Work-related cardiovascular disease

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To my family and friends

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ABSTRACT

The overall aim of this thesis was to study occupational risk factors for cardiovascular disease, particularly, occupational noise, job strain and shift work.

Incidence of cardiovascular disease was analysed in a general population sample, the Primary Prevention Study, in relation to exposure to noise and job strain. The results indicated that exposure to noise increased the risk of developing coronary heart disease. Simultaneous exposure to job strain further increased the risk. We could not demonstrate an increased risk of stroke. Female workers in the paper industry exposed to shift work and noise were analysed regarding mortality from cardiovascular disease in a longitudinal cohort study. Female workers exposed to noise $\geq$90 dB(A) or the combination of shift work and noise had an increased mortality from acute myocardial infarction but not from stroke. A cohort study of Swedish seafarers was performed. There was no increased mortality for seafarers who had worked on passenger ferries only. However, seafarers who had worked on different types of vessels had an increased total mortality and in addition an increased mortality from cardiovascular disease among relatively younger seafarers. The association between exposure to job strain and presence of coronary calcium was studied in the SCAPIS pilot study, a general population sample. The power of the study was limited, but exposure to high strain job or active job could potentially increase the risk in men, but not in women, where it could rather be exposure to passive job, however the results were insignificant.

The results of the thesis strengthen earlier observations of a health hazardous effect from exposure to noise, job strain and shift work. The results are also in parity with international studies on increased mortality among seafarers.

Keywords: Occupational noise, shift work, job strain, seafarer, cardiovascular disease.

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SAMMANFATTNING PÅ SVENSKA

Hjärtkärlsjukdom är vanligt förekommande och den vanligaste dödsorsaken i Sverige. Det finns många olika faktorer som påverkar utvecklingen av hjärtkärlsjukdom såsom genetiska förutsättningar, fysisk aktivitet och kost. Arbetsrelaterade riskfaktorer bidrar sannolikt också till uppkomst av hjärtkärlsjukdom. Yrkesmässig stress, bullerexponering och skiftarbete är några av de faktorer som har studerats och där man har en stark misstanke om samband men det kan inte anses vara helt klarlagt.

En av studierna utgick från den Primärpreventiva studien, en uppföljning av män i Göteborg födda 1915 - 1925. Männens exponering för buller och stress, i form av höga krav och låg kontroll, uppskattades med hjälp av jobb-exponeringsmatriser. Männens insjuknande i hjärtkärlsjukdom följdes upp via register. Resultaten visade att exponering för buller ökade risken för att insjukna i kranskärlssjukdom, såsom hjärtinfarkt. Samtidig exponering för höga krav och låg kontroll ökade risken ytterligare. Någon ökad risk för stroke kunde inte påvisas.

Kvinnor som arbetat i svensk pappersindustri och som varit exponerade för skiftarbete och buller studerades beträffande deras dödlighet i hjärtkärl-sjukdomar. Analyserna visade att det fanns en ökad dödlighet i hjärtinfarkt bland kvinnor exponerade för buller 90 dB(A) eller mer jämfört med den allmänna befolkningen i Sverige, särskilt för kvinnor som var exponerade för en kombination av skiftarbete och buller. Det fanns ingen ökad dödlighet i stroke.

En kohortstudie genomfördes av svenskt sjöfolk. Resultaten visade att det inte fanns någon ökad dödlighet för de som arbetat på enbart passagerarfartyg. Däremot för de som arbetat på olika typer av fartyg så fanns det en generellt ökad dödlighet och utöver det en ökad dödlighet i hjärtkärlsjukdom, både hjärtinfarkt och stroke bland relativt unga personer.

Mängden kalk i hjärtats kranskärl, koronart kalcium, är relaterat till risken för framtida hjärtinfarkt. Eventuellt samband mellan stress och koronart kalcium undersöktes genom SCAPIS pilotstudie. Resultaten bör tolkas med försiktighet, men pekade på att höga krav och låg kontroll hos män respektive låga krav och låg kontroll hos kvinnor skulle kunna öka risken för koronart kalcium, dock med statistisk osäkerhet.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Eriksson HP, Andersson E, Schiöler L, Söderberg M, Sjöström M, Rosengren A, Torén K. Longitudinal study of occupational noise exposure and joint effects with job strain and risk for coronary heart disease and stroke in Swedish men. BMJ Open 2018;**8**e019160.doi:10.1136/bmjopen-2017-019160.

II. Eriksson HP, Söderberg M, Neitzel RL, Torén K, Andersson E. Shift work, noise exposure and risk of cardiovascular mortality in a Swedish cohort of female industrial workers. Submitted.

III. Eriksson HP, Forsell K, Andersson E. Mortality from cardiovascular disease in a cohort of Swedish seafarers. Submitted.

IV. Eriksson HP, Torén K, Rosengren A, Andersson E, Söderberg M. Adverse psychosocial job exposure and risk of coronary artery calcification. Manuscript.

CONTENT

ABBREVIATIONS

BMI	Body mass index
CAC	Coronary calcium
CACS	Coronary calcium score
dB(A)	The A-weighted sound pressure level in decibels
CI	Confidence interval
CHD	Coronary heart disease
CVD	Cardiovascular disease
HR	Hazard ratio
JDC	Job demand control
JEM	Job exposure matrix
OR	Odds ratio
PR	Prevalence ratio
RR	Relative risk
SMR	Standardized mortality ratio
SR	Seafarers Registry
TWA	The eight-hour time-weighted average sound level

1 INTRODUCTION

Work-related diseases are multifactorial diseases in which the work environment plays a partial role in causation (WHO). In this thesis, cardiovascular diseases are studied, the etiology is multi factorial and occupational exposures are likely to be a part of the development among the working and previously working population. The effect from an occupational exposure can be discernible during the working years but also many years after the exposure. The understanding of which occupational factors that contribute to the development of cardiovascular diseases is of importance for preventive reasons and to clarify how many cases of illness that could be avoided if the occupational exposure would not be present, in order to prioritize preventive measures.

1.1 CARDIOVASCULAR DISEASE

Cardiovascular disease, CVD, is frequent and the most common cause of death occurring in Sweden. Even though incidence and mortality from myocardial infarction and stroke has significantly declined in recent years in Sweden (The National Board of Health and welfare 2018a).

According to a report from the National Board of Health and Welfare in Sweden, in 2017, 25,300 persons developed an acute myocardial infarction which corresponds to an incidence of 340 cases per 100,000 inhabitants. Of them 24% were mortal within 28 days. Myocardial infarctions increase markedly with increasing age and is more common among men than women, although the difference have decreased over time, still, incidence and mortality were twice as high during 2017 among men. According to the same report, myocardial infarction is related to education, there are more cases of myocardial infarction among persons with a low education compared to persons with a high education (The National Board of Health and welfare 2018a).

In 2017, 25,800 persons had a stroke in Sweden, including intracerebral bleeding and ischemic stroke, which corresponds to an incidence of 360 stroke cases per 100,000 inhabitants. Of the 25,800 persons, 26% died within 28 days. Stroke can occur in all ages but is more common in older ages, 75% of those affected are 70 years old or more (The National Board of Health and welfare

2018b). Stroke is more common among men, mortality due to stroke among men is also higher, except for the ages 85 years and above.

It is well known that factors such as smoking, hereditary factors, high blood pressure and altered blood lipids can increase the risk of cardiovascular disease (Rapsomaniki et al. 2014). Socioeconomic status, SES, is also a factor that affects the risk of developing CVD, both coronary heart disease, CHD, and stroke is inversely related to SES for both men and women (Backholer et al. 2017), and for women the risk of having a low SES might even be higher, regarding CHD, according to an international review and meta-analysis (Backholer et al. 2017).

1.2 OCCUPATIONAL RISKS

Occupation is part of the socioeconomic status and there are several risk factors in the occupational environment that have been associated with an increased risk of developing coronary heart disease and stroke. For instance, psychosocial factors including shift work and stress, noise exposure, chemical exposure and ionizing radiation (SBU 2015, SBU 2017). According to a report on work-related mortality in Sweden in 2016, performed on behalf of the Swedish Work Environment Authority, stress, shift work, engine exhaust, noise and persistent physically heavy work causes each more than 500 deaths per year (Andersson et al. 2019). However, the associations cannot be considered completely established and the mechanisms are to some extent unclear.

1.2.1 NOISE

Exposure to noise is also frequent in many occupational environments. Noise exposure is health hazardous and can cause hearing impairment (Lie et al. 2016). There are studies indicating that occupational exposure to noise can increase the risk of cardiovascular disease (Theorell et al. 2016). A Canadian study of 30,000 lumber mill workers presented an increased risk of myocardial infarction both in relation to duration of employment and in relation to noise levels (Davies et al. 2005). The highest risk was found among those who were currently working and had been employed 20 years or more with relative risks (RRs) between 2.0 and 4.0. An 18-year follow-up of 6,005 men from the Helsinki Heart Study showed an increased risk, 1.48 (95% confidence interval, CI 1.28-1.71) of coronary heart disease in relation to continuous noise

exposure exceeding 85 dB(A) (Virkkunen et al. 2005). Exposure to impulse noise showed similar risk estimates. In a case-control study from Sweden, subjects with myocardial infarction and controls were classified using a job-exposure matrix for occupational noise (Selander et al. 2013). There was an increased odds ratio (OR), for occupational noise exceeding 75 dB(A), but with adjustments for age, sex, smoking, socioeconomic status and air pollution the risk decreased and became insignificant.

Regarding stroke and the association to occupational noise there are few longitudinal studies. A Japanese study comprising 14,568 subjects from the general population with self-reported noise levels were followed for approximately 15 years. In adjusted models the hazard ratio (HR) for intra-cerebral bleeding was 2.1 (95% CI 1.01-4.4) (Fujino et al. 2007). The risk of ischemic stroke was HR 1.7 (95% CI 0.7-4.1). A Danish study of more than 200,000 workers who were followed for six years on stroke morbidity, exposure to occupational noise was assigned to each worker according to company, calendar year and occupation. The assigned noise levels were obtained from measurements on 1,077 workers. The study did not show any increased risk of stroke in relation to occupational noise exposure (Stokholm et al. 2013).

A recent review article from 2016 suggested a strong association between noise and hypertension but a weak association to other cardiovascular diseases (Skogstad et al. 2016). However, a recent American study of male workers at metal manufacturing plants found no association between exposure to noise and hypertension (Tessier-Sherman et al. 2017). Thus, it is not completely established whether occupational noise can increase the risk of cardiovascular disease and the mechanism are not clear either. The mechanisms behind environmental noise exposure and the increased risk of cardiovascular disease have been studied more extensively (Basner et al. 2014). Noise exposure activates the autonomic and endocrine systems, the blood pressure increases, the heart rate is affected and stress hormones are released (Basner et al. 2014).

1.2.2 SHIFT WORK

Shift work is presently a frequently occurring form of work but historically night shift was forbidden in Sweden until the 1960s for female industrial workers. But now, according to an investigation by Statistics Sweden in 2018, one of five employees works on a shift schedule in Sweden (Statistics Sweden 2019). Shift work is also more common among younger persons in Sweden, among persons aged16–24 years old, 42% declare that they are shift workers compared to persons in the ages 35-44 where 17% declare shift work according to the same investigation. There are many variations of shift schedules but shift work is usually defined as work that is not scheduled during the usual daytime hours.

Shift work can reduce sleep, cause excessive sleepiness and has been found to have a probable impact on health (Kecklund et al. 2016). A systematic review and meta-analysis from 2018, found a 26% higher risk of morbidity in CHD and approximately 20% increased mortality from CVD and CHD among shift workers. The association between shift work and CVD appeared after five years of shift work (Torquati et al. 2018). CVD was in this review considered as CHD, cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease, deep vein thrombosis and pulmonary embolism (Torquati et al. 2018). In a Swedish nested case–control study consisting of 138 shift workers and 469 day-workers the crude OR for shift workers' risk of experiencing an ischemic stroke was 1.0 (95% CI 0.6–1.8) for both the men and the women (Hermansson et al. 2007).

There are studies on shift working women in health care presenting an increased risk of cardiovascular disease. In a cohort study of 189,158 nurses, longer duration of rotating night shift work was associated with an increase in CHD risk (Vetter et al. 2016). A cohort study of 80,108 nurses showed an association between rotating night shift work and ischemic stroke risk. There was a linear trend between the number of years of rotating night shift work and ischemic stroke risk, with a 4% increase in ischemic stroke risk for each 5 years of shift work (Brown et al. 2009). But there are few studies regarding shift work among industrially employed women.

In a Swedish study published in 1986, 504 paper mill workers were followed for 15 years regarding ischaemic heart disease, shift work was compared to day work. There was an increasing risk with increasing time of shift work. After 11-15 years of shift work RR 2.2 $p<0.04$ and after 16-20 years RR 2.8, $p<0.03$. The association was independent of smoking and age. The risk for

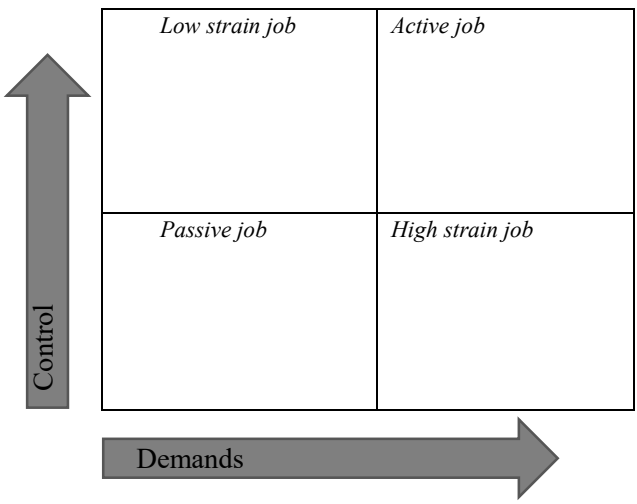
ischaemic heart disease fells after 20 years of shift work, the authors concluded that this was due to a positive selection in the group (Knutsson et al. 1986).

It has not been completely elucidated how shift work can increase the risk of CVD but shift work can cause disturbed meal patterns (Souza et al. 2019), circadian misalignment and sleep loss to varying extents which may be part of the course of events (Kervezee et al. 2018, Strohmaier et al. 2018). Shift work may also increase the risk of development of the metabolic syndrome (Wang et al. 2014). Larger studies on shift work and impact on health are complex to perform due to the many types of shift work that can vary over time for each individual, there is a risk of misclassification, and there are often combined exposures such as shift work and noise which complicates the analyses. A Finnish study of industrially employed men showed an increased risk of ischemic heart disease when exposure to shift work occurred as well as when exposure for noise occurred, and when both exposures occurred together (Virkkunen et al. 2006). Possibly, there are also individual differences in tolerance to different types of shift work (Hittle et al. 2018), which may change with increasing age (Schuster et al. 2019). Humans have predispositions for different hours of sleep/awake times, often called morning-, intermediate- and evening chronotypes (Hittle et al. 2018). Circadian misalignment could occur when the working hours does not match the individuals chronotype (Hittle et al. 2018). However, there are studies indicating that evening chronotypes are more susceptible to night shift (Hulsegge et al. 2019, Ritonja et al. 2019) regarding cardiometabolic risk factors.

1.2.3 JOB STRAIN

Exposure to work related stressors can be estimated according to different models and the most frequently used is the job demand-control model, JDC (Karasek 1979). The job demand-control model emphasizes the joint effect between demands and control. The demand dimension assesses psychological work demands such as work load, intensity and time pressure. The control dimension assesses to what extent the individual can influence the order, volume and content of their tasks (decision latitude). According to the model, high demands and low decision latitude, defined as a high strain job, is considered as the job condition that is most health hazardous. When job demands and job decision latitude are both high, the job is defined as active, which is considered as demanding but also associated with learning and developing opportunities. The opposite, low demands and low decision latitude is defined as passive job and implies a decline in overall activity and reduced stimulating activity according to the model. Finally, high decision latitude and low demands is considered as a low strain job and the least health hazardous and often used as a reference to high strain jobs in studies, Figure 1.

Figure 1.



Exposure to a high strain job has been associated with increased risk of cardiovascular disease in many studies. A review article from 2015 presented increased risk of coronary heart disease RR 1.34 (95% CI 1.18-1.52) and ischemic stroke RR 1.24 (95% CI 1.05-1.46) in subjects exposed to job strain (Kivimäki et al. 2015). A recent Italian study published in 2017 of 4,100 men presented increased risk of coronary heart disease among manual and non-manual male workers exposed to job strain or active job but not for managers and proprietors (Ferrario et al 2017). It has also been showed that men with a history of cardiovascular or metabolic disease could be even more sensitive to high strain (Kivimäki et al. 2018a). A multicohort study assessing the associations between work stressors and mortality in men and women with and without cardiometabolic disease found an increased mortality among male subjects with cardiometabolic disease exposed to high strain (Kivimäki et al. 2018a).

Regarding stroke and job stressors, a Swedish study from 2008 of almost 3 million participants using a JEM for assessment of the exposure found increased risks of stroke from exposure to low control (Toivanen 2008). The HR of the lowest versus the highest job control quartile was 1.25 (95% CI 1.17–1.32) for any stroke among the women and for the men HR 1.24 (95% CI 1.21–1.28), age- and workhour-adjusted.

The mechanisms between occupational stress exposure and cardiovascular disease are not clear. Although the acute stress response has been well documented and includes altered function of the hypothalamus-pituitary-adrenal cortex axis and the autonomic nervous system (Kivimäki and Steptoe. 2018b). There are likely several mechanisms involved that link job strain to the development of cardiovascular disease, possibly the metabolic syndrome, weight gain, hypertension and altered behaviour due to exposure to stress such as increased smoking and less physical activity (Kivimäki et al. 2015).

1.3 PAPER INDUSTRY

The forest industry is an important industry in Sweden and employs approximately 70,000 persons. The pulp- and paper mills constitutes an important part of the forest industry. 11 million tons of pulp is produced every year. There are different types of pulp, which are produced in different ways, e.g. through boiling of wood chips in chemicals or by decomposing the wood and then mechanically processing of the exposed fibers. Pulp is the raw material for paper, cardboard and some textiles. 10 million tons of paper is

produced every year. There are several occupational exposures in the pulp- and paper industry such as noise, chemicals, wood- and paper dust and shift work (Torén 1996). The exposure level depends on the type of process. Soft tissue mills frequently also have a high level of paper dust exposure (Torén 1996).

There are studies indicating increased cardiovascular mortality among workers in the paper industry (Andersson et al. 2007). A Norwegian study of female paper mill workers showed an increased mortality from ischemic heart disease (Langseth et al. 2006). An earlier Swedish study on male workers in pulp and paper mills presented an increased risk of coronary heart disease among men with a longer duration of shift work, compared to day workers (Karlsson et al. 2005). The shift workers also had an increased risk of mortality due to stroke. The association between occupational noise and CVD have not been studied in the paper industry, only in saw mills, another forest industry (Davies et al. 2005).

1.4 SEAFARERS

Approximately 10,000 Swedish citizens were working on Swedish vessels in 2016 (Svensk Sjöfart 2018). The number of Swedish seafarers and Swedish merchant vessels has decreased over the years. Historically mostly males have worked at sea but during the last 20 years, the percentage of women among Swedish seafarers has increased from 18% to 29% (Svensk Sjöfart 2018). Seafarers occupational environment is regulated and controlled by the Swedish Transport Agency. There is a requirement of an approved medical certificate in order to work at sea, also regulated by Swedish Transport Agency and international regulations.

Due to multiple factors, seafarers have an increased morbidity and mortality according to international studies (Brandt et al. 1994, Rafnsson et al. 1994, Poulsen et al. 2014). Previous studies have presented increased risks of infectious diseases (Roberts et al. 2016), accidents (Roberts et al. 2014), mental illness (Iversen 2012) and cancer among seafarers (Nilsson 1998, Ugelvig et al. 2018). Another probable cause of illness and death among seafarers (Alves et al. 2010, Holt et al. 2017) is CVD (Brandt et al. 1994, Oldenburg et al. 2016). Yet, it is not known if the risk of CVD is increased compared to the general population; the studies are scarce and with differing outcomes (Roberts and Jaremin. 2010, Jaremin and Kotulak. 2003), and it has not been studied recently among Swedish seafarers.

In a doctoral thesis from 1960, mortality among seafarers was studied between 1945 and 1954 and an increased mortality from CVD was found, especially among officers (Otterland 1960). In an earlier Swedish register-based study on different occupational groups, published in 1992, an increased incidence of myocardial infarction among deck officers was reported (Hammar et al. 1992).

There are probable risk factors among seafarers for CVD such as shift work (Torquati et al. 2018). One type of shift work on board is the "6 h on/6 h off duty system, where you are on duty 6 h and then off duty 6 h, it is questionable whether 6 h is enough for recovery and frequently the 6 h off duty period is disrupted by work tasks. Other probable risk factors for CVD among seafarers are noise exposure (Skogstad et al. 2016, Forsell et al. 2017) and psychosocial stress (Kivimäki et al. 2015, Forsell et al. 2017). Furthermore, according to international studies, seafarers also have risk factors such as an increased amount of obesity, smoking and lack of physical exercise (Pougnet et al. 2013, Oldenburg et al. 2014), and Danish studies have presented increased rates of hypertension (Tu et al. 2016), and the metabolic syndrome (Moller Pedersen et al. 2013) among seafarers. Once developing a CVD, the chance of survival could be affected due to an extended time to qualified medical investigation and treatment (Jaremin and Kotulak.. 2003).

1.5 CORONARY CALCIUM

Calcification of the coronary arteries, CAC, is part of the atherosclerosis process. CAC develops during a long time through macrophages, inflammatory mechanisms, apoptosis and general influence from mineral metabolism factors in the coronary arteries (Nakahara et al. 2017). CAC increases with increasing age and develops at a later age among women compared to men (Sandfort et al. 2017). The presence of CAC is a marker of atherosclerotic plaque burden and a predictor of CHD and mortality (Liew et al. 2017). As CAC and plaque burden increase, there is an equivalent increase in the risk of CHD events. Whereas, the absence of coronary calcium is strongly associated with lack of future coronary events (Sarwar et al. 2009). The amount of CAC is frequently quantified through the Agatston scoring method where calcium deposit areas are multiplied by a density factor, based on the results from a computed tomography investigation (Sandfort et al. 2017).

There are few studies on the association between adverse psychosocial stress exposure and development of CAC. In the longitudinal study; Coronary Artery

Risk Development in Young Adults, CAC was measured in 3,695 participants, aged 18-30 at baseline. The analyses could not find any associations to job strain at either 10- or 18-year of follow-up from the first measures of psychosocial variables, when the subjects were aged 28-48 years. However, blue collar workers displayed a tendency to a higher prevalence of positive CAC compared to workers in other occupations (Greenlund 2010). Likewise, in a cross-sectional study where CAC scans were performed in 1,111 healthy volunteers, 138 asymptomatic patients and 600 symptomatic patients, and exposure to job strain was assessed through a questionnaire, no association between CAC and job strain was found (Rozanski et al. 2011).

1.6 JOB EXPOSURE MATRICES

A job exposure matrix, JEM, can be used in large epidemiological studies to assess the exposure when information on type of occupation has been collected/is known. The exposure of interest can be estimated based on the JEM instead of a questionnaire or a detailed interview with each study participant about their occupational exposure. A general JEM presents the level of a specific exposure for different occupational titles in a population but there are more detailed JEMs for specific branches or workplaces. JEMs list occupations/departments on one axis and exposure agent on the other and the cell of the matrix indicate the level of exposure in a certain occupation. The data in the matrix are usually based on previous measurements or investigations (Teschke 2003). In this thesis the following JEMs are used; one general for assessments of noise (Sjöström et al. 2013) and one specific for paper mills (Neitzel et al. 2018), and also one psychosocial JEM with assessments of demand and control (Johnson et al. 1990, 1993, Fredlund et al. 2000) and one specific on shift work.

2 AIM

The overall aim of this thesis was to study work-related risk factors for cardiovascular disease, particularly, occupational noise, job strain and shift work were addressed.

Paper I: In the first paper, the aim was to investigate whether occupational noise exposure increased the risk of coronary heart disease and cerebrovascular disease and to analyse interactions with occupational stress, job strain, in a longitudinal study of Swedish men.

Paper II: In the second paper, the aim was to analyse mortality from cardiovascular disease in a cohort of industrially employed women exposed to shift work and occupational noise, compared to the general population.

Paper III: In the third paper, the purpose was to investigate whether Swedish seafarers have increased mortality from cardiovascular disease compared to the general population and investigate potential differences in mortality over time, between different duties on board and different vessels among the seafarers.

Paper IV: In the fourth paper, the purpose was to investigate whether there is an association between exposure for occupational stress, job strain, and the presence of calcium in the coronary arteries.

3 MATERIAL AND METHODS

This thesis is based on four studies, paper I-IV. Paper I-III are longitudinal cohort studies and paper IV is a cross-sectional study, table 1.

Table 1. Overview of design and sample in each paper

Paper	I	II	III	IV
Design	Cohort	Cohort	Cohort	Cross-sectional
Data collection	Primary prevention study	Paper mill cohorts	Swedish Seafarers cohort	SCAPIS pilot study
Inclusion criteria	Random sample of males born in Gothenburg 1915-1925. Employed at follow up. No previous coronary heart disease or stroke.	Females working in the production of paper mills employed >1 year.	Females and males born after 1920, with Swedish personal identity number and a minimum of 30 days of registration with the Seafarers´ Register between 1985-2013	Residents in Gothenburg. Females and males aged 50-64 years. No previous cardiac stent or by pass surgery.
Sample size	5,753	4,496	85,169	777
Outcome	Incidence of cardiovascular disease	Mortality from cardiovascular disease	Mortality from cardiovascular disease	Coronary calcium
Statistical method	Hazard ratio using Cox proportional hazards regression	Standardized mortality ratio	Standardized mortality ratio	Prevalence ratio using Cox regression and robust variance

3.1 STUDY POPULATION

In paper I, the studied population came from the Primary Prevention Study, a general population sample consisting of 10,000 men born between 1915 and 1925 (Wilhelmsen et al. 1986). Between 1970 -1973, 7,494 of the 10,000 men participated in screening examinations. A follow-up examination was carried out three years later, where 7,133 men participated. In this study, we used the follow-up data as our baseline since they included occupational data and health parameters.

In paper II, we merged women from three existing Swedish paper mill cohorts into one female cohort, consisting of 4,496 women working in the production in paper mills, figure 2. One of the three previous cohorts used in this study was a soft tissue paper mill cohort with four mills, which consisted of workers employed for more than 1 year during 1960 to 2008. The other two used cohorts from pulp and paper mills, two sulfate mills and four sulfite mills consisted of workers employed for more than 1 year during 1950 to 1999. Thus, 67% of the 4,496 women were derived from the soft tissue paper mill cohort, and the remaining 33% were derived from the two pulp and paper mill cohorts.

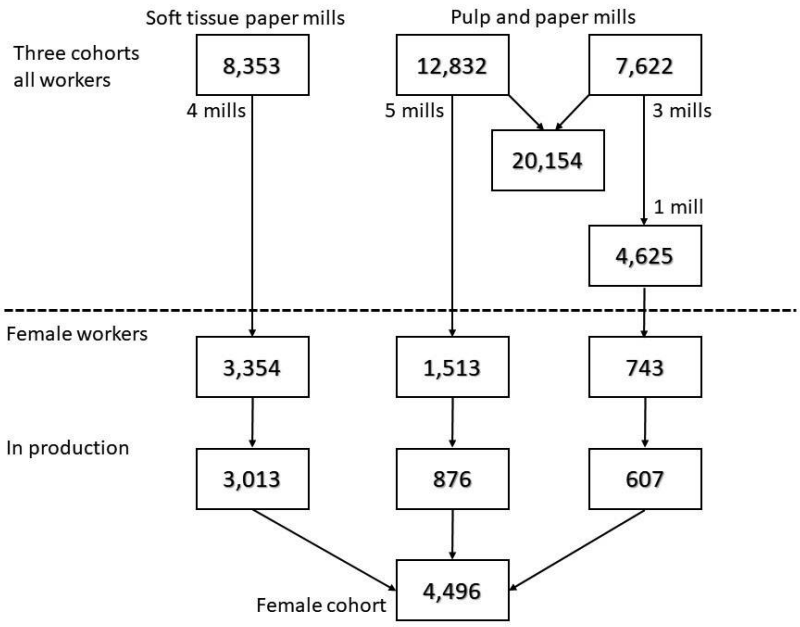


Figure 2. Flow chart of cohorts used for this study, number of workers, female workers and our final female cohort. Two of three pulp and paper mills in the third cohort did not include any women.

In paper III, the study population consisted of seafarers in Sweden registered with the Seafarers´ Registry as seafarers between 1985 and 2013. Subjects with records of a minimum of 30 days of work on a vessel during that period were included. Those who lacked a Swedish personal identity number, i.e. foreign workers, were excluded as were subjects born before 1920. Both women and men were included. In total, there were 85,169 subjects after exclusions.

In paper IV, the study population was derived from the SCAPIS pilot study (Bergström et al 2015). In 2012, 2,243 men and women registered as residents in Gothenburg, aged 50–64 years, were randomly selected and invited to participate in this study. A total of 1,111 subjects accepted and of them totally 777 participants had complete data on CAC, job demand-control and used covariates.

3.2 ASSESSMENT OF EXPOSURE

3.2.1 ASSESSMENT OF NOISE EXPOSURE

Noise exposure was estimated through a previously established general JEM, in paper I, (Sjöström et al. 2013). This noise JEM was based on 145 measurement reports and 569 measurements. It classifies 321 occupations on noise levels and covers the period from 1970 to 2004 in 5-year intervals. The eight-hour time-weighted average sound levels, TWAs, were categorised into three different levels in the JEM: low <75 dB(A); medium 75–85 dB(A); and high >85 dB(A). There was also an assessment of likelihood of peak noise exposure. The subjects in our study were classified into three groups for TWA levels and noise peaks, according to their occupation at baseline.

In paper II, we used a specific noise JEM, developed for the soft paper mill cohorts (Neitzel et al. 2018), for assessment of the noise exposure among the workers in the soft tissue mills. It was based on 100 stationary and 209 full-shift personal dosimetry measurements made at the soft tissue paper mills by occupational hygienists from our department as well as 812 stationary and 36 full-shift personal dosimetry measurements made by the mills. Information from focus groups, researchers and historical books on the production of the mills was also used. Based on these data, a semi-quantitative JEM was established in which noise exposures were classified into one of seven different ranked categories for each department and each year. The categories were: <75 dB(A), 75-79.9 dB(A), 80-84.9 dB(A), 85-89.9 dB(A), 90-94.9 dB(A), 95-99.9 dB(A), ≥100 dB(A) (Neitzel et al. 2018). A noise JEM was also developed for every pulp mill where a similar procedure was done, we used information from researchers, historical books and measurements from American pulp mills and for one of the pulp mills we had detailed data on noise levels that was used.

We had information from personnel files regarding department and job title for the workers so the JEMs were applied to assign a TWA level for every year of mill work for every worker.

3.2.2 ASSESSMENT OF PSYCHOSOCIAL WORK CONDITIONS

In the first paper, job demand-control was estimated using a previously developed JEM. Initially constructed by Johnson et al. (1990, Johnson and Stewart. 1993), based on data from the annual Swedish Living Conditions

Survey (ULF) 1977 and 1979 and then further developed by Fredlund et al. (2000) using questionnaire data from the Swedish Work Environment Survey 1989-97 (n=48,894). This JEM has index scores of job demand and control (decision latitude) initially for 261 occupations and in the later version for 320 occupations, by gender and age. All subjects in this study were assigned a certain score based on occupation, age and being male, through this psychosocial JEM. Using the median of the distribution as cut-off, which is standard procedure, demand and control were dichotomized as high or low. The participants were then allocated into four categories: high strain (high demand-low control), active (high demand-high control), passive (low demand-low control) and low strain (low demand-high control).

In paper IV, job demand control was estimated using the Swedish version of Karasek & Theorell's Job Content Questionnaire, labelled The Swedish Demand-Control-Support Questionnaire (DCSQ) (Sanne et al. 2005, Chungkham et al. 2013). The demand and control variables were positively inverted so that high scores were equivalent to high demands or high control and then summed separately. Since job demand and control were analysed using sum scores, subjects with <50% missing items received imputed values, mean scores of the remaining items in each variable were imputed on individual level. Each variable was then dichotomized into high or low by the median values of the distributions. The dichotomized variables were combined into the following categories: high strain (high demand-low control), active (high demand-high control), passive (low demand-low control) and low strain (low demand-high control) and the participants were allocated into these categories.

3.2.3 ASSESSMENT OF SHIFT WORK

In paper II, a shift work JEM was developed, specific for each of the mills in the study, based on: information from personnel files; group-level questionnaire data; information from focus groups consisting of people responsible for the working environment, managers, and employees; information collected from key persons; researchers with knowledge of the paper mills; and historical information from books. Each department and year were classified as either no shift work, shift work without nights or rotating shift work including nights. Shift work without nights was common among female workers until the 1980s, especially at the soft tissue mills.

3.3 ASSESSMENT OF OTHER VARIABLES

3.3.1 THE METABOLIC SYNDROME

In paper IV, the participants were classified as having metabolic syndrome or not according to the criteria for clinical diagnosis of the metabolic syndrome in the statement from the American Heart Association and the National Heart, Lung, and Blood Institute (Grundy et al. 2005).

Presences of any three of the following five parameters were regarded as constitution of the metabolic syndrome:

- elevated waist circumference, ≥88 cm in women and ≥102 cm in men
- elevated triglycerides, ≥1,7 mmol/l or drug treatment for elevated triglycerides
- reduced HDL cholesterol, <1,3 mmol/l in women and <1,03 mmol/l in men or treatment with statins
- elevated blood pressure, systolic blood pressure ≥130 and diastolic blood pressure ≥85 or hypertensive drug treatment
- elevated fasting glucose; ≥5,5 mmol/l or treatment with antidiabetic drugs or insulin

3.3.2 SEAFARERS

Information was retrieved from the Seafarers registry, held by the Swedish Transport Agency, on dates of seafaring work, type of vessel and duty onboard for each seafarer and for each period of service. Based on this, the seafarers were categorized into different groups. Firstly, we divided the subjects into two categories, seafarers who had worked *solely on passenger ferries* and seafarers who had worked on *different types of vessels*.

Secondly, type of duty on board was divided into four categories: *solely service* means only having served in the service section of a vessel; *deck officer (ever)* means ever having worked as a deck officer; *engine officer/crew (ever)* means ever having worked in the engine room as officer or crew; and *deck crew* means having worked as deck crew and possibly also having served in the service section.

Thirdly, the seafarers were subdivided into groups based on time registered as a seafarer, *<1 year, 1–5 years, 5–10 years, 10–20 years,* and *>20 years.*

3.4 OUTCOMES

Outcomes were classified according to the diagnostic codes of the International Statistical Classification of Diseases and Related Health Problems, 6^{th}–10^{th} revisions (ICD-6 to ICD-10).

In paper I, outcomes were cardiovascular diagnoses using the Swedish national register on cause of death and the Swedish hospital discharge register from the National Board of Health and Welfare. The outcomes were classified according to ICD-8 code until 1986, ICD-9 was used from 1987 to 1996, and ICD-10 was used from 1997 onwards. Coronary heart disease was defined as 410-414 (ICD-8, 9) and as I20-I25 (ICD-10) from the death register and as acute myocardial infarction 410 and I21 from the discharge register, respectively. Stroke events, including both ischemic stroke and intracerebral bleeding, were defined as death or hospitalisation with ICD codes 431-438 (ICD-8, 9) and I61-I69 (ICD-10).

In paper II, reference data regarding mortality for the general population were retrieved from the National Board of Health and Welfare. Outcomes studied were mortality from cardiovascular diagnoses and total mortality, from the Swedish Cause of Death Register. Coronary heart disease was defined as ICD-6/7 codes 420 and 422.1, ICD-8/9 codes 410–414 and as ICD-10 codes I20–I25. Cerebrovascular disease, including both ischaemic stroke and intracerebral bleeding, and also subarachnoid bleeding, was defined as ICD 6/7 330-334 ICD-8/9 430–438 and ICD-10 I60–I69. From 1969 onward, acute myocardial infarction, ICD-8/9 410 and ICD-10 I21 could be analysed.

In paper III, outcomes were cardiovascular diagnoses from the Swedish Cause of Death Register and total mortality from Statistics Sweden. Coronary heart disease was defined as ICD-8/9 codes 410–414 and as ICD-10 codes I20–I25, myocardial infarction as ICD-8/9 410 and ICD-10 I21. Cerebrovascular disease, including both ischaemic stroke and intracerebral bleeding, was defined as ICD-8/9 430–438 and ICD-10 I60–I69. Ischaemic stroke was defined as ICD-8/9 433–434 and ICD-10 I63–I64 and intracerebral bleeding as ICD-8/9 431 and ICD-10 I61.

The outcome in paper IV was coronary calcium score, CACS, which was estimated using a computed tomography investigation of the coronary arteries.

The calcium content in each coronary artery was measured, summed and quantified using the Agatston score (Sandfort et al. 2017) and CACS 0 was compared to CACS ≥100.

3.5 STATISTICS

The data in paper I was analysed with Cox regression. HRs, and 95%, CIs, were calculated. The participants were stratified by their noise exposure; low, medium and high noise levels and also by likelihood of noise peaks; unlikely, maybe, and likely. Hospital care or mortality from coronary heart disease or stroke was considered events and time was measured as months since baseline. The observation period stopped at the age of 75. We adjusted for age only and in a risk factor adjusted model also for ever-smoking, cholesterol, diabetes, hypertension and body mass index, BMI. The interaction between occupational noise exposure and high strain was analysed by dividing the population into subjects exposed to high strain versus subjects not exposed to high strain. HRs and tests for trend were calculated.

In paper II the person-years at risk were calculated starting from the first time of employment in the paper mills until time of death or the end of follow up, 31 December 2013. The person years were stratified by 5-year age groups and 1-year calendar periods. The expected number of deaths for these strata was calculated using the female general population as a reference. SMRs were calculated with 95% CI. Subjects were categorized into exposure groups, based on their shift- and noise exposure. We analyzed three levels of noise and shift work. Noise levels were grouped as; <90 dBA, ≥90 dBA for <10 years, and ≥90 dB for ≥10 years. Shift work was grouped as; no nights, rotating shift work including nights for <10 years, and rotating shift work including nights for ≥10 years. SMR was also calculated for person-years in different age groups, <65 years and ≥65 years, the usual age of retirement in Sweden.

In paper III, the person-years at risk were calculated from first time of work at sea registered in the Seafarers registry until first emigration, time of death or end of follow-up, 31 December 2013. The person years were stratified by gender, 5-year age groups and 1-year calendar periods. The expected number of deaths for these strata was calculated using the general population as a reference. The SMRs with 95% CIs were calculated stratified for gender, type of vessel, position held, and time registered as a seafarer. The SMR was also calculated for person-years in different age groups: <46, 46–55, 56–65, and >65 years. Further analyses were done on seafarers who started their sea

service before 1985 and after 1985, respectively, and by dividing the observation period into two periods, 1985–1999 and 2000–2013.

In paper IV the participants were divided in three groups according to their CACS; CACS 0, CACS 1-99 and CACS ≥100. Associations between psychosocial work variables, job demand-control, and CACS were calculated with prevalence ratios (PR), using Cox regression with robust variance and 95% CI. The groups CACS 1-99 and CACS ≥100, respectively, were compared to CACS 0. All analyses were cross-sectional. The following covariates were used: age, gender, smoking status, university education, socioeconomic area and the metabolic syndrome.

4 RESULTS

4.1 PAPER I

There were 1,004 events of coronary heart disease during the follow-up period of 94,222 person years. For the participants exposed to medium levels of noise the risk of coronary heart disease was HR 1.15 (95% CI 1.01-1.31) and high levels of noise HR 1.27 (95% CI 0.99-1.63), respectively, age-adjusted. Exposure to noise peaks also increased the risk of coronary heart disease HR 1.19 (95% CI 1.03-1.38). In the risk factor-adjusted models, all estimates were slightly diminished, but the statistical significance was kept on noise peaks. Analysing the cohort excluding the subjects with hypertension and diabetes at baseline (n=4,400), the HR for coronary heart disease was 1.20 (95% CI 1.03-1.41) for participants exposed to medium level of noise exposure and 1.49 (95% CI 1.11- 1.99) for those exposed to a high level of noise exposure and for the subjects with likely exposure to noise peaks the HR was 1.30 (95% CI 1.09-1.55). When analysing the risk of coronary heart disease in subjects younger than 65 years the risk estimates increased, but the confidence intervals turned wider and included unity.

There were 517 stroke events during the follow-up period. There was no increased risk of stroke in any category of noise exposure, medium levels, high levels or peak noise exposure.

Among those classified as exposed to high strain (high demands and low control) and occupational noise >75 dB(A), the risk for coronary heart disease further increased HR 1.80, (95% CI 1.19-2.73) age-adjusted, Table 2, and risk factor-adjusted: HR 1.73, (95% CI 1.14-2.61). Interaction analyses on stroke were negative.

Table 2. Interaction between occupational noise exposure and high strain. Hazard ratios (HR) with confidence intervals for coronary heart disease and stroke in subjects exposed for high strain versus not exposed for high strain in relation to exposure for occupational noise among all men (n=5,753).

	Age adjusted HR(95% CI)	
	High strain(n events)	Not high strain(n events)
Coronary heart disease, all, n=1004 events		
Low noise, <75 dB(A)	1.00 (ref) n=29	1.00 (ref) n=451
Medium and high noise, >=75 dB(A)	1.80 (1.19-2.73) n=99	1.10 (0.96-1.25) n=425
p for interaction	p=0.03	
Noise peaks unlikely	1.00 (ref) n=92	1.00 (ref) n=530
Noise peaks maybe	1.39 (0.88-2.19) n=23	1.00 (0.81-1.22) n=112
Noise peaks likely	1.25 (0.70-2.23) n=13	1.20 (1.03-1.40) n=234
p for interaction	p=0.43	
Stroke, all, n=517 events		
Low noise, <75 dB(A)	1.00 (ref) n=17	1.00 (ref) n=245
Medium and high noise, >=75 dB(A)	1.33 (0.76-2.33) n=43	1.01 (0.84-1.21) n=212
p for interaction	p=0.35	
Noise peaks unlikely	1.00 (ref) n=47	1.00 (ref) n=289
Noise peaks maybe	0.68 (0.29-1.60) n=6	0.86 (0.64-1.15) n=53
Noise peaks likely	1.44 (0.65-3.19) n=7	1.07 (0.87-1.33) n=115
p for interaction	p=0.66	

4.2 PAPER II

During the follow up period of 167,262 person years, there were 1,191 deaths, out of which 29% were due to cardiovascular disease.

The cohort median value of number of years of employment within the paper mill industry was 6 years, and 37% had been employed >10 years. 64% had worked only before 1987. The median TWA noise level in dB(A) (25-75 percentiles) was 89.2 (84.2-92.5). The overall total mortality or mortality from coronary heart disease or cerebrovascular disease was not increased compared to the general population. However, the mortality from acute myocardial infarction in the cohort was increased, SMR 1.20 (95% CI 1.01-1.41), especially before the age of 65 years, SMR 1.50 (95% CI 1.00-2.15), Table 3.

Participants exposed to shift work with no nights and noise exposure <90 dB(A) had no increased mortality from acute myocardial infarction. Among those exposed to noise ≥90 dB(A) for more than 10 years, the mortality from myocardial infarction was SMR 1.41 (95% CI 1.02-1.89). For those who were below 65 years at death and exposed to noise ≥90 dB(A), the mortality from myocardial infarction was even higher, SMR 1.95 (95% CI 1.24-2.93). Analysing participants having worked rotating night shift more than 10 years the SMR from myocardial infarction was 1.33 (95% CI 0.91-1.89). For the combined exposure of noise ≥90 dB(A) and shift work (no nights) the SMR from myocardial infarction was 1.31 (95% CI 0.97-1.73), Table 4, and among them, for the participants below 65 years of age, the mortality from myocardial infarction was SMR 2.41 (95% CI 1.20-4.31).

Table 3. Mortality from cardiovascular disease 1956-2013 among shift working female paper mill employees in relation to shift work and noise. Standardized mortality ratios (SMR) with 95% confidence intervals (CI). If less than 5 cases, expected cases are shown in parentheses.

		Myocardial infarction (from 1969)		Cerebrovascular disease	
	N	Case	SMR (95% CI)	Case	SMR (95% CI)
Total cohort	4,496	144	1.20 (1.01-1.41)	116	0.95 (0.78-1.13)
Shiftwork:					
No night shift	2,097	84	1.15 (0.92-1.42)	64	0.86 (0.66-1.09)
Rotating shift <10 years	1,538	29	1.22 (0.82-1.76)	32	1.31 (0.90-1.85)
Rotating shift ≥10 years	861	31	1.33 (0.91-1.89)	20	0.85 (0.52-1.31)
Noise:					
Noise <90 dB(A)	1,997	49	1.08 (0.80-1.42)	41	0.87 (0.63-1.19)
Noise ≥90 dB(A) <10 years	1,897	52	1.18 (0.88-1.55)	42	0.94 (0.68-1.27)
Noise ≥90 dB(A) ≥10 years	602	43	1.41 (1.02-1.89)	33	1.06 (0.73-1.49)
Total cohort age <65 years		29	1.50 (1.00-2.15)	11	0.95 (0.58-1.04)
Shiftwork age <65 years:					
No night shift		15	1.48 (0.83-2.44)	4	(10.0)
Rotating shift <10 years		7	1.35 (0.54-2.79)	6	1.20 (0.44-2.60)
Rotating shift ≥10 years		7	1.72 (0.69-3.55)	1	(3.9)
Noise age <65 years:					
Noise <90 dB(A)		6	0.79 (0.29-1.72)	1	(7.4)
Noise ≥90 dB(A) <10 years		15	1.82 (1.02-3.00)	7	0.92 (0.16-2.22)
Noise ≥90 dB(A) ≥10 years		8	2.26 (0.97-4.45)	3	(3.9)

Table 4. Mortality from cardiovascular disease and total mortality 1956-2013 among shift working female paper mill employees in different groups of shift work and noise exposure. Standardized mortality ratios (SMR) with 95% confidence intervals (CI). If less than 5 cases, expected cases are shown in parentheses.

		Myocardial infarction (from 1969)		Cerebrovascular disease	
	N	Case	SMR (95% CI)	Case	SMR (95% CI)
Total cohort	4,496	144	1.20 (1.01-1.41)	116	0.95 (0.78-1.13)
Shift and noise:					
No nights, noise <90 dB(A)	1,316	35	0.99 (0.69-1.37)	31	0.84 (0.57-1.20)
No nights, noise >90 dB(A)	781	49	1.31 (0.97-1.73)	33	0.87 (0.60-1.22)
Rotating shift, noise <90 dB(A)	681	14	1.41 (0.77-2.36)	10	0.98 (0.47-1.81)
Rotating shift, noise >90 dB(A)	1,718	46	1.24 (0.91-1.66)	42	1.11 (0.80-1.50)
Age at death	Age				
No nights, noise <90 dB(A)	<65	4	(5.5)	1	(5.4)
No nights, noise <90 dB(A)	≥65	31	1.03 (0.70-1.47)	30	0.96 (0.65-1.37)
No nights, noise >90 dB(A)	<65	11	2.41 (1.20-4.31)	3	(4.6)
No nights, noise >90 dB(A)	≥65	38	1.15 (0.82-1.58)	30	0.90 (0.60-1.28)
Rotating shift, noise <90 dB(A)	<65	2	(2.0)	0	(1.9)
Rotating shift, noise <90 dB(A)	≥65	12	1.51 (0.78-2.64)	10	1.22 (0.58-2.24)
Rotating shift, noise >90 dB(A)	<65	12	1.66 (0.86-2.91)	7	1.00 (0.40-2.06)
Rotating shift, noise >90 dB(A)	≥65	34	1.14 (0.79-1.59)	35	1.14 (0.79-1.58)

4.3 PAPER III

Seafarers working on passenger ferries

There was no increased total mortality or increased mortality from CHD or cerebrovascular disease in seafarers who had worked on passenger ferries only.

Seafarers working on different vessels

There was no increased mortality in CHD when analysing the seafarers, who had worked on different types of vessels, as one group. However, when dividing the seafarers into subgroups, we found increased mortalities. For the age group <46 years, the SMR for CHD was significantly increased, 1.48 (95% CI 1.06–2.01), and their SMR for total mortality was also increased, SMR 1.36 (95% CI 1.25–1.48), Table 5. The mortality varied along the length of registration in the Seafarers registry, SR, and was the highest for seafarers who had worked 10-20 years. As an example, male seafarers who were <46 years old and had been registered for 10–20 years, the SMR for CHD was 2.46 (95% CI 1.31–4.20). But for seafarers registered >20 years in the SR, there was no increased mortality in CHD. It was the categories male deck crew and male engine officer/crew (ever) <46 years that had significantly increased SMRs for CHD when calculating mortality according to type of duty on board.

When we divided the male seafarers with regard to start of sea service, we observed that, for male seafarers who started before 1985 and were <46 years, the SMR for CHD remained significantly increased. For male seafarers < 46 years, who started their sea service after 1985, the SMR for CHD was similar compared to the subjects who started before 1985 but no longer significantly increased.

Dividing the observation period into two periods, 1985–1999 and 2000–2013, showed that mortality from CVD remained significantly increased for the years 1985–1999 for males <46 years and the total mortality also remained significantly increased. During the observation period 2000–2013, the SMRs for CVD were insignificant, even though there was a borderline increased mortality from CHD for men aged 56–65 years, SMR 118 (95% CI 99-140). The total mortality for the seafarers having served on different types of vessels as one group decreased during the observation period 2000-2013; however, it was significantly increased for male seafarers of the ages 46–55 years, SMR 1.27 (95% CI 1.13–1.42) and 56–65 years, SMR 1.30 (95% CI 1.21–1.40).

SMR from cerebrovascular disease was also calculated. Male seafarers <46 years had a significantly increased mortality from cerebrovascular disease, SMR 1.93 (95% CI 1.16–3.02) Table 5.

When analysing the female seafarers, the SMR for mortality from CHD was 1.22 (95% CI 0.87–1.65) and from cerebrovascular disease, 1.14 (95% CI 0.72–1.71). We found no significantly increased mortality in cardiovascular disease for women when dividing them into different ages. However, the total mortality was increased for the ages 46–55 years, SMR 1.40 (95% CI 1.07–1.81). Table 5.

Table 5. Mortality from cardiovascular disease and total mortality, 1985–2013, among Swedish seafarers serving on different types of vessels, compared with the general population, shown as standardized mortality ratio (SMR) with observed cases (O) and 95% confidence intervals (CIs), by gender and age at death. Where fewer than three cases were reported, expected values are shown in parentheses.

	Age <46 yrs			Age 46–55 yrs			Age 56–65 yrs			Age >65 yrs		
	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI
Male seafarers on different vessels												
Total mortality	557	1.36	1.25–1.48	618	1.21	1.12–1.31	1,116	1.19	1.12–1.26	1,656	0.88	0.84–0.92
Coronary Heart disease	41	1.48	1.06–2.01	100	1.00	0.81–1.21	232	1.00	0.88–1.14	356	0.84	0.76–0.93
Myocardial infarction	23	1.29	0.82–1.94	55	0.85	0.64–1.10	130	0.88	0.74–1.04	191	0.78	0.67–0.89
Cerebro-vascular disease	19	1.93	1.16–3.02	17	0.78	0.46–1.25	50	1.05	0.78–1.38	110	0.75	0.62–0.90
Stroke	0		(1.5)	3	0.61	0.13–1.79	12	0.74	0.38–1.30	56	0.82	0.62–1.06
Cerebral haemorrhage	9	2.18	1.00–4.13	8	0.81	0.35–1.59	25	1.37	0.89–2.03	23	0.73	0.46–1.10
Female seafarers on different vessels												
Total mortality	47	1.20	0.88–1.60	60	1.40	1.07–1.81	64	1.12	0.87–1.44	163	1.10	0.94–1.29
Coronary heart disease	0		(1.0)	3	1.13	0.23–3.29	9	1.43	0.65–2.72	29	1.23	0.82–1.76
Myocardial infarction	0		(0.7)	2		(1.8)	3	0.72	0.15–2.10	13	0.94	0.50–1.60
Cerebro-vascular disease	1		(1.3)	4	2.02	0.55–5.17	2		(2.9)	16	1.15	0.65–1.86

4.4 PAPER IV

Among the 777 participants 20% of the men and 5% of the women had CACS ≥100, respectively. For women there was no association between exposure for high strain and having CACS ≥100 PR 1.02 (95% CI 0.24-4.31), adjusted for age, education, smoking, socioeconomic area and metabolic syndrome. For women reporting passive job, the risk of having CACS ≥100 was PR 2.40 (95% CI 0.83-6.92). Male participants reporting high strain job had a risk PR 1.54 (95% CI 0.88-2.69) of having CACS ≥100 and those reporting active job; PR 1.67 (95% CI 0.92-3.06), respectively, Table 6.

Table 6. Groups of coronary calcium score (CACS) analysed in relation to exposure for job demand-control. High strain job, active job and passive job are compared with low strain job with prevalence ratios (PR) and 95% confidence intervals (CI).

	CACS=1-99 compared to CACS=0		CACS≥100 compared to CACS=0	
	PR (95% CI) age-adjusted*	PR (95% CI) adjusted**	PR (95% CI) age-adjusted*	PR (95% CI) adjusted**
Women, N - N	82 - 293	82 - 293	18 - 293	18 - 293
High strain job	0.79 (0.45-1.40)	0.83 (0.46-1.50)	0.75 (0.17-3.21)	1.02 (0.24-4.31)
Active job	0.92 (0.53-1.59)	0.93 (0.54-1.57)	0.59 (0.12-2.80)	0.70 (0.16-3.02)
Passive job	0.93 (0.58-1.50)	1.06 (0.64-1.73)	1.44 (0.49-4.20)	2.40 (0.83-6.92)
Men, N - N	137 - 170	137 - 170	77 - 170	77 - 170
High strain job	1.18 (0.78-1.80)	1.21 (0.79-1.84)	1.56 (0.86-2.83)	1.54 (0.88-2.69)
Active job	1.23 (0.77-1.97)	1.18 (0.75-1.86)	1.51 (0.78-2.95)	1.67 (0.92-3.06)
Passive job	1.12 (0.75-1.67)	1.16 (0.78-1.74)	1.09 (0.58-2.06)	1.27 (0.68-2.37)

*all subjects adjusted for age and gender

**adjusted for age, education, smoking, socioeconomic area and metabolic syndrome, all subjects also adjusted for gender

5 DISCUSSION

This thesis explores and gives further evidence for the association between the occupational exposures noise, shift work and job strain and cardiovascular diseases.

In the first paper we analysed exposure to noise, interaction with job strain and risk of cardiovascular disease in a longitudinal study of men. Exposure to occupational noise increased the risk of CHD but there was no increased risk of stroke. The study also suggested an interaction between noise exposure and job strain.

In the second paper, female paper mill workers with combined exposure to shift work and noise had a significantly increased risk of mortality from acute myocardial infarction, but not from stroke.

In the third paper, relatively younger male seafarers who had worked on different types of vessels had an increased mortality from CVD.

In the fourth study we had insufficient power, but our results indicated that exposure to high strain job or active job could increase the risk of CAC in men, but in women, it could rather be exposure to passive job, but the results were insignificant.

5.1 NOISE AND CARDIOVASCULAR DISEASE

We found evidence for an association between occupational noise and coronary heart disease in paper I and II, in parity with previous longitudinal studies. A prospective 18 year follow up Finnish study showed an increased risk for coronary heart disease associated to continuous noise exposure exceeding 85 dB(A), and exposure to impulse noise (Virkkunen et al. 2005). In paper II, this finding was most pronounced among those exposed to high levels of noise with a long duration of employment and below 65 years of age. As in a Canadian study of lumber mill workers exposed to noise where there was an increased risk of fatal acute myocardial infarction associated to duration of employment and to noise levels (Davies et al. 2005).

We found no increased risk of or mortality from stroke in paper I or II in relation to noise exposure. There are opposing results from earlier studies on the association between stroke and occupational exposure. A Danish study

(Stokholm 2013) did not show an increased risk of stroke from exposure to occupational noise. In an Australian study of 2,942 subjects there was a significant association between the incidence of stroke and those exposed to very high levels of noise (Gopinath et al 2011). In a Japanese study (Fujino et al. 2007) comprising 14,568 subjects, the risk of intra-cerebral bleeding was HR 2.1 (95% CI 1.0-4.4) and the HR for ischemic stroke was 1.7 (95% CI 0.7-4.1). However, the noise levels were self-reported. Stroke comprises different subtypes such as ischemic stroke, intra-cerebral bleeding and sometimes also subarachnoid bleeding is included in the stroke concept in studies. All those clinical subtypes of stroke may be related to different risk factors.

5.2 SHIFT WORK AND CARDIOVASCULAR DISEASE IN THE PAPER INDUSTRY

In paper II, in addition to noise, shift work and mortality from CVD was studied among female workers in the paper industry. Among participants who had worked rotating night shift more than 10 years, the SMR from myocardial infarction was insignificantly raised, 1.33 (95% CI 0.91-1.89). However, almost all subjects in our study were exposed to shift work, but there were relatively few subjects that were exposed to shift work only and not to noise, hence we had a lack of power when studying the effects of shift work. Exposure to noise is frequently combined with exposure to shift work in industrial settings. It is a complex task to separate the health effects from these exposures. There could also be synergistic effects. A study of industrially employed men in Finland showed an increased risk of ischemic heart disease when exposure to shift work occurred as well as when exposure to noise occurred, and also, when both exposures occurred simultaneously (Virkkunen et al. 2006).

There is frequently also an exposure to dust in industries, especially in the paper industry. For the soft tissue mill cohort we have assessed paper dust exposure in a JEM in a similar way as for noise. Applying this paper dust assessment did not show any risk of mortality from acute myocardial infarction or other cardiovascular diseases from paper dust. Applying all three JEM's did not change the results for noise and shift work which is why we omitted the paper dust exposure from the current analyses. Pulp mills are much less dusty than soft tissue mills. Chemicals are more frequently used in pulp mills, but the risk of mortality from myocardial infarction was similar between the two types of paper mills.

5.3 JOB STRAIN, CORONARY CALCIUM AND CARDIOVASCULAR DISEASE

In paper I, noise exposure and the interaction with job strain was studied. Job strain further increased the risk of CHD in accordance with the findings by Selander et al. (2007) in a case control study, where job strain further increased the risk for coronary heart disease when occupational noise exposure occurred. Exposure to job strain job has been associated with increased risk of CVD, a review from 2015 presented increased risk of CHD RR 1.34 (95% CI 1.18-1.52) (Kivimäki and Kawachi. 2015). A study published after this review, showed increased risk of CHD among male manual and male non-manual workers exposed to job strain or active job (Ferrario et al. 2017).

In paper IV job strain and the risk of CAC was studied. Few previous studies have investigated the association between job strain and CAC and the results have been negative. (Greenlund et al. 2010, Rozanski et al. 2011).

In our study, the PR of having CACS ≥100 among men exposed to high strain or active job, was non-significantly elevated. For women there was no association between exposure to high strain and having CACS ≥100 but among women reporting passive job, the PR of having CACS ≥100 was non-significantly elevated. However, the power of the study was limited. Lack of associations could also be due to the relatively young age of the participants, as CAC relates to an older age (Liew et al. 2017). In our study, CAC was more frequent among men and in older ages, as reported in a previous prospective cohort study where they investigated the amount of CAC in a cohort of 6,814 participants 45 to 84 years of age (McClelland et al. 2006).

5.4 SEAFARERS AND CARDIOVASCULAR MORTALITY

In paper III, mortality from CVD was studied among seafarers. We found an increased mortality from CHD and cerebrovascular disease for male seafarers <46 years old, who had worked on different types of vessel in the positions “deck crew” or “engine officer/crew (ever)”, particularly those who had served as seafarers for several years. In a Danish cohort study on seafarers from 1970–1985, a significantly increased mortality rate from CHD was presented only for the engine crew (Brandt et al. 1994). The occupational exposure is likely different among different positions at sea and has likely varied over time. This

increased mortality in our study among these relatively young men with a longer experience as seafarers could indicate a relation to work.

There was an insignificant tendency towards increased mortality from CHD at a later age for the female participants in paper III, compared to the male participants. There is generally a development of CHD later in life for women compared to men (Bello and Mosca. 2004). The lack of significant results for the females in our study may be due to lack of statistical power; there are fewer female seafarers and hence, there were fewer females in the cohort. We cannot conclude that there is no increased mortality for female seafarers from CHD.

However, the total mortality was increased for both male and female seafarers who had worked on different types of vessels. Previous studies have shown increased mortality and morbidity in seafarers compared with individuals in land-based occupations (Brandt et al. 1994, Rafnsson and Gunnarsdottir. 1994, Poulsen et al. 2014). We found no increase in mortality from cardiovascular disease or total mortality for seafarers, who had worked solely on passenger ferries. The occupational environment is likely different on passenger ferries with less chemical exposure and more regular work schedules. However, the seafarers in our study who had worked solely on passenger ferries had worked for less time at sea compared to the seafarers who had worked on different types of vessels.

The mortality from CHD was not significantly increased for seafarers who started their sea service after 1985 or the observation period 2000–2013, but this may be partly due to lack of power, their shorter time as seafarers and their younger ages. However, there was a borderline increased mortality from CHD for men aged 56–65 years, SMR 118 (95% CI 99-140) during 2000-2013. The increase in total mortality decreased over time. In a Danish study analysing mortality in seafarers 1986-2009, the total mortality diminished over time; however, there was no clear decrease in mortality from heart diseases (Borch et al. 2012).

5.5 REGISTER STUDIES

Register studies have several strengths such as that the data already exist, large samples can be studied and there is no differential misclassification or attrition bias (Thygesen and Ersbøll. 2014). In paper I-III we have used national register with high coverage and good quality to collect information on the outcome, cardiovascular diseases. There are also limitations with register studies such as; important information can be unavailable, potential confounder

information is lacking, missing information on data quality, differences in coding of the data (Thygesen and Ersbøll. 2014).

In paper II-III we had no information on risk factors for cardiovascular diseases such as smoking which is considered important information. However, in paper II, a previously performed subgroup analysis on 1,686 subjects with adjustment for smoking, showed no substantially changes of the risk estimates, compared to unadjusted for smoking, but had low power. This adjustment was possible due to information from survey data. Regarding paper III and lack of individual data on smoking, in 1977 in Sweden, 67% of male deck officers, 51% of male engine officers and 35% of male engine crew were smokers, compared with 44% of the general male population (Nilsson 1998). In a Swedish questionnaire survey from 2014 answered by 1,972 seafarers, 11% of the respondents were current daily smokers, with no marked difference between men and women (Forsell et al. 2015). Among the service personnel, the proportion of smokers was higher, 23%. In the present study, paper III, there was no increased mortality from cardiovascular diseases among the service personnel. In the Swedish general population, 9% of men and 11% of women were daily smokers in 2015, according to the Public Health Agency of Sweden.

In paper III, we had no information on site of death for the seafarers. Possibly, the increased mortality from CVD could be partially attributed to long distance to advanced medical treatment. Yet, long distance is not likely to explain the entire increase as the high mortality figures were also related to seafarer age, type of vessel, and length of registration as a seafarer. In a Polish study on seafarers, pre-hospital mortality from myocardial infarction was increased compared to the general working population, but the incidence was not increased. The authors concluded that work-related factors reduce survival at sea in the case of a myocardial infarction (Jaremin and Kotulak. 2003).

5.6 JOB EXPOSURE MATRICES

In paper I and II JEMs were used for classification of exposure to noise, shift work and job strain. JEMs decrease the risk of information bias and dependent misclassification. However, variability of exposure within occupational categories in different workplaces is usually not considered which can result in independent misclassification of the exposure which increases the risk of underestimation of possible associations. Also, JEMs are likely time dependent since occupational exposures change over time (Niedhammer 2018). However, in paper II we have used noise JEMs and a shift work JEM that are constructed

specifically for studies of the mills and they are based on measurements and specific information from the studied time period.

5.7 HEALTHY WORKER

It is common in epidemiological studies to compare workers death rates in a specific job with death rates in the general population. This comparison can be biased since the general population contains people who do not work because of ill health. And as a consequence, the death rates for the studied workers can be lower than those for the general population. This selection bias is called the healthy worker effect (Rothman 2012). That apply to paper II-III where we compared our mortality rates with the general population. So, this could reduce our estimates, but despite the healthy worker effect, we found an increased total mortality in paper III.

In paper III, mortality from CHD was increased among subjects that had worked 10-20 years at sea. But after 20 years of registered seamanship the mortality from CHD declined, this could partly be due to a healthy worker effect, the healthiest persons are still working and the persons with poor health has left their occupation or at least their occupation at sea. As in an Icelandic study where the mortality from ischaemic heart disease was the highest among seafarers who had worked for 8–10 years, SMR 1.56 (95% CI 1.14–2.7); but then the mortality decreased (Rafnsson and Gunnarsdottir. 1994).

5.8 CLASSIFICATION OF SEAFARERS

In paper III, we divided the seafarers into those who had worked solely on passenger ferries and those who had worked on different types of vessels. It is common for seafarers to work on several types of vessels during their working years. Therefore, in our study, paper III, it was not possible to analyse each type of vessel separately on that type of vessels specific risk of mortality. The seafarers who had worked on passenger ferries solely had no increased mortality, but few of these seafarers had served at sea before 1985 and they had also worked for less years at sea. However, the occupational exposure of passenger ferries and other types of vessels differ considerably, including more regular work, and less chemical exposure on passenger ferries.

Seafarers have also frequently worked in different types of duties and the exposures also differ among different duties. The seafarers were divided into four categories in our study: *solely service* means only having served in the service section of a vessel; *deck officer (ever)* means ever having worked as a deck officer; *engine officer/crew (ever)* means ever having worked in the engine room as officer or crew; and *deck crew* means having worked as deck crew and possibly also having served in the service section. It was the categories deck crew and engine officer/crew that had significantly increased mortalities from CHD in paper III. A Norwegian register study detected an increased overall mortality, but no significantly increased mortality from CVD, for seafarers working on tankers compared with seafarers working on other ships. The increased risk was related to work as a mate; there was no increased risk for those working as captains (Moen et al. 1994). And in Danish cohort study on seafarers an increased mortality from CHD was presented for the engine crew only, compared with the general population (Brandt et al. 1994).

6 CONCLUSION

General conclusion: Exposure to occupational noise is a probable risk factor for coronary heart disease. We found no increased risk of cerebrovascular disease in relation to exposure to noise or shift work, however this could be due to a lack of power in the studies, an increased risk cannot be excluded.

Among men exposed to noise >75 dB(A) there is a likely increased risk of coronary heart disease. Furthermore, noise and exposure to high strain may interact and additionally increase the risk of coronary heart disease.

Women working in the production of paper mills have an increased mortality from myocardial infarction, especially subjects less than 65 years and those exposed for a combination of shift work and noise levels of 90 dB(A) or more. The effect of noise is difficult to separate from the effect of shift work and vice versa since these exposures often cooccur.

Relatively younger male Swedish seafarers who have worked on different types of vessels have an increased mortality from coronary heart disease as well as cerebrovascular disease, particularly those who have served as seafarers for several years, even though it has diminished over time. Our results corroborate earlier international studies regarding increased general mortality among seafarers. There was no increased mortality, general or in CVD among seafarers working solely on passenger ferries.

There was a lack of power in the fourth study and the results were insignificant but indicated that occupational exposure to high strain or active job could increase the risk of development of coronary artery calcium in men. However, in women, it could be exposure to low demands and low control that increases the risk of coronary artery calcium.

7 FUTURE PERSPECTIVES

Shift work is a common occupational exposure that is complicated to study since it is often combined with other occupational hazardous exposures, particularly in industries. Several studies have been performed on shift working nurses but studies on female industrial workers are infrequent and need to be performed, particularly on groups with similar occupational exposures and with detailed assessment of the shift schedules.

We found an increased total mortality among seafarers which needs to be analyzed further to comprehend what causes this increased amount of deaths, compared to the general population. It should also be addressed why there is an increased mortality among younger seafarers in cardiovascular disease; with the methodology used in our study it was not possible to analyze this further. The incidence of cardiovascular disease among seafarers should also be studied to see if it is increased compared to the general population, we have only studied the mortality.

There is an increasing number of studies on the cardiovascular risks of noise exposure. Hearing protection is more frequently used but it is not clear whether it protects sufficiently. Could noise exposure impose a cardiovascular risk in spite of hearing protection?

In our study on occupational stress and coronary calcium we had a lack of power, and there are few previous studies addressing the same question so further studies are needed. If we will have the possibility we will perform the same analysis on the full SCAPIS study, in this study the SCAPIS pilot study was analysed.

Occupational settings and exposures have changed over time. Perhaps also attitudes towards different demands in occupational life has changed. The job strain model was elaborated during the end of the 1970´s. Should occupational stress be study through another model in coming studies?

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REFERENCES

Alves PM, Leigh R, Bartos G, Mody R, Gholson L, Nerwich N. 2010. Cardiovascular events on board commercial maritime vessels: a two-year review. Int Marit Health. 62(3):137-42.

Andersson E, Persson B, Bryngelsson IL, Magnuson A, Torén K, Wingren G et al. 2007. Cohort mortality study of Swedish pulp and paper mill workers-nonmalignant diseases. Scand J Work Environ Health 33(6):470-8.

Andersson M, Slunga Järvholm L, Järvholm B. 2019. Kunskapssammanställning 2019:3 Arbetsrelaterad dödlighet – delrapport 1, Beräkning av antalet dödsfall 2016 uppdelat på olika exponeringar i arbetet. Umeå Universitet. Arbetsmiljöverket.

Backholer K, Peters SAE, Bots SH, Peeters A, Huxley RR, Woodward M. 2017. Sex differences in the relationship between socioeconomic status and cardiovascular disease: a systematic review and meta-analysis. J Epidemiol Community Health 71(6):550-7.

Basner M, Babisch W, Davis A, Brink M, Clark C, Janssen S et al. 2014. Auditory and non-auditory effects of noise on health. Lancet. 383(9925):1325–32.

Bello N, Mosca L. 2004. Epidemiology of coronary heart disease in women. Prog Cardiovasc Dis. 46(4):287-95.

Bergström G, Berglund G, Blomberg A, Brandberg J, Engström G, Engvall J, et al. 2015. The Swedish CArdioPulmonary BioImage Study: objectives and design. J Intern Med. 278(6):645-59.

Borch DF, Hansen HL, Burr H, Jepsen JR. 2012. Surveillance of maritime deaths on board Danish merchant ships, 1986-2009. Int Marit Health. 63(1):7-16.

Brandt LP, Kirk NU, Jensen OC, Hansen HL. 1994. Mortality among Danish merchant seamen from 1970 to 1985. Am J Ind Med. 25(6):867-76.

Brown DL, Feskanich D, Sánchez BN, Rexrode KM, Schernhammer ES, Lisabeth LD. 2009. Rotating night shift work and the risk of ischemic stroke. Am J Epidemiol. 169(11):1370-7.

Chungkham HS, Ingre M, Karasek R, Westerlund H, Theorell T. 2013. Factor structure and longitudinal measurement invariance of the demand control support model: an evidence from the Swedish Longitudinal

Occupational Survey of Health (SLOSH). PLoS One. 8(8):e70541. doi: 10.1371/journal.pone.0070541.

Davies HW, Teschke K, Kennedy SM, Hodgson MR, Hertzman C, Demers PA. 2005. Occupational exposure to noise and mortality from acute myocardial infarction. Epidemiology. 16(1):25-32.

Ferrario MM, Veronesi G, Bertù L, Grassi G, Cesana G. 2017. Job strain and the incidence of coronary heart diseases: does the association differ among occupational classes? A contribution from a pooled analysis of Northern Italian cohorts. BMJ Open. 7(1):e014119. doi: 10.1136/bmjopen-2016-014119.

Forsell K, Eriksson H, Järvholm B, Lundh M, Andersson E, Nilsson R. 2015. Arbetsmiljö och säkerhet på svenska fartyg, rapport 151. Arbets- och miljömedicin Sahlgrenska Universitetssjukhuset. http://www.amm.se/wp-content/uploads/2016/12/2015-Nr.-151.pdf (Hämtad 2019-08-07).

Forsell K, Eriksson H, Järvholm B, Lundh M, Andersson E, Nilsson R. 2017. Work environment and safety climate in the Swedish merchant fleet. Int Arch Occup Environ Health. 90(2):161-8.

Fredlund P, Hallqvist J, Diderichsen F, Marklund S (red). 2000. Psykosocial yrkesexponeringsmatris. Arbete och Hälsa. Stockholm: CM Gruppen.

Fujino Y, Iso H, Tamakoshi A; JACC study group. 2007. A prospective cohort study of perceived noise exposure at work and cerebrovascular diseases among male workers in Japan. J Occup Health. 49(5):382-8.

Gopinath B, Thiagalingam A, Teber E, Mitchell P. 2011. Exposure to workplace noise and the risk of cardiovascular disease events and mortality among older adults. Prev Med. 53(6):390-4.

Greenlund KJ, Kiefe CI, Giles WH, Liu K. 2010. Associations of job strain and occupation with subclinical atherosclerosis: The CARDIA Study. Ann Epidemiol. 20(5):323-31.

Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA et al. 2005. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 112(17):2735-52.

Hammar N, Alfredsson L, Smedberg M, Ahlbom A. 1992. Differences in the incidence of myocardial infarction among occupational groups. Scand J Work Environ Health. 18(3):178-85.

Hermansson J, Gillander GK, Karlsson B, Lindahl B, Stegmayr B, Knutsson A. Ischemic stroke and shift work. 2007. Scand J Work Environ Health. 33(6):435-9.

Hittle BM, Gillespie GL. 2018. Identifying shift worker chronotype: implications for health. Ind Health. 56(6):512-23.

Holt TE, Tveten A, Dahl E. 2017. Medical emergencies on large passenger ships without doctors: the Oslo-Kiel-Oslo ferry experience. Int Marit Health. 68(3):153-8.

Hulsegge G, Picavet HSJ, van der Beek AJ, Verschuren WMM, Twisk JW, Proper KI. 2019. Shift work, chronotype and the risk of cardiometabolic risk factors. Eur J Public Health. 29(1):128-34.

Iversen RT. The mental health of seafarers. 2012. Int Marit Health. 63(2):78-89.

Jaremin B, Kotulak E. 2003. Myocardial infarction (MI) at the work-site among Polish seafarers the risk and the impact of occupational factors. Int Marit Health. 54(1-4):26-39.

Johnson JV, Stewart WF, Fredlund P, Hall E, Theorell T. 1990. Psychosocial Job Exposure Matrix. Stress Research Report Nr 221. Stockholm, National Institute for Psychosocial Factors and Health and WHO Psychosocial Centre. Stockholm.

Johnson JV, Stewart WF. 1993. Measuring work organisation exposure over the life course with a job-exposure matrix. Scand J Work Environ Health. 19(1):21-8.

Karasek RA. 1979. Job demands, job decision latitude, and mental strain: implications for job redesign. Adm Sci Q. 24(2):285–308.

Karlsson B, Alfredsson L, Knutsson A, Andersson E, Torén K. 2005. Total mortality and cause-specific mortality of Swedish shift- and dayworkers in the pulp and paper industry in 1952-2001. Scand J Work Environ Health. 31(1):30-5.

Kecklund G, Axelsson J. 2016. Health consequences of shift work and insufficient sleep. BMJ. 1;355:i5210. doi: 10.1136/bmj.i5210.

Kervezee L, Kosmadopoulos A, Boivin DB. 2018. Metabolic and cardiovascular consequences of shift work: The role of circadian disruption and sleep disturbances. Eur J Neurosci. doi: 10.1111/ejn.14216.

Kivimäki M, Kawachi, I. 2015. Work Stress as a Risk Factor for Cardiovascular Disease. Curr Cardiol Rep. 17: 74. doi.org/10.1007/ s11886-015-0630-8

Kivimäki M, Pentti J, Ferrie JE, Batty GD, Nyberg ST, Jokela M et al. 2018a. Work stress and risk of death in men and women with and without cardiometabolic disease: a multicohort study. Lancet Diabetes Endocrinol. 6(9):705-13.

Kivimäki M, Steptoe A. 2018b. Effects of stress on the development and progression of cardiovascular disease. Nat Rev Cardiol. 15(4):215-29

Knutsson A, Akerstedt T, Jonsson BG, Orth-Gomer K. 1986. Increased risk of ischaemic heart disease in shift workers. Lancet. 2(8498):89-92.

Langseth H, Kjærheim K. 2006. Mortality from non-malignant diseases in a cohort of female pulp and paper workers in Norway. Occup Environ Med. 63(11):741-5.

Lie A, Skogstad M, Johannessen H, Tynes T, Mehlum IS, Nordby KC et al. 2016. Occupational noise exposure and hearing: a systematic review. Int Arch Occup Environ Health. 89(3):351-72.

Liew G, Chow C, van Pelt N, Younger J, Jelinek M, Chan J, et al. 2017. Cardiac Society of Australia and New Zealand Position Statement: Coronary Artery Calcium Scoring. Heart Lung Circ. 26(12):1239-51.

McClelland RL, Chung H, Detrano R, Post W, Kronmal RA. 2006. Distribution of coronary artery calcium by race, gender, and age: results from the Multi-Ethnic Study of Atherosclerosis (MESA). Circulation. 113(1):30-7.

Moller Pedersen SF, Jepsen JR. 2013. The metabolic syndrome among Danish seafarers. Int Marit Health. 64(4):183-90.

Nakahara T, Dweck MR, Narulan N, Pisapia D, Narula J, Strauss HW. 2017. Coronary artery calcification: from mechanism to molecular imaging. JACC Cardiovasc Imaging. 10(5):582-93.

Neitzel RL, Andersson M, Eriksson H, Torén K, Andersson E. 2018. Development of a job exposure matrix for noise in the Swedish soft tissue paper industry. Ann Work Expo Health. 62(2):195–209.

Niedhammer I, Milner A, LaMontagne AD, Chastang JF. 2018. Study of the validity of a job-exposure matrix for the job strain model factors: an update and a study of changes over time. Int Arch Occup Environ Health. 1(5):523-36.

Nilsson R. 1998. Cancer in seamen with special reference to chemical health hazards. Dissertation, Gothenburg University, Sweden

Oldenburg M. 2014. Risk of cardiovascular diseases in seafarers. Int Marit Health. 65(2):53-7.

Oldenburg M, Herzog J, Harth V. 2016. Seafarer deaths at sea: a German mortality study. Occup Med (Lond). 66(2):135-7.

Otterland A. 1960. A sociomedical study of the mortality in merchant seafarers. Analysis of deaths in the population of active seafarers registered in Sweden 1945-1954. Dissertation, Gothenburg University, Sweden.

Pougnet R, Pougnet L, Loddé BL, Canals-Pol ML, Jegaden D, Lucas D et al. 2013. Cardiovascular risk factors in seamen and fishermen: review of literature. Int Marit Health. 64(3):107-13.

Poulsen TR, Burr H, Hansen HL, Jepsen JR. 2014. Health of Danish seafarers and fishermen 1970-2010: What have register-based studies found. Scand J Public Health. 42(6):534-45.

Rafnsson V, Gunnarsdottir H. 1994. Mortality among Icelandic seamen. Int J Epidemiol. 23(4):730-6.

Rapsomaniki E, Timmis A, George J, Pujades-Rodriguez M, Shah AD, Denaxas S et al. 2014. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. Lancet 383(9932):1899-911.

Ritonja J, Tranmer J, Aronson KJ. 2019. The relationship between night work, chronotype, and cardiometabolic risk factors in female hospital employees. Chronobiol Int. 36(5):616-28.

Roberts SE, Jaremin B. 2010. Cardiovascular disease mortality in British merchant shipping and among British seafarers ashore in Britain. Int Marit Health. 62(3):107-16.

Roberts SE, Nielsen D, Kotłowski A, Jaremin B. 2014. Fatal accidents and injuries among merchant seafarers worldwide. Occup Med (Lond). 64(4):259-66.

Roberts SE, Carter T. British merchant seafarers 1900-2010: A history of extreme risks of mortality from infectious disease. 2016. Travel Med Infectious Dis. 14(5):499-504.

Rothman KJ. 2012. Epidemiology An introduction. 2. uppl. Oxford: Oxford University Press.

Rozanski A, Gransar H, Kubzansky LD, Wong N, Shaw L, Miranda-Peats R et al. 2011. Do psychological risk factors predict the presence of coronary atherosclerosis? Psychosom Med. 73(1):7-15.

Sandfort V, Bluemke DA. CT calcium scoring. 2017. History, current status and outlook. Diagn Interv Imaging. 98(1):3-10.

Sanne B, Torp S, Mykletun A, Dahl AA. 2005. The Swedish Demand-Control-Support Questionnaire (DCSQ): factor structure, item analyses, and internal consistency in a large population. Scand J Public Health. 33(3):166-74.

Sarwar A, Shaw LJ, Shapiro MD, Blankstein R, Hoffmann U, Cury RC et al. 2009. Diagnostic and prognostic value of absence of coronary artery calcification. JACC Cardiovasc Imaging. 2(6):675-88.

SBU. Arbetsmiljöns betydelse för hjärt-kärlsjukdom. En systematisk litteraturöversikt. Stockholm: Statens beredning för medicinsk och social utvärdering (SBU); 2015. SBU-rapport nr 240. ISBN 978-91-85413-84-3.

SBU. Arbetsmiljöns betydelse för hjärt-kärlsjukdom – Exponering för kemiska ämnen. En systematisk översikt och utvärdering av medicinska, sociala och etiska aspekter. Stockholm: Statens beredning för medicinsk och social utvärdering (SBU); 2017. SBU-rapport nr 261. ISBN 978-91-88437-03-7.

Schuster M, Oberlinner C, Claus M. 2019. Shift-specific associations between age, chronotype and sleep duration. Chronobiol Int. 36(6):784-95.

Selander J, Bluhm G, Nilsson M, Hallqvist J, Theorell T, Willix P et al. 2013. Joint effects of job strain and road-traffic and occupational noise on myocardial infarction. Scand J Work Environ Health. 39(2):195-203.

Sjöström M, Lewné M, Alderling M, Willix P, Berg P, Gustavsson P. et al. 2013. A job-exposure matrix for occupational noise: Development and validation. Ann Occup Hyg. 57(6):774-83.

Skogstad M, Johannessen HA, Tynes T, Mehlum IS, Nordby KC, Lie A. 2016. Systematic review of the cardiovascular effects of occupational noise. Occup Med (Lond). 66(6):10-6.

Souza RV, Sarmento RA, de Almeida JC, Canuto R. 2019. The effect of shift work on eating habits: a systematic review. Scand J Work Environ Health. 45(1):7-21.

Statistics Sweden. 2019. Andel som arbetar skift eller schema bland anställda 16-64 år ULF/SILC 2018. Statistiska Centralbyrån. https://www.scb.se/hitta-statistik/statistik-efter-amne/levnadsforhallanden/levnadsforhallanden/undersokningarna-av-levnadsforhallanden-ulf-silc/pong/tabell-och-diagram/sysselsattning/andel-som-arbetar-skift-eller-schema-bland-anstallda-16-64-ar-2018/ (Hämtad 2019-08-07).

Stokholm ZA, Bonde JP, Christensen KL Hansen AM, Kolstad HA. 2013. Occupational noise exposure and the risk of stroke. Stroke. 44(11):3214-6.

Strohmaier S, Devore EE, Zhang Y, Schernhammer ES. 2018. A review of data of findings on night shift work and the development of DM and CVD Events: a synthesis of the proposed molecular mechanisms. Curr Diab Rep. 18(12):132. doi: 10.1007/s11892-018-1102-5.

Svensk sjöfart. 2018. Sjöfarten i siffror. Svensk Sjöfart http://www.sweship.se/svensk-sjofart-i-korthet/sjofarten-i-siffror/ (hämtad 2019-08-09).

Teschke K. 2003. Exposure surrogates: job exposure matrices, self-reports, and expert evaluations. Nieuwenhuijsen MJ (red). Exposure assessment in occupational and environmental epidemiology. Oxford New York: Oxford university press, 119-32.

Tessier-Sherman B, Galusha D, Cantley LF, Cullen MR, Rabinowitz PM, Neitzel RL. 2017. Occupational noise exposure and risk of hypertension in an industrial workforce. Am J Ind Med. 60(12):1031-8.

The National Board of Health and Welfare. 2018a. Statistik om hjärtinfarkter 2017. Socialstyrelsen. https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/statistik/2018-12-42.pdf. (Hämtad 2019-08-07).

The National Board of Health and Welfare. 2018b. Statistik om stroke 2017. Socialstyrelsen. https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/statistik/2018-12-39.pdf. (Hämtad 2019-08-07).

Theorell T, Jood K, Järvholm LS, Vingård E, Perk J, Östergren PO et al. 2016. A systematic review of studies in the contributions of the work environment to ischaemic heart disease development. Eur J Public Health. 26(3):470-7.

Thygesen LC, Ersbøll AK. 2014. When the entire population is the sample: strengths and limitations in register-based epidemiology. Eur J Epidemiol. 29(8):551-8.

Toivanen S. 2008. Job control and the risk of incident stroke in the working population in Sweden. Scand J Work Environ Health. 34(1):40-7.

Torén K, Hagberg S, Westberg H. 1996. Health effects of working in pulp and paper mills: exposure, obstructive airways diseases, hypersensitivity reactions, and cardiovascular diseases. Am J Ind Med. 29(2):111-22.

Torquati L, Brown WJ, Kolbe-Alexander T. 2018. Shift work and the risk of cardiovascular disease. A systematic review and meta-analysis including dose–response relationship. Scand J Work Environ Health. 44(3):229-38.

Tu M, Jepsen JR. Hypertension among Danish seafarers. 2016. Int Marit Health. 67(4):196-204.

Ugelvig Petersen K, Volk J, Kaerlev L, Lyngbeck Hansen H, Hansen J. 2018. Cancer incidence among merchant seafarers: an extended follow-up of a Danish cohort. Occup Environ Med. 75(8):582-5.

Vetter C, Devore EE, Wegrzyn LR, Massa J, Speizer FE, Kawachi I et al. 2016. Association between rotating night shift work and risk of coronary heart disease among women. JAMA. 315(16):1726-34.

Virkkunen H, Kauppinen T, Tenkanen L. 2005. Long-term effect of occupational noise on the risk of coronary heart disease. Scand J Work Environ Health. 31(4):291-9.

Virkkunen H, Härmä M, Kauppinen T, Tenkanen L. 2006. The triad of shift work, occupational noise, and physical workload and risk of coronary heart disease. Occup Environ Med. 63(6):378-86.

Wang F, Zhang L, Zhang Y, Zhang B, He Y, Xie S. 2014. Meta-analysis on night shift work and risk of metabolic syndrome. Obes Rev. 15(9):709-20.

WHO. Occupational and work-related diseases. World Health Organization. https://www.who.int/occupational_health/activities/occupational_work_diseases/en/ (hämtad 2019-08-12)

Wilhelmsen L, Berglund G, Elmfeldt D, Tibblin G, Wedel H, Pennert K et al. 1986. The multifactor primary prevention trial in Goteborg, Sweden. Eur Heart J. 7(4):279-88.