LINKING WORKPLACE FACTORS TO CARDIOVASCULAR DISEASE OUTCOMES

SHIFT WORK, LONG HOURS, AND CARDIOVASCULAR DISEASE: A REVIEW   *by Kyle Steenland, PhD*

Data from industrialized countries suggests that irregular patterns of work, such as shift work and extensive overtime work, have become increasingly common. In conjunction with this trend, there are more epidemiologic studies of the health effects of such irregular patterns of work, a number of which focus on heart disease. The following is a review of the literature, with comments on possible mechanisms linking irregular hours and heart disease as well as on the methodologic difficulties of studying this topic. Shift work and heart disease are the primary focus here, because most of the epidemiologic efforts have been directed at this area, but the epidemiology of overtime work and heart disease also is reviewed.

Shift Work and Heart Disease

DEFINITION AND PREVALENCE OF SHIFT WORK

Shift work refers to work patterns other than the standard day shift. It therefore includes both rotating shifts in which the worker works a rotating pattern of days, evenings, and nights, and permanent shift work in which a worker works steadily during evenings or nights (second or third shift). Most of the epidemiology regarding the health effects of shift work has focused on rotating shifts. There are many forms of rotating shifts. A worker may work a week of days, a week of evenings, and a week of nights, with weekends off. He or she may work three shift rotations changing more frequently, including sometimes double shifts (16 hours), or perhaps alternative day and night work.

The prevalence of shift work varies from country to country, but most data suggest that in Western industrial countries approximately 10–20% of workers now work rotating shifts. Taylor and Pocock cite a figure of 25% for England in 1968; Tenkanen, et al. cite an estimate of 15–20% for Europe currently; and Knutsson, et al. report an estimated 10–12% in Sweden in the early 1990s.[134,254,256] Gordon, et al. cite a figure of 26% for men and 18% for women in the United States in 1980.[80] It appears that in both Europe and the U.S. the proportion of workers on rotating shifts has been increasing since WW II.[80] For some particular occupations such as nursing, the proportion of workers on rotating shifts is very high. In Boston, for example,

OCCUPATIONAL MEDICINE: State of the Art Reviews—
Vol. 15, No. 1, January–March 2000. Philadelphia, Hanley & Belfus, Inc.

7

60% of nurses reported in 1988 that they had a history of shift work.[127] Permanent shift work appears to be more rare than rotating shift work; for example, Akerstedt, et al. report Swedish data showing a prevalence of only 7% for permanent shift work.[2]

MECHANISMS FOR SHIFT WORK AND HEART DISEASE

Shift work might reasonably be considered a risk factor for heart disease because: (1) shift work, especially rotating shift work, disrupts **circadian rhythms**, which are are linked to a number of CV risk factors such as blood pressure, heart rate, and catecholamine levels, (2) shift work is either correlated with or leads to poorer **lifestyle factors** which in turn are related to increased CV disease, e.g., reduced physical activity, poorer diet, increased cigarette consumption, and less social contact, and (3) shift work involves more **occupational stress** because such jobs are more demanding and often involve less control on the part of the worker, and increased stress may increase heart disease. These possible mechanisms clearly are not exhaustive. For example, Harma mentions the known decrease in fibrinolysis in early morning hours which might preferentially affect night workers, or some unknown aspect directly related to sleep deprivation itself.[92] Bøggild and Knutsson provide a more thorough review of potential mechanisms.[25] Note that for the second pathway described above, shift work could be either causal or simply a marker for confounders (standard heart disease risk factors), which when controlled would eliminate any association between shift work and heart disease.

The (continual) disruption of circadian rhythm for rotating shift workers is probably the strongest proposed mechanism, with important and documented effects on the CV system (see Chapter 5 for a review). However, key questions remain about exactly how this disruption might lead to increased disease in shift workers, and whether they can adapt to such disruption.

Shift work could cause either acute or chronic effects on the heart, i.e., acute effects while performing shift work, or chronic effects years later. Disruption of circadian rhythms might be suspected of having acute effects, although chronic alterations of blood pressure, for example, might lead to heart disease at a later date. A worse pattern of lifestyle characteristics and increased stress could reasonably be associated with either acute or chronic effects on the heart. Whether the presumed effects are acute or chronic, they may be more easily observed in younger men, during working ages, simply because single risk factors for heart disease are more easily detected at younger ages before a large number of risk factors begin to cause much higher heart disease rates.[108] On the other hand, if the effects were chronic, they might not become apparent until older ages and perhaps not until after workers had left the workplace.

METHODOLOGIC ISSUES IN STUDYING SHIFT WORK AND HEART DISEASE

As a general recommendation, in light of the potential for a long lag period between shift work and overt CV disease, studies should include followup of workers after leaving work. Analyses should pay careful attention to different possible lag times between the beginning of shift work and observable heart disease. Assuming some appreciable lag, studies restricted to workers currently employed might more profitably focus on the development of intermediate CV risk factors (e.g., blood pressure, cholesterol) rather than manifest CV disease (which in many cases will cause the worker to leave the workforce). However, cross-sectional studies of intermediate risk factors among the currently employed are limited due to the usual problem of determining temporal sequence, so longitudinal studies with baseline measures before shift work would be far preferable.

There are several additional aspects of shift work that potentially complicate any epidemiologic study of its relation to heart disease. Shift workers may be a select population, and it may be difficult to find a comparable reference population of day workers. Shift workers may be selected into shift work because they are healthier to begin with and the employer believes they are better adapted to shift work. However, the opposite scenario is also possible—shift workers may already have an unhealthy lifestyle and, therefore, may be willing to work irregular hours because they won't suffer any lifestyle change. There are few data on this issue. McNamee, et al. found a significantly reduced risk of ischemic heart disease in the first 10 years after starting shift work, which then was no longer apparent, suggesting an initial selection of shift workers for good health.[172] Knuttson and Akerstedt studied 53 men who applied for day work or shift work and found that the applicants for shift work were more accustomed to irregular sleep patterns, but there were no differences in traditional CV risk factors.[135]

In addition to selection into shift work for health-related reasons, shift workers may have unhealthier lifestyles and lower educational backgrounds than day workers, biasing upwards studies of heart disease. Such biases are minimized if one compares workers to workers, making the same general social class likely, especially if they are in the same workplace. This potential bias is more of a concern in broad-based studies such as population-based case-control studies including many social classes, or in cohort studies including subjects from many different workplaces.

There is reasonable evidence that some percentage of new shift workers switch back to day work because they cannot tolerate shift work. Harma, et al. provide evidence that 20% of shift workers switch back to day work within a year due to intolerance of shift work.[93] Koller reports cross-sectional data indicating 22% of workers with a history of shift work had abandoned shift work due to health or family problems.[140] Akerstedt, et al. cite evidence from Sweden in the 1940s that approximately 10% of workers with a history of shift work had transferred back to day work for health reasons within 10 years.[2] Angersbach, et al. report in a study of 600 workers that 11% had switched from shift work to day work, two-thirds of whom did so for health reasons.[11] These same authors found a higher prevalence of health problems in these workers who had dropped out of shift work, compared with day workers or workers who had stayed in shiftwork. McNamee, et al. found an increased risk of heart disease death in the first 5 years after a shift worker switched back to day work (odds ratio 2.69 [1.04–6.96]).[172] On the other hand, Bøggild, et al. found no increased risk for shift workers who switched back to day work.[26] Nachreiner has provided an overview of the recent literature on workers' tolerance of shift work.[182]

The phenomenon of workers, particularly unhealthier workers, switching back from shift work to day work is an example of a **healthy shift-worker survivor bias**, which tends to create a bias towards the null in studies of shiftwork and CV disease. This potential bias is particularly important in prevalence studies comparing shift workers to non-shift workers, and in longitudinal studies that seek a trend in risk with shift work duration rather than compare those ever employed in shift work to those never employed in shift work.

While the healthy shift-worker survivor bias concerns workers switching from shift work to day work, there is also the more general problem of the **healthy worker survivor bias**, which refers to the tendency of sick workers to leave the workforce altogether. Heart disease is a serious illness that often results in the removal of workers from the workplace. One approach, when comparing shift workers to day workers, is to compare illness or mortality rates when both groups are working or when both groups are not working.[245]

It is difficult to summarize these possible biases to say that the overall "net" likely bias is negative or positive. Judgement of the likely sum effect of such biases depends on study design and can best be done for each study individually

EPIDEMIOLOGIC STUDIES OF SHIFT WORK

Cardiovascular Risk Factors. Disruption of circadian rhythms, poor lifestyle, and increased stress presumably operate via a worse profile of CV risk factors among shift workers versus day workers. However, the healthy shift-worker survivor bias and the healthy worker survivor bias might make it more difficult to observe such a worse profile, particularly in prevalence studies. The data on CV risk factors as shown in Table 1 do not indicate a consistently worse profile of risk factors among shift workers. Almost all of these studies are cross-sectional, assessing the prevalence of risk factors at a given point in time. Shift work is defined in these studies by either current status as a shift worker or by a history of shift work. Some studies excluded day workers who had ever been shift workers, but most did not, thereby allowing a possible healthy shift-worker survivor bias.

Blood pressure usually exhibits a trough at night and peak during the day. The study by Baumgart, et al. listed in Table 1 shows that shift workers rapidly alter this pattern and exhibit a peak at night while working; other investigators have duplicated these findings.[44,250,294] However, most studies do not indicate that shift workers have a higher mean blood pressure, which would be expected to lead to more heart disease (an exception is the study by Prunier-Poulmaire, et al., but it is somewhat suspect due to a small day worker referent group that was doing a different kind of job, and the fact that 18 of 21 self-reported health conditions were significantly worse in shift workers, suggesting a possible selection bias). It is possible that a different diurnal pattern of blood pressure troughs and peaks could increase risk of heart disease, but this is currently unknown.

The lack of consistent prevalence findings of more CV risk factors does not strengthen the case that shift work increases CV risk, but neither does it fatally weaken it. First, the evidence is not totally negative; second, the healthy worker biases may play a role in negative studies. Even if a consistent profile of worse CV risk factors (either lifestyle factors such as smoking or physiologic measures such as blood pressure) was found among shift workers in prevalence studies, the question would still be open as to whether shift work was *directly responsible for* the increased prevalence of risk factors or simply *associated with* such factors. In the former case, shift work would truly be a cause of CV disease, and epidemiologic analyses would not control for risk factors because they would be intermediate variables on a causal pathway. In the latter case, shift work might or might not be a true cause of heart disease, but if it were, it would not operate via causing an increase in known risk factors. Thus, epidemiologic analyses would have to control for known risk factors because they would be considered confounding variables. This problem—whether known risk factors for an outcome should be considered intermediate or confounding variables—is a common one in epidemiologic studies.[281] Adequate studies to sort out this problem require a longitudinal design in which shift workers and day workers are studied at baseline and then followed to determine whether CV risk factors develop preferentially in shift workers.

Cardiovascular Disease. The principal epidemiologic studies comparing CV mortality or incidence among shift workers and day workers or non-shift workers are listed in Table 2. The focus is on studies of *rotating* shift workers. There is only one study of permanent shift workers in the literature; this study focused on fatal

TABLE 1. Selected Recent Studies of Cardiovascular Risk Factors in Shift Workers*

Study†	Population	Design	Findings, Shift Versus Day Work; Comments
Nakamura, et al. 1999	66 male Japanese blue-collar shift workers, 239 day workers, same plant	Prevalence data measured in annual health checkup	Workers rotating 3 shifts, but not those rotating 2 shifts, had significantly higher cholesterol and obesity than day workers
Prunier-Poul-maire, et al. (1998)	French custom officials, 262 shift workers, 40 day workers working in airplanes	Prevalence data, self-reported high blood pressure	Older workers with more rotating shifts reported significantly higher blood pressure; however, they also reported significantly increased health problems for 16 of other 19 health conditions
Knuttson and Nilsson 1998	Sample of 2548 men and 2836 women from 1990 Swedish census, 17% shiftworkers or nightworkers	Prevalence data on current smoking	More current smoking for shift or night workers, odds ratio 1.3 (1.1–1.6), controlling for age, stress, sex
Tenkanen, et al. 1997	1806 Finnish workers (564 shift workers) in several industries, age 40–55 in 1982	Prevalence data in 1982 for risk factors, shift work as of 1982	No differences in smoking, alcohol, obesity, physical activity, or cholesterol; more reported stress
Lasfargues, et al. 1996	676 male and 524 female night workers vs. pair-matched controls, both from 150,000 volunteers for health checkup in France, aged 30–50, 1991–3	Prevalence data, matching on broad socioeconomic strata (manual worker, clerical, manager), age, and sex	No difference in blood pressure, alcohol, self-reported health status. Cholesterol significantly lower in male night workers. Significantly higher triglycerides, smoking, obesity, WBC, sleep problems in night workers. Not clear whether night workers rotated shifts.
Kawachi, et al. 1995	79,109 U.S. nurses age 30–55 in 1976, 60% current or past shift workers as of 1988	Prevalence data in 1988 for risk factors, any history of shift work (both self-reported)	More smoking, high blood pressure, diabetes, obesity, physical activity, less alcohol, no difference in high cholesterol (all age-adjusted)
Skipper et al. 1990	464 U.S. nurses, 54% rotating shifts, 23% days, 12% evenings or nights	Self-reported 1988 prevalence data, age-adjusted, shift work as of 1988	No differences between rotating shift workers and others for physical or mental health, except increased stress for rotating shifters
Romon, et al. 1992	71 French shift workers with more than one year vs. 70 age-matched day workers with no past shift work	Prevalence data, measured in 1988	Higher triglycerides, less alcohol, no differences in cholesterol obesity, cigarettes, blood pressure, nutrients
Knutsson, et al. 1990	12 shift workers, 13 day workers, Swedish paper mill	Prospective over 6 months, shift work as of time of study	No difference in change in lipids or blood pressure over 6 months
Bursey 1990	57 English shift workers (> 5 yr), 57 day workers over 40 (never shift work)	Prevalence data measured at time of study, matching on age, cigarettes, blue-collar status	No difference in obesity, blood pressure, cholesterol, EKG

TABLE 1. Selected Recent Studies of Cardiovascular Risk Factors in Shift Workers* (Cont).

Study†	Population	Design	Findings, Shift Versus Day Work; Comments
Baumgart, et al. 1989	17 English shift workers serving as their own controls	Continuous blood pressure measured morning and night shifts	No difference in mean blood pressure between night and day shifts; evidence of an 8-hour lag in the diurnal variation of blood pressure as soon as night work began
Costa, et al. 1990	158 toll collectors night or shift work vs. 44 day workers, same company, aged 35 or older	Prevalence data	No difference in cholesterol, obesity, blood pressure, triglycerides unadjusted for age, no difference in summary measure of cardiovascular risk factors after age adjustment
Knutsson, et al. 1988	361 shift workers, 240 day workers, blue-collar workers at 3 Swedish plants	Prevalence data measured 1975–1976, shift work as of time of study	More smoking, higher triglycerides, no differences in age, cholesterol, obesity, blood pressure
Gordon, et al. 1986	828 men, 833 women, random sample of U.S., 22% rotating shift workers	Prevalence data self-reported 1980, shift work self-reported as of 1980	Men and women reported more drinking, job stress, emotional problems. No association with age, education, or income, or smoking. Women reported more tranquilizer use.

* For a more complete review of such studies, including non-English publications, see reference 25.
† McNamee et al. 1996 omitted because of lack of age-adjusted data.

heart disease while working (assuming an acute effect) and showed no harmful effects of evening or night work.[246]

The data in Table 2 are rather sparse, and the results are not consistent. Four studies show a significant increase in CV disease for shift workers, while four do not. The 1997 study by Tenkenen, et al. is one of the strongest because it was done within a clinical trial and had good data on heart disease risk factors and outcomes (data were analyzed with and without treated subjects, to make sure results were not confounded by drug treatment).[256] Subjects worked at a variety of workplaces and represented different social classes (restriction of the data to blue-collar workers lowered the relative risk about 25%, indicating some confounding by social class). Overall, analyses indicated that the excess risk shown by shift workers (approximately 40%, borderline significant) was not much affected by adjustment for risk factors such as blood pressure, cholesterol, smoking, or occupational stress. This finding suggests that shift work does cause heart disease, but not via an increase in prevalence of any known or suspected risk factors (e.g., occupational stress), at least as measured in this study. Indeed, Tenkanen, et al. hypothesize another mechanism possibly related to both stress and circadian rhythms—an alteration of fibrinolysis among shift workers. They provide some data showing that the heart disease risk of shift workers versus day workers was somewhat less for those who were taking gemfibrozil as part of a clinical trial. (Gemfibrozil is a lipid-lowering drug that subsequently was found to increase fibrinolysis.) In a followup paper, Tenkanen, et al. found that higher relative risks occurred for shift workers who smoked, suggesting an interaction.[255] However, they did not provide a test of significance for this interaction.

TABLE 2. Studies of Shift-Work and Cardiovascular Disease*

Study†	Population	Design	Findings, Shift Versus Day Work; Comments
Bøggild, et al. 1999	5249 men aged 40–59 in 1971, from 14 companies	Cohort study with 22-yr followup, fatal/non-fatal IHD	RR 1.0 (0.9–1.2) for shift workers, control for most risk factors
Knutsson, et al. 1999	2006 cases first myocardial infarction, 2642 controls	Population based case-control study	RR 1.3 (1.1–1.6) for men and RR 1.3 (0.9–1.8) for women for shift work in last 5 years. Control for smoking, education
Tenkanen, et al. 1997 Tenkanen, et al. 1998	1806 Finnish workers (564 shift workers) in several industries, age 40–55 in 1982, generally long-term shift workers	Cohort study with 6-yr followup, IHD, (ICD 410-414) via death or hospital discharge	RR for IHD 1.4 (1.0–1.9), adjustment for cigarettes, lipids, blood pressure, obesity, alcohol, job strain. No analysis by duration of shift work
McNamee, et al. 1996	Male manual workers at single plant, age < 50 when first employed between 1950–1992, 467 IHD deaths as per death certificate, 467 controls	Nested case-control study, shift work based on personnel records, any history > 1 mo (2/3 exposed)	OR 0.5 (0.3–0.8) in first 10 years after shift work began, OR 0.9 (0.7–1.2) thereafter. No trend with duration of shift-work, control for BP, smoking, job status, obesity measured before employment
Kawachi, et al. 1995	79109 female nurses aged 42–67 in 1988, free of IHD, 60% with history of shift work	Cohort study with 4-yr followup, 292 fatal and nonfatal CHD	RR 1.3 (1.0–1.7) for shift work, RR 1.2 (0.9–1.6) for < 6 yr shift work, RR 1.5 (1.1–20) for 6 yr. Adjustment for risk factors in 1990 (little effect of adjustment on RRs)
Knutsson, et al. 1986	504 paper mill workers in 1968, 394 shift workers, few ex-shift workers, at a single plant	Cohort study 15-yr followup, 43 cases of IHD (angina or MI)	RR 1.4 (n.s.), increasing risk of IHD with increasing duration of shift work until 20 years (RR 2.8, 16–20 yr.), when RR drops possibly due to survivor effect, control over smoking, age
Angersbach, et al. 1980	210 shift workers, 142 day workers, 41 ex-shift workers, all who stayed employed over 11 years, at a single plant	Followup morbidity study over 1966–77 based on company medical records	No differences in cardiovascular complaints registered in company clinic; study limited by restriction to active workers
Taylor and Pocock 1972	Male manual workers with 10+ years employment after 1946 and born before 1920, from 10 companies, 4188 shift workers with 10+ years shift work, 3869 day workers with 10+ years day work and < 6 mo shift work, 555 ex-shift workers with 6+ mo shift work	Cohort study with followup through 1968, 444 CHD deaths, comparison to general population via SMRs	SMR 0.9 (0.8–1.1) for day workers, 1.0 (0.9–1.2) for shift workers, 1.2 (0.9–1.7) for ex-shift workers SMR 1.2 (1.0–1.5) for shift workers under age 60, primarily in one company adjustment only for age, no analysis by duration of shift work

* Cross-sectional studies are omitted. † Three studies potentially relevant to rotating shift workers are omitted (Alfredsson, et al. 1982, Alfredsson, et al. 1985, Tuchsen 1993) because they are not based on a well-defined population of shift workers. The exposure variable in these three studies is defined as work in an occupation presumed to involve more frequent shift work than other occupations. These studies all show some increase in mortality among workers in jobs presumed to involve more shift work. However, the imprecision of the definition of shift work and the possibility of confounders related to occupation make these studies of less value than the ones listed. (IHD = ischemic heart disease, ICD = ischemic coronary disease, CHD = coronary heart disease, MI = myocardial infarction)

The study by Kawachi, et al. of U.S. nurses is a second well-designed study with a positive result (RR = 1.31, 95% CI 1.02–1.68).[127] Adjustment for traditional risk factors generally did not change results much, again suggesting that any shift work effect is not mediated through the risk factors usually considered for heart disease, although in this study only self-reported data on risk factors was available. A significant trend of increased risk with increasing duration of rotating shift work was shown. There is no suggestion in the data that those who left shift work shortly after entering it (the "drop-outs") had a higher heart disease risk. This could be because few nurses were able to switch back to day work, even if they had health problems.

The third positive study, by Knutsson, et al., is a smaller study without extensive control over conventional CV risk factors.[136] It is consistent with the Kawachi, et al. study in that there is an overall excess risk of about 40% for shift workers, and a significant increasing trend in risk with increasing duration of shift work, at least until 20 years. Employees who have been shift workers for more than 20 years show a decreased risk, which the authors interpret as a survivor effect—shift workers who survive more than 20 years are a particularly hardy group unaffected by heart disease. However, no such survivor effect was seen in the Kawachi, et al. study.

The fourth positive study, also by Knutsson, et al. is unusual in that it is a population-based case-control study in which shift work in the last five years was determined by interview.[134] Shift work (14–15% did shift work, about the same for men and women) in this study is not rotating shifts per se, but includes those reporting night work (about 3–4% did night work). The limited time window for shift work and the lack of detailed information on the reported shift work are limitations in this study. The categorization of exposed (shift work) versus nonexposed is likely to be less precise than in cohort studies; this fact would ordinarily bias findings towards the null. Nonetheless, a modest but significant relative risk of 1.3 was found for both men and women. Adjustment for self-reported job strain did not change the findings, nor was there any interaction with the job strain variable. The principal concern in this study is possible upward bias in the odds ratio due to uncontrolled confounding. Shift workers were of lower socioeconomic class than non-shift workers, and smoked more. Education and smoking (current, former, never) were controlled in the analysis, but residual confounding by social class may have occurred, and there was no control for risk factors such as obesity, blood pressure, and cholesterol. While it could be argued that these last factors might be intermediate variables which should not be included in the model, this case has not been proved, and it is at least equally plausible that these variables act as confounders.

The four remaining studies in Table 2, in contrast, are largely negative. There are no obvious flaws in the designs of the studies by Bøggild, et al., McNamee, et al., and Taylor and Pocock to explain why they are negative.[26,172,254] The Bøggild, et al. study is one of the better analyses overall, as it is a cohort study with good baseline data on possible confounders, some validation data indicating that self-reported data on shift work were reasonably accurate, and a recontact of 75% of the cohort 15 years after baseline to again ascertain shift-work status.[26] Workers worked in 14 different companies and came from different social classes. Although workers with any night work are mixed with rotating shift workers, evidence presented suggests that most shift workers rotated. There is no suggestion of any excess risk for shift workers in this study, with or without controlling for traditional risk factors. There is some evidence in these data that inadequate control over social class, in studies with heterogenous populations of workers, might be an important confounder in shift-work studies.

The McNamee, et al. study was done in a workforce at a single plant.[172] This study showed no effect overall of shift work, nor with duration of shift work (in contrast to Kawachi, et al. 1995 and Knuttson, et al. 1986). McNamee, et al. conducted a number of time-specific analyses, including analyses by years since beginning shift work; the latter revealed a significant excess risk for ex-shift workers shortly after leaving shift work (odds ratio 2.69, 1.04–6.96, 14 cases, 6 controls) compared to day workers. However, this finding may have been a reflection of sick workers leaving employment rather than a health effect specific to shift work.

The Taylor and Pocock study is an older study that is limited by the lack of a direct comparison between shift workers and day workers (all groups are compared to the general population), but which is based on large numbers and had a good division of workers between long-term shift workers, day workers, and ex-shift workers.[254] Despite the lack of a direct comparison between worker groups, this study can be considered negative. There is an interesting finding of a modest excess for shift workers under 60 years of age, but the authors state that this is largely due to one particular company and that there may be additional reasons (not specified) why young workers at this company might have high heart disease rates.

The final study in this group, by Angersbach, et al., is a morbidity study based on company medical records and restricted to workers who remained employed during an 11-year period.[11] This is an important limitation in so much as the effects of shift work on the heart might cause workers to leave employment, or might first occur only after employment, so this study must be given less weight than the others. A similar study of illness among active workers was conducted, but it did not report CV disease separately.[253]

SUMMARY OF EPIDEMIOLOGIC EVIDENCE FOR HEART DISEASE–SHIFT WORK LINK

Taken as a whole, the epidemiologic data suggest that a modest association between shift work and heart disease may exist. There are plausible biological mechanisms (via disruption of circadian rhythms) by which shift work could result in heart disease. However, the epidemiologic studies are still relatively few in number, and they are not consistent. Therefore a causal relationship between shift work and heart disease cannot be inferred. It is a difficult subject to study epidemiologically, and we must wait for additional data before drawing more definitive conclusions.

Those studies that do show a shift work effect do not suggest that this effect is mediated by changes in conventional heart disease risk factors; however, these risk factors may not have been well measured or may not have been the true risk factors of interest. Furthermore, there may be effects of shift work on the CV system that are not well understood and are not well explained by the current proposed mechanisms. There is some evidence of selection biases operating that could bias findings towards the null, but there is other evidence that some positive findings in general populations may have been confounded positively by social class.

REGULATIONS CONCERNING SHIFT WORK

Kogi recently reviewed international regulations on the organization of work, principally the recommendations of the International Labor Organization (ILO) dating from 1990, and the directive of the European Council of 1993 which (at least in theory) must be enforced within the European Economic Community. These regulations apply more generally to all work organization, but a number of points are directly relevant to shift work. The ILO recommendations call for: (1) advice to the

worker at regular intervals on how to cope with shift work, (2) transfer to a similar day job when the worker is found unfit for shift work, (3) special compensation for shift work, (4) consultation between worker and employer on the details of the shift work, and (5) at least 11 hours rest in each 24-hour period (no consecutive full-time shifts). The European directive is similar. It calls for: (1) a minimum daily rest period of 11 hours in a 24-hour period, (2) a rest period of at least 35 consecutive hours per 7-day period, (3) maximum of 48 work hours per week, and (4) transfer to day work when problems with night work are recognized.

In the U.S. there are no general regulations covering shift work, although there are some regulations for particular sets of transportation workers (pilots, truck drivers, and railroad workers). The U.S. National Institute for Occupational Safety and Health has published guidelines for shift work.

Overtime Work and Heart Disease

Overtime work is commonly thought to be stressful and fatiguing and may be correlated with sleep deprivation, thereby involving two of the same mechanisms hypothesized for heart disease and shift work. There are data indicating that, in general, being at work (versus not being at work) increases blood pressure, so that longer working hours implies more time with increased blood pressure.[210] Finally, there are more recent data indicating that long hours of overtime may increase average blood pressure as measured over 24 hours. One model for an effect of long hours on heart disease suggests that this increased blood pressure contributes to an acute myocardial infarction.

Studies of long hours and heart disease involve many of the same methodologic issues as studies of shift work and heart disease; it is important to compare populations of workers that are as similar as possible with respect to potential confounders to avoid selection biases, and longitudinal studies with careful attention to temporal sequence of exposure are preferred.

Overtime work as a risk factor for heart disease is difficult to separate from the more general literature regarding stress, since overtime work generally is considered stressful. There are a few early studies suggesting that long working hours are among the stressful factors that increase the risk of heart disease.[224,264] More recently, Falger and Shouten studied cases of male acute myocardial infarction versus hospital and neighborhood controls.[68] With hospital controls (but not neighborhood controls), they found that self-reported prolonged overtime (time period not defined) caused a significant two-fold excess risk for acute myocardial infarction after controlling for smoking, age, education, and self-reported exhaustion. The focus in these studies has been more on stress rather than on overtime work per se.

There are two other studies in which working long hours is inferred for study subjects based on occupational category, using ancillary surveys of work habits by different occupations.[37,88] These studies can provide only indirect evidence and are not reviewed here.

The most important studies to date attempt to separate the independent effects of long hours and stress, either by explicit attempts to measure both these variables and by matching, or by quantitatively measuring hours worked.[95,111,243] Two of the studies concern long hours and blood pressure, while one is a case-control study of long hours and myocardial infarction. All three come from Japan, where working long hours is common and where death from overwork, or "Karoshi," is a publicly recognized phenomenon, despite the lack of formal epidemiologic evidence.

Hayashi, et al. studied 10 normotensive men working long hours (more than 60 hours overtime a month) and 11 normotensive controls (less than 30 hours overtime a month) (Group A).[95] Blood pressure was recorded during a routine checkup. Investigators also studied 15 exposed men and 11 controls who had mild hypertension (group B), as well as a group of normotensive men whose hours varied between heavy overtime and light overtime (group C). Groups A, B, and C all worked for the same company, and group C members worked in the same department; exposed and controls were similar with respect to age, body mass, and smoking habits. Hourly blood pressure, recorded over a month and averaged, showed significantly higher blood pressure for the exposed versus controls in groups A and B. Group C, perhaps the most interesting because it was studied longitudinally and avoided potential confounding (subjects were their own controls), showed a significant increase in blood pressure (diastolic and systolic) and a significant decrease in sleep when working more overtime (average 96 hours/month, versus 43 hours/month during the control period).

Iwasaki, et al. studied systolic blood pressure among 71 salesmen in the same company divided into two groups by length of work week in the previous month.[111] Based on a single blood pressure measurement, the group with more hours (65 hours/week) had higher systolic blood pressure for one age group (age 50–59) than did the group with shorter working hours (57 hours/week), despite the fact that the difference in hours worked was not extreme. Smoking and body mass were comparable between exposed and nonexposed. This study provides only weak evidence of an exposure effect due to its cross-sectional nature, the possibility of confounding, and reliance on a single blood pressure measurement.

In the most thorough study to date, Sokejima and Kagamimori compared 195 Japanese survivors of first heart attacks to 331 controls who were free of heart disease and matched by age and occupation to the patients.[243] Controls were chosen via lists of workers who had had yearly routine medical exams. Occupational matching was by eight broad occupational categories. Data on medical history, blood pressure, cholesterol, glucose tolerance, body mass, and smoking habits were obtained for both cases and controls, as were data on psychosocial conditions at work and time spent in sedentary work. The last two factors were not associated with heart disease in the analysis, while the former, more established risk factors were. Working hours in the month before infarction or interview (for controls) did not differ between cases and controls (average 9.2 hours). However, when the data were categorized, patients had significantly increased likelihood of having worked either short or long hours in the previous month (either > 11 hours on the average, or < 7) compared to controls, suggesting a U-shaped relationship between working hours and heart disease. The authors speculated that the increase in risk for those with short working hours might have been due to these subjects suffering from early disease (and therefore working less), or from a protective effect of working a full work day. The authors also found that there was a significant trend of increasing risk of infarction with a larger increase in working hours during the year prior to infarction, so that a change towards longer working hours increased risk. This finding is consistent with a postulated increase in blood pressure contributing to a heart attack.

In summary, although the literature is sparse, there is some suggestion that long hours can increase blood pressure and lead to increased heart disease, independent of other stressful conditions at work. These findings must be viewed as preliminary, but are intriguing enough to warrant more studies on overtime work and heart disease.

CHEMICAL AND PHYSICAL FACTORS   *by Larry Fine, MD, PhD*

Recently, much of the interest in the relationship between work and cardiovascular disease (CVD) has focused on psychosocial factors. However, there are a host of occupational chemical and physical factors that have been studied to investigate their possible relationship to CVD. Some of these exposures, such as cold weather, noise, and passive smoking, are common.

Cold Weather

Several epidemiologic studies have observed a definite relationship between environmental exposure to temperature below 18°C and small increases in the acute mortality from coronary artery disease (CAD) and CVD in individuals older than 50 years.[66] These increases in risk of death from cold exposures in Europe occurred to a greater degree in regions with warmer winters, in populations with cooler homes, and among people who wore fewer clothes and were less active outdoors. In a large study of 50- to 69-year-old men in London between 1986 and 1992, it was found that cold exposures of normal life are sufficient to induce prolonged hemoconcentration and increases in both systolic and diastolic blood pressure (BP). These changes occurred on the first cold day and persisted for a few days.[55] The increases in mortality appear preventable by adequate indoor heating and adequate protection against cold while outdoors.

In a study of the population of Yakutsk, which has extremely cold winters with mean October to March temperatures of –27°C, mortality from CVD and CAD among individuals 50–59 years old did not change. In comparison to other Siberian cities, this lack of mortality associated with cold stress seemed to result from the wearing of exceptionally warm clothing and the reduction of outdoor excursions at temperatures below –20°C.[54] These studies suggest that older workers who have regular or intermittent outdoor exposure in the winter may be at slightly increased risk of mortality from CVD and CAD; however, the excess risk seems to be prevented by adequate clothing (e.g., overcoats, gloves, and hats) and opportunities to rest in warm indoor environments. The mortality of older workers with outdoor exposures is an area for future study.

The relationship between mortality and cold exposure may be of interest in climates with mild winters, since the effects observed in Europe are seen in, for example, Italy and Greece. In addition, studies of cold temperatures may be of interest even in workers with exposures below 20°C, whether indoors or outdoors. ST-segment depression with or without anginal symptoms during ambulatory electrocardiac monitoring is suggestive of transient myocardial ischemia. Results from the CORDIS study found significant increases in the rate of silent ST-segment depression among women workers working at ambient temperatures lower than 20°C after adjusting for possible confounding factors such as age, type of work, smoking, and relative weight. It seems biologically plausible that sudden exposure to cold could induce coronary artery spasm, since the cold pressor test can provoke abnormalities of myocardial perfusion not only in patients with structural coronary disease or variant angina, but also normal subjects.[124a,221a]

Heat Exposures and Warm Weather

Acute myocardial infarction (MI) may occur (although rarely) after severe heat exhaustion or heat stroke, as they are associated with widespread tissue injury.[77] The risk of acute ischemia with heat stroke or heat exhaustion in working populations is unknown. In a study of Hajj pilgrims suffering from heat stroke, 21% had localized

ST-T electrocardiographic changes consistent with acute myocardial ischemia.[3] Heat waves in the United States are clearly associated with increase in overall mortality among the elderly. One European study found excessive total daily CV mortality among males between the ages of 45 and 65 when maximum air temperature exceeded 33°C.[240a]

Heat stroke and exhaustion are certainly acute risk factors for myocardial ischemia in an individual with CAD. For exposures less intense than those that cause heat stroke or exhaustion, the risk of cardiac ischemia in an individual with CAD appears to be related to the magnitude of the heat stress.[230,251c] One epidemiologic study of open-hearth steelworkers did not find an elevated risk of death from CAD.[217] However, a second study of French Potash miners concluded that there was an increased risk of IHD from the hot underground mining environment. One possible reason for the negative study is the selection of strong, healthy workers, both at hire and during employment.[288]

Further studies of heat waves to determine if active working adults have elevated mortality patterns and more studies of occupational groups with intermittent exposures to high temperatures would be interesting. Prompt recognition and therapy for heat stroke and heat exhaustion may prevent or limit myocardial ischemia in workers with underlying coronary disease.[50]

Noise

Research on noise exposure and hypertension or elevations in blood pressure has focused on two aspects: objective measures of noise exposure, usually exceeding 80 dB, and duration of exposure. A few studies have defined noise as any exposure that is considered by the exposed worker to be an annoyance. Two recent reviews have reached somewhat different conclusions about the relationship between objectively measured noise exposure and hypertension.[65,267] Experiments in animals suggest that noise exposure in spontaneously hypertensive rats can increase the number of ischemic myocardial lesions.[99] This issue is not entirely resolved, but there may be a dose-response relationship between noise and hypertension; the importance of duration of exposure has not been clarified.[70,101,295] The proponents of a causal relationship between noise and hypertension have noted that the likely increases in BP would result in modest increases (1.1–1.2) in the relative risk for CAD.[65] Overall, there is considerable, if conflicting, evidence that prolonged exposure to high noise levels causes significant, chronic elevation of BP.

A few studies address the effect of noise on other cardiac risks, such as cholesterol. However, the results are not definitive, but raise the hypothesis that noise exposure could affect lipid levels.[174] One interesting and provocative study found a borderline significant relationship in men between transient episodes of ST-depression on ambulatory electrocardiac monitoring and industrial noise exposure.[81] Since noise exposure is still common, further research on the relationship between CVD and chronic, high-level noise exposure is important.

Passive Smoking

A review by Kristensen underlined the importance of passive smoking at work as a risk factor for premature CVD in Denmark.[65] A risk assessment based on measured levels of environmental tobacco smoke (ETS) in office air and salivary cotinine in nonsmoking U.S. workers estimated that 4000 heart disease deaths occurred annually among office workers from occupational exposures to passive smoking.

This number was based on an estimated prevalence of unrestricted smoking in U.S. office workplaces of 28%.[221]

In some workplaces with particularly high levels of exposure to passive smoking, such as casinos, CAD risk may be even greater.[268] Environmental sampling was performed to evaluate occupational exposure to ETS among casino employees. The geometric mean serum cotinine level of the 27 participants who provided serum samples was 1.34 nanograms per milliliter (ng/ml) pre-shift, and 1.85 ng/ml post-shift. Both measurements exceeded the geometric mean value of 0.65 ng/ml for participants in the third National Health and Nutrition Examination Survey (NHANES III) who reported exposure to ETS at work.[268] This evaluation demonstrates that a sample of employees working in a casino gaming area were exposed to ETS at levels greater than those observed in a representative sample of the U.S. population, and that the serum and urine cotinine of these employees increased during the working shift. The number of these high-exposure environments in the U.S. is unknown.

Physical Exercise and Vibration

Numerous studies consistently find that higher levels of physical activity, whether at work or leisure, are associated with lower risks of CAD and CVD.[158] The biological processes proposed to explain the beneficial effect of higher levels of physical activity are very plausible.[158] Because of the negative effect of a lack of physical activity, sedentary work can be viewed as an occupational risk factor for CAD.[65] The relative risk of death from CAD is about 2.0 for sedentary compared with active occupations. Unfortunately, the level of physical activity in the population may be on the decline overall because of changes on the job and in transportation.

Uncertainty exists about the level and type of physical activity on the job may be protective.[284] Three specific physical occupational factors have been suggested as possible risk factors.[246] While increasing the level of physical activity is beneficial in preventing CAD, *irregular* heavy physical exertion (such as 6 or more metabolic equivalents) is associated in most studies with substantially increased risk of an acute MI in the first hour after the exertion.[289a] However, while the relative risk is high, the absolute risk is low, and habitual physical activity greatly reduces the risk of heavy physical exertion.

Evidence that lifting may be an occupational risk factor is limited. Associations with lifting may be due to some other confounding factor.[246] However, a significant increase in SMR for MI related to heavy lifting has been found; when combined with hectic work, the risk was even higher. Resistance weight training has been used safely in the rehabilitation of patients with cardiac disease.[19]

Both segmental and whole body exposure to vibration have been postulated to have acute effects on the CV system. Since there are some data supporting this hypothesis, further investigation of this association would be of some interest.[8a,61a]

Chemical Exposures and Cardiovascular Disease

A few occupational exposures, such as carbon monoxide, carbon disulfide (CS_2), methylene chloride, and nitrate esters, have been definitely linked to selected CV conditions. The evidence for these exposures is by far the strongest when the level of occupational exposure is high. For some chemicals (e.g., lead, arsenic, and 2,3,7,8-tetrachlorodibenzo-p-dioxin) evidence is more limited or substantial occupational exposures are less common. Low-level exposures to carbon monoxide, lead, and carbon disulfide are common.

CARBON DISULFIDE

CS_2 was definitively associated with increased risk of CAD in Finnish epidemiologic studies which showed that higher exposures before 1970 were linked to high relative risks for CAD, and that following substantial reduction in exposure the risk declined to less than 1.[192] Overall, the several other epidemiologic cohort mortality studies strengthen the evidence that CS_2 can cause CAD in workers exposed for long time periods and at high levels.[166,251b] The mechanism may be primarily a direct adverse effect on the CV system, since the risk of dying from heart disease has been largely restricted to currently or recently exposed workers in some of the cohort mortality studies. The importance of this hypothesis is that the adverse effect may be reversible to some extent.

There is some debate about the level of exposure associated with increased risk of CAD.[211] The most recent cohort mortality study concluded that exposure to relatively low levels of CS_2 increases the risk of CV mortality.[251a] As with many occupational adverse effects, the precise shape of the dose-response curve between mortality from CAD and exposure to CS_2 remains an important area of research.

CS_2 has been associated with several effects that suggest direct and indirect mechanisms for the increased risk of CAD. Interestingly, in both Belgian and Japanese CS_2 workers, but not Finnish workers, an increased prevalence of microaneurysms of the retinal artery has been reported.[196a,277] The other effects that have been noted are ECG abnormalities, a negative inotropic effect, an increase in LDL-cholesterol, and increased diastolic BP.[57,62,147]

NITRATE ESTERS

Nitrate esters such as nitroglycerin (NTG) and ethylene glycol dinitrate (EGDN) caused angina and more rarely cardiac sudden death in highly exposed workers in the past.[18,105,244a] Following withdrawal from exposure, coronary artery spasm has been postulated as occurring. In the occupational setting, skin exposure to the nitrate esters is the principal route of exposure. In the studies of mortality from CAD in exposed explosives workers, it is not clear whether the effects are solely acute after withdrawal from exposure or also occur during acute overexposure. There are substantial case studies and epidemiologic evidence to confirm this hypothesis of an acute effect of nitrate esters. Only one study found evidence that there may be a chronic effect that persists several years after exposure ceases.[105] This study suggested that CV effects of NTG and EGDN might be more complex than simply the precipitation of coronary spasm after acute withdrawal from exposure. It is possible that the nitrates also lead in some manner to increased diastolic BP, since one study also found, in addition to a chronic increase in CAD mortality, a nonsignificant increase in CVD mortality.[106] Older clinical reports suggested that sudden death rarely occurs in exposed workers without pre-existing CAD. However, Stayner found that workers hired after 1970 who were screened every 6 months for hypertension as well as resting and exercise ECG abnormalities did not have an excess risk of death from NTG exposure.[244a] This absence of an effect could be due to a combination of lower exposures and effective screening to identify more high-risk workers. Prospective studies of currently exposed workers are needed to determine whether there is any remaining excess risk.

CARBON MONOXIDE

Substantial exposure to carbon monoxide (CO) is more common than substantial exposure to either nitrate esters or CS_2. CO exerts its adverse effects via its avid binding to hemoglobin, resulting in decreased delivery of oxygen to the tissues.[58] In

addition, CO binds to the cytochrome oxidase system in the mitochondria of cardiac muscle, raising the possibility that CO exposure could directly decrease myocardial contractility. A limited number of occupational exposures to CO can result in carboxyhemoglobin levels greater than 25%. When the carboxyhemoglobin level exceeds 25%, the reduction in tissue oxygen delivery can cause myocardial ischemia or infarction, dysrhythmias, or even sudden death.[58] These high levels of exposure can occur from exposure to combustion sources, such as during fire fighting activities or use of gasoline engines in confined spaces (e.g., gasoline-powered washers for cleaning of flood debris in basements). For example, in one study of structural fire fighting, 10% of the samples exceed 1500 ppm of CO.[112]

The acute cardiac effects of CO even at low levels of exposure are dependent on the ability of the coronary arteries to increase blood flow to the myocardium in response to the hypoxic stress of CO. Workers with significant CAD may be affected at lower levels of exposure. In addition, CO exposure from workplace combustion sources are additive with the CO exposure that smokers receive from their cigarettes. One study showed that smokers in workplaces with low levels of CO exposure (3–12 ppm), far below the OSHA exposure limit (50 ppm or 55 mg/m^3), had carboxyhemoglobin levels of 2.1–7.6%.[285] Levels above 4% carboxyhemoglobin have been associated with reduced time to onset of angina during exercise tests.[132] Higher workplace exposures, for example at the OSHA recommended exposure limit, could raise the carboxyhemoglobin level of the nonsmoker above 4%. Workers with CAD may have an increased number of angina attacks in occupational environments with CO exposure.

Overall, mortality studies of exposed workers provide some evidence that CO exposure may be associated with an increase in mortality from CAD while the exposure continues. Some of these studies are positive and others are negative.[90,141,249a] Some of the positive studies involved workers who are exposed to more than one agent. For example, one found a significant increase in mortality from sudden death presumably due to CAD in furnace workers in ferroalloy plants.[104] The increase was not explained by smoking or alcohol consumption; however, these workers were exposed to manganese, CO, and heat. Interestingly, two studies have found evidence of an increase in hypertension morbidity or mortality; however, in both studies workers did have multiple exposures.[104,141] The latter observation raises the hypothesis that chronic CO exposure could potentiate other CV effects.

One of the few studies with a detailed exposure assessment for CO, no other potential cardiac toxic exposures, and a good internal comparison group is that comparing tunnel workers to toll booth operators.[249a] The tunnel workers had a 35% increased mortality from CAD. The excess declined after 1970 when the CO levels were reduced by improved ventilation (prior to 1970, levels averaged over 50 ppm). The excess mortality was limited to the first few years after employment ceased.

Overall, the epidemiologic studies do suggest that high-level CO exposure may cause at least moderate increases in the risk of CAD. It is not surprising that studies of the adverse effects of CO in physically active occupations with intermittent exposures, such as fire fighting and foundry work, have had mixed results. Acute exposures in fire fighting or to a combustion source in a confined space and that cause carboxyhemoglobin level above 25% may pose a cardiac hazard even for individuals with a normal CV system, while lower levels of exposure may pose a hazard for individuals with significant CAD. These lower exposures in the individual with CAD would be potentially more hazardous if other factors were present that could increase the risk of cardiac ischemia, such as cigarette smoking, high altitude, or substantial physical exercise.

METHYLENE CHLORIDE

Methylene chloride (dichloromethane) is metabolized to CO. Any worker who presents with a clinical picture consistent with CO toxicity and a history of solvent exposure should be evaluated for methylene chloride exposure. Exposures as low as 75 ppm of methylene chloride can produce similar levels of carboxyhemoglobin as exposure to CO at 35 ppm. Methylene chloride has been a common solvent in furniture-stripping solutions.[171] The risk of methylene chloride exposure is related to the duration and intensity of the exposure. Two epidemiologic studies of occupationally exposed chemical workers involved in the production of methylene chloride have not found an association with CAD.[75,198]

LEAD

Occupational exposures to lead are still common in some industries, such as construction and manufacturing of lead batteries. The identification of subtle subclinical effects of lead at low exposure levels has led to reduction in recommended occupational exposure limits from 80 to 40 micrograms/dl.[80a] At these lower levels of exposure it is possible that lead may be contributing to hypertension.[150] This concern was first raised by studies in the general population. One recent review of the animal, epidemiologic occupational, and general population studies concluded that there is a weak positive relationship between both systolic and diastolic BP and lead exposure. A two-fold increase in blood lead concentration was associated with a 1 mm increase in systolic pressure and 0.6 mm increase in diastolic pressure.[244b] The reviewers were not sure that the relationship was causal. They believed that there were several possible plausible mechanisms, including interference of lead with calcium metabolism, a possible direct effect of lead on the vascular smooth muscle, or potentiation of sympathetic stimulation by lead. The most recent cross-sectional studies of workers are also inconsistent. The issue of whether occupational exposures to lead contribute to hypertension is not totally resolved.

SOLVENTS AND DYSRHYTHMIAS

A limited number of chemicals have been associated with atrial and ventricular dysrhythmias by mechanisms unrelated to ischemia; such events may occur even in individuals with anatomically normal coronary vessels.[286] Some organic solvents, particularly fluorocarbons such as chlorofluorocarbon 113, are implicated in the occupational setting.[189] Suspected proarrhythmic agents are bromofluorocarbons, methyl chloroform, methylene chloride, and trichloroethylene.[126] The strongest evidence for this relationship is from case reports following very high, intentional exposures (e.g., glue sniffing).[51] Other evidence comes from clinical studies and experimental animal investigations.[126] The animal studies suggest that a wide range of solvents at very high levels of exposure are cardiac toxins; however, the risk in usual working situations is probably small.[220]

The pathogenesis of solvent-related dysrhythmias likely involves potentiating the effect of endogenously secreted catecholamines to cause arrhythmias. The combined effect of the solvent and catecholamines results in atrial or ventricular arrhythmias.[126] At very high levels of exposure other mechanisms are possible, such as decreased myocardial contractility or hypoxia from respiratory depression.

There are several case reports of sudden death or atrial fibrillation following exposure to chlorofluorocarbon 113 in confined spaces. The most volatile fluorocarbons are the most hazardous. Epidemiologic studies of workers exposed to fluorocarbons in nonconfined spaces and presumably at lower levels of exposures are not consistent.[51] A positive study found an association between history of episodes of

palpitation among pathology residents and exposure to fluorocarbons in the preparation of frozen sections from surgical specimens.[244] A negative study involved ambulatory EKG monitoring and exposure measurements to fluorocarbon-113 in sixteen sedentary aerospace workers. The frequency of ventricular and atrial premature beats and other evidence of dysrhythmias on a low exposure day (64 ppm personal time-weighted average [TWA]) were compared to a higher exposure day (442 ppm TWA).[62] There is also an equivocal study among refrigerator repairmen.[61]

In summary, occupational exposures to fluorocarbon-113 at levels below the OSHA standard of 1000 ppm have not been associated with cardiac dysrhythmias.

Several epidemiologic mortality studies of solvent-exposed workers have been conducted, principally in aerospace, rubber, chemical, and dry cleaning industries. Each of these studies has limitations in determining if there is an association between acute solvent exposure and cardiac mortality. Most were designed to concentrate on the relationship between chronic solvent exposure and cancer rather than acute exposure and CVD. The majority of cardiac deaths occurred years after exposure ceased. Most did not have detailed exposure measurements; therefore, the potential for misclassification of exposure is substantial. A review of the epidemiologic literature shows no *consistent* association between solvents, with the exception of CS_2, and elevated risks of mortality from heart disease.[286]

A few studies do indicate one or more positive associations. A case-control study in the rubber industry found no evidence of association between the most solvent exposures and heart disease, but did find limited evidence of an association between ethanol or phenol exposure and mortality from CAD.[287] A recent cross-sectional study reported associations between occupational exposures to benzene or xylene, but not to phenol, and the prevalence of hypertension, atrial, and ventricular ectopic beats.[142] A significant but slight increase in mortality from CAD was reported among aerospace workers exposed to trichloroethylene or toluene.[22] This study had an internal reference group and careful exposure assessment. The 10–20% increases in this study generally were not dose related, and there were overlapping exposures to several solvents. In another study of trichloroethylene there was no evidence of an increased risk from CV mortality in the workers with long duration or higher levels of exposure.[13]

PSYCHOSOCIAL FACTORS: REVIEW OF THE EMPIRICAL DATA AMONG MEN   by Karen Belkić, MD, PhD, Paul Landsbergis, PhD, Peter Schnall, MD, Dean Baker, MD, Töres Theorell, MD, PhD, Johannes Siegrist, PhD, Richard Peter, PhD, and Robert Karasek, PhD

In 1958, a case-control study by Russek and Zohman revealed that of 97 male coronary patients under age 40, 91% were judged to have been exposed to "occupational stress and strain," based on a detailed occupational history, compared to 20% of healthy controls.[224] In the same year, Friedman, Rosenman and Carroll published their seminal paper demonstrating a significant relation between serum cholesterol and blood clotting times, and cyclic variation in occupational stress among accountants.[76] Since these early studies there has been a burgeoning body of evidence demonstrating a relationship between psychosocial factors at the workplace and cardiovascular disease (CVD).

Approximately 20 years ago, the **Job Strain Model** was introduced by Karasek.[123] Systematic investigation of psychosocial workplace factors and CVD was dramatically advanced by this model, which can be readily applied in epidemiologic studies. The first hypothesis is that strain occurs when there is excessive psychological

workload demands together with low job decision latitude. This combination provokes arousal, as well as distress, activating both the sympathoadrenomedullary and adrenocortical axes, and yielding a highly deleterious combination.[71,74] A third dimension, social isolation, was later added to the Job Strain Model.[114] The second hypothesis is that high demands together with high decision latitude lead to active learning of new behaviors, and possibly improved health through long-term positive changes in coping behaviors. (See Chapter 3 for a detailed discussion of the theoretical construct.)

More recently, the **Effort-Reward Imbalance (ERI) Model** was introduced by Siegrist and colleagues.[233–235] In comparison to the Job Strain Model with its emphasis on moment-to-moment control over the work process (i.e., decision latitude), the ERI Model provides an expanded concept of control, emphasizing macro-level long-term control vis-à-vis rewards such as career opportunities, job security, esteem, and income. The ERI Model assesses the balance between these rewards and effort, positing that work stress results from an imbalance between high effort and low control over long-term rewards. Effort is seen to stem both extrinsically from the demands of the job and intrinsically from the individual's tendency to be overly committed to these work demands. (See Chapter 3 for further discussion.) In addition to research using these two models, several other psychosocial risk factors are being examined for their potential explanatory value with regard to CV outcomes. Threat-avoidant vigilant work, also termed "disaster potential," represents a plausible construct for which there is some empirical data, reviewed herein.

The following review results from *in extenso* English language publications in peer-reviewed journals as these pertain to samples of men, in whom the majority of this research has been conducted. The empirical evidence with regard to workplace psychosocial factors and CVD outcomes among women is described toward the end of this chapter.

The Job Strain Model

ISCHEMIC HEART DISEASE AND OTHER HARD CVD ENDPOINTS

Table 3 presents the data concerning exposure to job strain and/or its major dimensions, in relation to ischemic heart disease or other hard CVD endpoints. A brief description of how the job strain variable was assessed in each study, the variables for which adjustment is made, and significant positive as well as null and negative findings are shown. (For more details concerning methods for evaluating job strain and other psychosocial workplace factors, see Chapter 6.)

There were eight case-control studies of job strain and CVD. Those investigations which obviated self-report bias by imputing job strain exposure on the basis of occupational title revealed major significant findings with regard to aspects of control[6,8,87,265] and/or to exposure to high psychological demands together with low control.[6,8,88] The other five studies, relying on self-report data, also revealed primarily significant positive associations. An exception is the very small study of Emdad, et al., which, unlike the others, restricted itself to a single occupational group (professional drivers) having a limited range of variation on demands and control, and, thus, less statistical power to detect an effect of job strain.[64]

Self-report data of Hallqvist, et al. provided another important facet of causal evidence by showing a dose-response relationship between strength of exposure to job strain and relative risk of myocardial infarction.[87] The significant, positive Synergy Index reveals that exposure to the combination of high demands and low control confers greater risk than the additive effects of the dimensions.

TABLE 3. Studies of Job Strain and Ischemic Heart Disease among Men

			Case Control Studies			
First Author (Year)	Study Participants	Form(s) of Job Strain Variable	Illness Outcome	Significant Positive Associations (Adjusted Confounders)		Null or Sig. Negative Assoc. (Adjusted Confounders)
Alfredsson, et al. (1982 & 1983)	Swedish, < 65 y.o. N = 334 cases, N = 882 population controls	Imputed: Hectic/various aspects of control as quadrant terms	Hospitalized and/or fatal MI	Total study (Age) Monotony Rushed tempo + low influence over work tempo Rushed tempo + not learning new things 40–54 y.o. (Age & immigrant status or education) Hectic work + no influence on pace Hectic work + few possibilities to learn new things	RR 1.32 1.35 1.45 ≈ 1.7 ≈ 2	Rushed tempo = NS Low influence over work tempo = NS Not learning new things = NS Rushed tempo + monotony = NS (Age)
Billing, et al. (1997)	Swedish, < 70 y.o. Cases: N = 531 male, 236 female Population controls: N = 34 male, 15 female	Self-report: PSJSQ Main effects only	Chronic, stable angina pectoris, clinic patients	Skill discretion Control (Age)	p < .001 < .01	ψ demand = NS Decision authority = NS (Age)
Bobák, et al. (1998)	Czech, 25–64 y.o. N = 179 cases N = 784 controls All full-time employed	Self-report: ψ Demands (3 items) Decision-latitude (8 items) Quartile term (21% job strain)	First nonfatal MI	Highest decision latitude quartile (Age, district, education, hypertension, other coronary RF)	RR 0.43	Job strain = NS Highest ψ demands quartile RR = 0.52 (Age, district, education, hypertension, other coronary RF)
Emdad, et al. (1997)	Swedish, < 52 y.o. N = 13 cases N = 12 hypertensive controls, All professional drivers	Self-report: PSJSQ Demand/control Quotient term	Hospitalized IHD			Job strain = NS ψ demand = NS Decision latitude = NS Skill discretion = NS Control = NS (Age)

(Table continued on next page.)

TABLE 3. Studies of Job Strain and Ischemic Heart Disease among Men *(Continued)*

First Author (Year)	Study Participants	Form(s) of Job Strain Variable	Illness Outcome	Significant Positive Associations (Adjusted Confounders)				Null or Sig. Negative Assoc. (Adjusted Confounders)
		Self-report:			(Quartile) RR		(Optimal) RR	
Hallqvist, et al. (1998), Theorell, et al. 1998)	Swedish, 45–64 y.o. N = 1047 cases N = 1450 population controls	PSJSQ Quartile term and optimal term (reflects optimum balance between exposure contrast and power)	First hospitalized and/or fatal MI	Self-report:				Self-report:
				Job strain	2.2	→	9.2	• Non-manual workers
				Synergy index	4.0	→	7.5	Job strain = NS
				• Manual workers				ψ demands = NS
				Job strain	10.0	→	46.1	Decision latitude = NS
				Synergy index	11.1	→	23.9	• Manual workers
		Imputed:		Decision latitude			2.3	ψ demands = NS
		PSJEM Decision latitude Quartiles		(Hypertension, smoking, BMI)				(Hypertension, smoking, BMI)
				Imputed			OR	Imputed
				Decision latitude (Age, catchment area)			1.7	Decision latitude = NS (Age, catchment area, social class, coronary RF)
		Imputed:		White collar			RR	Blue collar
Hammar, et al. (1994)	Swedish, 30–64 y.o. N = 13,205 cases N = 22,599 population controls	Hectic/aspects of Decision-latitude Quadrant term (relaxed quadrant as referent)	First MI	Hectic work and low influence over work hours (Age, county, calendar year)			1.4	Single factors = NS Hectic work and other factors = NS White collar Single factors = NS (Age, county, calendar year)
		Self-report:					RR	
Sihm, et al. (1991)	Danish, < 55 y.o. N = 52 cases N = 72 community and hospital controls	Workload/elements of control Quadrant term	Survivors of MI	Heavy workload + contradictory demands			1.96	Workload = NS Autonomy = NS
				Heavy workload + low responsibility			1.78	Influence = NS
				Low workload + good social interaction (Age, SES)			0.58	Contradictory demands = NS Growth + development = NS (Age, SES)
		Self-report:					p	ψ demands = NS
Theorell, et al. (1987)	Swedish, < 45 y.o. N = 85 cases N = 116 community controls	3 Quotient terms: Demands (2 items) ÷ Influence (3 items) Intellectual discretion or variety (1 item each)	Hospitalized nonfatal MI	Variety of work tasks			0.01	Influence over work = NS
				ψ demands/variety of work tasks			0.01	Intellectual discretion = NS
				ψ demands/intellectual discretion (Age, education, coronary risk factors)			0.04	ψ demands/influence over work = NS *(Age education, coronary risk factors)*
			Coronary artery atheromatosis					Degree coronary atheromatosis and quotient terms or main effects = NS

TABLE 3. Studies of Job Strain and Ischemic Heart Disease among Men *(Continued)*

<div align="center">Cross Sectional Studies</div>

First Author (Year)	Study Participants	Form(s) of Job Strain Variable	Illness Outcome	Significant Positive Associations (Adjusted Confounders)		Null or Sig. Negative Assoc. (Adjusted Confounders)
Johnson, et al. (1988)	N = 7165, Swedish, 16–65 y.o. population sample	Self-report: ψ Demands (2 items) Control (11 items) Support (5 items) Quadrant term (relaxed quadrant as referent)	Self-reported CVD (N = 409)	Blue collar High ψ demands/low control High ψ demands/low control/ low support White collar High ψ demands/low support *(Age, dimensions of isostrain)* 3-Factor multiplicative interaction ratio = 1.09	PR 3.55 7.22 1.81	All High ψ demands = NS Control = NS White collar High ψ demands/low control = NS *(Age, dimensions of isostrain)*
Johnson, et al. (1989)	N = 7219, Swedish, 25–65 y.o. population sample	Self-report: ψ Demands (2 items) Control (11 items) Support (5 items) Compare high to low quintile	Self-reported CVD (N = 407)	All Isostrain Blue collar Isostrain *(Age)*	PR 1.77 2.04	White collar Isostrain *(Age)* = NS
Karasek, et al. (1987)	N = 5000, Swedish, mean age 37.1 ± 12.1, white collar, trade-union members	Self-report: Workload (3 items) Decision latitude (4 items) Main effects only	Self-reported heart disease	*(Age, marital status)* Workload Conflict Clarity Decision/latitude Social support	SOR 1.24 1.18 1.12 0.92 0.90	
Karasek, et al. (1988)	U.S., 18–79 y.o. N = 2409 HES, N = 2424 HANES population sample (87% white)	Imputed: QES Quadrant term (20% job strain)	MI (N = 39 HES) (N = 30 HANES)	Job strain—HES —HANES ψ Demands—HANES Decision latitude—HES —HANES *(Age, race, education, SBP, other coronary RF)*	SOR 1.5 1.6 2.1 –1.5 –2.0	ψ Demands—HES = NS *(Age, race, education, SBP, other coronary RF)*

(Table continued on next page.)

TABLE 3. Studies of Job Strain and Ischemic Heart Disease among Men *(Continued)*

First Author (Year)	Study Participants	Form(s) of Job Strain Variable	Illness Outcome	Significant Positive Associations (Adjusted Confounders)		Null or Sig. Negative Assoc. (Adjusted Confounders)
Hlatky, et al. (1995)	N = 1132 males, N = 357 females U.S. patients undergoing coronary angiography (88% white, 60% white collar)	Self-report: JCQ Predefined cutpoints: (23% job strain men, 43% in women) Job strain index = quotient	Degree of coronary atheromatosis			Job strain = Quadrant term = NS Index = NS *(Age, gender, blood pressure, coronary risk factors, history of MI, typical angina)*

Cohort Studies

First Author (Year)	Study Participants	F/u (y)	Form(s) of Job Strain Variable	Illness Outcome	Significant Positive Associations (Adjusted Confounder)		Null or Sig. Negative Assoc. (Adjusted Confounder)
Alfredsson, et al. (1985)	N = 958,096 total*, Swedish, 20–64 y.o., population-based	1	Imputed: Hectic/various aspects of control as quadrant terms	Hospitalized MI (N = 1059)	*(Age)* Punctuality Few possibilities to learn new things Hectic and monotonous work Hectic work and few possibilities to learn new things *(Age + marital status, nationality, income, smoking or heavy lifting at work)*	SMR 121 113 118 ≈ 125	*(Age)* Hectic work = NS Monotonous work = NS

* Total not by gender, gender-stratified analysis done—males in this table

First Author (Year)	Study Participants	F/u (y)	Form(s) of Job Strain Variable	Illness Outcome	Significant Positive Associations (Adjusted Confounder)		Null or Sig. Negative Assoc. (Adjusted Confounder)
Bosma, et al. (1997 & 1998)	N = 6896, U.K., 35–55 y.o. civil servants	5.3	Self-report: ψ Demands (4 items) Control (15 items) Median cutpoint quadrant Term and interaction term Observer: 4 items	Self-report Angina, CHD event, Dx. IHD	*(Age & f/u time)* Low control (SR) & angina pectoris Low control (SR) & diagnosed IHD Low control (SR) & any CHD event Low control (O) & any CHD event Job strain (SR) & any CHD event	OR 1.54 1.6 1.55 1.43 1.45	Job strain (SR) & angina pectoris = NS Job strain (SR) & diagnosed IHD = NS Job strain (O) & all outcomes = NS *(Age & f/u time)*
Johnson, et al. (1989)	N = 7219, Swedish, 25–65 y.o. population-based	9	Self-report: ψ Demands (2 items) Control (11 items) Support (5 items) Compare high to low quintile	CVD mortality (N = 193)	*(Age)* Isostrain: Total group Blue collar	RR 1.92 2.58	Isostrain: White collar = NS *(Age)*

TABLE 3. Studies of Job Strain and Ischemic Heart Disease among Men *(Continued)*

First Author (Year)	Study Participants	F/u (y)	Form(s) of Job Strain Variable	Illness Outcome	Significant Positive Associations (Adjusted Confounders)		Null or Sign. Negative Assoc. (Adjusted confounders)
Johnson, et al. (1996)	N = 12,517, Swedish 25–74 y.o. population-based (nested case-control N = 2422 controls)	14	Imputed: ψ Demands (2 items) Control (12 items) Support (4 items) Interaction terms	CVD mortality (N = 521)	Low control Low control/low support *(Age, class, nationality, physical job demands, education, exercise, smoking, last year employed)*	**RR** 1.83 2.62	ψ demands = NS Job strain = NS *(Same adjustment as for positive findings)*
Karasek, et al. (1981)	N = 1461, Swedish, 15–61 y.o., population-based (Nested* case-control: N = 66 controls)	9	Self-report: ψ demands (2 items) Intellectual Discretion (2 items) Personal Schedule Freedom (3 items)	CVD & cerebro-vascular mortality (N = 22)	High ψ demands High ψ demands & low personal freedom schedule *(Age, education, smoking, CHD sx at baseline)*	**OR** 4.0 4.0	Low intellectual discretion = NS Low personal freedom schedule = NS *(Same adjustment as for positive findings)*
		6		Self-report CHD	High ψ demands Low Intellectual Discretion *(Age, education, smoking, overweight)*	**SOR** 1.29 1.44	Personal Schedule Freedom = NS *(same adjustment as for positive findings)*
Theorell, et al. (1991a)	N = 79, Swedish, < 45 y.o. employed, first MI survivors	5	Self-report: 3 Quotient terms: Demands (2 items) + Influence (3 items), Intellectual discretion or variety (1 item each)	Mortality from repeat MI (N = 13)	Demands + variety (univariate) Demands + intellectual discretion *(Biomedical risk factors)*	**P** 0.03 0.02	Demands = NS Single aspects of decision latitude = NS
Alterman, et al. (1994)	N = 1683 U.S., 38–56 y.o. Chicago Western Electric healthy employees of European ancestry (74% blue collar)	25	Imputed: QES Tertile term (7% job strain))	CHD mortality	High decision latitude *(Age, SBP, cholesterol, smoking, alcohol, family history CVD)*	**RR** 0.76	Job strain (Age) = NS ψ Demands (Age) = NS Decision latitude *(Education + age, SBP, cholesterol, smoking, alcohol, family history CVD) = NS*

(Table continued on next page.)

TABLE 3. Studies of Job Strain and Ischemic Heart Disease among Men *(Continued)*

First Author (Year)	Study Participants	F/u (y)	Form(s) of Job Strain Variable	Illness Outcome	Significant Positive Associations (Adjusted Confounders)		Null or Sig. Negative Assoc. (Adjusted Confounders)
Hlatky, et al. (1995)	N = 1132 men, N = 357 women U.S. patients undergoing coronary angiography (88% white, 60% white collar)	4	Self-report: JCQ (Cutpoints: ψ demands > 32, decision latitude < 28) Men: 23% job strain Women: 43% job strain Job strain index = quotient term	Incident nonfatal MI (N = 70) Cardiac deaths (N = 42)			In patients with significant CAD: Job strain index & quadrant term = NS for cardiac death & cardiac events ("Established prognostic factors" including ejection fraction, CAD extent, myocardial ischemia) In patients without significant CAD: Job strain index & quadrant term = NS for cardiac events (N = 6 total) (Age, gender, ejection fraction, insignificant CAD)
Reed, et al. (1989)	N = 4737, U.S. Hawaiians of Japanese descent, 45–65 y.o. population-based	18	Imputed: QES Quartile Term Multiplicative Score Vector Score	Incident definite CHD (N = 359)			All calculated forms of Job Strain = NS ψ Demands = NS Decision latitude = NS In acculturated group: Low job strain (vector score) p < 0.05 (Age, blood pressure & other coronary risk factors)
Steenland, et al. (1997)	N = 3575, U.S. 25–74 y.o., population-based 58% blue collar	12–16	Imputed: QES Quartile term (17% job strain)	Incident heart disease (N = 519)	Job control (highest compared to lowest quartile) (Age, education, blood pressure, other coronary risk factors)	OR 0.71	Stratified analysis blue and white collar: Job strain, ψ Demands, Low control = NS High control & high demand OR = 0.69 for blue collar (As for positive findings)

ψ = psychological, Dx = diagnosed, HES = Health Examination Survey, HANES = Health and Nutrition Examination Survey, IHD = ischemic heart disease, JCQ = job content questionnaire, NS = nonsignificant, OR = odds ratio, PSJSQ = psychological job strain questionnaire (Swedish), PSJEM = Psychosocial Job Exposure Matrix, QES = quality of employment surveys, RF = risk factors, RH = relative hazard, RR = relative risk, SES = socioeconomic status, SMR = standard mortality ratio, SR = self-reported.

Notes: Significant positive associations require a lower limit of the 95% confidence intervals > 1.0 and/or p < 0.05. The N for women is indicated only if the analysis was *not* gender stratified.
 * The study by Karasek, et al. (1981) analyzes incident cases of CVD death compared to matched controls selected from the cohort. As per Hulley, et al.,[100] we term this a "nested case control study" and include it within the cohort studies.

Of the five cross-sectional investigations of job strain and CVD, four relied upon self-report of exposure to the job strain dimensions and of the disease outcome. Johnson and Hall found that the interaction among demand, control, and support was more than multiplicative (by 9%), with a three-factor multiplicative interaction ratio = 1.09.[114] Karasek, et al. used the imputational method to assess exposure to job strain, together with objective verification of the presence of myocardial infarction (MI).[124] Thus, this population-based, cross-sectional data can be considered free of self-report bias of any kind and reveals a significant positive association between exposure to job strain, as well as each of its main dimensions, and MI.

Among the ten cohort studies of job strain and CVD, six report significant positive results with regard to exposure to various types of low control,[7,9,29,30,116,247] and four show significant associations with exposure to some form of high psychological demands coupled with low control.[7,29,30,119,259a] Significant positive results were seen for exposure to high psychological demands alone[119] and for isostrain (high psychological demands, low control and low social support at work).[115]

Four cohort studies had predominantly null results.[9,103,218,247] Three of these had followup periods of 12–25 years without assessment of employment status subsequent to intake, such that the participants were likely to have been temporally far removed from these job exposures.[9,218,247] In two of these the mean age at CHD occurrence is high, and with advancing age the impact of CVD risk factors declines.[9,218] The three also used the imputation method for determining exposure to job strain (see Chapter 6). While providing a convenient means of converting coded occupational titles into exposure data and obviating self-report bias, the imputation method provides no assessment of within-occupation variability and, due to nondifferential misclassification, underestimates actual associations between job characteristics and health outcomes.[143] Thus, while significant positive associations found using the imputational method provide powerful evidence for the model, negative or nonconfirmatory studies may be due, at least in part, to loss of statistical power.[226] This is particularly problematic with respect to psychological demands, which show the largest amount of variance within rather than between occupations, and this variance is therefore not reflected in the averaged values.[261]

Particular attention in the clinical cardiologic arena has been paid to the study of Hlatky and colleagues in which exposure to job strain was reported not to be significantly associated cross-sectionally with degree of angiographically-assessed coronary atherosclerosis, nor prospectively with cardiac events.[103] In immediate response to the publication of these results, the American Heart Association issued the following statement: "Although psychological stress in the workplace is widely believed to increase the risk of coronary heart disease, scientific evidence supporting this belief 'is relatively sparse' according to scientists publishing a new study. Their research suggests that job strain is not an important coronary risk factor."[10] We believe that this conclusion is incorrect. This study does not appear to have been designed initially to test the job strain hypothesis. The original purpose of this research seems to have been to examine employment patterns among patients with coronary artery disease.[168] The sampling technique used (evaluation of all patients with chest pain undergoing coronary angiography) may have been suitable to that purpose. However, it is not appropriate for research intended to explore the role of psychosocial stress factors in CVD.

A close examination of the study reveals a number of major, interconnected flaws which inextricably undermine its internal validity. By choosing consecutive stable patients with chest pain, who were undergoing coronary angiography at a university hospital, as the study sample, with the cross-sectional endpoint being degree

of coronary atherosclerosis, the chances are high that the etiologic relationship between exposure and outcome is severely distorted.[109,215] This overreporting of chest pain would lead a large number of patients without coronary artery disease (CAD), but *with* self-reported job strain, to present to the medical system, and insofar as a substantial number of these persons were sent to angiography, this would lead to a lowered odds ratio for CAD related to job strain. This form of **selection bias** is an example of *differential* misclassification, which tends to bias the results negatively. Existing effects between job strain and CAD are less likely to be detected because the frequency of reported chest pain is higher, by at least an order of magnitude,[219] in the study patients than in the population of a similar age.

Patients with chest pain and normal coronary arteries have been recognized as a group with a high prevalence of occupational and behavioral difficulties.[42,154,195,200,206,208] Major problems with confounding also exist in the Hlatky, et al. study. The patients with normal coronary arteries or insignificant CAD more often had white-collar jobs than did the patients with significant CAD (p = 0.0001), and yet no adjustment for socioeconomic status was made. Lack of gender stratification further obfuscates etiologic relations. By self-report data, 43% of the women fell into the job strain category compared to 23% of the men. Women comprised 48% of patients with normal coronary arteries versus 14% of those with significant CAD. No mention was made of Syndrome X, characterized by enhanced ventricular pain sensitivity,[199] and whose prevalence among women is high.[282] There is also evidence that the CAD patients reporting low decision-latitude and/or job strain had disproportionately stopped working at 1 year followup[168]; this further attenuates any association between point exposure to job strain at entry into the study and subsequent cardiac events.

One cohort study examined the important issue of cumulative exposure to psychological demands, control, and social support.[116] These authors emphasize that the etiological fraction for CV disease mortality attributable to long-term exposure to low work control is substantially larger (35%) than previously estimated for job strain assessed at a single point in time (7–16%). By assessing cumulative exposure it becomes apparent that the magnitude of the CV effects due to unhealthy work conditions has been heretofore largely *underestimated*.

These studies, taken together, predominantly demonstrate a significant, positive relation between exposure to low control and/or job strain and subsequent CVD. The evidence, while limited, suggests the existence of a dose-response relationship (both in terms of intensity of point exposure[87] and temporal duration[116]) between exposure to job strain or low control and CVD outcomes. The cohort studies provide another important piece of confirmatory evidence of causality, based upon their demonstration that the temporal nature of the association is in the expected direction.

BLOOD PRESSURE

Ambulatory Blood Pressure Studies. As elaborated in Chapter 5, there are numerous potential mediating mechanisms by which psychosocial workplace factors can increase the risk of developing ischemic heart disease. Elevation in arterial blood pressure (BP) and hypertension represent one of the most well-recognized and important risk factors, with ambulatory, as opposed to casual, clinic BPs being of greatest prognostic importance, particularly when recorded during work.

Table 4 summarizes the data relating job strain and/or its major dimensions to ambulatory BP. Of the 11 cross-sectional ambulatory BP studies, five reveal a significant positive effect of exposure to job strain upon ambulatory systolic blood pressure (SBP) recorded during work.[41,159,227,228a,276] In the four of these five studies in

TABLE 4. Studies of Job Strain and Ambulatory Blood Pressure among Men

Cross-Sectional Studies

First Author (Year)	Study Participants	Form(s) of Job Strain Variable	Significant Positive Effects: SBP (Adjusted Confounders)	Significant Positive Effects: DBP (Adjusted Confounders)	Null or Sig. Negative Assoc. (Adjusted Confounders)
Blumenthal, et al. (1995)	N = 61, U.S., 29–59 y.o. mild, unmedicated hypertensives	Self report: JCQ Quadrant term (24% job strain) (% men not specified)			– 4 SBP (significance unspecified) DBP = NS (Age, education, income, job status)
Cesana, et al. (1996)	N = 527, No. Italian, 25–64 y.o. population sample	Self-report: JCQ Quadrant and tertile terms	Quadrant Tertile Normotensives: Work +3.4 → +4.2 24 h +2.8 → +4 (Age, education, overwt index, PA)		Borderline hypertensives Quadrant term work and 24 h: SBP and DBP = NS Tertile term: SBP work: –4.6, 24h: –3 DBP work: –1.7, 24h: –1 Normotensives Quadrant and tertile term: Work & 24 h DBP = NS (As SBP)
Härenstam, et al. (1988)	N = 66, Swedish, (age unspecified), prison staff	Self-report: Job demands (14 items) Decision-latitude (2 items) Skill discretion (6 items) Main effects only	Skill discretion predicts Work SBP p < 0.01 Leisure SBP p < 0.001 (Age, status, nightwork, ETOH, BMI)		
Knox, et al. (1985), Theorell, et al. (1985)	N = 71, Swedish, 26–32 y.o. from military recruit lists	Imputation: Hectic (1 item) Control over work pace (1 item) Quadrant term (28% job strain)			SBP: Work and home = NS DBP: Work and home = NS
Light, et al. (1992)	N = 65, U.S., 18–47 y.o. 58% white, 42% black 71% white collar	Self-report: JCQ Quadrant term (23% job strain-men)	Job strain: Work + 6.0 (Age, BMI, status, PA, posture, race)	Job strain: Work + 4.0 (As SBP)	ψ demand, decision latitude, skill discretion work SBP + DBP = NS (As SBP)

(Table continued on next page.)

TABLE 4. Studies of Job Strain and Ambulatory Blood Pressure among Men *(Continued)*

First Author (Year)	Study Participants	Form(s) of Job Strain Variable	Significant Positive Effects: SBP (Adjusted Confounders)			Significant Positive Effects: DBP (Adjusted Confounders)			Null or Sig. Negative Assoc. (Adjusted Confounders)
Schnall, et al. (1992), Landsbergis, et al. (1994)	N = 262, U.S., 30–60 y.o. from 8 worksites, 84% white	Self report: JCQ Quadrant term (21% job strain) and 9th cell term	**Job strain** / Work / Home / Sleep + 6.7 → / + 6.5 → / + 6.2 **ψ demands** Work (p = 0.015) *(Age, race, education, BMI, smoking, PA, urine Na⁺, TAB, worksite, ETOH)*	Quadrant +6.7 → +6.5 →	9th cell +11.5 +8.6 (no data)	**Job strain** Work *(As SBP)*	Quadrant +2.7 →	9th cell +4.1	Job strain: DBP home & sleep = NS ψ demands = NS (except work SBP) Decision latitude = NS *(As SBP)*
Schnall, et al. (1998)	N = 195, U.S., 33–63 y.o. from 8 worksites, 84% white	Self-report: JCQ Quadrant term (16% job strain)	**Job strain** Work + 6.4 Home + 6.9 Sleep + 5.0 *(Age, race, BMI, smoking, ETOH)*			**Job strain** Work + 5.0 Home + 4.9 *(As SBP)*			Job strain sleep DBP = NS *(As SBP)*
Steptoe, et al. (1995)	N = 49, U.K., 20–29 y.o. firefighters	Self-report: ψ demands (3 items) Control (3 items) Skill utilization (4 items) (51% job strain)	**Job strain & systolic reactor:** Afternoon work + 12.4 *(Groups with and without job strain, high-low reactivity did not differ significantly in age, BMI, ETOH, smoking, baseline BP, inter alia)*						Job strain: Work SBP & DBP = NS
Steptoe, et al. (1999)	N = 60 men, N = 102 women* UK, mean age = 39 teachers	Self-report: 10 items/quotient term with cutpoints (49% job strain total) (% in men unspecified)	**Low job strain:** Evening work + 3.1 *(Age, BMI, baseline SBP)*			**Low job strain** Evening work + 2.1 *(Age, BMI)*			Job strain: Work SBP & DBP = NS Evening SBP & DBP = NS *(Age,BMI)*
Theorell, et al. (1991b)	N = 161, Swedish, 35–55 y.o. borderline HTN (DBP = 85–94) employed	Imputed: ψ demands (2 items) Control (12 items) Quotient term with 3 levels: high, medium, low				**Low physical demand:** **Job strain** / Work / Leisure / Sleep +7.4 → +5.9 → +7.4 →	Medium +7.4 → +5.9 → +7.4 →	High +11.9 +9.9 +10.2	High physical demand: DBP work, leisure & sleep = NS High & low physical demand SBP work, leisure & sleep = NS

* Results not gender-stratified

TABLE 4. Studies of Job Strain and Ambulatory Blood Pressure among Men *(Continued)*

First Author (Year)	Study Participants	Form(s) of Job Strain Variable	Significant Positive Effects: SBP (Adjusted Confounders)	Significant Positive Effects: DBP (Adjusted Confounders)	Null or Sig. Negative Assoc. (Adjusted Confounders)
van Egeren, et al. (1992)	N = 17, U.S., 21–52 y.o. university employees, sedentary work, (88% white)	Self report: JCQ Cutpts of Schnall, 1990 (24% job strain-men N = 4)	Job strain Work +9 Home +5 (Age, baseline BP, BMI, TAB, caffeine)	Job strain Work +4 (As SBP)	Home DBP, sleep SBP & DBP = NS (As SBP)

Cohort Ambulatory BP Studies

First Author (Year)	Study Participants	F/u (y)	Form(s) of Job Strain Variable	Significant Positive Effects: SBP (Adjusted Confounders)	Significant Positive Effects: DBP (Adjusted Confounders)	Null or Sig. Negative Assoc. (Adjusted Confounders)
Schnall, et al. (1998)	N = 195, U.S., 30–60 y.o. from 8 worksites, 84% white	3	Self report: JCQ Quadrant term (21% job strain)	Job strain at T1 & T2 vs. at neither Work +11.1 Home +11.1 Sleep +10.8 Job strain at T1, not at T2 Work −5.3 Home −4.7 (Age, BMI, race, smoking, ETOH)	Job strain at T1 & T2 vs. at neither Work +9.1 Home +7.3 Job strain at T1, not at T2 Work −3.2 Home −3.3 (As SBP)	Job Strain at T1 & Tw vs. at neither DBP sleep = NS Job strain at T1, not at T2 SBP & DBP sleep = NS (As SBP)
Theorell, et al. (1988)	N = 40, Swedish, 26–60 y.o., 6 different occupations	1	Self report: PSJSQ Quotient term—4 levels	Highest repeated job strain Work +4		Highest repeated job strain: Work DBP = NS Leisure SBP & DBP = NS

Case-Control Ambulatory BP Study

First Author (Year)	Study Participants	Form(s) of Job Strain Variable	Significant Positive Effects (Adjusted Confounders)		Null or Sig. Negative Assoc. (Adjusted Confounders)
Schnall, et al. (1990)	N = 215, U.S., 30–60 y.o. from 8 worksites, 84% white	Self report: JCQ Quadrant term (21% job strain)	Job strain Case defined at work ambulatory BP > 85 Case defined at work ambulatory BP > 90 Case defined at work ambulatory BP > 95 (Age, BMI, type A behavior, 24 h urine Na+ excretion, physical activity on the job, education, smoking, ETOH, work site)	OR 3.1 3.6 24.4	

BMI = body mass index, ETOH = alcohol, JCQ = job content questionnaire, NS = nonsignificant, OR = odds ratio, PA = physical activity, PSJSQ = psychosocial job strain questionnaire (Swedish), TAB = Type A behavior.

which recordings were continued outside work, ambulatory SBP was found to be significantly elevated during leisure, nonwork time among those exposed to job strain. One additional study, in which only main effects were assessed, shows that low skill discretion is a significant, independent predictor of ambulatory SBP during work, as well as during leisure time.[91] High psychological demands also were found to be associated with a significant elevation in ambulatory SBP during work.[228a] Ambulatory diastolic blood pressure (DBP) was significantly higher during work among those exposed to job strain, with a "carry-over effect" to leisure time in two studies.[159,227,228a,259,276]

Significant dose-response relationships were reported in three studies: when job strain was defined at a more extreme level (e.g., the top tertile of demands or the bottom tertile of latitude, or their combination—the 9th cell term; see Chapter 6), the blood pressure effect also was greater. Thus, analyzing the Schnall, et al. 1992 study and the Landsbergis, et al. study together, when job strain was defined by the usual quadrant term work ambulatory SBP showed a +6.7 mmHg effect, but when the 9th cell was used the effect rose to +11.5.[152,228a] In the study of borderline hypertensives by Theorell and colleagues, exposure to "medium" levels of job strain (and low levels of physical demand) was associated with a +7.4 mmHg effect on ambulatory DBP during work, compared to +11.9 among those exposed to "high" job strain.[259] Self-report bias was obviated in this study by use of the imputation method.

In contrast, both Blumenthal, et al. and Cesana, et al. obtained null or negative results when job strain was assessed by self-report among borderline, unmedicated hypertensives.[23,41] The latter group of authors have suggested that this may reflect a denial phenomenon. This formulation is concordant with Theorell's observations that an underreporting of a stressor may be associated with overreaction physiologically, among those with a positive family history of hypertension.[257]

In the Knox, et al. study and the Theorell, et al. 1985 study, use of the imputation method based upon single items to define the major job strain dimensions may have contributed to nondifferential misclassification.[133,262] Two single-occupation studies by Steptoe and colleagues also reveal a number of null cross-sectional ambulatory BP findings. In a group of firefighters, 51% were deemed to have been exposed to job strain, based upon a small number of items for each dimension.[249] Using similar methodology, 49% of teachers (not gender stratified) were said to have been exposed to job strain.[248] Nondifferential misclassification due to limited range of variation of actual job characteristics may explain these results. Nevertheless, when job strain exposure status was combined with systolic reactivity, a significant positive effect upon afternoon work SBP was found (+12.4) among the firefighters. Among the teachers, the difference in BP between evening and day work was significantly less among those with high (–0.64/–2.45) versus low (–3.72/–4.5) job strain (not gender stratified).

The case-control study of Schnall, et al. reveals a significant positive relation between exposure to job strain and hypertensive status, as defined by work ambulatory BP.[228] Furthermore, as the definition of hypertension was made progressively more rigorous (work ambulatory BP > 85, 90, and 95 mmHg), the odds ratio for exposure to quartile-term job strain increased correspondingly (3.1, 3.6, and 24.4, respectively).

Both cohort ambulatory BP studies report significant positive findings. In the Schnall, et al. 1998 study, exposure to job strain at baseline and 3 years later showed a +11.1 mmHg effect on workplace and home ambulatory SBP compared to those

unexposed at both times.[227] The DBP effect also was marked. Furthermore, those men who reported being exposed to job strain at baseline but not 3 years later showed a significant drop in work and home ambulatory BP at 3-year followup, after controlling for major confounders.

Casual Blood Pressure Studies. Studies of job strain in relation to casual BP (usually measured in the clinic or other unspecific setting outside the workplace) are generally less consistent than those using ambulatory recordings at the workplace. Significant positive effects of exposure to job strain among men were found with respect to casual SBP in the cross-sectional studies of Cesana, et al., among normotensives but not borderline hypertensives, and of Melamed, et al., in which exposure to hectic, short-cycle, repetitive work was compared to jobs with substantial variety or longer cycle.[41,173] Kawakami and colleagues reported a significantly elevated SBP and DBP among day workers exposed to job strain, but not among those working rotating shifts.[130] In only one of the five large databases assessed by Pieper, et al. was exposure to job strain using the imputation method significantly associated with casual SBP and DBP.[209] However, a summary estimate of all five working population samples revealed a significant relation between a low decision-latitude and SBP. In a similar vein, Curtis, et al. found a significant inverse relation between hypertensive status based on casual BP readings and self-reported decision latitude at work.[52]

In contrast, in other studies neither exposure to job strain nor its major dimensions (when analyzed) were associated with hypertensive status or BP levels, based on casual BP readings.[4,9,40,64,110,252] (In the Carrère, et al. study, BP was measured immediately pre- and post-work.) In the investigations of Greenlund, et al. and Netterstrøm, et al., nonsignificant relations (gender-adjusted but not stratified) between job strain or its major dimensions and casual BP measures were found, with a few unexpected inverse relations in the latter study.[82,186] A cohort study by Chapman, et al. revealed that exposure to deadlines at work was associated with a significant increase in SBP, while other single or interaction terms reflecting job strain and/or its major dimensions showed no significant relations to SBP nor DBP among men.[43]

The papers of Albright, et al., Carrère, et al., and Emdad, et al. are on single occupations, and therefore are of limited range of variance.[4,40,64] The major issue, however, for most of these studies, is that casual BPs are highly variable and, in the clinic setting, may be influenced by psychosocial factors related to the clinic visit itself, the so-called "white coat effect."[207] Worksite point measurements of BP appear to be more reliable than casual clinic BP (see Chapter 7). Schnall and colleagues found that workers exposed to job strain showed an increased likelihood of having hypertension, classified on the basis of worksite point measurements of BP.[228] Furthermore, as the definition of hypertension was made more stringent, the odds ratio increased, providing additional evidence of the reliability of workplace point estimates, as well as the criterion validity of the relation between job strain and BP elevation.

Thus, with respect to casual BP, we find limited evidence that job strain or its dimension(s) has a major impact. This is in contradistinction to studies that measure ambulatory BP and examine averaged BPs during work, as well as other periods, as the outcome. These studies show strong, consistent effects of job strain or its major dimension(s) on BP. Furthermore, there is some evidence, albeit not totally consistent, of a dose-response relationship with respect to ambulatory BP and exposure to increasingly severe job strain. In addition, there is cohort data demonstrating not only the expected temporal relationship between exposure and outcome,[227] but also the effect of cumulative exposure. Finally, the data, albeit observational rather than a

controlled intervention, indicate that "*a change in exposure* is associated with a *change in morbidity*."[227] Hernberg has categorized the latter as "the most conclusive evidence of causality."[100]

OTHER CARDIAC RISK FACTORS

Some studies indicate that exposure to job strain and/or its major dimensions is associated with other standard cardiac risk factors among men. There are theoretical background discussions on how work organizations can influence health-related behaviors that impact upon the CV system.[113,151]

With regard to **cigarette smoking**, it has been proposed that workplace stressors have less impact on smoking prevalence than on smoking intensity, since people often begin smoking before entering the labor market.[283] Accordingly, the focus here is on results concerning smoking intensity among current smokers. Green and Johnson found, after controlling for sociodemographic factors, that male chemical plant employees in higher-strain work smoked significantly more cigarettes, and more of them had increased the number of cigarettes smoked, compared to those with lower-strain jobs.[81] Hellerstedt and Jeffery also reported a significantly greater number of cigarettes smoked per day among men in high-strain jobs compared to passive jobs, after sociodemographic adjustment.[98] Kawakami, et al. found that high-strain jobs *and* passive jobs with low social support were associated with increased smoking intensity.[130] Other studies also reveal a significant positive association between job strain and/or its major dimensions and smoking intensity among men.[176,209]

However, in a study of young adults, after adjusting for age, education, and type A behavior, Greenlund and colleagues found no significant relation between self-reported job demands, decision latitude, job strain, and smoking intensity.[82] Among male professional drivers, no significant relation was found between self-reported job strain, psychological demands, decision latitude, and smoking intensity.[63] Two imputational studies, in which sociodemographic adjustment was not made, also reveal no association between exposure to job strain and/or its major dimensions, and how much workers smoke.[9,218] In the one prospective study in which changes in smoking prevalence were examined, men whose job decision latitude increased over 3 years had a substantial reduction in cigarette smoking. The greatest increase in decision latitude was found among those 13 men who quit smoking.[151]

Sedentary behavior during nonwork time was found to be significantly associated with less social interaction at work, as well as with fewer opportunities to learn new things on the job (an integral part of the decision-latitude), in a population-based sample of Swedish men, after adjusting for age and education.[113] Similarly, another study found a significant inverse relation between low decision-latitude and number of exercise sessions per week, after sociodemographic adjustment.[98] However, no significant association was found between sedentary leisure time and job strain or its major dimensions in the study of Landsbergis, et al.[151]

Obesity, as assessed by detailed anthropometric measurements, has been found among Hispanic men in the U.S. (HHANES study) to be significantly associated with exposure to job strain, decision authority, and psychological demands (imputation method), after adjusting for age, education, and smoking status.[78] Netterstrøm and colleagues reported that both self-reported and imputed exposure to job strain were associated with a significantly elevated body mass index (BMI) in a sample of men and women; these results were adjusted for, but not stratified by, gender.[186] In contrast, a number of other studies relying upon BMI show no relation between job

strain or its major dimensions and BMI among men.[98,110,151,218] In a study of male professional drivers, an inverse relation was found between self-reported job strain and self-reported BMI.[63] This finding was attributed to denial, which has been shown to deleteriously impact upon cardiac risk among professional drivers.[187,292]

Hellerstedt and Jeffery found a significant relation between **high-fat diet** and exposure to high psychological demands, as well as job strain.[98]

Psychosocial stressors may promote atherogenic processes (see Chapter 5). Here, we briefly summarize the epidemiologic data concerning these metabolic parameters and job strain and/or its major dimensions. Ishizaki, et al. found that low psychological demands significantly predicted tissue plasminogen activator levels, independently of traditional cardiac risk factors.[110] Elevated fibrinogen was reported by Brunner and colleagues in the Whitehall II study to be associated with low workplace control, as assessed both by self-report and external observer.[36] In the former case, this effect remained after adjustment for socioeconomic status. However, Ishizaki, et al. found neither job strain nor its major dimensions significantly associated with plasma fibrinogen levels. Moller and Kristensen also failed to find that job strain was a significant, independent predictor of plasma fibrinogen levels, using a multivariate model that included social class.[178]

Of the studies that have examined the relations between serum cholesterol and/or its constituent fractions, and job strain or its major dimensions, no significant results among men have been reported.[9,67,82,110,130,173,180,186,218] Netterstrøm, et al. reported that HbA1C was significantly associated with imputed exposure to job strain in a sample of men and women; these results were adjusted for, but not stratified by, gender.[186] Other studies assessing glucose intolerance showed no significant relation to job strain or its major dimensions among men.[67,82,110,173]

Thus, there is preliminary evidence that job strain or its major dimension(s) may impact on cardiac risk factors besides BP. Some noteworthy results are seen regarding smoking intensity. There are some suggestive data regarding links to the coagulation mechanisms and other metabolic indices contributing to the atherogenic process; however, there are also substantial null findings. Much additional research is needed before definitive conclusions can be reached in this area.

The Effort-Reward Model

ISCHEMIC HEART DISEASE AND OTHER HARD CVD ENDPOINTS

Measures of effort-reward imbalance (ERI) at work have been found to predict new manifestations of coronary heart disease in Germany, Finland, and England (Table 5). In a prospective study of 416 German factory workers aged 25–55, a number of measures of high effort and low reward independently and strongly predicted CHD incidence over 6.5 years after adjusting for other behavioral and somatic risk factors.[239] These measures included status inconsistency (OR 4.4), job insecurity (OR 3.4), work pressure (OR 3.5), and overcommitment (OR 4.5). A combined "low reward/high effort" variable was also a significant predictor (OR 3.4) in a separate analysis. If advanced, subclinical CHD (OR 6.2) or stroke (OR 8.2) is added to the case definition, the association with ERI becomes even more substantial.[233]

Among men in the British Whitehall study, exposure to a combination of high effort and low reward more than doubled the risk of newly reported CHD over 5.3 years.[30] Finally, in a prospective study of Finnish men, those facing high work demands, low work resources, and low income had a more than doubled risk of myocardial infarction or dying from heart disease after 8.1 years, compared to men with low demands,

TABLE 5. Studies of the Effort-Reward Imbalance Model and Cardiovascular Outcomes for Men

				Cohort Studies		
First Author (Year)	Study Participants	Form(s) of Exposure Variable	F/u (y)	Illness Outcome	Significant Positive Associations (Adjusted Confounders)	Null or Sig. Negative Assoc. (Adjusted Confounders)
Siegrist, et al. (1990)	416 male German blue-collar workers from 3 factories	Low security, career opportunities: job insecurity or status inconsistency High effort: work pressure or overcommitment	6.5	Acute MI or SCD (n = 263 in analysis)	Status inconsistency — OR 4.4 Overcommitment — 4.5 Low security, career opportunities *or* high effort — 4.5 Low security, career opportunities *and* high effort — 30.6 *(Age, BMI, SBP, lipids)*	Job instability, piecework, shiftwork, noise, increase in workload = NS; low promotion prospects Not significant controlling for other measures of low security, career opportunities and high effort Job insecurity Work pressure
Siegrist & Peter (1994); Siegrist (1996)				Acute MI, SCD, or advanced (sub-clinical) CAD (n = 329 in analysis)	Work pressure — 2.5 Low security, career opportunities, *or* high effort — 2.4 Low security, career opporunities, *and* high effort — 6.2	Overcommitment
Siegrist, et al (1992); Siegrist (1996)				Acute MI, SCD, or stroke	Overcommitment — 3.6 Status inconsistency — 2.9 Low security, career opportunities, *and* high effort — 8.2 *(Age, BMI, BP, lipids, smoking, exercise)*	
Lynch (1997a)	N = 940, Eastern Finnish men, 42–60 y.o., population-based	• Stress from work demands scale (11 items split at high 20%) • Economic rewards scale (income, split at low 20%)	4.2	Progression of carotid athero-sclerosis (plaque height, max. & mean IMT)	High demands, low income — p For change in max. IMT — 0.03 For change in plaque height — 0.008 *(Age, baseline IMT)* For change in plaque height — 0.04 *(Age, HDL, LDL, triglycerides, smoking, alcohol, BMI, SBP, treated hypertension or hyperlipidemia)*	Groups with other combinations of demands and income = NS *(Age, baseline IMT)*

TABLE 5. Studies of the Effort-Reward Imbalance Model and Cardiovascular Outcomes for Men *(Continued)*

First Author (Year)	Study Participants	Form(s) of Exposure Variable	F/u (y)	Illness Outcome	Significant Positive Associations (Adjusted Confounders)		Null or Sig. Negative Assoc. (Adjusted Confounders)
Lynch, et al. (1997b)	N = 2297, Eastern Finnish men, 42–60 y.o., population-based	• Stress from work demands scale (11 items) • Resources scale (5 items) (skill discretion/emotional rewards of work; interesting, enjoyable, meaningful work) • Economic rewards scale (income, split at low 40%) Referent = low, high, high	8.1	Acute MI	High demands, low resources, low rewards	RH	Groups with other combinations of demands, resources, rewards = NS (Age)
					(Age, alcohol, smoking, physical activity)	2.3	
					(Age, depression, marital status, hopelessness)	2.2	
					(Age, fibrinogen, SBP, BMI, CV fitness, lipids, other bioRF)	1.9	
				CVD mortality	High demands, low resources, low rewards		
					(Age, alcohol, smoking, physical activity)	2.6	
					(Age, fibrinogen, SBP, BMI, CV fitness, lipids, other bioRF)	2.3	
Bosma, et al (1998)	10,308 British civil servants (33% women), 35–55 y.o.	High effort: competiveness, overcommit., hostility Low reward: poor promotion prospects, blocked career	5.3	Newly reported CHD (results for men)	High effort and low reward	OR	High effort *or* low reward
					(Age, BMI, smoking, BP, lipids, employment grade, negative affectivity, length of followup, job control)	2.2	

<center>**Cross-Sectional Study**</center>

First Author (Year)	Study Participants	Form(s) of Exposure Variable	Illness Outcome	Significant Positive Associations (Adjusted Confounders)		Null or Sig. Negative Assoc. (Adjusted Confounders)
Peter, et al (1999b)	2098 Swedish men and women, 45–64 y.o., population-based case-control SHEEP study	Effort-reward imbalance: ratio > 1 Job strain: latitude bottom 25% or demands top 25%	Acute nonfatal MI (results for men)		OR	
				Effort-reward imbalance (no job strain)	1.4	
				Effort-reward imbalance *and* job strain	2.3	
				(Age, BMI, smoking, HPT, lipids, exercise, diabetes, family history, SES)		

bioRF = biological risk factors, CAD = coronary artery disease, CVD = cardiovascular disease, HPT = hypertension, IMT = intima-media thickness, MI = myocardial infarction, SCD = sudden cardiac death.

high resources, and high income.[165] In addition, in this sample a combination of high work demands and low income was significantly associated with progression of carotid atherosclerosis.[164] (In the German and Finnish studies, some measures of high effort or low reward were not associated with heart disease, as shown in Table 5.)

BLOOD PRESSURE

As seen in Table 6, in the cross-sectional study of 179 male German middle managers aged 40–55, forced job change (low reward) (OR 3.3) and a variable combining frequent interruptions (effort) and forced job change (OR 5.8) were strongly associated with hypertension.[205] Similarly, in a cross-sectional study of Stockholm area residents, an effort-reward ratio greater than one was associated with hypertension (OR 1.6) among men.[202] The combination of ERI and shiftwork among Stockholm men led to an even stronger association (OR 2.2) with hypertension.[203]

In the prospective study of 416 German blue-collar workers from three factories, low promotion prospects at work (OR 2.7), competitiveness at work (OR 2.8), and feelings of sustained anger (OR 5.4) predicted coronary high risk status.[238] (High risk was defined as the 13.6% of the sample with both hypertension and high lipid levels.) In addition, a variable combining overtime work (effort) and fear of job loss, job instability, and layoffs (low reward) was similarly associated (OR 3.3) with a comanifestation of hypertension and atherogenic lipids.[233] (In all of these studies of hypertension, some of the measures of high effort or low reward were not associated with hypertension; see Table 6.)

OTHER CARDIAC RISK FACTORS

Cardiac risk factors other than hypertension may represent additional pathways by which ERI may contribute to CVD. Among German blue-collar workers, LDL/HDL ratio was associated with high work demand, increased workload, and job insecurity, combined with occupational instability.[235] In German managers, LDL cholesterol was predicted by a combination of workload and lack of support.[237] In Swedish men, cholesterol/HDL ratio, but not plasma fibrinogen, was associated with ERI.[202,203] Among the German managers, fibrinogen was associated with a combination of overcommitment and lack of social ("reciprocal") support, but not with combinations of other measures of effort or reward.[237]

COMMENTS ON THE NULL FINDINGS AND GENERAL INTERPRETATION

Despite the positive findings, some questions remain about which specific work factors are responsible for increasing CHD risk, and whether these variables are additive or interactive.

Specific Predictors of Risk. In the earlier studies, the set of variables used to measure effort and reward was not always identical, as some studies used "proxy" measures.[30,164,165] In addition, Siegrist, et al. applied a less restrictive measurement approach where subjects were considered "exposed" to ERI when at least one of the effort and one of the reward variables were positive.[238,239] Thus, we cannot be sure which work characteristic contributed to this combined risk factor. More recently, a standardized summary measure of ERI has been constructed based on a predefined algorithm.[202–204] To illustrate this issue, in the three studies of hypertension (Table 6), only the German middle-manager study found associations between outcome and measures of extrinsic effort.[205] Extrinsic effort was not associated with hypertension in the Swedish WOLF study.[202] In the German blue-collar study, work pressure was not associated with outcome, and forced piecework was not in the analysis (due to

TABLE 6. Studies of the Effort-Reward Imbalance Model and Hypertension for Men

Cohort Studies

First Author (Year)	Study Participants	Form(s) of Exposure Variable	F/u (y)	Illness Outcome	Significant Positive Associations (Adjusted Confounders)		Null or Sig. Negative Assoc. (Adjusted Confounders)
Siegrist, et al. (1991); Siegrist (1996)	416 male German blue-collar workers from 3 factories	Low security, career opportunities: job instability, low promotion prospects. Overcommitment: competitiveness, sustained anger. High effort-low reward: overtime *and* job instability *or* fear of job loss	6.5	Comanifestation of hypertension and high LDL-cholesterol (n = 314 in analysis)	Low promotion prospects Competitiveness Sustained anger High effort-low reward *(Age, BMI, smoking, exercise)*	OR 2.7 2.8 5.4 3.3	Work pressure, job instability: forced piecework and status inconsistency were not in the analysis, due to attempts to find the most parsimonious model

Cross-Sectional Studies

First Author (Year)	Study Participants	Form(s) of Exposure Variable	Illness Outcome	Significant Positive Associations (Adjusted Confounders)		Null or Sig. Negative Assoc. (Adjusted Confounders)
Peter & Siegrist (1997); Siegrist (1996)	179 healthy German male middle managers, 40–55 y.o.	High extrinsic effort: time pressure, frequent interruptions. High intrinsic effort: overcommitment (upper tertile), sustained anger. Low reward: lack of support, status incongruence, status discrepancy, forced job change	Hypertension (≥ 160/95 mmHg) (n = 170 in analysis)	Bivariate analysis: Time pressure Frequent interruptions Forced job change Freq. interruptions + forced job change All exposure variables in model: Forced job change Effort-reward imbalance measures: Freq. interruptions *or* forced job change Freq. interruptions + forced job change *(Age, BMI, smoking, exercise)*	OR 3.3 2.3 5.8	Overcommitment Sustained anger Lack of support Status incongruence Status discrepancy Time pressure Frequent interruptions
Peter, et al (1998) Peter, et al (1999a)	N = 2228, Swedish men, 30–55 y.o., population-based WOLF study	Effort-reward imbalance: (ratio > 1): overcommitment (upper tertile), extrinsic effort (above median), low reward (above median) Rotating shift workers (vs day shift)	Hypertension (≥ 160.95 mmHG) (results for men)	Bivariate analysis: Effort-reward imbalance Low reward Effort-reward imbalance *(Age, smoking, BMI, exercise)* Effort-reward imbalance *(Age, smoking, BMI, exercise, lipids, SES)* Effort-reward imbalance + rotating shift *(Age, smoking, BMI, exercise)*	OR 1.7 1.6 2.2	Overcommitment Extrinsic effort

BMI = body mass index, SES = socioeconomic status.

colinearity).[238] Only in one later analysis of the sample was overtime (plus low reward measures) associated with high CHD risk.[233] Similarly, "forced job change" in the middle manager study and "low promotion prospects" in the blue-collar study were the only low reward measures associated with hypertension. ("Status inconsistency" was not in the analysis of the blue-collar sample due to colinearity with other reward measures.)

In the CHD studies (Table 5), no extrinsic measure was included in the Whitehall study analysis,[30] and a very broad measure of work demands was used in the Finnish studies.[164,165] Low status control (low job security) was essentially the measure of low reward in the German blue-collar sample and the Whitehall study, while economic reward and social support were added as measures of reward in the Finnish and the Swedish SHEEP studies.

Interaction Versus Additive Burden. As with the Job Strain Model, the question arises as to whether measures of high effort and low reward combine with each other additively to increase CHD risk, or whether they interact with each other ("synergism," see Chapter 3). In some analyses, as seen in Tables 5 and 6, synergism appears to exist. In the blue-collar study and the middle manager study, for example, the relative risk of CHD due to measures of high effort combined with low reward is substantially greater than the sum of the risks due to these two components separately.[205,233] However, no statistical tests of interaction were conducted. A number of more recent analyses used a combined high effort-low reward ratio variable, which prevents observation of possible interaction.

In summary, several studies, both cross-sectional and prospective, have shown significant positive associations between measures of high effort/low reward and elevated lipid levels, hypertension, and CVD. The magnitude of the relationship is similar to that typically found for job strain with respect to these outcomes. Furthermore, preliminary evidence indicates that the effects of job control and ERI are statistically independent of each other in prediction of CHD[30] and that the combined effects of exposure to job strain and ERI upon CVD are much stronger than the separate effects of each.[204]

Threat-Avoidant Vigilant Work

A particularly heavy psychological burden occurs when one must continuously maintain a high level of vigilance to avoid disastrous consequences, which could occur with a momentary lapse of attention or a wrong decision. Among several of the occupations shown to be at high risk for CVD (e.g., bus, taxi, and truck drivers; air traffic controllers; sea pilots), threat-avoidant vigilant activity is a prominent aspect of work. Experimental animal studies have shown an association between performance of threat (shock) avoidance tasks and cardiac electrical instability.[46,162]

A few epidemiologic studies have specifically examined aspects of threat-avoidant vigilant activity with regard to CVD outcomes. In a cohort study by Menotti and Seccareccia of 99,029 Italian men employed by the railroad system, occupational psychologists rated jobs with respect to level of "responsibility at work."[175] Levels were based on the "economic and financial implications of decisions taken at work, as well as the relevance of possible damage and hazards both economic and for human life as a consequence of possible mistakes made at work." The age-adjusted mortality rates due to MI were significantly greater ($p < 0.001$) for each of three ascending levels of responsibility at work compared to the lower levels. Job dimension data from expert ratings were imputed to a CV disability data base (N = 9855).[181] For the dimension of having to be "alert to changing conditions," age-adjusted ORs of

1.85, 2.17 and 2.8 were found for the second, third, and highest quartiles, respectively. The "hazardous job situation" dimension showed age-adjusted ORs 2.07, 3.32, and 4.09, for the second, third, and highest quartiles, respectively. (Confidence intervals were not provided; the author identified job dimension scores having an OR of at least 2 as meriting additional research attention.) In the imputational study by Alfredsson, et al., an SMR of 132 (116–149) was calculated for hospitalization for MI, among Swedish men whose jobs entailed risk of explosion.[7] Occupational titles were used to impute job characteristics based upon observational analysis and interviews in a study of 6213 Finnish municipal employees.[251] These authors identified requisites for "alertness of the senses" and dangerous work as quantitatively important stressors among male transport workers, with high prevalence of self-reported hypertension and CHD.

These epidemiologic studies provide suggestive evidence for an association between aspects of threat-avoidant work and CVD outcomes. Further investigation is needed, with more precise, well-controlled risk estimates, and accounting of biomedical and psychosocial risk factors.

SOCIAL CLASS, OCCUPATIONAL STATUS, AND CVD by
Michael Marmot, FFPHM—Supported by an MRC research professorship and by the John D. and Catherine T. MacArthur Research Foundation Research Network on Socioeconomic Status and Health

A dominant feature of the occurrence of cardiovascular disease (CVD) in most industrialized societies is the higher rate in people of lower socioeconomic position. The Whitehall studies of British civil servants showed that the link between socioeconomic position and CVD was not confined to higher rates among the poor.[169,170] The poor do have high rates, but there is a social gradient: the lower the social status, the higher the CV risk. A review by Kaplan and Keil covers a wealth of studies showing a similar social gradient in the U.S.[118]

What implications does the social gradient have for questions of etiology and in particular for the role of work? In the U.K., we traditionally used Registrar General's social classes, which are based on occupation. It has never been clear whether the differences in CVD observed using these classes are due to occupation or to other features correlated with occupational status.

Elsewhere in this volume we show how ideas on the effects and meaning of social stratification have been shaped by Marx, Durkheim, and Weber. It is useful to think of three "meanings" of socioeconomic position, in terms of the ways they may affect health. First, low social position may be related to **material deprivation**, and absolute material deprivation (poverty) may be related to risk of illness. Second, socioeconomic position may be related to **standing in society** which may, in turn, relate to shared values, culture, and lifestyle. Third, socioeconomic position is a measure of position in the social hierarchy, which is related to **power relationships**. People higher in the hierarchy have more control over their own, and other people's, lives. These power relations operate in the workplace, but not exclusively so.

Figure 1 shows standardized mortality ratios from ischemic heart disease (IHD) by Registrar General's social classes in England and Wales.[56] Focusing on the 1991–93 period, we see that IHD is markedly higher among men in social class V, unskilled manual workers. The gradient is shown clearly. Men in social class I have a mortality ratio about 35% lower than the England and Wales average, and men in social class IV
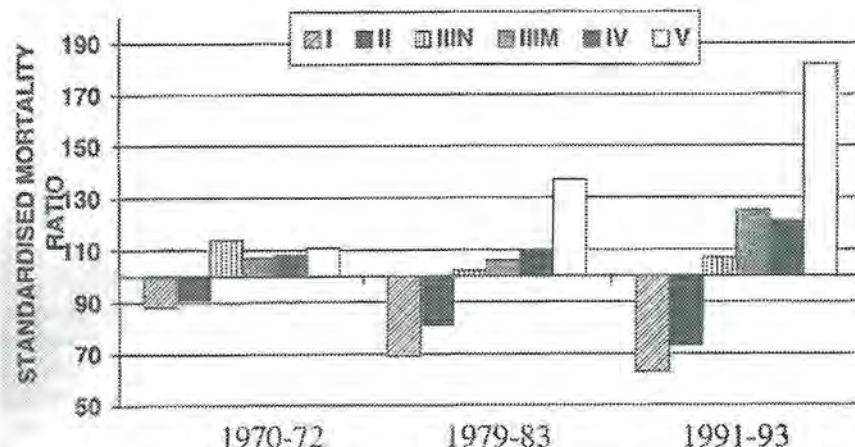
FIGURE 1. Ischemic heart disease by social class in England and Wales, males 1970–93. (Data from Drever F, Whitehead M, Roden M: Current patterns and trends in male mortality by social class (based on occupation). Popul Trends 86:15–20, 1996; with permission.)

have mortality 25% higher. The high mortality of men in the lowest social class could be attributed, in part, to the effect of absolute deprivation. It is difficult to attribute the rest of the gradient to differing degrees of material deprivation. In contemporary Britain, the overwhelming majority of these men in classes I to IV are adequately housed, nourished, and clothed, with adequate provision of safe water and food, and safe handling of sewage. In addition, the steepening of the gradient over the 20-year period shown occurred at a time when material prosperity was increasing for the top 80% of the population. Absolute deprivation does not, therefore, provide a ready explanation for the gradient in IHD mortality. Using data on U.S. counties grouped according to the proportion in white-collar occupations, Wing, et al. showed that the inverse social gradient in CHD mortality has become progressively steeper between 1968 and 1982.[29]

The other two concepts of social stratification are more likely to provide explanations for the gradient. The research task is to distinguish influences associated with power relations that are linked to work from influences related to general social standing that are linked more to lifestyle. Neither of the other two models alone gives a fully adequate accounting of the changing social class relations of IHD. Extending the comparisons in Figure 1, there is evidence from England, Wales, and the Netherlands that in the 1950s and earlier, heart disease mortality may have been more common in people of higher socioeconomic position.[146] Lifestyle may play some role in this; there is evidence that when the smoking epidemic first hit, it was at least as common among people of higher status but, with time, higher status people gave up smoking or declined to take up the habit to a greater degree than people of lower status. Physical activity may have followed a similar course. With the decline of physical activity in the workplace, the greater tendency for high-status people to be physically active in leisure time may have conferred increasing protection on them. One particular feature of diet—consumption of fresh fruit and vegetables that contain antioxidants and other protective nutrients—also may be related to the lower rate of heart disease in people of higher status.

The evidence from the Whitehall and Whitehall II studies is that these lifestyle factors may account for some, but by no means all, of the social gradient in CVD. In the Whitehall studies there was a social gradient in smoking, consumption of fruit
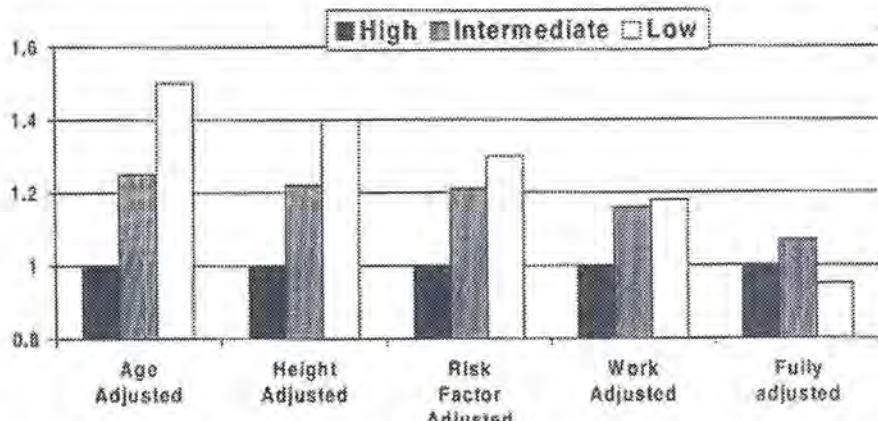
FIGURE 2. Odds ratio for new coronary heart disease in Whitehall II by employment grade, males. (From Marmot MG, Bosma H, Hemingway H, et al: Contribution of job control and other risk factors to social variations in coronary heart disease incidence. Lancet 350:235–239, 1997.)

and vegetables, and sedentary lifestyle, but only for a limited extent in obesity and blood pressure level, and not at all in plasma cholesterol. In Whitehall I (CHD mortality) and Whitehall II (CHD incidence), adjusting for coronary risk factors related to lifestyle accounted for about a third of the social gradient.[165,179] Among nonsmokers the social gradient in CHD incidence and mortality was similar to the gradient in smokers. In Whitehall II, low control in the workplace was related to CHD incidence[29] and accounted for about half the social gradient[169] (Fig. 2).

In seeking to interpret this finding of the importance of the psychosocial work environment, consider two related questions: Did low control appear to be associated with CHD because low control is associated with low socioeconomic status, and *other* factors account for the association of low socioeconomic status with disease; in other words was there confounding? Did low control appear to be an important mediator of the relation between social position and CHD because low control is simply a measure of low socioeconomic position? Several convincing lines of argument indicate that these results were not simply the result of problems of confounding and/or measurement.

In the Whitehall II study and in a Czech case-control study, the relation between low control and CHD was not removed by adjusting for socioeconomic status.[34,79] This finding implies that within a particular employment level, those with more control over their work have lower incidence of CHD than those with less control.

In separate studies in Sweden, first Johnson and Hall and then Hallqvist showed that job strain according to the demand/control model (DCM) was more strongly related to CHD in blue-collar than in white-collar workers.[83,114] Of course, it could be argued that manual workers with more control, and lower coronary risk, are of higher status compared to manual workers with less control. This, however, is not an argument against the importance of low control in the workplace because it may be precisely this particular feature of low social status that is responsible for part of the social gradient in disease. One approach to deciding if it is low control or other characteristics associated with low social status that are related to CHD is multivariate analyses. In the Whitehall II study, multivariate analysis showed an independent effect of low

control. The second approach is to explore biological markers, such as plasma fibrinogen, which is a risk factor for coronary disease. In Whitehall II, smoking, obesity, and lack of exercise were associated with plasma fibrinogen level. Independent of this finding, low control at work also was associated with plasma fibrinogen level.[36]

In the Whitehall II study and the Czech case-control study, high demand was not associated with coronary risk. The fact that these civil servants were office-based workers may be relevant. In Sweden, the DCM was related to disease more strongly in manual than in nonmanual workers. Thus, the degree to which the full DCM predicts disease may be influenced by the nature of employment in different settings.

These findings do suggest that low control in the workplace is independently related to CHD and makes an important contribution to the social gradient in CHD, along with other risk factors, including those related to lifestyle and early life. There still is a problem, however. A social gradient in CHD exists in people who are not working in formal employment: homemakers, the unemployed, and retired people. Low control *in the workplace* does not apply to them, but they may be affected by power relations that apply throughout society. High-status people among these groups who are "not working" may have power, control, and mastery that derives from their general position in the social hierarchy, rather than the workplace. This is in accord with the results of studies in nonhuman primates that show high-status animals to have less atherosclerosis and less activation of stress hormones.[232]

Kawachi and Kennedy and others have shown a relation between income inequality and mortality internationally; in the U.S., the relation was shown at the state level. Their interpretation of this finding is that income inequality is a marker for the quality of the social environment which, in turn, affects disease risk.[128,129,289] One reason for focusing on the role of work as one of the causes of the social gradient is that redesign of the workplace is more feasible than redesign of society, and may have other beneficial consequences.

WOMEN, WORK, AND CVD   *by Chantal Brisson, PhD*

In several industrialized countries, CVDs are the leading cause of death in women, as they are in men, and generate an equal amount of heart disease expenditure in both groups.[60,224a] CHD, the largest component of CVD, shows a lower rate in women than in men in younger age groups, but approaches similar rates for women and men in older groups.[73] Therefore, the study of CHD in women of working age is more difficult than the study of men of similar age because larger populations of working women have to be enrolled to obtain a sufficient number of CHD events. Over the last two decades, CVD mortality rates have shown consistent decreases.[15,266] However, in several countries there has been no decrease in women[69,216,278] or the decrease has been less marked than in men.[102,278] This difference could be due to changes that have occurred in women's lives since the 1970s—such as paid employment.[193] It is estimated that the proportion of women aged 25–49 involved in paid work will be 82% in the year 2000 in countries of the European Union.[177]

Gender Differences in Work and Home Exposures

Most women and men are employed in jobs where their own gender has a large majority.[12,177,194] Jobs held predominantly by women are concentrated in the services.[177] In countries participating in the Organisation de Coopération et de Développement Économiques, four service industries contained half of working women: office work, sales, health care, and teaching.[194]

Women □ **Men**
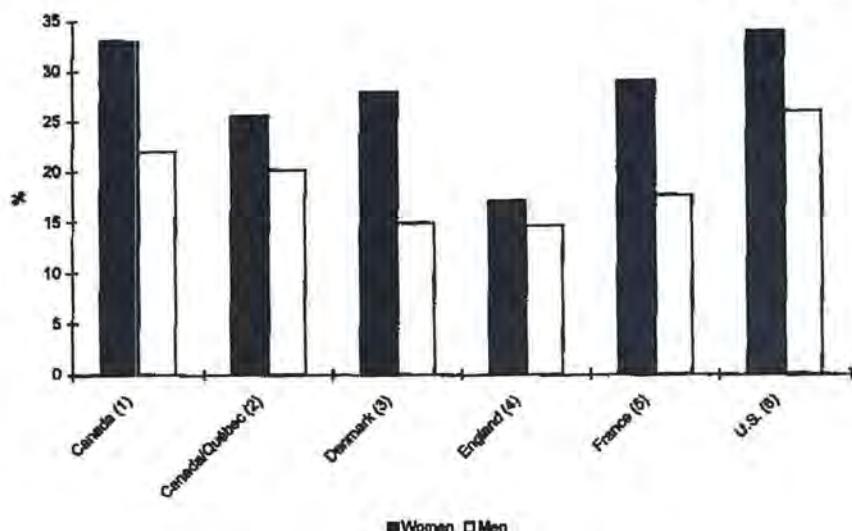
Notes: Prevalences cannot be compared between countries because different methods were used to categorize exposure groups.

(1) Random population sample—3847 male and 2587 female workers. Psychological demands and decision latitude assessed with 7 items from Job Content Questionnaire (JCQ). Median splits used to define high job strain.[34]

(2) Stratified random population sample—721 male and 389 female workers. Psychological demands and decision latitude assessed with full JCQ. Median splits used to define high job strain.[156]

(3) 748 male and 756 female white- and blue-collar workers living in 11 municipalities in Copenhagen County. Psychological demands and decision latitude assessed with 2 and 7 items. Job strain defined as combination of low degree of decision latitude (score ≥ 3) and high work pace (work pace reported too high or time pressure).[186]

(4) 6895 male and 3413 female London civil servants. Psychological demands and decision latitude assessed respectively with 4 and 9 items. Medians splits used to define high job strain.[30]

(5) 8277 male and 3170 female workers from the Gazel cohort. Psychological demands and decision latitude assessed with full JCQ. Median splits used to define high job strain.[188]

(6) 4018 mailhandlers from U.S. Postal Service. Psychological demands and decision latitude assessed respectively with 5 and 9 items from JCQ. Median splits used to define high job strain.[39]

FIGURE 3.   Prevalence (%) of high job strain by gender in six populations from five countries.

    Given this gender division of jobs it is expected that job characteristics potentially related to CV diseases also will differ. This clearly is the case regarding high job strain, defined as the combination of high psychological demands and low job decision latitude.[122] Indeed, studies conducted in Canada, Denmark, England, France, and the U.S. all found a higher prevalence of job strain in women than in men (Fig. 3).[30,34,39,156,186,188] It is particularly the level of control that is lower in women's jobs.[29,39,82,84,122,156,188] In some studies, higher psychological demands were observed in women,[39,82,156] but other studies found little difference between women and men on this factor.[85,131]

    Potentially stressful exposures related to family responsibilities are also more prevalent in women than in men. Indeed, despite their increasing involvement in paid work, women spend more hours than men in child caring and housework.[20,157,160,293] For example, in countries of western Europe women spent an average of 35 hours/week in child caring and housework before 1975, and 31 hours/week after 1975. Men spent 8 and 11 hours, respectively during the same periods.[94]

Job Strain

JOB STRAIN AND CARDIOVASCULAR DISEASES

High job strain has been defined by Karasek as the combination of high psychological demands and low decision latitude.[122] *Psychological demands* refers to the quantity of work, the mental requirements, and the time constraints. *Decision latitude* refers to the ability to make decisions about one's own work and the possibility of being creative and using and developing skills. The Job Strain Model emphasizes that high psychological demands are not, in themselves, a great source of strain if they are combined with decision latitude, i.e., influence on one's own work, since this influence enables a person to adequately meet the demands to which he or she is subject.

From 1981 on, a number of studies investigated the effect of job strain on CHD risk.[6,7,9,29,30,83,86,88,103,114–116,119,124,148,218,247,260,265] In the area of stress at work and CHD, these studies constitute the largest group using a common conceptual model.[125,144,226] Some recent studies found a high CHD risk mainly in workers exposed to low decision latitude.[29,30,86,116,247,265] Others found little effect.[9,103,218] Some studies also found that low social support at work had a main effect on CHD and could amplify the effect of job strain on CHD risk.[114,115]

Few of the previous studies were conducted among women. Table 7 shows studies using a prospective cohort or case-control design in women. A majority (five) of these studies found that women exposed to high job strain or one of its components had significant increases in CHD risk. Three evaluated job strain using the job title method,[7,86,88] which relies on the attribution of an inferred mean score to all women having the same job title.[229] This method may lead to misclassification of exposure in that it does not take into account the within-occupational variance that can be important in many occupations.[124,229] Misclassification may lead to an underestimation of the true effect, and may explain why studies using the job title method tended to show lower relative risk (1.3–1.6) than other studies (2.5–5.0).

In two of the four studies using the individual method (reporting by the subject of her job characteristics), the measure of psychological demands[83] or decision latitude[148] was a proxy of the original job strain measure.[120] In a third study these measures were taken after the occurrence of the myocardial infarction.[197] Therefore, the

TABLE 7. Effect of Job Strain on CHD Risk in Women

Author	Year	Country	Study Design	Number of Subjects	Job Strain Evaluation Method	RR (95% CI or p Value)	
Lacroix	1984	U.S.	Cohort	389	Individual	2.9 (p ≤ .01)	(1)
Alfredsson	1985	Sweden	Cohort	319,365	Job title	1.6 (1.1–2.3)	
Haan	1988	Finland	Cohort	902	Individual	5.0 (p = .03)	(2)
Hall	1993	Sweden	Cohort	5921	Job title	1.3 (0.9–1.8)	(3)
Hammar	1994	Sweden	Case-control	4667	Job title	1.3 (1.1–1.6)	
Bosma	1997–98	England	Cohort	3413	Individual	1.7 (1.1–2.6)	(4)
Orth-Gomer	1998	Sweden	Case-control	584	Individual	2.5 (1.2–5.3)	

(1) In the subsample of clerical women, the RR was 5.2 (p < .001).

(2) The study population includes both men (N = 603) and women (N = 299).

(3) RR for women exposed to low decision latitude only. The RR for women exposed to low work social support was of similar magnitude.

(4) RR observed for women exposed to low decision latitude only. The RR for job strain exposure was 1.1 (0.8–1.7).[30]

high risk found in these studies must be interpreted with caution. In Bosma's study, the population was very specific (London civil servants); therefore the absence of an effect of job strain could be specific to this population.[30] Similar limitations, and others not mentioned here,[125,144,226] also are present in studies conducted in men.

In two studies, an elevated risk was observed only for women exposed to low decision latitude,[29,86] which parallels what has been noted previously in some studies of men. In the Hall, et al. study the combination of low decision latitude and low work social support seemed to be associated with higher risk.[86] In several studies including both women and men, the effect of job strain on CHD risk tended to be of similar magnitude in both groups.[7,30,83,88]

JOB STRAIN AND BLOOD PRESSURE

A number of studies have reported that workers exposed to high job strain had increased blood pressure.[23,130,149,159,227,228,258,259,263,276] However, null results also have been found.[4,32a,43,82,91,186,209,249,262] Studies conducted among women are presented in Table 8. Four out of six studies that used ambulatory measures of BP found an effect of job strain.[23,149,258,276] Two studies that did not were conducted on very small samples of 64[159] and 22[263] women, and the percentage of participants was either not provided[159] or very low (22%).[263] Five of six studies using casual measures of BP at rest did not find an effect of job strain.[32a,43,52,82,186] These findings demonstrate that the *type* of BP measure is an important factor explaining the discrepancy in the results. Ambulatory BP measures: (1) take into consideration the normal BP level at work and outside work rather than the level measured in a clinic-type situation; (2) control for BP variability related to the observer or to the presence of medical personnel; and (3) may have about twice the precision of a single measure. In studies using ambulatory measures, women exposed to high job strain had increases in BP of 4–7 mmHg. A similar pattern of results has been observed in studies using ambulatory BP measures in men.[149]

There is evidence that the effect of job strain on BP is persistent beyond working hours. For example, in the study by Laflamme, et al. among women holding a university degree, those exposed to high job strain had an average of 6 mmHg (p = .012) higher systolic BP than nonexposed women over the 24 hours of a working day (Fig. 4).[149] The difference was, on average, 5.5 mmHg (p < 0.05) in the morning, 10.5 mmHg (p < 0.001) in the afternoon, and 8.5 mmHg (p = .005) in the evening.

There is also some evidence of a stronger effect when duration of exposure increases. Indeed, Laflamme, et al. measured job strain at two different times (T1 and T2) with a median of 14.4 months between the two measures. Among women holding a university degree, those with high strain at both T1 and T2 had a significant elevation in systolic BP of 7.7 mmHg (p = .001), on average, over the 24 hours when compared to women unexposed at both T1 and T2 (Fig. 5). Women exposed only at T1 and women exposed only at T2 had a slight but nonsignificant elevation in BP when compared to women unexposed at both times. These findings are consistent with a larger effect on BP when duration of exposure is prolonged, and with an effect that diminishes when exposure ceases. Such findings are consistent with those observed in a 3-year longitudinal study conducted in men.[227]

Most available studies on job strain and BP are cross-sectional. The cross-sectional design is subject to differential selection and information bias.[45] For example, it is plausible that individuals employed in high-strain jobs will tend to move, in time, to a low-strain job. Evidence of such a selection effect has been found.[149]

TABLE 8. Effect of Job Strain on Blood Pressure in Women

Author	Year	Country	Study Design	Number of Subjects	BP Evaluation Method	Differences in BP Between Exposed and Nonexposed (mmHg)		
						Diastolic (95% CI or p value)	*Systolic (95% CI or p value)*	
Theorell	1988	Sweden	Cohort	22	Ambulatory	N.S.	4 (N.S.)	(1)
Chapman	1990	Australia	Cohort	534	Casual	N.S.	N.S.	
Netterstrom	1991	Denmark	Cross-sectional	1209	Casual	–.4 (N.S.)	1.7 (N.S.)	(2)
Van Egeren	1992	U.S.	Cross-sectional	37	Ambulatory	4.0 ($p = .04$)	12.0 ($p = .001$)	(3)
Light	1992	U.S.	Cross-sectional	64	Ambulatory	–2.2 (N.S.)	–1 (N.S.)	
Theorell	1993	Sweden	Cross-sectional	56	Ambulatory	3.7 ($p < .05$)	4.4 ($p < .05$)	(4)
Blumenthal	1995	U.S.	Cross-sectional	38	Ambulatory	N.S.	5.0 (N.A.)	
Greenlund	1995	U.S.	Cross-sectional	601	Casual	0.2 (N.S.)	1.0 (N.S.)	(5)
Curtis	1997	U.S.	Cross-sectional	453	Casual	0.7 (–2.0–3.4)	–0.4 (–4.1–3.4)	
Laflamme	1998	Canada	Cross-sectional	71	Ambulatory	6.4 ($p = .01$)	8.0 ($p = .005$)	(6)
Brisson	1999a	Canada	Cross-sectional	212	Casual	6.5 (1.1–11.9)	N.S.	(7)
Brisson	1999c	Canada	Cross-sectional	3864	Casual	0.2 (N.S.)	0.4 (N.S.)	

N.S. = nonsignificant, N.A. = unavailable
(1) Differences between occasion with highest and lowest strain on four assessments during a 1-year followup.
(2) Study population includes both men (N = 664) and women (N = 545). Job strain evaluation based on job title yielded comparable estimates.
(3) Study population includes both men and women.
(4) Differences estimated from published article using corresponding multiple regression coefficients. Differences corresponded to an increase of 0.15 on job strain score as observed between female physicians (low) and waitresses (high) in a previous study.[260]
(5) Results observed among black women. Similarly, no effect observed among white women.
(6) Results observed among university-educated women (N = 71). No effect observed among women without a university degree (N = 139).
(7) Results observed in women who had children (N = 212). No effect observed in women without children (N = 150). For all women (N = 362), the difference was 4.1 (0.6–7.6) for diastolic BP. Similar trends observed for systolic BP, although not statistically significant.

Indeed, in that study, twice as many women moved to another job among women exposed to high strain (23.8%) as among those exposed to low strain (12.4%) at T1 ($p = .003$). If job strain is related to higher BP, this selection effect may lead to an underestimation of the true association in cross-sectional studies. The absence of an association among less-educated women also could be due to selection.

The increases in BP observed in women exposed to high job strain are clinically significant. Indeed, it has been demonstrated in a meta-analysis of nine prospective studies conducted among women and men that a persistent elevation of 5 mmHg of diastolic BP increases the risk of strokes by 34% and the risk of coronary heart disease by 21%.[166] The association between daytime ambulatory BP and these disease endpoints is stronger than that of casual BP.[201]
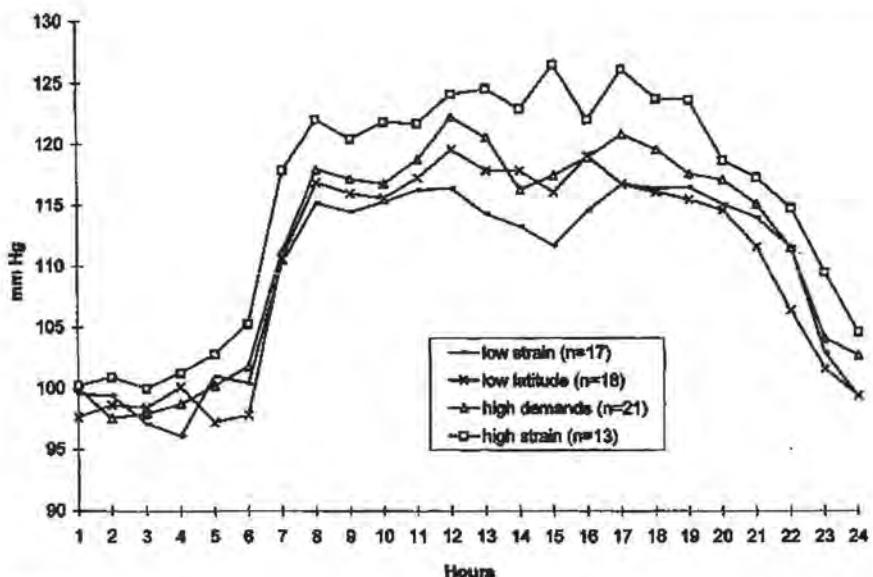
FIGURE 4. Hourly mean systolic blood pressure by current job strain exposure among white-collar women holding a university degree (1 mmHg ≈ 0.133 kPa). (From Laflamme N, Brisson C, Moisan J, et al: Job strain and ambulatory blood pressure among female white-collar workers. Scand J Work Environ Health 24(5):334–343, 1998; with permission.)
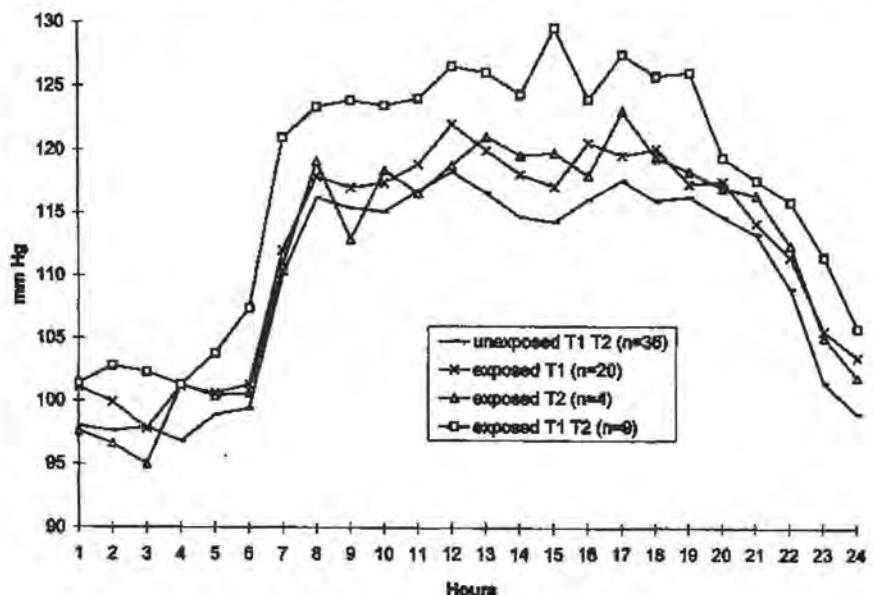
FIGURE 5. Hourly mean systolic BP by cumulative job strain exposure among white-collar women holding a university degree (T1 = 1991–1993, T2 = 1993–1994, 1 mmHg ≈ 0.133 kPa). (From Laflamme N, Brisson C, Moisan J, et al: Job strain and ambulatory blood pressure among female white-collar workers. Scand J Work Environ Health 24(5):334–343, 1998; with permission.)

Little is known about the long-term effect of job strain on BP in women or men. Indeed, very few of the previous studies used a prospective design or evaluated the effect of exposure duration. Well-designed prospective studies are needed to evaluate the effect of prolonged exposure to job strain and the effect of exposure withdrawal on BP. The issue of exposure withdrawal is particularly relevant for assessing the potential benefits of intervention studies aimed at reducing job strain in the workplace.

JOB STRAIN AND OTHER CARDIOVASCULAR RISK FACTORS

Psychosocial factors at work may contribute to the risk of CVD by the adoption of unhealthy behaviors (e.g., smoking, sedentary activity, high fat intake).[226] A number of studies found that some psychosocial factors at work were associated with the prevalence[9,98,113,121] or the intensity[81,98,176,283] of smoking; the prevalence of sedentary behavior[98,113]; and obesity.[78,98] However, null results also have been observed.[107,151,176,186,209] Studies largely are conducted among men. Only one previous study used a prospective design.[151]

In studies conducted among women, job strain was not consistently associated with CVD risk factors. None of the four studies on the association with smoking found an effect.[31,82,98,186] However, the prevalence of smoking was associated with psychological demands in two studies.[31,98] Two studies observed that women with high job strain had a higher BMI than nonexposed women.[98,186] However, other studies failed to find an association.[31,280] Job strain was not associated with cholesterol (total and HDL)[186] or high fat intake.[98] Brisson[31] found an association between job strain and sedentary behavior, but Hellerstedt[98] did not. Sedentary behavior was associated with lower decision latitude[98,113] and with psychological demands.[113] The two studies on plasma fibrinogen observed an association with high job strain[186] and with low job control.[36]

TABLE 9. Effect of Job Strain and Family Load in White-Collar Women

Time Period	High FL	High Job Strain	n	Systolic BP (mmHg)	Diastolic BP (mmHg)
Work 9h–16th	no	no	42	116.3 ± 1.2	74.3 ± 1.0
	no	yes	7	119.7 ± 3.0	77.8 ± 2.4
	yes	no	14	119.9 ± 2.1	76.3 ± 1.7
	yes	yes	6	127.3 ± 3.2**	80.6 ± 2.6*
Evening 17h–21h	no	no	42	116.7 ± 1.2	74.4 ±1.0
	no	yes	7	119.1 ± 3.0	76.5 ± 2.4
	yes	no	14	119.1 ± 2.1	74.9 ± 1.7
	yes	yes	6	128.6 ± 3.3***	81.2 ± 2.6*
Night 0h–6h	no	no	42	98.6 ±1.0	57.8 ± 0.9
	no	yes	7	98.8 ± 2.5	58.0 ± 2.1
	yes	no	14	100.2 ± 1.8	58.7 ± 1.5
	yes	yes	6	105.4 ± 2.7*	63.4 ± 2.3*
All day (24 hours)	no	no	42	110.0 ± 1.0	68.4 ± 0.8
	no	yes	7	112.5 ± 2.4	71.0 ± 2.0
	yes	no	14	113.0 ± 1.7	69.9 ± 1.4
	yes	yes	6	119.7 ± 2.6***	74.7 ± 2.2**

* $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$; FL = family load.
Values are means ± standard errors adjusted for age, smoking, and use of oral contraceptives. Exposed categories are compared with the reference category (first category of each variable). Significance of the differences is estimated by Student's t test.
From Brisson C, Laflamme N, Moisan J, et al: Effect of family responsibilities and job strain on ambulatory blood pressure among white-collar women. Psychosom Med 61(2):205–213, 1999; with permission.

JOB STRAIN AND FAMILY RESPONSIBILITIES

Several authors have reported that the high prevalence of job strain in women and its combination with large-family responsibilities may lead to high CV risk.[72,85,96,117,153,163,226] In the Framingham study, employed women who had three or more children had a higher incidence of CV diseases than employed women who had no children or than housewives with three or more children.[97] Frankenhaeuser has shown that among women managers, BP remained elevated in the evening after work, unlike men managers, who showed a decrease.[72] Brisson, et al. found that, among women having children, those exposed to high strain had a significant increase in diastolic BP, while among women without children, little effect was observed.[33]

In another study, Brisson, et al. investigated specifically the combined effect of high job strain and large-family responsibilities on ambulatory BP.[32] Significant effects were found among white-collar women holding a university degree (Table 9). The combined exposure of large-family responsibilities and high job strain tended to have a greater effect on BP than the exposure to either one of these factors. The combination of large-family responsibilities and high job strain was associated with higher systolic and diastolic BPs for all three periods (work, evening, and night), which also suggests a persistent effect beyond the work setting. Family responsibilities were measured with a composite index taking into account the presence of children, their age, and the proportion of domestic work performed. Further studies are needed to evaluate the combined effect of large-family responsibilities and high job strain on BP and the possible modifying effect of education on these associations.

Effort-Reward Imbalance at Work and Cardiovascular Outcomes

The Effort-Reward Imbalance Model was developed by Siegrist to explore adverse health effects of psychosocial factors at work. This model defines stressful experience at work as an imbalance between high effort spent and low reward received.[233] Effort comes from two sources: an extrinsic source (the demands of the job) and an intrinsic source (the motivation of the individual worker). Rewards at work are distributed in money, esteem, and status control.[233]

In the Whitehall study, Bosma, et al. have observed that this model and the decision latitude dimension from Karasek's model had independent effects,[30] suggesting the complementarity of the two models. The Swedish WOLF Study found that women who exercised high effort at work but received not enough reward had a higher prevalence of hypertension than other women (adjusted OR 1.6, 95% CI, 0.9–2.7).[202] This study also found that high intrinsic effort (overcommitment) was related to increased LDL-cholesterol in women (POR 1.4, 95% CI, 1.1–1.8).

Other Job Conditions and Cardiovascular Diseases

Shiftwork[47,256,270] and long working hours[64,95,274] have been associated with CVD in studies conducted among men. Few studies were conducted in women. In a case-control study, Knutsson, et al. found that women exposed to shiftwork had higher risk of MI than unexposed women (OR 1.3, 95% CI, 0.9–1.8 for women aged 45–70 and OR 3, 95% CI, 1.4–6.5 for women aged 45–55).[134] Alfredsson, et al. reported that at 1-year followup, the SMR for hospitalization for MI was 131 (95% CI, 105–162) for women working in occupations with long working hours and 152 (95% CI, 119–191) for women in occupations with irregular working hours.[7] For men, moderate overtime was a protective factor against hospitalization for MI. This gender difference could be explained by the fact that it may be more difficult for women to combine their family responsibilities with overtime.[161,179]

In another prospective study, the age-adjusted relative risk of CHD was 1.4 (95% CI, 1.1–1.8) in nurses who reported ever doing shiftwork. This excess risk persisted after adjustment for smoking and other CV risk factors. Among nurses reporting 6 or more years of shiftwork, the adjusted relative risk was 1.5 (95% CI, 1.1–2.0).[127] Brugère, et al. have observed no association between shiftwork and the prevalence of hypertension among 8928 women followed by occupational medicine specialists.[35]

HIGH-RISK OCCUPATIONS FOR CARDIOVASCULAR DISEASE
by Finn Tüchsen, MSc

The burden of CVD is unequally distributed across various occupations. The identification of occupational groups at high cardiac risk can be extremely helpful in generating etiologic hypotheses. Culpable single factors, e.g., exposure to carbon disulfide, and more complex psychosocial exposures, e.g., work comprising high psychological demand and low decision latitude, might be identified. However, combined exposures or some measure of total occupational burden (see Chapter 3) may best explain why certain occupations consistently show high risk of CVD.

Knowledge about occupational exposures and CVDs can be obtained from studies within a single occupation, insofar as there is sufficient variance, as well as from studies comparing one occupation with a reference occupation and studies comparing all occupations with a common standard. Each of these designs has strengths and weaknesses. The following pages focus on the latter study design.

Mortality and Morbidity Studies of "All" Occupations

EARLY STUDIES USING PROPORTIONAL MORTALITY RATIOS

Information from the Great Britain decennial census has been used together with national death registration data to study socioeconomic differences in mortality.[184] The first study of disease-specific mortality by occupation was published in 1851, and since then updates have been published every 10 years.[196] This design is not very reliable for CVD, however, because the proportional mortality ratio (PMR) measure should only be used for rare diseases. Another serious problem is that the occupational title is taken from the death certificate, and the title might be a consequence of the disease rather than a valid proxy measure for the occupational exposure. The most recent update illustrates clearly these methodological problems. For men, the occupation with the highest PMR was clergymen (PMR 120). The authors concluded: "The ranking of PMRs did not point to any obvious occupational hazards, and the jobs at the top of the ranking were not those that would be considered unusually stressful. Nor were they sedentary occupations." The problem with this design is that CVD accounts for one third of the mortality of the men and 23% for the women. As expected, the differentiation in PMR was low among men and higher among women. The highest PMR found was 178 among female railway signal workers. Larger differentials were observed for rarer diseases, like stroke.

A NEW GENERATION OF STUDIES BASED ON CENSUS DATA

A new generation of mortality and/or morbidity studies based on census data in Denmark,[53,272] Norway,[28] Finland,[167,191,225] and Sweden[7,88,89] has successfully overcome the aforementioned shortcomings. Additional studies come from West

Germany[27] and Western Australia.[279] Information on occupation is collected prior to and independently of followup for death, and there is practically no loss to followup. While the Nordic studies followed the entire population, a comparable longitudinal study covering England and Wales was based on a 1% sample.[79] These cohort studies with a 5-year and later a 10-, 15- and 20-year followup may control well for the "healthy worker" effect. Furthermore, some of them use the economically active and not the entire population as their standard population. This is especially important when studying CVD because of the very strong selection effect of these diseases.

Data from all five Nordic countries also have been pooled into one data set.[190] The occupations had to be aggregated to 55 broad occupations because there were some differences in the detailed classifications between the countries. In Italy, a cross-sectional mortality study was published in 1995, together with a followup study of morbidity.[49,271] Recently, Danish and Swedish data were pooled to obtain better estimates for occupations with few employees.[5] The study supported the hypothesis that working in a brewery, cannery, slaughterhouse, or dairy, or in the chemical, paper, or rubber and plastics industries may lead to increased risk of MI. Alfredsson, et al. also draw our attention to the large differences among occupational groups. In a case control study including most of the Swedish population, they found a nine-fold higher risk in metal process workers (RR 2.8) than judges (R 0.3).[145]

All these studies may produce positive findings due to chance and multiple comparisons. One way to avoid such misinterpretations is to focus on the occupations found to be at high risk in more than one country or study (Table 10).

Professional Drivers: The Most Consistent Evidence of Elevated Risk. In these studies, professional drivers, particularly urban transport operators, emerge as the workers with the most consistent evidence of elevated risk. The high risk in bus drivers has been known for several decades. A recent review cites 34 of 40 studies as confirming the increased risk of ischemic heart disease and hypertension among professional drivers.[16] These authors conclude: "Such a consistent and large body of data concerning cardiac risk does not appear to exist for any other specific occupational group." One particularly well-controlled study revealed that, after a mean of 11.8 years of followup, 103 middle-aged male mass-transit drivers in Gothenberg had an OR 3.0 (95% CI, 1.8–5.2) for incident CHD compared to 6596 men from other occupational groups, after adjusting for age, serum cholesterol, BP, smoking, body mass index (BMI), diabetes, positive family history of CHD, leisure and occupational physical activity, and sociodemographic factors.[223] Another study reported that the risk of hospitalization for stroke is also increased among professional drivers in Denmark.[269] Compared to employed referents, the age-specific standardized hospitalization ratio was 114 (95% CI, 108.2–120.4) among men and 130 (100–168) among women. Furthermore, there was a gradient of risk within the occupation that appeared to be stress-related. Netterstrom and Juel found that objective workload based on traffic intensity was a significant, independent predictor of acute MI incidence among bus drivers in Denmark.[185] For high versus low traffic intensity, the RR was 2.7 (95% CI, 0.9–7.6) in Copenhagen, and 3.4 (1.2–9.5) in the province.

Methodologic Issues

For some occupations there is conflicting or weak evidence about high risk. These null or negative studies underscore the need for more and better designed research. For example, there are conflicting findings concerning the risk in police. According to a study by Tüchsen and colleagues, it may only be higher ranking policemen who are at elevated risk for CVD.[271] It is also helpful to detect low-risk

TABLE 10. Occupations at Increased Risk of Either Acute Myocardial Infarction or Ischemic Heart Disease Mortality or Morbidity in More than One Study

Men		Women
Air traffic controllers	Lorry drivers	Bus drivers
Bakers	Paper industry workers	Cleaners
Bus drivers	Police	Home help
Butchers	Prison wardens	Rubber and plastics workers
Cannery workers	Rubber and plastics workers	Paper workers
Cooks	Ship's deck officers and	Self-employed in hotel and catering
Fire fighters	sea pilots	Taxi drivers
Fishermen	Taxi drivers	Unskilled worker in tube,
Foundry workers	Waiters	sheet, and steel construction
Hairdressers	Warehousemen, storekeepers	Waitresses

Lower limit of the 95% confidence intervals must have been > 1 for each study considered to be positive. Cohort studies: references 28, 49, 79, 167, 191, 271, 279. Case control studies: references 5, 27, 89.

groups, to maximize the risk differences among occupational groups.[5,145] Note, however, that the magnitude of the risk in such studies is not necessarily representative for the groups as a whole, because it depends on the precise definition of both the index group and the standard group.

The need for improved design also includes conducting quantitative studies of the various occupational exposures with variable degrees of exposure. There are few studies in this field that take exposure intensity and peak values into consideration. However, length of exposure has been a valuable variable in some studies. For example, the prevalence of hypertension among San Francisco Municipal Transit vehicle operators was found to increase "in a step-wise fashion" with length of exposure to that job.[214] The increase from one category to the next (pre-employment, < 10 years, 10–20 years, > 20 years) controlling for age, race, gender, BMI, and alcohol
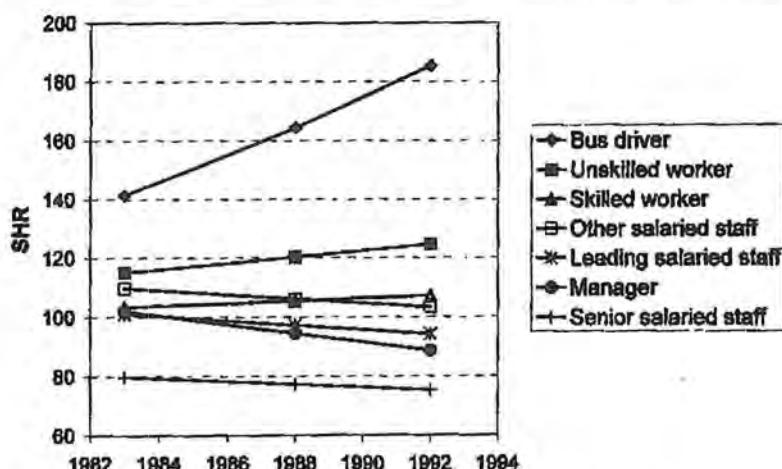
FIGURE 6. Time trend in predicted standardized hospitalization ratios due to ischemic heart disease among male employment status groups and single occupations in Denmark, 1981–1993. (From Tüchsen F, Endahl LA: Increasing inequality in ischaemic heart disease morbidity among employed men in Denmark 1981–1993: The need for a new preventive policy. Int J Epidemiol 28:640–644, 1999; with permission.

consumption showed OR 1.19 (95% CI, 1.0–1.41) for mild hypertension and OR 1.25 (1.03–1.52) for moderate to severe hypertension.

Future Analysis

One may expect that the next generation of occupational mortality and morbidity studies will focus on changes in relative risk over time. A recent study from Denmark demonstrates the potential in such analyses.[273] An unexpected increase in inequality of CHD risk over time was found (Fig. 6). Bus drivers not only had a high risk, but the risk was increasing. These results convinced Danish authorities that a large-scale workplace health promotion program among bus drivers had to be initiated; such a program is now in progress in Copenhagen.

REFERENCES

1. The world's women 1970–1990: Trends and statistics. New York, United Nations, 1991.
2. Akerstedt T, Knutsson A, Alfredsson L, Theorell T: Shift work and cardiovascular disease. Scand J Work Environ Health 10:409–414, 1984.
3. Akhtar MJ, al-Nozha M, Al-Harthi S, Noah M: Electrocardiographic abnormalities in patients with heat stroke. Chest 104:411–414, 1993.
4. Albright CL, Winkleby MA, Ragland DR, et al: Job strain and prevalence of hypertension in a biracial population of urban bus drivers. Am J Public Health 82:984–989, 1992.
5. Alfredsson L, Bach E, Hammar N, Tuchsen F: Acute myocardial infarction in selected occupations in Denmark and Sweden. Copenhagen, Nordic Council of Ministers. TemaNord: 507, 1996.
6. Alfredsson L, Karasek R, Theorell T: Myocardial infarction risk and psychosocial work environment: An analysis of the male Swedish working force. Soc Sci Med 16:463–467, 1982.
7. Alfredsson L, Spetz C, Theorell T: Type of occupation and near-future hospitalization for myocardial infarction and some other diagnoses. International Journal of Epidemiology 14:378–388, 1985.
8. Alfredsson L, Theorell T: Job characteristics of occupations and myocardial infarction risk: Effect of possible confounding factors. Soc Sci Med 17:1497–1503, 1983.
8a. Al-Nashash H, Qassem W, Zabin A, Othman M: ECG response of the human body subject to vibrations. J Med Eng Technol 20:2–10, 1996.
9. Alterman T, Shekelle RB, Vernon SW, Burau KD: Decision latitude, psychologic demand, job strain and coronary heart disease in the Western Electric Study. Am J Epidemiol 139:620–627, 1994.
10. American Heart Association: Job strain not a predictor of heart attack in patients. NR:95-4308, 1995.
11. Angersbach D, Knauth P, Loskant H, et al: A retrospective cohort study comparing complaints and diseases in day and shift workers. Int Arch Occup Environ Health 45:127–140, 1980.
12. Anker R: Gender and jobs: Sex segregation of occupations in the world. Geneva, International Labour Office, 1998.
13. Axelson O, Seleden A, Andersson K, Hogstedt C: Updated and expanded Swedish cohort study on trichloroethylene and cancer risk. JOM 36:556–562, 1994.
14. Baumgart P, Walger P, Fuchs G, et al: Diurnal variations of blood pressure in shift workers during day and night shifts. Int Arch Occup Environ Health 61:463–466, 1989.
15. Beaglehole R, Stewart AW, Jackson R, et al: Declining rates of coronary heart disease in New Zealand and Australia, 1983–1993. Am J Epidemiol 145:707–713, 1997.
16. Belkic K, Emdad R, Theorell T: Occupational profile and cardiac risk: Possible mechanisms and implications for professional drivers. Int J Occup Med Environ Health 11:37–57, 1998.
17. Belkic K, Savic C, Theorell T, et al: Mechanisms of cardiac risk among professional drivers. Scand J Work Environ Health 20:73–86, 1994.
18. Ben-David A: Cardiac arrest in an explosives factory worker due to withdrawal from nitroglycerin exposure. Am J Ind Med 15:719–722, 1989.
19. Beniamini Y, Rubenstein JJ, Faigenbaum AD, et al: High-intensity strength training of patients enrolled in an outpatient cardiac rehabilitation program. J Cardiopulm Rehabil 19:8–17, 1998.
20. Biernat M, Wortman CB: Sharing of home responsibilities between professionally employed women and their husbands. J Pers Soc Psychol 60:844–860, 1991.
21. Billing E, Hjemdahl P, Rehnqvist N: Psychosocial variables in female vs male patients with stable angina pectoris and matched healthy controls. Eur Heart J 18:911–918, 1997.
22. Blair A, Hartge P, Stewart PA, et al: Mortality and cancer incidence of aircraft maintenance workers exposed to trichloroethylene and other organic solvents and chemicals: Extended follow up. Occup Environ Med 55:161–171, 1998.
23. Blumenthal JA, Thyrum TE, Siegel WC: Contribution of job strain, job status and marital status to laboratory and ambulatory blood pressure in patients with mild hypertension. J Psychosom Res 39:133–144, 1995.
24. Bobak M, Hertzman C, Skodova Z, Marmot M: Association between psychosocial factors at work and non-fatal MI in a population based case-control study in Czech men. Epidemiology 9:43–47, 1998.
25. Bøggild H, Knutsson A: Shift work, risk factors, and cardiovascular disease. Scand J Work Environ Health 25:85–89, 1999.
26. Bøggild H, Suadicani P, Hein J, Gyntelberg F: Shift-work, social class, and ischemic heart disease in middle-aged and elderly men: A 22-year follow-up in the Copenhagen Male Study. (In press), 1999.

27. Bolm-Audorff U, Siegrist J: Occupational morbidity data in myocardial infarction. A case-referent study in West Germany. J Occup Med 25:367–371, 1983.
28. Borgan J-K, Kristoffersen LB: Dodelighet i yrker og sociookonomiske grupper 1970–1980. Oslo, Statistick sentralbyra, 1986.
29. Bosma H, Marmot MG, Hemingway H, et al: Low job control and risk of coronary heart disease in Whitehall II (prospective cohort) study. Br Med J 314:558–565, 1997.
30. Bosma H, Peter R, Siegrist J, Marmot M: Two alternative job stress models and the risk of coronary heart disease. Am J Public Health 88:68–74, 1998.
31. Brisson C, Larocque B, Moisan J, et al: Psychosocial constraints at work, smoking, sedentary behavior and body mass index: A prevalence study among 8,000 white collar workers. J Occup Environ Med (accepted), 1999c.
32. Brisson C, Laflamme N, Moisan J, et al: Effect of family responsibilities and job strain on ambulatory blood pressure among white-collar women. Psychosomatic Medicine 61:205–213, 1999d.
32a. Brisson C, Laflamme N, Moisan J, et al: Job strain and blood pressure at rest: A cross-sectional study among 4000 white-collar women (submitted) 1999e.
33. Brisson C, Laflamme N, Vezina M: Job strain and blood pressure in a random population sample of women. Am J Industr Med (accepted), 1999a.
34. Brisson C, Larocque B, Laflamme N, et al: Les contraintes psychosociales chez les Canadiennes et les Canadiens. (submitted), 1999b.
35. Brugere D, Barrit J, Butat C, et al: Shiftwork, age, and health, an epidemiologic investigation. In J Occup Environ Health 3(Suppl 2):S15–S19, 1997.
36. Brunner EJ, Smith GD, Marmot MG, et al: Childhood social circumstances and psychosocial and behavioral factors as determinants of plasma fibrinogen. Lancet 347:1008–1013, 1996.
37. Buell P, Breslow L: Mortality from CHD in California men who work long hours. J Chron Dis 11:615–625, 1960.
38. Bursey R: A cardiovascular study of shift workers with respect to coronary artery disease risk factor prevalence. J Soc Occup Med 40:65–67, 1990.
39. Cahill J, Landsbergis PA: Job strain among post office mailhandlers. Int J Health Serv 26:731–750, 1996.
40. Carrere S, Evans GW, Palsane MN, Rivas M: Job strain and occupational stress among urban public transit operators. J Occup Psychol 64:305–316, 1991.
41. Cesana G, Ferrario M, Sega R, et al: Job strain and ambulatory blood pressure levels in a population-based employed sample of men from northern Italy. Scand J Work Environ Health 22:294–305, 1996.
42. Channer KS, Papouchado M, James MA, Rees JR: Anxiety and depression in patients with chest pain referred for exercise testing. Lancet 2:818–823, 1985.
43. Chapman A, Mandryk JA, Frommer MS, et al: Chronic perceived work stress and blood pressure among Australian government employees. Scand J Work Environ Health 16:258–269, 1990.
44. Chau N, Mallion J, de Gaudemaris R, et al: Twenty-four-hour ambulatory blood pressure in shift workers. Circulation 80:341–347, 1989.
45. Checkoway H, Pearce NE, Crawford-Brown DJ: Research Methods in Occupational Epidemiology. New York, Oxford University Press, 1989.
45a. Chen CJ, Chiou HY, Chiang MH, et al: Dose-response relationship between ischemic heart disease mortality and long-term arsenic exposure. Arterioscler Thromb Vasc Biol 16:504–510, 1996.
46. Corley KC, O'Shiel F, Mauck HP: Myocardial degeneration and cardiac arrest in squirrel monkeys. Physiologic and psychologic correlates. Psychophysiology 14:322–328, 1977.
47. Costa G: The problem: Shiftwork. Chronobiology International 14:89–98, 1997.
48. Costa G, Betta A, Uber D, Alexopoulos C: Estimate of coronary risk in a group of Italian shiftworkers. In Costa G, Cesana G, Kogi K, Wedderburn A (eds): Shiftwork: Health, Sleep, and Performance. New York, Peter Lang, 1990. pp 363–369.
49. Costa G, Lagorio S, Faggiano F: Mortalita per professione in Italia negli anni '80. Roma, ISPELS (Collana Quaderni ISPELS no. 2), 1995.
50. Costrini AM, Pitt HA, Gustafson AB, Uddin DE: Cardiovascular and metabolic manifestations of heat stroke and severe heat exhaustion. Am J Med 66:296–302, 1979.
51. Cunningham SR, Dalzell GWN, McGirr P, Khan MM: Myocardial infarction and primary ventricular fibrillation after glue sniffing. Brit Med J 294:739, 1987.
52. Curtis AB, James SA, Raghunathan TE, Alcser KH: Job strain and blood pressure in African Americans: The Pitt County Study. Am J Public Health 97:1297–1302, 1997.
53. Danmarks Statistick: Dodelighed og erhverv 1970–75. Copenhagen, Danmarks Statistik, 1979.
54. Donaldson GC, Ermakov SP, Komarov YM, et al: Cold related mortalities and protection against cold in Yakutsk, eastern Siberia: Observation and interview study. BMJ 317:978–982, 1998.
55. Donaldson GC, Robinson D, Allaway SL: An analysis of arterial disease mortality and BUPA health screening data in men, in relation to outdoor temperature. Clin Sci (Colch) 92:261–268, 1997.
56. Drever F, Whitehead M, Roden M: Current patterns and trends in male mortality by social class (based on occupation). Population Trends 86:15–20, 1996.
57. Drexler H, Ulm K, Hardt R, et al: Carbon disulphide. IV. Cardiovascular function in workers in the viscose industry. Int Arch Occup Environ Health 69:27–32, 1996.
58. Dwyer EM, Turino GM: Carbon monoxide and cardiovascular disease. N Engl J Med 21:1474, 1989.
59. Eaker ED: Myocardial infarction and coronary death among women: Psychosocial predictors from a 20-years follow-up of women in the Framingham study. Am J Epidemiol 135:854–864, 1992.
60. Eaker ED: Psychosocial risk factors for coronary heart disease in women. Cardiology Clinics 16:103–111, 1998.
61. Edling C, Ohlson C-G, Ljungkvist G, et al: Cardiac arrhythmia in refrigerator repairmen exposed to fluorocarbons. Brit J Ind Med 47:207, 1990.

61a. Egan CE, Espie BH, McGrann S, et al: Acute effects of vibration on peripheral blood flow in healthy subjects. Occup Environ Med 53:663–669, 1996.

62. Egeland GM, Bloom TF, Schnorr TM, et al: Fluorocarbon 113 exposure and cardiac dysrhythmias among aerospace workers. AJIM 22:851–857, 1992.

63. Emdad R, Belkic K, Theorell T, Cizinsky S: What prevents professional drivers from following physicians' cardiologic advice? Psychoth Psychosom 67:226–240, 1998.

64. Emdad R, Belkic K, Theorell T, et al: Work environment, neurophysiologic and psychophysiologic models among professional drivers with and without cardiovascular disease: Seeking an integrative neurocardiologic approach. Stress Med 13:7–21, 1997.

65. European Heart Network: Social factors, work, stress and cardiovascular disease prevention in the European Union. Brussels, Belgium, The European Heart Network, 1998.

66. Eurowinter Group: Cold exposure and winter mortality from ischaemic heart, cerebrovascular disease, respiratory disease, and all causes in warm and cold regions of Europe. Lancet 349:1341–1346, 1997.

67. Everson SA, Lynch JW, Chesney MA, et al: Interaction of workplace demands and cardiovascular reactivity in progression of carotid atherosclerosis: Population based study. British Medical J 314:553–558, 1997.

68. Falger PRJ, Schouten EGW: Exhaustion, psychologic stress in the work environment and acute myocardial infarction in adult men. J Psychosom Res 36:777–786, 1992.

69. Falkeborn M, Persson I, Terent A, et al: Long-term trends in incidence and mortality from acute myocardial infarction and stroke in women: Analyses of total first events and of deaths in the Uppsala Health Care Region, Sweden. Epidemiology 7:67–74, 1996.

70. Fogari R, Zoppi A, Vanasia A, et al: Occupational noise exposure and blood pressure. J Hypertens 12:475–479, 1994.

71. Forsman L: Individual and group differences in psychophysiological responses to stress with emphasis on sympathetic-adrenal medullary and pituitary-adrenal cortical responses. Department of Psychology. Stockholm, University of Stockholm, 1983.

72. Frankenhaeuser M, Lundberg U, Fredriksson M, et al: Stress on and off the job as related to sex and occupational status in white-collar workers. J Organizational Behav 10:321–346, 1989.

73. Fraser GE: Preventive Cardiology. New York, Oxford University Press, 1986.

74. Fredriksson M, Sundin O, Frankenhaeuser M: Cortisol excretion during the defence reaction in humans. Psychosom Med 47:313–319, 1985.

75. Friedlander BR, Hearne FT: Epidemiological investigation of employees chronically exposed to methylene chloride. J Occup Med 20:657, 1978.

76. Friedman M, Rosenman RH, Carroll V: Changes in the serum cholesterol and blood clotting time in men subjected to cyclic variations of occupational stress. Circulation 17:852–861, 1958.

77. Garcia-Rubira JC, Aguilar J, Romero D: Acute myocardial infarction in a young man after heat exhaustion. Int J Cardiol 47:297–300, 1995.

78. Georges E, Wear ML, Mueller WH: Body fat distribution and job stress in Mexican-American men of the Hispanic Health and Nutrition Examination Survey. Am J Human Biol 4:657–667, 1992.

79. Goldblatt P: Longitudinal Study 1971–1981. Mortality and Social Organisation. London, Office of Population Censuses and Surveys (HMSO, Series LS no. 6), 1990.

80. Gordon N, Cleary P, Parker C, Czeisler C: The prevalence and health impact of shiftwork. Am J Pub Health 76:1225–1228, 1986.

80a. Goyer RA: Lead toxicity: Current concerns. Environ Health Perspect 100:177–187, 1993.

81. Green KL, Johnson JV: The effects of psychosocial work organization on patterns of cigarette smoking among male chemical plant employees. Am J Public Health 80:1368–1371, 1990.

82. Greenlund KJ, Liu K, Knox S, et al: Psychosocial work characteristics and cardiovascular disease risk factors in young adults: The CARDIA study. Coronary Artery Risk Disease in Young Adults. Soc Sci Med 41:717–723, 1995.

83. Haan MN: Job strain and ischaemic heart disease: An epidemiologic study of metal workers. Ann Clin Res 20:143–145, 1988.

84. Hall EM: Gender, work control and stress: A theoretical discussion and an empirical test. Int J Health Sci 19:725–745, 1989.

85. Hall EM: Double exposure: The combined impact of the home and work environments on psychosomatic strain in Swedish women and men. Int J Health Services 22:239–260, 1992.

86. Hall EM, Johnson JV, Tsou TS: Women, occupation, and risk of cardiovascular morbidity and mortality. Occup Med 8:709–719, 1993.

87. Hallqvist J, Diderichsen F, Theorell T, et al: The SHEEP Study Group: Is the effect of job strain on myocardial infarction due to interaction between high psychological demands and low decision latitude? Results from Stockholm Heart Epidemiology Program (SHEEP). Soc Sci Med 46:1405–1415, 1998.

88. Hammar M, Alfredsson L, Theorell T: Job characteristics and the incidence of myocardial infarction: A study of men and women in Sweden, with particular reference to job strain. Int J Epidemiol 23:277–284, 1994.

89. Hammar N, Alfredsson L, Smedberg M, Ahlbom A: Differences in the incidence of myocardial infarction among occupational groups. Scand J Work Environ Health 18:178–185, 1992.

90. Hansen ES: A cohort study on the mortality of firefighters. Brit J Ind Med 47:805, 1990.

91. Harenstam A, Theorell T: Work conditions and urinary excretion of catecholamines: A study of prison staff in Sweden. Scand J Work Environ Health 14:257–264, 1988.

92. Harma M: New work times are here—are we ready (editorial). Scand J Work Environ Health 24 Suppl 3:3–6, 1998.

93. Harma M: Individual differences in tolerance to shiftwork: A review. Ergonomics 35:101–109, 1993.

94. Hatt S: Gender, work and labour markets. Suffolk, Ipswich Book, 1997.

95. Hayashi T, Kobayashi Y, Yamaoka K, Yano E: Effect of overtime work on 24-hour ambulatory blood pressure. J Occup Environ Med 38:1007–1011, 1996.

96. Haynes SG: The effect of job demands, job control, and new technologies on the health of employed women. A review. In Frankenhaeuser M (ed): Women, Work, and Health: Stress and Opportunities. New York, Plenum Press, 1991, pp 157–169.
97. Haynes SG, Feinleib M: Women, work and coronary heart disease: Prospective findings from the Framingham Heart Study. Am J Public Health 70:133–141, 1980.
98. Hellerstedt WL, Jeffery RW: The association of job strain and health behaviours in men and women. Int J Epidemiol 26:575–583, 1997.
99. Hermann HJ, Rohde HG, Schulze W, et al: Effects of noise stress and ethanol intake on hearts of spontaneously hypertensive rats. Basic Res Cardiol 89:510–523.
100. Hernberg S: Evaluation of epidemiologic studies in assessing the long term effects of occupational noxious agents. Scand J Work Environ Health 6:163–169, 1980.
101. Hessel PA, Sluis-Cremer GK: Occupational noise exposure and blood pressure: Longitudinal and cross-sectional observations in a group of underground miners. Arch Environ Health 49:128–134, 1994.
102. Higgins M, Thom T: Trends in CHD in the United States. International Journal of Epidemiology 18:s58–s66, 1989.
103. Hlatky MA, Lam LC, Lee KL, et al: Job strain and the prevalence and outcome of coronary artery disease. Circulation 92:327–333, 1995.
104. Hobbesland A, Kjuus H, Thelle DS: Mortality from cardiovascular diseases and sudden death in ferroalloy patients. Scand J Work Environ Health 23:334–341, 1997.
105. Hogstedt C, Andersson K: A cohort study of mortality among dynamite workers. J Occup Med 21:553, 1979.
106. Hogstedt C, Axelson O: Mortality from cardio-cerebrovascular diseases among dynamite workers—an extended case-referent study. Ann Acad Med Singapore 13(Suppl 2):399–403, 1984.
107. House JS, Strecher V, Metzner HL, Robbins CA: Occupational stress and health among men and women in the Tecumseh Community Health Study. J Health Soc Beh 27:62–77, 1986.
108. Howard G, Goff D: A call for caution in the interpretation of the observed smaller relative importance of risk factors in the elderly. Ann Epidemiol 8:411–414, 1998.
109. Hulley SB, Cummings SR: Designing Clinical Research: An Epidemiologic Approach. Baltimore, Williams & Wilkins, 1988.
110. Ishizaki M, Tsuritani I, Noborisaka Y, et al: Relationship between job stress and plasma fibrinolytic activity in male Japanese workers. Int Arch Occup Environ Health 68:315–320, 1996.
111. Iwaski K, Sasaki T, Oka T, Hisanaga N: Effect of working hours on biological functions related to cardiovascular system among salesmen in a machinery manufacturing company. Ind Health 36:361–367, 1998.
112. Jankovic J, et al: Environmental study of firefighters. Ann Occup Hyg 35:581–602.
113. Johansson G, Johnson JV, Hall EM: Smoking and sedentary behavior as related to work organization. Soc Sci Med 32:837–846, 1991.
114. Johnson JV, Hall EM: Job strain, workplace social support, and cardiovascular disease: A cross-sectional study of a random sample of the Swedish working population. Am J Public Health 78:1336–1342, 1988.
115. 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 15:271–279, 1989.
116. Johnson JV, Stewart W, Hall EM, et al: Long-term psychosocial work environment and cardiovascular mortality among Swedish men. Am J Public Health 86:324–331, 1996.
117. Jones F, Bright JEH, Searle B, Cooper L: Modelling occupational stress and health: The impact of the demand-control model on academic research and on workplace practice. Stress Med 14:231–236, 1998.
118. Kaplan GA, Keil JE: Socioeconomic factors and CVD: A review of the literature. Circulation 88:1973–1998, 1993.
119. Karasek R, Baker D, Marxer F, Ahlbom A, Theorell T: Job decision latitude, job demands, and cardiovascular disease: A prospective study of Swedish men. Am J Public Health 71:694–705, 1981.
120. Karasek R, Brisson C, Kawakami N, et al: The Job Content Questionnaire (JCQ): An instrument for internationally comparative assessments of psychosocial job characteristics. J Occup Health Psychology 3:322–355, 1998.
121. Karasek R, Gardell B, Lindell J: Work and nonwork correlates of illness and behaviour in male and female Swedish white collar workers. J Occup Behav 8:187–207, 1987.
122. Karasek R, Theorell T: Healthy Work: Stress, Productivity, and the Reconstruction of Working Life. New York, Basic Books, 1990.
123. Karasek RA: Job demands, job decision latitude and mental strain: Implications for job redesign. Adm Sci Q 24:285–308, 1979.
124. Karasek RA, Theorell T, Schwartz JE, et al: Job characteristics in relation to the prevalence of myocardial infarction in the U.S. Health Examination Survey and the Health and Nutrition Examination Survey. Am J Public Health 78:910–918, 1988.
124a. Kaski JC, Crea F, Meran D, et al: Local coronary supersensitivity to diverse vasoconstrictive stimuli in patients with variant angina. Circulation 74:1255–1265, 1986.
125. Kasl SV: The influence of the work environment on cardiovascular health: A historical, conceptual, and methodological perspective. J Occup Health Psychol 1:42–56, 1996.
126. Kaufman JD, Silverstein MA, Moure-Eraso R: Atrial fibrillation and sudden death related to occupational solvent exposure. Am J Ind Med 25:731–735, 1994.
127. Kawachi I, Colditz G, Stampfer M, et al: Prospective study of shift work and risk of coronary heart disease in women. Circulation 92:3178–3183, 1995.
128. Kawachi I, Kennedy BP: Health and social cohesion: Why care about income inequality? Br Med J 314:1037–1040, 1997.
129. Kawachi I, Kennedy BP, Lochner K, Prothrow-Stith D: Social capital, income inequality, and mortality. Am J Public Health 87:1491–1498, 1997.

130. Kawakami N, Haratani T, Araki S: Job strain and arterial blood pressure, serum cholesterol, and smoking as risk factors for coronary heart disease in Japan. Int Arch Occup Environ Health 71:429–432, 1998.
131. Kawakami N, Kobayahi F, Araki S, et al: Assessment of job stress dimensions based on the job demands—Control model of employees of telecommunications and electric power companies in Japan: Reliability and validity of the Japanese version of the Job Content Questionnaire. Int J Behav Med 2:358–375, 1995.
132. Kleinman MT, Leaf DA, Kelly E, et al: Urban angina in the mountains: Effects of carbon monoxide and mild hypoxemia on subjects with chronic stable angina. Arch Environ Health 53:388–397, 1998.
133. Knox S, Theorell T, Svensson J, Waller D: The relation of social support and working environment to medical variables associated with elevated BP in young males: A structural model. Soc Sci Med 21:525–531, 1985.
134. Knutsson A, et al: Shiftwork and myocardial infarction: A case-control study. Occup Environ Med 56:46–50, 1999.
135. Knutsson A, Akerstedt T: The healthy-worker effect: Self-selection among Swedish shift workers. Work and Stress 6:163–167, 1992.
136. Knutsson A, Akerstedt T, Jonsson BG, Orth-Gomer K: Increased risk of ischaemic heart disease in shift workers. Lancet 8498:89–92, 1986.
137. Knutsson A, Akerstedt T, Jonsson B: Prevalence of risk factors for coronary artery disease among day and shift workers. Scand J Work Environ Health 14:317–321, 1988.
138. Knutsson A, Andersson H, Berglund U: Serum lipoprotein in day and shift workers: A prospective study. Br J Ind Med 47:132–134, 1990.
139. Knutsson A, Nilsson T: Tobacco use and exposure to environmental tobacco smoke in relation to certain work characteristics. Scand J Soc Med 26:183–189, 1998.
140. Koller M: Health risks related to shift work. An example of time-contingent effects of long-term stress. Int Arch Occup Environ Health 53:59–75, 1983.
141. Koskela RS: Cardiovascular diseases among foundry workers exposed to carbon monoxide. Scand J Work Environ Health 20:286–293, 1994.
142. Kosteva K: Study of the cardiovascular effects of occupational exposure to organic solvents. Int Arch Occup Environ Health 71(Suppl):S87–91, 1998.
143. Kristensen TS: The demand-control-support model: Methodological challenges for future research. Stress Medicine 11:17–26, 1995.
144. Kristensen TS: Job stress and CVD: A theoretic critical review. J Occup Health Psychol 1:246–260, 1996.
145. Kristensen TS, Kronitzer M, Alfredsson L: Social factors, work, stress and cardiovascular disease prevention. Brussels, The European Heart Network, 1998.
146. Kunst AE, Looman CWN, Mackenbach JP: Socioeconomic mortality differences in the Netherlands in 1950–1984: A regional study of cause specific mortality. Soc Sci Med 31:141–152, 1990.
147. Kuo HW, Lai JA, Lin M, Su ES: Effects of exposure to carbon disulfide (CS2) on electrocardiographic features of ischemic heart disease among viscose rayon factory workers. Int Arch Occup Environ Health 70:61–66, 1997.
148. LaCroix A, Haynes SG: Occupational exposure to high demand/low control work and coronary heart disease incidence in the Framingham cohort. Am J Epidemiol 120:481, 1984.
149. Laflamme N, Brisson C, Moisan J, et al: Job strain and ambulatory blood pressure among female white-collar workers. Scand J Work Environ Health 24:334–343, 1998.
150. Landrigan PJ: Toxicity of lead at low dose. Brit J Ind Med 46:593, 1989.
151. Landsbergis PA, Schnall PL, Deitz DK, et al: Job strain and health behaviors: Results of a prospective study. Am J Health Promo 12:237–245, 1998.
152. Landsbergis PA, Schnall PL, Warren K, et al: Association between ambulatory blood pressure and alternative formulations of job strain. Scand J Work Environ Health 20:349–363, 1994.
153. Landsbergis PA, Schurman SJ, Israel BA, et al: Job stress and heart disease: Evidence and strategies for prevention. New Solutions Summer:42–58, 1993.
154. Lantigua LJ, Sprafkin RP, Mc Croskery JH, et al: One-year psychosocial follow-up of patients with chest pain and angiographically normal coronary arteries. Am J Cardiol 62:209–213, 1988.
155. Larfargues G, Sylvaine V, Caces B, et al: Relations among night work, dietary habits, biological measures, and health status. Int J Behav Med 3:123–134, 1996.
156. Larocque B, Brisson C, Blanchette C: Coherence interne, validite factorielle et validite discriminante de la traduction francaise des echelles de demande psychologique et de latitude decisionnelle de "Job Content Questionnaire" de Karasek. Revue d'epidemiologie et de sante publique 46:371–381, 1998.
157. Le Bourdais C, Hamel PJ, Bernard P: Le travail et l'ouvrage. Charge et partage des taches domestiques chez les couples quebecois. Sociologie et Societes 19:37–55, 1987.
158. Lee IM, Paffenbarger RS Jr, Hennenkens CH: Pysical activity, physical fitness, and longevity. Aging (Milano) 9:2–11, 1997.
159. Light KC, Turner JR, Hinderliter AL: Job strain and ambulatory work blood pressure in healthy young men and women. Hypertension 20:214–218, 1992.
160. Lundberg U, Mardberg B, Frankenhaeuser M: The total workload of male and female white-collar workers as related to age, occupational level, and number of children. Scand J Psychol 35:315–317, 1994.
161. Loudoun RJ, Bohle PL: Work/non-work conflict and health in shiftwork: Relationships with family status and social support. Int J Occup Environ Health 3(Suppl 2):S71–S77, 1997.
162. Lown B: Role of higher nervous activity in sudden cardiac death. Jpn Circ J 54:581–602, 1990.
163. Lundberg U: Work and stress in women. In Orth-Gomer K, Chesney M, Wenger N (eds): Women, Stress, and Heart Disease. Mahwah, NJ, Lawrence Erlbaum Associates, 1998, pp 41–56.
164. Lynch J, Krause N, Kaplan GA, et al: Workplace demands, economic reward and progression of carotid atherosclerosis. Circulation 96:302–307, 1997a.

165. Lynch J, Krause N, Kaplan GA, et al: Work place conditions, socioeconomic status, and the risk of mortality and acute myocardial infarction: The Kuopio Ischemic Heart Disease Risk Factor Study. Am J Public Health 87:617–622, 1997b.
166. MacMahon S, Peto R, Cutler J, et al: Blood pressure, stroke, and CHD. Part 1, Prolonged differences in blood pressure: Prospective observational studies corrected for the regression dilution. Lancet 335:765–774, 1990.
167. Marin R: Occupational Mortality 1971–80. Helsinki, Tilastokeskus, 1986.
168. Mark DB, Lam LC, Lee KL, et al: Identification of patients with coronary disease at high risk for loss of employment. A prospective validation study. Circulation 86:1485–1494, 1992.
169. 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 350:235–239, 1997.
170. Marmot MG, Shipley MJ, Rose G: Inequalities in death—specific explanations of a general pattern. Lancet i:1003–1006, 1984.
171. McCammon CS, Wells VE, Glaser RA, et al: Worker exposure to methylene chloride during furniture stripping as determined by air, breath and blood samples. J Applied Ind Hyg, 1991.
172. McNamee R, Binks K, Jones S, et al: Shiftwork and mortality from ischaemic heart disease. Occ Env Med 53:367–373, 1996.
173. Melamed S, Ben-Avi I, Luz J, Green MS: Repetitive work, work underload and coronary heart disease risk factors among blue-collar workers—the CORDIS Study. Cardiovascular Occupational Risk Factors Determination in Israel. J Psychosomatic Research 39:19–29, 1995.
174. Melamed S, Froom P, Kristal-Boneh E, et al: Industrial noise exposure, noise annoyance, and serum lipid levels in blue-collar workers—the CORDIS Study. Arch Environ Health 52:292–298, 1997.
175. Menotti A, Seccareccia F: Physical activity at work and job responsibility as risk factors for fatal coronary heart disease and other causes of death. J Epidemiol Commun Health 39:325–329, 1985.
176. Mensch BS, Kandel DB: Do job conditions influence the use of drugs. J Health Soc Behav 29:169–184, 1988.
177. Meulders D, Plasman R, Vander Stricht V: Position of women in the labour market in the European community. Aldershot, Darmouth Publishing Company, 1998.
178. Moller L, Kristensen TS: Plasma fibrinogen and ischaemic heart disease risk factors. Arteriosclerosis and Thrombosis 11:344–350, 1991.
179. Morehouse RL: Shiftwork: The special challenges for women. AAOHN J 43:532–535, 1995.
180. Muntaner C, Nieto FJ, Cooper L, et al: Work organization and atherosclerosis: Findings from the ARIC study. Artherosclerosis Risk in Communities. Am J Prev Med 14:9–18, 1998.
181. Murphy LR: Job dimensions associated with severe disability due to CVD. J Clin Epidemiol 44:155–166, 1991.
182. Nachreimer F: Individual and social determinants of shiftwork tolerance. Scand J Work Environ Health 24 Suppl 3:35–42, 1998.
183. Nakamura K, Shimai S, Kikuchi S, et al: Shift work and risk factors for coronary heart disease in Japanese blue-collar workers: Serum lipids and anthropometric characteristics. Occup Med 47:142–146, 1999.
184. National Health Statistics: Occupational Health Decennial Supplement, series DS no. 10. London, Her Majesty's Stationary Office, 1995.
185. 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 14:231–238, 1988.
186. Netterstrom B, Kristensen TS, Damsgaard MT, et al: Job strain and cardiovascular risk factors: A cross-sectional study of employed Danish men and women. Br J Ind Med 48:684–689, 1991.
187. Netterstrom B, Suadicani P: Self-assessed job satisfaction and ischaemic heart disease mortality: A 10-year follow-up of urban bus drivers. Int J Epidemiol 22:51–56, 1993.
188. Niedhammer I, Bugel I, Goldberg M, et al: Psychosocial factors at work and sickness absence in the Gazel cohort: A prospective study. Occup Environ Med 55:735–741, 1998.
189. NIOSH: NIOSH Alert Request for Assistance in Preventing Death from Excessive Exposure to Chlorofluorocarbon 113 (CFC-113). Cincinnati, OH, U.S. Department of Health and Human Services, Public Health Service, Centers for Disease and Prevention Control, National Institute for Occupational Safety and Health, Publication No. 89-109, 1989.
190. Nordic Statistical Secretariat: Occupational Mortality in the Nordic Countries 1971–1980. Copenhagen, Statistical Reports of the Nordic Countries, 1988.
191. Notkola V, Pajunene A, Leino-Arjas P: Occupational mortality by cause in Finland 1971–1991 and occupational mobility. Helsinki, Statistics Finland, Health:1, 1997.
192. Nurminen M, Hernberg S: Effects of intervention on the cardiovascular mortality of workers exposed to carbon disulfide: A 15 year follow up. Brit J Ind Med 42:32–35, 1985.
193. OCDE (Organization de cooperation et de developpement economiques): Eco-Sante, version 1.5., 1993.
194. OCDE (Organization de cooperation et de developpement economiques): L'avenir des professions a predominance feminine. Paris, Organisation de cooperation et de developpement economiques, 1998.
195. Ockene IS, Shaw MJ, Alpert JS, et al: Unexplained chest pain in patients with normal coronary arteriograms. N Engl J Med 303:1249–1252, 1980.
196. Office of Population Censuses and Surveys: Occupational mortality 1979–80, 1982–83. Great Britain. Decennial Supplement. London, Her Majesty's Stationary Office, 1986.
196a. Omae K, Takebayashi T, Nomiyama T, et al: Cross-sectional observation of the effects of carbon disulphide on artriosclerosis in rayon manufacturing workers. Occup Environ Med 55: 1998.
197. Orth-Gomer K: Psychosocial risk factor profile in women with CHD. In Orth-Gomer K, Chesney M, Wenger N (eds): Women, Stress, and Heart Disease. Mahwah, NJ, Lawrence Erlbaum Associates, 1998, pp 25–38.
198. Ott MG, Skory LK, Holder BB, et al: Health evaluation of employees occupationally exposed to methylene chloride: Mortality. Scand J Work Environ Health 9(Suppl 8), 1983.
199. Pasceri V, Lanza GA, Buffon A, et al: Role of abnormal pain sensitivity and behavioral factors in determining chest pain in Syndrome X. J Am Coll Cardiol 31:62–66, 1998.

200. Pasternak RC, Thibault GE, Svoia M, et al: Chest pain with angiographically insignificant coronary arterial obstruction. Clinical presentation and long-term follow-up. Am J Med 68:813–817, 1980.
201. Perloff D, Sokolow M, Cowan RM, Juster RP: Prognostic value of ambulatory blood pressure measurements: Further analyses. J Hypertens 7 Suppl 3:S3–S10, 1989.
202. Peter R, Alfredsson L, Hammar N, et al: High effort, low reward and cardiovascular risk factors in employed Swedish men and women: Baseline results from the WOLF study. J Epidemiol Community Health 52:540–547, 1998.
203. Peter R, Alfredsson L, Knutsson A, et al: Is a stressful psychosocial work environment mediating the effects of shiftwork on cardiovascular risk factors in men? Scand J Work Environ Health (accepted for publication), 1999a.
204. Peter R, Hallqvist J, Reuterwall C, et al: The SHEEP Study Group: Psychosocial work environment and myocardial infarction: Improving risk prediction by combining two alternative job stress models in the SHEEP Study. (Submitted), 1999b.
205. Peter R, Siegrist J: Chronic work stress, sickness absence, and hypertension in middle managers: General and specific sociological explanations? Social Sci Med 45:1111–1120, 1997.
206. Pickering TG: Job strain and the prevalence and outcome of coronary artery disease [letter; comment]. Circulation 94:1138–1139, 1996.
207. Pickering TG: White coat hypertension. In Laragh JH, Brenner BM (eds): Hypertension: Pathophysiology, Diagnosis, and Management. New York, Raven Press, Ltd., 1995, pp 1913–1927.
208. Pickering TG: Should studies of patients undergoing coronary angiography be used to evaluate the role of behavioral risk factors for coronary heart disease? J Behav Med 8:203–213, 1985.
209. Pieper C, LaCroix AZ, Karasek RA: The relation of psychosocial dimensions of work with coronary heart disease risk factors: A meta-analysis of five United States data bases. Am J Epidemiol 129:483–494, 1989.
210. Pieper C, Warren K, Pickering TG: A comparison of ambulatory blood pressure and heart rate at home and work on work and non-work days. J Hypertens 11:177–183, 1993.
211. Price B, Bergman TS, Rodriguez M, et al: A review of carbon disulfide exposure data and the association between carbon disulfide exposure and ischemic heart disease mortality. Reg Toxicol Pharmacol 26:119–128, 1997.
212. Reference deleted.
213. Prunier-Poulmaire S, Gadbois C, Volkoff S: Combined effects of shift systems and work requirements on customs officers. Scand J Work Environ Health 24 suppl 3:134–140, 1998.
214. Ragland DR, Greiner BA, Holman BL, Fisher JM: Hypertension and years of driving in transit vehicle operators. Scand J Soc Med 25:271–279, 1997.
215. Ragland DR, Helmer DC, Seeman TE: Patient selection factors in angiographic studies: A conceptual formulation and empirical test. J Behav Med 14:541–553, 1991.
216. Rasnason V: Mortality from ischemic heart disease in Iceland, 1951–1985. Ann Epidemiol 1:493–503, 1991.
217. Redmond CK, Gustin J, Kamon E: Long-term mortality experience of steelworkers. VIII. Mortality patterns of open hearth steelworkers (a preliminary report). J Occup Med 17:40–43, 1975.
218. Reed DM, LaCroix AZ, Karasek RA, et al: Occupational strain and the incidence of coronary heart disease. Am J Epidemiol 129:495–502, 1989.
219. Reeder BA, Lui L, Horlick L: Sociodemographic variation in the prevalence of cardiovascular disease in Saskatchewan: Results from the Saskatchewan Heart Health Survey. Can J Cardiol 12:271–277, 1996.
220. Reinhardt CF, et al: Cardiac arrhythmias and aerosol sniffing. Arch Environ Health 22:265, 1971.
221. Repace JL, Jinot J, Bayard S, Emmons K, Hammond SK: Air nicotin and saliva cotinine as indicators of workplace passive smoking exposure and risk. Risk Anal 18:71–83, 1998.
221a. Rodger JC, Railton R, Parekh P, Newman P: Effects of cold stimulation on myocardial perfusion: An investigation using thallium-201 scintigraphy. Br Heart J 52:57–62, 1984.
222. Romon M, Nuttens M, Fievet C, et al: Increased triglyceride levels in shift workers. Am J Med 93:259–262, 1992.
223. Rosengren A, Anderson K, Wilhelmsen L: Risk of coronary heart disease in middle-aged male bus and tram drivers compared to men in other occupations: A prospective study. Int J Epidemiol 20:82–87, 1991.
224. Russek HI, Zohman BL: Relative significance of heredity, diet, and occupational stress in coronary heart disease of young adults. Am J Med Sci 235:266–275, 1958.
224a. Santé Canada: Les maladies cardio-vasculaires et les accidents vasculaires cérébraux au Canada. Santé Canada, Direction générale de la protection de la santé-Laboratoire de lutte contre la maladie, 1997.
225. Sauli H: Occupational Mortality 1971–75. Helsinki, Tilastokeskus, 1979.
226. Schnall PL, Landsbergis PA, Baker D: Job strain and CVD. Annu Rev Public Health 15:381–411, 1994.
227. Schnall PL, Landsbergis PA, Schwartz J, et al: A longitudinal study of job strain and ambulatory blood pressure: Results from a 3-year follow-up. Psychosom Med 60:697–706, 1998.
228. Schnall PL, Pieper C, Schwartz JE, et al: The relationship between "job strain," workplace diastolic blood pressure, and left ventricular mass index. Results of a case-control study [published erratum appears in JAMA 1992 Mar 4;267(9):1209]. JAMA 263:1929–1935, 1990.
228a. Schnall PL, et al: Relation between job strain, alcohol, and ambulatory BP. Hypertension 19:488–494, 1992.
229. Schwartz JE, Pieper C, Karasek RA: A procedure for linking psychosocial job characteristic data to health surveys. Am J Public Health 78:904–909, 1988.
230. Sheldahl LM, Wilke NA, Sougherty S, Tristani FE: Cardiac responses to combined moderate heat and exercise in men with coronary artery disease. Am J Cardiol 70:186–191, 1992.
231. Reference deleted.
232. Shively CA, Clarkson TB: Social status and coronary artery atherosclerosis in female monkeys. Arterioscler Thromb 14:721–726, 1994.
233. Siegrist J: Adverse health effects of high-effort/low-reward conditions. J Occup Health Psychol 1:27–41, 1996.
234. Siegrist J: Threat to social status and cardiovascular risk. Psychotherapy and Psychosomatics 42:90–96, 1984.

235. Siegrist J, Matschinger H, Cremer P, Seidel D: Atherogenic risk in men suffering from occupational stress. Atherosclerosis 69:211–218, 1988.
236. Siegrist J, Peter R: Job stressors and coping characteristics in work-related disease: Issues of validity. Work & Stress 8:130–140, 1994.
237. Siegrist J, Peter R, Cremer P, Seidel D: Chronic work stress is associated with atherogenic lipids and elevated fibrinogens in middle aged men. Journal of Internal Medicine 242:149–156, 1997.
238. Siegrist J, Peter R, Georg W, et al: Psychosocial and biobehavioral characteristics of hypertensive men with elevated atherogenic lipids. Atherosclerosis 86:211–218, 1991.
239. Siegrist J, Peter R, Junge A, et al: Low status control, high effort at work and ischaemic heart disease: Prospective evidence from blue collar men. Social Science & Medicine 31:1127–1134, 1990.
240. Siegrist J, Peter R, Motz W, Strauer BE: The role of hypertension, left ventricular hypertrophy and psychosocial risks in cardiovascular disease: Prospective evidence from blue-collar men. Eur Heart J 13 Suppl D:89–95, 1992.
240a. Sierra Pajares Ortiz M, Diaz Jimenez H, Montero Rubio JC, et al: Daily mortality in the Madrid community during 1986–1991 for 45- to 64-year-olds: Relationship to air temperature. Rev Esp Salud Publica 2:149–160, 1997.
241. Sihm I, Delholm G, Hansen ES, et al: The psychosocial work environment of younger men surviving acute myocardial infarction. European Heart Journal 12:203–209, 1991.
242. Skipper J, Jung F, Coffey L: Nurses and shiftwork: Effects on physical health and mental depression. J Advanced Nursing 15:835–842, 1990.
243. Sokejima S, Kagamimori S: Working hours as a risk factor for acute myocardial infarction in Japan: Case-control study. Brit Med J 317:775–780, 1998.
244. Speizer FE, Wegman DH, Ramirez A: Palpitation rates associated with fluorocarbon exposure in a hospital setting. N Engl J Med 292:624, 1975.
244a. Stayner LT, A.L. D, Thun M, et al: Cardiovascular mortality among workers exposed to nitroglycerin and dinitrotoluene. Scand J Work Environ Health 18:34–43, 1992.
245. Steenland K, Deddens J, Salvan A, Stayner L: Negative bias in exposure-response trends in occupational studies: Modeling the healthy worker survivor effect. Am J Epidemiol 143:202–210, 1996.
246. Steenland K, Fine L: Shift work, shift change, and risk of death from heart disease at work. Am J Ind Med 29:278–281, 1996.
247. 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 31:256–259, 1997.
247a. Steenland K, Piscitelli L, Deddens J, et al: Cancer, heart disease, and diabetes in workers exposed to 2,3,7,8-tetrochlorodibenzo-p-dioxin. J Nat Cancer Inst 91:779–786, 1999.
248. Steptoe A, Cropley M, Joekes K: Job strain, blood pressure and response to uncontrollable stress. J Hypertens 17:193–200, 1999.
249. Steptoe A, Roy MP, Evans O, Snashall D: Cardiovascular stress reactivity and job strain as determinants of ambulatory blood pressure at work. J Hypertension 13:201–210, 1995.
249a. Stern FB, Halperin WE, Hornung RW, et al: Heart disease mortality among bridge and tunnel officers exposed to carbon monoxide. Am J Epidemiol 128:1276–1288, 1988.
249b. Staessen JA, Roels S, Lauwerys RR, Amery A: Low-level lead exposure and blood pressure. J Hum Hypertens 9:303–328, 1995.
250. Sternberg H, Rosenthal T, Shamiss A, Green M: Altered circadian rhythm of blood pressure in shift workers. J Hum Hypertens 9:349–353, 1995.
251. Suurnakki T, Ilmarinen J, Wagar G, et al: Municipal employees' cardiovascular diseases and occupational stress factors in Finland. Int Arch Occup Environ Health 59:107–114, 1987.
251a. Swaen GM, Braun C, Slangen JJ: Mortality of Dutch workers exposed to carbon disulfide. Int Arch Occup Environ Health 66:103–110, 1994.
251b. Sweetnam PM, Taylor SW, Elwood PS: Exposure to carbon disulphide and ischaemic heart disease in a viscose rayon factory. Br J Ind Med 44:220–227, 1987.
251c. Taggart P, et al: Cardiac responses to thermal, physical, and emotional stress. Br Med J 3:71–76, 1972.
252. Tarumi K, Hagihara A, Morimoto K: An inquiry into the relationship between job strain and blood pressure in male white-collar workers. Jpn J Ind Health 35:269–276, 1993.
253. Taylor P: A comparison of sickness absence, lateness, and other absence behavior in an oil refinery from 1962–1965. Brit J Ind Med 24:93–102, 1967.
254. Taylor P, Pocock S: Mortality of shift and day workers 1956–1968. Brit J Ind Med 29:201–207, 1972.
255. Tenkanen L, Sjoblom T, Harma M: Joint effect of shift work and adverse life-style factors on the risk of coronary heart disease. Scand J Work Environ Health 24:351–357, 1998.
256. Tenkanen L, Sjoblom T, Kalimo R, et al: Shift work, occupation, and coronary heart disease over 6 years of follow-up in the Helsinki Heart Study. Scand J Work Environ Health 23:257–265, 1997.
257. Theorell T: Family history of hypertension—an individual trait interacting with spontaneously occurring job stressors. Scand J Work Environ Health 16 Suppl 1:74–79, 1990.
258. Theorell T, Ahlberg-Hulten G, Jodko M, et al: Influence of job strain and emotion on blood pressure in female hospital personnel during work hours. Scand J Work Environ Health 19:313–318, 1993.
259. Theorell T, de Faire U, Johnson J, et al: Job strain and ambulatory blood pressure profiles. Scand J Work Environ Health 17:380–385, 1991b.
259a. Theorell J, et al: The effects of the strain of returning to work on the risk of cardiac death after an MI before age 45. Int J Cardiol 30:61–67, 1991.
260. Theorell T, Hamsten A, de Faire U, et al: Psychosocial work conditions before myocardial infarction in young men. International Journal of Cardiology 15:33–46, 1987.

261. Theorell T, Karasek R: Current issues relating to psychosocial job strain and cardiovascular disease research. Journal of Occupational Health Psychology 1:9–26, 1996.
262. Theorell T, Knox S, Svensson J, Waller D: Blood pressure variation during a working day at age 28: Effects of different types of work on blood pressure level at age 18. J Human Stress 2:36–41, 1985.
263. Theorell T, Perski A, Akerstedt T, et al: Changes in job strain in relation to changes in physiological states—a longitudinal study. Scand J Work Environ Health 14:189–196, 1988.
264. Theorell T, Rahe RH: Behavior and life satisfactions of Swedish subjects with myocardial infarction. J Chron Dis 25:139–147, 1972.
265. Theorell T, Tsutsumi A, Hallqvist J, et al: SHEEP Study Group. Decision latitude, job strain and myocardial infarction. Am J Public Health 88:382–388, 1998.
266. Thomas JT, Epstein FH: Heart disease, cancer, and stroke mortality trends and their interrelations. An international perspective. Circulation 90:574–582, 1994.
267. Thompson SJ: Review: Extraaural health effects of chronic noise exposure in humans. Schriftenr Ver Wasser Boden Lufthyg 88:91–117.
268. Trout D, Decker J, Mueller C, et al: Exposure of casino employees to environmental tobacco smoke. J Occup Environ Med 40:270–276, 1998.
269. Tüchsen F: Stroke morbidity in professional drivers in Denmark 1981–1990. Int J Epidemiol 26:989–994, 1997.
270. Tüchsen F: Working hours and ischaemic heart disease in Danish men: A 4-year cohort study of hospitalization. Int J Epidemiol 22:215–221, 1993.
271. Tüchsen F, Andersen O, Costa G, et al: Occupation and ischemic heart disease in the European Community: A comparative study of occupations at potential high risk. Am J Ind Med 30:407–414, 1996.
272. Tüchsen F, Bach E, Marmot M: Occupation and hospitalization with ischaemic heart disease: A new nation wide surveillance system based on hospital admissions. Int J Epidemiol 21:450–459, 1992.
273. Tüchsen F, Endahl LA: Increasing inequality in ischaemic heart disease morbidity among employed men in Denmark 1981–1993: The need for a new preventive policy. Int J Epidemiol 28:640–644, 1999.
274. Uehata T: Long working hours and occupational stress-related cardiovascular attacks among middle-aged workers in Japan. J Human Ergol 20:147–153, 1991.
275. van Amelsvoort LGPM: Coronary heart disease among truck drivers. Report of the International Workshop on the Epidemiology of CHD among European Truck Drivers. Bilthoven, European Commission, 1995.
276. van Egeren LF: The relationship between job strain and blood pressure at work, at home, and during sleep. Psychosom Med 54:337–343, 1992.
277. Vanhoorne M, De Bacquer D, De Backer G: Epidemiological study of the cardiovascular effects of carbon disulphide. Int J Epidemiol 21:745–752, 1992.
278. Volmink JA, Newton JN, Hicks NR, et al: Coronary event and case fatality rates in an English population: Results of the Oxford myocardial infarction incidence study. Heart 80:40–44, 1998.
279. Waddell VP, Holman CD, Armstrong BK, et al: Variation in hospital morbidity in the male workforce of Western Australia. Br J Ind Med 45:139–147, 1988.
280. Wamala SP, Wolk A, Orth-Gomer K: Determinants of obesity in relation to socioeconomic status among middle-aged Swedish women. Preventive Med 26:734–744, 1997.
281. Weinberg C: Toward a clearer definition of confounding. Am J Epidemiol 137:1–8, 1993.
282. Wenger NK: Cardiovascular disease in the elderly and in women. In Goldman L, Braunwald E (eds): Primary Cardiology. Philadelphia, WB Saunders, Co., 1998, pp 70–81.
283. Westman M, Eden D, Shirom A: Job stress, cigarette smoking and cessation: The conditioning effects of peer support. Soc Sci Med 20:637–644, 1985.
284. Whaley MH, Blair SN: Epidemiology of physical activity, physical fitness, and coronary heart disease. J Cardiovasc Risk 2:289–295, 1995.
285. Wickramatillake HD, Gun RT, Ryan P: Carbon monoxide exposures in Australian workplaces could precipitate myocardial ischaemia in smoking workers with coronary artery disease. Aust N Z Public Health 22 (Suppl 3):389–393, 1998.
286. Wilcosky TC, Simonsen NR: Solvent exposure and cardiovascular disease. Am J Ind Med 19:569–586, 1991.
287. Wilcosky TC, Tyroler HA: Mortality from heart disease among workers exposed to solvents. J Occup Med 25:879, 1983.
288. Wild P, Moulin JJ, Ley FX, Schaffer P: Mortality from cardiovascular diseases among potash miners exposed to heat. Epidemiology 6:243–247, 1995.
289. Wilkinson R: How can secular improvements in life expectancy be explained? In Blane D, Brunner E, Wilkinson R (eds): Health and Social Organization. London, Routledge, 1996, pp 109–122.
289a. Willich SN, Lewis M, Lowel H, et al: Physical exertion as a trigger of myocardial infarction. Triggers and mechanisms of myocardial infarction study group. N Engl J Med 329:1684–1690, 1993.
290. Wing S, Dargent-Molina P, Casper M, et al: Changing association between community structure and ischaemic heart disease mortality in the United States. Lancet 2:1067–1070, 1987.
291. Winkleby MA, Ragland DR, Fisher JM, Syme SL: Excess risk of sickness and disease in bus drivers: A review and synthesis of epidemiological studies. Int J Epidemiol 17:255–262, 1988.
292. Winkleby MA, Ragland DR, Syme SL: Self-reported stressors and hypertension: Evidence of an inverse association. Am J Epidemiol 127:124–134, 1988.
293. Wright EO, Shire K, Hwang S-L, et al: The non-effects of class on the gender division of labor in the home: A comparative study of Sweden and the United States. Gender & Society 6:252–282, 1992.
294. Yamasaki F, Schwartz JE, Gerber LM, et al: Impact of shift work and race/ethnicity on the diurnal rhythm of blood pressure and catecholamines. Hypertension 32:417–423, 1998.
295. Zhao YM, Zhang SZ, Selvin S, Spear RC: A dose response relation for noise induced hypertension. Br J Ind Med 48:179–184.

Journal Title: Occupational medicine

Volume: 15
Issue: 1
Month/Year: 2000
Pages: 7-68

Article Author: Steenland-K; Fine-L; Belkic-K; Landsbergis-P; Schnall-P; Baker-D; Theorell-T; Siegrist-J; et. al.

Article Title: Research findings linking workplace factors to cardiovascular disease outcomes

Imprint:

Call #:

Location: NIOSHM

Item #: