SHIFT WORK, STRESS AND HEART DISEASE AMONG PARAMEDICS

by

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ABSTRACT

Shift work and work-related stress is a rising concern among the workforce population because of the potential link to cardiovascular disease (CVD). While these exposures are common in emergency services, there are few studies examining if these factors increase CVD risk among paramedics. The aim of this dissertation is to address this research gap.

The first study examined neuroendocrine activity related to shift work and job strain. Shift workers (n=14) reported higher job strain than daytime workers (n=7) and exhibited neuroendocrine dysregulation through salivary biomarkers (alpha-amylase and cortisol) and subclinical CVD indicators (heart rate variability and endothelial functioning). The sampling protocol developed in this study can be used for future, large-scale field studies.

The second and third studies used records of emergency runs attended by British Columbia (BC) paramedics between 1990/1 and 2002 to derive exposures, and administrative records from the BC Linked Health Database to ascertain CVD cases.

The second study used a nested case-control design with 11 years follow-up (n = 183 – 742). Three controls were matched per case by age, sex and first year of employment. Results of conditional logistic regression did not support hypotheses that shift work was associated with hypertension, chronic coronary syndrome nor acute coronary syndrome; nor that time away from shift work may reduce the risk of CVD. However, development of novel shift work metrics which incorporated periods of neuroendocrine dysregulation and recovery should be considered in future studies.

The third study used a case-crossover design to compare exposures during 4 days prior to onset of acute coronary events to exposures in 4 randomly chosen days in the month prior for each acute coronary case (n=65). Results suggest non-significant increased risks of acute coronary syndrome were associated with busy work days, high-stress emergencies and discrepancies between dispatched information and diagnosis at the scene. A delay in onset of acute coronary events was also observed. Results suggest current psychological debriefing sessions may not be effective and that considerations should be made to improve mental health programs to reduce psychological strain.
PREFACE

Chapters 2, 4 and 5 of this dissertation were written as stand-alone manuscripts for publication in peer-reviewed academic literature. Chapter 2 has been published in the Journal of Occupational and Environmental Hygiene, Chapter 4 is under review in the Scandinavian Journal of Work, Environment and Health, and Chapter 5 is in preparation for submission to the Annals of Emergency Medicine.

Data collection for Chapter 2 was approved by the University of British Columbia Clinical Research Ethics Board (H08-01232). For Chapters 4 and 5, all research protocols received approval for behavioural ethics at the University of British Columbia (H11-03065) and Data Access of BC Ambulance Service and Ministry of Health data was accomplished through Population Data BC Data Access Request (DAR 05-003).

Chapter 2: Job Strain and Shift work influences on biomarkers and subclinical heart disease indicators: a pilot study


I conceptualized the idea, designed the study, collected all samples, completed the analyses and wrote the manuscript. Paul Demers provided assistance with developing the initial study protocol. Aleck Ostry provided guidance in deriving Karasek’s job demand and control domains from the Sources of Occupational Stress questionnaire. Hugh Davies supervised all drafts of the manuscript. All authors provided feedback and revisions for the final manuscript. My overall contribution: 90%.

Chapter 4: Risk of acute/chronic forms of heart disease with shift work, and the influence of recovery time

A version of this chapter has been submitted to the Scandinavian Journal of Work, Environment and Health as: Wong IS, Demers, PA, Ostry, AS, Davies, HW. The association of chronic shift work
exposure with chronic heart disease; and the inclusion of recovery time to improve exposure assessment.

I conceptualized the idea, conducted the analyses and wrote the manuscript. Hugh Davies supervised all aspects of this study. Paul Demers proposed using a nested case-control design for this study and provided guidance with the analyses. Hugh Davies, Paul Demers and Aleck Ostry provided feedback and revisions for the final manuscript. My overall contribution: 90%.

Chapter 5: Emergency runs as triggers of acute coronary events among paramedics

A version of this chapter is in preparation to be submitted to the Annals of Emergency Medicine.

Hugh Davies conceptualized the idea of using a case-crossover study design for this study and supervised all aspects of the analyses. I developed the methodology after reviewing previous literature and consulting with other experts of case-crossover designs. I conducted all analyses and wrote the manuscript. Aleck Ostry provided guidance on how to identify and rank emergency runs in order of perceived stressfulness. Hugh Davies, Paul Demers and Aleck Ostry provided feedback and revisions for the final manuscript. My overall contribution: 95%.
TABLE OF CONTENTS

ABSTRACT .............................................................................................................................. ii
PREFACE ............................................................................................................................... iii
TABLE OF CONTENTS ......................................................................................................... v
LIST OF TABLES ................................................................................................................... ix
LIST OF FIGURES .................................................................................................................. x
LIST OF SYMBOLS AND ABBREVIATIONS ..................................................................... xi
ACKNOWLEDGEMENTS .................................................................................................. xiii
DEDICATION ........................................................................................................................ xv

1 INTRODUCTION AND LITERATURE REVIEW ......................................................... 1
  1.1 Neuroendocrine activity and etiology of cardiovascular disease ............................................. 2
  1.2 The Job Strain Model and psychosocial stress ........................................................................... 4
    1.2.1 Job strain and cardiovascular disease .................................................................................. 6
  1.3 Shift work: a physical and psychosocial stressor .................................................................... 21
    1.3.1 Evidence linking shift work and cardiovascular disease .................................................. 22
  1.4 Paramedics and cardiovascular disease .................................................................................. 37
  1.5 Dissertation objectives .......................................................................................................... 43
    1.5.1 Dissertation structure ......................................................................................................... 44

2 JOB STRAIN AND SHIFT WORK INFLUENCES ON BIOMARKERS AND SUBCLINICAL HEART DISEASE INDICATORS: A PILOT STUDY .............................. 48
  2.1 Synopsis ................................................................................................................................ 48
  2.2 Introduction .............................................................................................................................. 49
  2.3 Methods ................................................................................................................................... 52
    2.3.1 Study population and recruitment .................................................................................... 52
    2.3.2 Study protocol ...................................................................................................................... 52
    2.3.3 Study measures .................................................................................................................... 55
      2.3.3.1 Perceived job strain and general health ........................................................................ 55
      2.3.3.2 Biological markers of stress: salivary cortisol and alpha-amylase ................................ 56
      2.3.3.3 Heart rate variability ..................................................................................................... 58
      2.3.3.4 Endothelial dysfunction ............................................................................................... 60
      2.3.3.5 Statistical analysis ......................................................................................................... 61
  2.4 Results .................................................................................................................................... 61
    2.4.1 Study feasibility .................................................................................................................. 61
    2.4.2 Job strain, autonomic nervous system and hypothalamus-pituitary-adrenal activity ........ 65
  2.5 Discussion ................................................................................................................................. 70
5.2 Introduction ......................................................................................................................................... 108
5.3 Methods ............................................................................................................................................... 109
  5.3.1 Study population and case definition .......................................................................................... 109
  5.3.2 Exposure variables: potential triggers of acute coronary syndrome ............................................. 110
  5.3.3 Statistical analysis ......................................................................................................................... 117
5.4 Results .................................................................................................................................................. 118
  5.4.1 Cohort description ........................................................................................................................ 118
  5.4.2 Emergency run-related triggers of acute coronary syndrome (ACS) ........................................... 119
5.5 Discussion ............................................................................................................................................ 121
6 CONCLUSIONS, IMPLICATIONS AND FUTURE DIRECTIONS .............................................. 126
6.1 Objectives and key findings .............................................................................................................. 126
6.2 Scientific contributions ......................................................................................................................... 127
  6.2.1 Influences of shift work and job strain on neuroendocrine activity (Chapter 2) ............................ 127
  6.2.2 Risk of acute/chronic forms of heart disease with shift work, and the influence of recovery time (Chapter 4) ................................................................................................................. 128
  6.2.3 Emergency runs as triggers of acute coronary events among paramedics (Chapter 5) ............... 129
6.3 Synthesizing results to address gaps in previous research ................................................................... 130
  6.3.1 Developing occupation-specific standardized surveys .................................................................. 130
  6.3.2 Linking epidemiologic evidence with biological markers ............................................................ 130
  6.3.3 Reducing misclassification biases by improving exposure assessment and refining outcome measures ................................................................................................................................. 131
6.4 Challenges and limitations ................................................................................................................... 132
  6.4.1 Lack of statistical significance and precision in risk estimates ............................................... 132
  6.4.2 Data quality ................................................................................................................................... 133
  6.4.3 Deriving the metric “exposure to stressful emergencies” ............................................................... 135
6.5 Policy implications ................................................................................................................................. 136
  6.5.1 Mitigating the adverse health effects associated with shift work .............................................. 136
  6.5.2 Reducing emergency-related stressors ........................................................................................ 137
    6.5.2.1 Coping with traumatic events ................................................................................................ 138
    6.5.2.2 Reducing discrepancies between dispatched information and actual emergency on scene ................................................................. 140
  6.5.3 Maintaining healthy workers ........................................................................................................ 141
6.6 Future research directions .................................................................................................................... 143
  6.6.1 Extending studies of shift work, job strain and neuroendocrine dysregulation ......................... 143
  6.6.2 Dispatcher studies ......................................................................................................................... 144
  6.6.3 Recovery from shift work: biomarker studies and epidemiologic evidence .................................. 144
6.6.4 Identifying constructs related to emergency runs that may act as triggers of acute coronary events .......................................................... 146
6.6.5 Progression of risk factors for heart disease ...................................................... 147
6.7 Conclusion ............................................................................................................. 148

REFERENCES ............................................................................................................. 151

APPENDIX A PARAMEDIC CREW REPORT .............................................................. 172
LIST OF TABLES

Table 1.1   Summary of job strain and heart disease prospective cohort studies ................................. 8
Table 1.2   Summary of shift work and heart disease studies ................................................................... 25
Table 1.3   Summary of paramedic and heart disease studies ................................................................... 40
Table 2.1   Sampling protocol for salivary alpha-amylase, salivary cortisol, heart rate variability and endothelial functioning..................................................................................... 54
Table 2.2   Demographic characteristics and survey responses by shift and paramedic type comparisons ......................................................................................................................... 63
Table 2.3   Correlation of working day and rest day measurements ........................................................ 64
Table 2.4   Heart rate variability results by shift and paramedic type comparisons .................................. 67
Table 3.1   A comparison of demographic information, heart disease prevalence and non-occupational risk factors of heart disease between the convenience sample population used in the neuroendocrine sampling study and a random sample of the larger paramedic population ............................................................................. 81
Table 4.1   Descriptive characteristics of cases and controls for acute coronary syndrome, chronic coronary syndrome and hypertension .................................................................................... 96
Table 4.2   Correlation of shift work variables and covariates .................................................................. 97
Table 4.3   Risk of heart disease outcomes associated with shift work variable and covariates ............... 99
Table 4.4   Additive interaction effects of workload and (1) number of shift changes between shift work and non-shift work; and (2) ratio of average length of shift work to recovery, for chronic coronary syndrome and hypertension outcomes .................................................................................................................. 101
Table 5.1   Summary of survey rankings, primary care codes and dispatched and diagnosed codes grouped into categories of high, medium and low-stress emergencies; and frequency of dispatched and diagnosed emergencies ............................................ 115
Table 5.2   Odds ratios for acute coronary syndrome associated with emergency run-related exposures ................................................................................................................................................. 120
LIST OF FIGURES

Figure 1.1 Psychological demand / decision latitude model ...............................................................5

Figure 2.1 Alpha-amylase slope and calculated daily production for shift and paramedic
type comparisons ..........................................................................................................................66

Figure 2.2 Cortisol slope and calculated daily production for shift and paramedic type
comparisons .....................................................................................................................................68

Figure 2.3 Endothelial functioning by shift and paramedic type comparisons ...............................69

Figure 3.1 BC Ambulance Service new hires, retirees and working population by year ................83

Figure 5.1 Steps taken to categorize emergencies into high, medium and low stressors
using survey responses, existing literature, dispatch and diagnostic codes and
patient care codes. ..........................................................................................................................113
### LIST OF SYMBOLS AND ABBREVIATIONS

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>95% CI</td>
<td>95% Confidence Interval</td>
<td></td>
</tr>
<tr>
<td>ACS</td>
<td>Acute Coronary Syndrome</td>
<td></td>
</tr>
<tr>
<td>ANS</td>
<td>Autonomic Nervous System</td>
<td></td>
</tr>
<tr>
<td>Avg</td>
<td>Average</td>
<td></td>
</tr>
<tr>
<td>AUC</td>
<td>Area under the curve</td>
<td></td>
</tr>
<tr>
<td>BC</td>
<td>British Columbia</td>
<td></td>
</tr>
<tr>
<td>BCAS</td>
<td>British Columbia Ambulance Service</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
<td></td>
</tr>
<tr>
<td>CCHS</td>
<td>Canadian Community Health Survey</td>
<td></td>
</tr>
<tr>
<td>CCS</td>
<td>Chronic Coronary Syndrome</td>
<td></td>
</tr>
<tr>
<td>CISD</td>
<td>Critical Incidence Stress Debriefing</td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>Coronary Heart Disease</td>
<td></td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular Disease</td>
<td></td>
</tr>
<tr>
<td>$D$</td>
<td>Cohen's d; effect size</td>
<td></td>
</tr>
<tr>
<td>dB(A)</td>
<td>A-Weighted Decibels</td>
<td></td>
</tr>
<tr>
<td>ED</td>
<td>Endothelial Dysfunction</td>
<td></td>
</tr>
<tr>
<td>HF</td>
<td>High Frequency</td>
<td></td>
</tr>
<tr>
<td>Hz</td>
<td>Hertz</td>
<td></td>
</tr>
<tr>
<td>HPA</td>
<td>Hypothalamic-pituitary-adrenal</td>
<td></td>
</tr>
<tr>
<td>HRV</td>
<td>Heart Rate Variability</td>
<td></td>
</tr>
<tr>
<td>HTN</td>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>ICD</td>
<td>International Classification of Disease</td>
<td></td>
</tr>
<tr>
<td>Kcal</td>
<td>Kilocalorie</td>
<td></td>
</tr>
<tr>
<td>Kg</td>
<td>Kilogram</td>
<td></td>
</tr>
<tr>
<td>MET</td>
<td>Metabolic Equivalent of Task</td>
<td></td>
</tr>
<tr>
<td>mmHg</td>
<td>Millimeters of Mercury</td>
<td></td>
</tr>
<tr>
<td>MSP</td>
<td>Medical Services Plan</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>Number</td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td>Odds Ratio</td>
<td></td>
</tr>
<tr>
<td>pNN50</td>
<td>Percentage of intervals &gt;50ms different from the preceding interval</td>
<td></td>
</tr>
<tr>
<td>PNS</td>
<td>Parasympathetic nervous system</td>
<td></td>
</tr>
<tr>
<td>ptrend</td>
<td>p-value for trend</td>
<td></td>
</tr>
<tr>
<td>PTSD</td>
<td>Post-Traumatic Stress Disorder</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>Correlation Coefficient</td>
<td></td>
</tr>
<tr>
<td>Ref</td>
<td>Reference Group</td>
<td></td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
<td></td>
</tr>
<tr>
<td>RHI</td>
<td>Reactive Hyperemia Index</td>
<td></td>
</tr>
<tr>
<td>rMSSD</td>
<td>Square root of the mean of the squares of successive NN interval differences</td>
<td></td>
</tr>
<tr>
<td>RR</td>
<td>Relative Risk</td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>Systolic Blood Pressure</td>
<td></td>
</tr>
<tr>
<td>SCN</td>
<td>Suprachiasmatic Nucleus</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
<td></td>
</tr>
<tr>
<td>SNS</td>
<td>Sympathetic nervous system</td>
<td></td>
</tr>
<tr>
<td>Yr</td>
<td>Year</td>
<td></td>
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</table>
ACKNOWLEDGEMENTS

A PhD is never a solo effort but one which results from the support and collaboration of many. It is with this thought that I would like to acknowledge all those who made a significant contribution to this journey.

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The foundations of this dissertation were built upon contributions from Gregory Miller, Edith Chen and Nicholas Rohleder. Thank you for taking in this hygiene student and teaching me about hypothetical constructs, stress biomarkers, subclinical heart disease indicators and the progression cardiovascular disease from psychological stress.

This work could not have been possible without the contributions of Dug Andrusick, Garth Dinsmore, Tanya Hollist-Chyzowski, the British Columbia Ambulance Service and the Paramedics Union (CUPE 873). Thank you to all the men and women, who took the time to participate our studies, kept me safe during my ambulance rides and taught me all about paramedic work. I have gained a greater insight and newfound respect for the work that you do. I hope this dissertation will contribute in helping to make your profession a safe and healthy one.

Financial support for these studies was provided by WorkSafeBC and the Centre for Health and Environment Research. Support for my training was generously provided by the Canadian Institutes of Health Research, American Industrial Hygiene Foundation and the Western Regional Training Centre.
I would like to extend my thanks to many in the School of Population and Public Health for their support. Thank you to Kay Teschke and the UBC Bridge Program for giving me the best preparation for graduate school that anyone could ever have. I appreciate the opportunities provided by Michael Brauer to expand beyond occupational studies which allowed me to gain a well-rounded perspective of research. Thanks also to Lillian Tamburic for taking the time to teach me the basics of the health data used in this dissertation and helping make sense of what it means. My world was made much easier thanks to Karen Bartlett, Barbara Karlen, Beth Hensler and all the SPPH administrative staff for doing all the important “behind the scenes” work so that I could concentrate on my research.

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DEDICATION

To Derek,

for sharing in my curiosity of the world and reminding me of what is most important
INTRODUCTION AND LITERATURE REVIEW

Psychological stress has been increasingly recognized as an important contributor to, and modifiable risk factor for cardiovascular disease (CVD)\(^2\). The term “stress” has been defined as “a real or interpreted threat to the physiological or psychological integrity of an individual that results in physiological and/or behavioural consequences”\(^3\). Any activity or event that causes stress has been referred to as a “stressor”\(^4\), and the resulting responses to stress in the body is considered to be “strain”\(^5\). Stressors can be defined by varying degrees of intensity, and by duration as acute or chronic episodes and may have been implicated in differing stages of the etiology of cardiovascular disease\(^3,6\).

The workplace has been reported as the number one stressor in people’s lives and is more strongly linked to self-reported health complaints than any other life stressor\(^7,8\). The increasing prevalence of work-related psychosocial stress has been considered to be one of “the biggest health and safety challenges” among the workforce population\(^9\). It has been reported that 46% of employees in the United States are so severely stressed that they are at a point of psychological exhaustion that is greatly affecting their daily life (i.e. burnout)\(^10\). In 1998, 60% of workplace absences in the United Kingdom were reported to be stress-related\(^11\). It is estimated that the annual economic burden of workplace stress as defined by direct and indirect costs (e.g. absenteeism, presenteeism, disability management) is estimated to be $407 billion per year in the US and €20,000 million in the European Community\(^9,12\).

Shift work is a particular type of workplace stressor that has been identified as one of rising concern. It has been reported that the need for shift work may reflect the increasing demands on the global economy which may be transferred as an additional stressor on workers\(^13\). In Canada
alone, while the number of workers in daytime only schedules increased by 23.0% between 1996 and 2008, more growth was observed in regular night - and evening- shifts (38.5%), rotating-shifts (25.8%) and irregular schedules (37.4%)\textsuperscript{14}. Many of these workers have little choice with respect to their working schedules and there are few opportunities available for them to obtain a daytime-only schedule without extensive experience\textsuperscript{14}. Studies have shown that up to 80% of shift workers would prefer to work only during conventional daytime hours \textsuperscript{15}. While it is believed that shift work may contribute to work-related stress and increase the risk for CVD\textsuperscript{16}, the biological mechanisms underlying this causal pathway are not fully understood.

The following sections will describe the existing evidence and theories linking shift work and workplace stress with cardiovascular disease.

1.1 Neuroendocrine activity and etiology of cardiovascular disease

As a protective measure against stress, the body’s neuroendocrine systems invoke a series of hormonal responses to influence the function of target cells and organs in maintaining physiological homeostasis \textsuperscript{17}. Activity in the autonomic nervous system (ANS) is immediately initiated following exposure to a stressor, activating preganglionic sympathetic neurons, stimulating paravertebral ganglia and innervating organs such as the heart and adrenal medulla. The adrenal medulla responds by releasing catecholamines, epinephrine and norepinephrine, that bind adrenoreceptors to target organs such as the heart tissues to further increase sympathetic dominance over parasympathetic activity. Related physiological changes include reduced vagal activity leading to increased cardiovascular output and subsequent increase in blood pressure. This creates a heightened sense of attention and vigilance. ANS response is considered to be
transient, but prolonged sympathetic dominance can lead to imbalances in autonomic load and has been associated with progression of heart disease\textsuperscript{18}.

The hypothalamic-pituitary-adrenal axis (HPA) may follow by releasing the hormone, cortisol, to stimulate the stress response and suppress it once the threat has passed; or as an additional measure, to prepare the body for future threats\textsuperscript{19,20}. Cortisol plays a key role in regulating the immune system, glucose and lipid metabolism and maintenance of cardiac output by increasing vascular tone and decreasing vascular permeability\textsuperscript{21}.

Under conditions of healthy physiological functioning, the neuroendocrine systems create a feedback loop that turns off hormonal responses when the danger has passed. This state of biological homeostasis during environmental or physiological challenges has been termed “allostasis”\textsuperscript{17,22}. It is thought that long-term repeated reactivity to stress without sufficient recovery can lead to inadequate activation or cessation of neuroendocrine systems\textsuperscript{22}. This neuroendocrine dysregulation along with the behavioural and physiological consequences of how individual responds to stressors such as dietary habits, sleep disturbances, physical activity and social interactions is defined as “allostatic load”\textsuperscript{22}. It is believed that chronic allostatic load may result in high levels of inflammatory molecules (e.g. C-reactive protein and interleukin-6) which are believed to contribute to damaging the endothelium (i.e. lining cells of the vessel wall). These early lesions promote accumulation of lipids, macrophages and T lymphocytes in the vascular walls which may progress to development of coronary plaques\textsuperscript{23}. It is believed that chronic stress may accelerate the atherosclerotic process and acute stress may trigger a critical event in a person who already has a high degree of atherosclerosis\textsuperscript{24-26}. 
1.2 The Job Strain Model and psychosocial stress

Work-related psychosocial stress is defined as an individual’s response to a mismatch between their own knowledge and skills with the demands and pressures of their occupational environment\(^\text{27}\). The stress response may be positive (i.e. eustress) which can encourage personal growth and learning, but can become negative (i.e. distress) when the physiological and/or psychological demands of a stressor exceeds an individual’s capacity to cope\(^\text{4}\). While there is a wide variability between individuals in response to work-related stressors, evidence has shown that certain working conditions may be stressful to large groups of workers resulting in adverse physical and psychological consequences such as heart disease\(^\text{12,28}\). Identifying these working conditions to develop effective prevention strategies may improve worker health.

Several different models have been used in prior studies to quantify stressful working conditions (e.g. Effort-Reward Imbalance, Occupational Stress Index). However, in a recent review, Hansen et al. found that the Job Strain Model was the most frequently utilized to examine the association of work-related stress with neuroendocrine activity (28 out of 39 studies)\(^\text{29}\). The authors also reported that among 21 studies which found a significant positive association between neuroendocrine dysregulation and work stress measured by any method, 11 used the Job Strain Model. This suggests that the Job Strain Model may currently provide the most consistent biological evidence linking work-related stress with the progression of heart disease.

To quantify chronic work-related psychosocial stress using the Job Strain Model, a self-administered questionnaire is utilized to measure an individual’s perception of psychological demands and decision latitude (i.e. a combined measure task control and skill use and discretion)\(^\text{30}\). The scales of both domains can be combined to form a two-dimensional model.
with 4 categories [high-strain, low-strain, active work and passive work (Figure 1.1)] and provides the ability to delineate the difference between positive and negative stress (i.e. eustress and distress).

![Psychological demand / decision latitude model](image)

**Figure 1.1 Psychological demand / decision latitude model**

Adapted from Karasek, 1979

High-strain jobs (i.e. high psychological demands and low decision latitude) are recognized as leading to the most adverse reactions to residual psychological strain and result when workers feel a lack of control over occupational psychological demands. Conversely, low-strain jobs may be considered as the most ideal situation where a worker's job decision latitude allows them to respond to each challenge optimally. It is suggested that these workers are made both happier and healthier than average by work.

Passive work (i.e. low psychological demands and low decision latitude) is considered to be a situation detrimental to worker health. While workers are not exposed to a fast-paced environment, the lack of stimulus can lead to learned helplessness and may even result in a loss of previously acquired skills. This lack of stimulus at work has been shown to translate into
inactivity and social isolation during leisure time and may contribute to adverse health
behaviours. An active work environment is identified as being one with challenging situations
but where worker has enough skill discretion and decision latitude to maintain a sense of control
over their work environment. It is predicted that these types of jobs provide opportunities to
learn and grow, and can translate to being productive outside the work environment.

1.2.1 Job strain and cardiovascular disease

To date, over 70 studies have used the Job Strain Model to examine the association of chronic
job stress with CVD, but most were cross-sectional, precluding the ability to determine a causal
association. However, in recent years many well-designed prospective cohort studies have
been completed. Two systematic reviews and one meta-analysis have focused solely on these
types of studies to examine the best available evidence on the causal relationship between work
and heart disease. Among these reviews, 19 prospective cohort studies have been identified
up to March 2010. I have summarized these in Table 1.1. These studies varied considerably in
terms of sample size (range: 292 to 35,471), time of job strain measurement (e.g. baseline vs.
beginning and end of follow-up) and case ascertainment (e.g. administrative records vs. self-
report). Of these 19 studies, a moderate increased risk of CVD associated with job strain was
found in 17 studies, with statistical significance achieved in 7 studies. Decreased risks were
reported in 3 studies, however none were statistically significant. Relative risks for job strain
and CVD for most studies were generally between 1 and 2, but Uchiyama et al. found an
unusually high risk among a group of women (RR 9.05, 95% CI: 1.17 – 69.98). However, the
study population was restricted to those who were previously diagnosed with hypertension
which may result in elevated risks for cardiovascular events in comparison to studies of
normotensive subjects. In addition, job strain was assessed with a truncated version of the standard questionnaire and may have also biased results.
### Table 1.1 Summary of job strain and heart disease prospective cohort studies

(see footnote for abbreviations)

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size, Cases, Cohort, Follow-up period</th>
<th>Method of Exposure Assessment</th>
<th>Outcome</th>
<th>Risk Estimates for fully adjusted model</th>
<th>Adjustments</th>
<th>Notes</th>
<th>Review*</th>
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<td></td>
<td>(95% Confidence Interval)</td>
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<tr>
<td>Reed 1989 35</td>
<td>N = 8,006; Cases = 359 Japanese men, Hawaii Age 45-65 years 18 year FU</td>
<td>Imputed by job description</td>
<td>Physician diagnosed incident CHD measured 2 and 6 years after baseline; and through medical records, registry data and newspaper obituary notices Morbidity and mortality</td>
<td>RR 0.94 (0.65 – 1.36)</td>
<td>Age, smoking, blood pressure, cholesterol, physical activity, glucose</td>
<td>Checked occupational status with each follow-up examination (2 and 6 years after baseline). Only kept men that did not change status (n= 4,737)</td>
<td>1, 2</td>
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<tr>
<td>Johnson 1989 39</td>
<td>N = 7,219; Cases = 193 All men, white and blue collar workers Sweden Age 25 – 65 years 9 year FU</td>
<td>Self-report</td>
<td>Interviewed, then reported answers were assessed by 2 physicians – not clear when they were interviewed ; and registry data ICD 400-4, 410-4, 427, 429, 430-6, 440-5, 454-8 Morbidity and mortality</td>
<td>RR 1.92 (1.15 – 3.21), ptrend = 0.02 Blue collar: RR 2.58 (1.06 – 6.28), ptrend=0.08 White collar: RR 1.31 (0.58 – 2.96), ptrend=0.23</td>
<td>Age</td>
<td>Interviewed only once about job strain CVD self-reported with series of interview questions, then coded for ICD using a physician-developed coding system</td>
<td>1, 2</td>
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<tr>
<td>Alterman 1994 40</td>
<td>N = 1,638; Cases = 115 All men from Western Electric Works, most light assembly work, some managerial, engineering and clerical personnel US Age 38 – 56 years 10 year FU (morbidity) and 25 year FU(mortality)</td>
<td>Imputed by job description</td>
<td>Annual Physician exam &amp; ECG at baseline + Medical history ICD 410-414 Morbidity and mortality</td>
<td>Morbidity: RR 1.54 (0.85 – 2.80) Mortality: RR 1.03 (0.75 – 1.41)</td>
<td>Age, smoking, blood pressure, cholesterol, alcohol, family history of CVD, education</td>
<td>Interviewed only once about job strain, but noted the stability of the workforce and the rarity of job changes Using job titles to link job strain scores might not be ideal – missing objective measures of the work environment, and subjective perceptions</td>
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<td>Study</td>
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<tr>
<td>Steenland 1997</td>
<td>N = 3,575; Cases = 519</td>
<td>Imputed by job description</td>
<td>Hospital records or death registry ICD 410-414</td>
<td>OR 1.08 (0.81 – 1.49)</td>
<td>Age, blood pressure, education, BMI, cholesterol, smoking, diabetes</td>
<td>Only surveyed exposures at one point in time Completed separate analyses for blue and white collared workers. Blue collared workers in active jobs were less likely to have CVD in comparison to blue collared workers in other groups: RR 0.69 (0.48 – 0.99) Maybe exposure misclassification of job demands – occupations with high psychological demands were highly correlated with income and education = active jobs</td>
<td></td>
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<tr>
<td>Fauvel 2003</td>
<td>N = 292; Cases = 93</td>
<td>Self-report</td>
<td>Progression to Hypertension only – defined by increase &gt; 7 mmHg in SBP or DBP after 5 yr FU, or DBP &gt; 95 mmHg at end of FU</td>
<td>Trend: p &gt; 0.05</td>
<td>None</td>
<td>Baseline measurement of job strain The use of non-clinical definition of hypertension reduces confidence in findings.</td>
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<tr>
<td>Eaker 2004</td>
<td>Men 1,711</td>
<td>Imputed by job description</td>
<td>Clinically verified disease incidence CHD Morbidity</td>
<td>Men: RR 1.18 (0.69 – 2.0) Women: RR 0.61 (0.21 – 1.75) As calculated by Eller et al.</td>
<td>SBP, BMI, smoking, diabetes, cholesterol</td>
<td>Measured job strain only at one point in time Occupation was associated with CHD (p &lt; 0.001), not sure why authors did not include in adjustments Found that high job control among women increased risk for heart disease. Explains that it may because they were facing “cultural” pressures at the time the study was conducted that reflected society’s resistance to women in higher work roles. May have included those who were older than working age population</td>
<td>1, 2, 3</td>
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<tr>
<td>Kivimaki 2002</td>
<td>N = 812; Cases = 73</td>
<td>Self-report</td>
<td>Death registry CVD fatalities Mortality</td>
<td>HR 2.22 (1.04 – 4.73) Age, gender, occupational group, smoking, physical activity, blood pressure, cholesterol, BMI</td>
<td>Measured job strain only at baseline, but stratified cohort by job changes – found adverse effects of high job strain to be greatest for employees who remained with the same employer and occupation during the five years after baseline</td>
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<td>Study</td>
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<tr>
<td>Lee 2002</td>
<td>N = 35,038; Cases = 146</td>
<td>Self-report</td>
<td>Non-fatal MI, and fatal CHD Medical records, death registry Morbidity and Mortality</td>
<td>Total CHD RR 0.71 (0.42 – 1.19)</td>
<td>Age, follow-up period, smoking, alcohol, hypertension, diabetes, hypercholesterolemia, menopausal status, medication, diet, physical activity, parental history of MI, education, marital status, husband’s education</td>
<td>Assessed job strain at baseline</td>
<td>1, 2, 3</td>
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<tr>
<td></td>
<td>All women, Nurses Health Study US</td>
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<td>Non-fatal MI RR 0.63 (0.34 – 1.17)</td>
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<td>Age 46 – 71 years</td>
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<td>Fatal CHD RR 1.09 (0.40 – 2.92)</td>
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<td>4 year FU between 1992 and 1996</td>
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<td>Kuper 2003</td>
<td>N = 10,308; Cases: 828 all CHD; 266 fatal CHD/ non-fatal MI</td>
<td>Self-report</td>
<td>CHD morbidity and mortality Physician diagnosed, death registry</td>
<td>All CHD 1.35 (1.1 – 1.75)</td>
<td>Age, gender, employment grade, cholesterol, BMI, smoking, hypertension, physical activity, alcohol</td>
<td>Assessed job strain at baseline</td>
<td>1, 3</td>
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<td>Whitehall II study, men and women, civil servants, UK</td>
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<td>Fatal CHD/Non-fatal MI 1.16 (0.78 – 1.71)</td>
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<td>Avg 11 years FU</td>
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<td>Markovitz 2004</td>
<td>N = 3,200; Cases = 89</td>
<td>Self-report</td>
<td>Hypertension defn: • SBP ≥ 160 mmHg and DBP ≥ 95 mmHg or use of anti-hypertensive medication at end of FU</td>
<td>OR 2.06 (1.01 – 4.26) for increases in job strain ratio between beginning and end of follow-up</td>
<td>Age, baseline BMI, baseline SBP, family history of BP, smoking, examination site, education, change in BMI</td>
<td>Assessed Job strain at start and end of FU</td>
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<td>CARDIA, men and women US</td>
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<td>Age 20 – 32</td>
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<td>8 yr FU</td>
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<tr>
<td>De Bacquer 2005</td>
<td>N = 14,337; Cases = 87 Belgian job stress project All men, various occupations Age 35 – 59 years 3 yr Avg FU</td>
<td>Self-report</td>
<td>Sickness absence &gt; 3 weeks, validated with follow-up of with clinical records and formal diagnostic algorithm of gathering information of cardiac enzymes, ECG and necropsy findings</td>
<td>HR 1.26 (0.66 – 2.41)</td>
<td>Age, education, BMI, smoking, diabetes, systolic BP, cholesterol, job title</td>
<td>Assessment of job strain at baseline Inconsistent defn of CHD in comparison to other studies may have resulted in different findings in comparison to other studies</td>
<td>1, 2, 3</td>
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<tr>
<td>Uchiyama 2005</td>
<td>N = 1,615; Cases = 47 Hypertension followup study, men and women Japan Ages 40 – 65 years 5.6 yr Avg FU</td>
<td>Self-report</td>
<td>Physician diagnosed CVD morbidity at yearly checkups and mortality (not clear how mortality was ascertained)</td>
<td>All: RR 2.45 (0.87 – 6.93) Men: RR 1.86 (0.51 – 6.75) Women: RR 9.05 (1.17 – 69.86)</td>
<td>Age, BP, BMI, Cholesterol, proteinuria, left ventricular hypertrophy, ischemic ST-T change, atrial fibrillation, family history of stroke</td>
<td>Baseline job strain; yearly physician assessment for cardiovascular event Low number of cases, particularly among women may have lead to wide confidence intervals</td>
<td>1, 3</td>
</tr>
<tr>
<td>Netterstrom 2006</td>
<td>N = 659; Cases = 47 MONICA II study, all men Denmark Ages 30 – 60 years 9 yr Avg FU</td>
<td>Self-report</td>
<td>Hospital records or death registry CHD morbidity and mortality</td>
<td>HR 2.4 (1.0 – 5.7)</td>
<td>Age, SES, marital status, cholesterol, triglycerides, BMI, BP, smoking, alcohol, physical activity</td>
<td>Assessed baseline job strain; no significant risk of coronary risk factors associated with job strain at baseline No association when used imputed scores of job strain by job title Only 75% participation rate may lead to selection bias</td>
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<tr>
<td>Study</td>
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<td>Kornitzer 2006 48</td>
<td>N = 20,345; Cases = 129</td>
<td>Self-report</td>
<td>Depend on country: Belgium and France – sickness absences &gt; 28 days as reported by human resource departments. Physicians and hospitals were contacted to confirm caseness. Sudden deaths without a clinical diagnosis were classified as coronary deaths Spain – self-report of hospitalization ascertained by phone interview. Additional record linkages were made with MONICA register and mortality register. Sweden – registry and hospitalization data</td>
<td>HR 1.46 (0.96 – 2.25)</td>
<td>Age, smoking, BP</td>
<td>Baseline measurement of job strain Questionnaire used in Sweden was slightly different than others and was being calibrated with Karasek’s Job Strain Model may have lead to some exposure misclassification Differing exposure and outcome measures across different countries may have lead to exposure misclassification For France and Belgium: only industries who agreed to participate were included selection bias, whereas participants from Spain and Sweden represented a wider range of industries</td>
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<tr>
<td>Kuper 2006 49</td>
<td>N = 35,471; Cases = 210</td>
<td>Self-report</td>
<td>Hospital records or death registry CHD morbidity and mortality</td>
<td>Full-time workers: HR 1.0 (0.5 – 1.9) Part-time workers: HR 1.6 (0.7 – 3.7)</td>
<td>Age, SES, BMI, alcohol, smoking, diabetes, BP, physical activity</td>
<td>Baseline job strain; self-reported coronary risk factors and health behaviours Long follow-up would suggest that exposures may have changed particularly for women in part-time work exposure misclassification</td>
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<tr>
<td>Tsutsumi 2006 50</td>
<td>N = 6,509; Cases = 35 men and women, Japan</td>
<td>Self-report</td>
<td>Death registry CVD mortality</td>
<td>RR 1.98 (0.59 – 6.70)</td>
<td>Age, education, employment, smoking, alcohol, physical activity, BMI, hypertension, diabetes, cholesterol, community</td>
<td>Baseline job strain; excluded those who were currently seeking medical treatment for CVD</td>
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<td>Age 18 – 65 years 9.4 yr Avg FU</td>
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<td>More than 99% of participants were employed by companies with &lt; 300 employees → selection bias</td>
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<td>Low number of cases may be because Japan has the one of the lowest levels of IHD. This may be because of government sanctioned annual health checkups and follow-up preventative health strategies</td>
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<tr>
<td>André-Peterson 2007 51</td>
<td>N = 7,770; Cases = 291 Malmo cancer and diet study, men and women, Sweden</td>
<td>Self-report</td>
<td>Hospital records or death registry Fatal or non-fatal MI</td>
<td>Men: HR: 1.17 (0.53 – 2.99) Women: HR:1.29 (0.44 – 3.85)</td>
<td>Age, BP, anti-hypertensive drugs, diabetes, BMI&lt; treatment for hyperlipidemia, alcohol, smoking, education, occupation</td>
<td>Baseline job strain</td>
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<td>Age 47 – 73 years 7.8 yr Avg FU</td>
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<td>Authors took into account high domestic workload among women and concluded higher job strain among women may be attributed to duties at home</td>
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<td>Also examined the effects of social support and found that among women, social support played a more beneficial role in mitigating job stress</td>
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| Aboa-Éboulé 2007  | N = 942; Cases: 206                         | Self-report                   | Composite of:  
- fatal CHD (from death certificates, next-of-kin interviews, hospital charts) ICD9 410-414  
- non-fatal MI (cardiologist and vascular specialist diagnosed)  
- unstable angina (requiring hospitalization)  
CVD recurrence was assessed by interview at 6 years follow-up and compared to hospital and registry data | Assessment of job strain at baseline only:  
< 2.2 yr FU: HR: 0.58 (0.29-1.16)  
≥ 2.2 yr FU: HR: 1.45 (0.82-2.58)  
Chronic job strain (at baseline and at least 6 weeks after return to work):  
< 2.2 yr FU: HR: 0.86 (0.36-2.03)  
≥ 2.2 yr FU: HR: 2.38 (1.37-4.13) | Age, sex, hypertension, family history of CHD, BMI, comorbidities, social support, chemical and physical occupational exposures, hostile affect, suppressed anger, alcohol and smoking habits, physical activity, psychological distress, adverse work organization factors | Chronic job strain defined as self-reported strain at baseline (6 weeks after return to work) and 2 years later  
Recurrent MI was assessed 2.2 years later through interviews and checked against hospitalization records | none |
| Kivimaki 2008     | N = 3,160; Cases = 93                        | Self-report                   | Hospital records or death registry  
CHD and stroke Morbidity or mortality | HR 1.76 (1.05 – 2.95) | Age | Baseline measurement of job strain  
Inclusion of older employees (> 55 years) reduces risk and resulted in non-statistical significance: HR 1.22 (0.75 – 1.96)  
Interaction between job strain and age group (19 – 55 years vs. 56 – 65 years) on IHD | 2, 3 |
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<th>Study</th>
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<th>Adjustments</th>
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</table>
| Chandola 2008^4       | N = 10, 308; Cases = 522                   | Self-report                   | World Health Organization, MONICA criteria\(^3^\) | RR 1.33 (1.04 – 1.69) | Age, sex, employment grade, cholesterol, BP, anti-hypertensive medication, morning rise in cortisol, HRV, alcohol, smoking, physical activity, diet | Measured job strain at 2 points in time. Used summed score  
Showed dose-response relationship between frequency of stress and CVD  
Stronger association for those under 50 years of age  
RR 1.68 (1.17–2.42) |
| Netterstrom 2010^5^    | N = 1,146; Cases: 104                     | Self-report                   | Hospital records or death registry  
ICD8 410 – 414 and  
ICD10 I20 – I25 | Men: OR: 1.6 (0.7 – 3.7)  
Women: OR: 1.1 (0.3 – 4.2) | Age, social status, leisure-time physical activity, BMI, SBP, SES | Low number of cases \(\rightarrow\) low study power  
Purpose of the study was to examine the effectiveness of JSM in the current labour market, but used responses from 1992 – 1994 \(\rightarrow\) not certain if this would be indicative of the current market situation  
job demands among men over 50 years showed significant risk OR:2.3 (1.1 – 4.8) | none |
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<tr>
<td>Mäntyniemi 2012</td>
<td>N = 48,018 ; Imputed analyses: Cases: 53 Self-report analyses: Cases: 35 Finnish Public Sector Study, men and women employed in municipal services Finland Age: working age up to 55 years 4.6 yr Avg FU</td>
<td>Self-report and imputed</td>
<td>National pension registry ICD10 I20 – 25 - Disability pension requires physician’s diagnoses and is granted only if employee cannot return to work within 300 reimbursed sickness absence days during 2 consecutive years</td>
<td>Using imputed job strain scores: Men: HR: 2.37 (1.10 – 5.10) Women: HR: 0.98 (0.39 – 2.47) Using self-reported job strain scores: Men: HR: 0.99 (0.63 – 1.56) Women: HR: 1.65 (1.11 – 2.45)</td>
<td>Age, sex, SES, occupational physical demands, job contract, baseline fitness, CHD medication at baseline, baseline mental health, work unit information (e.g. number of employees)</td>
<td>Baseline job strain scores from individuals were used to create Job Exposure Matrices. Mean scores for each occupation were then applied to employees for imputed analyses 76% of subjects were women → selection bias Low number of cases – low statistical power Different statistical findings depending if scores are self-report or imputed. Self-reported exposure may have been biased from underlying subclinical CHD</td>
<td>none</td>
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</table>

**Abbreviations:**

- BMI = Body Mass Index
- BP = Blood Pressure
- CHD = Coronary heart disease
- DSP = Diastolic Blood Pressure
- Defn = definition
- FU = follow-up
- HR = Hazard Ratio
- ICD = International Classification of Diseases
- IHD = Ischemic Heart Disease
- IR = Incidence Ratio
- MI = Myocardial Infarction
- N= number
- OR = Odds Ratio
- RR = Relative Risk
- SBP = Systolic Blood Pressure
- SES = Socio-economic status
- US = United States
- UK = United Kingdom
- Yr = year

* Reviews:

1 = meta-analysis by Kivimaki et al. 32
2 = systematic review by Eller et al. 33
3 = systematic review by Backé et al. 34
In a meta-analysis of 11 prospective cohort studies using the Job Strain Model that were completed between 1979 and 2006, Kivimaki et al. estimated the summary risk for CHD incidence was 1.16 (95% CI: 0.94-1.43)\textsuperscript{32}. Systematic reviews completed by Eller et al. \textsuperscript{33} in 2009 and Backé et al. \textsuperscript{34} in 2012, included an additional 6 studies published after 2006 (Table 1.1). Backé et al. used a broader definition of heart disease (i.e. CVD instead of CHD) which resulted in the inclusion of 3 studies, with hypertension or stroke as outcome measures, that were not included in reviews by Kivimaki et al. or Eller et al. Despite the slight differences between reviews and although Eller et al. and Backé et al. did not provide a summary CVD or CHD incident risk estimate, all three reviews concluded that job strain may be associated with a moderate increased risk for heart disease.

All 3 reviews identified two common limitations that might be responsible for inconsistent evidence and null findings. Firstly, all studies which used job exposure matrices to impute job strain values by occupation title reported null findings\textsuperscript{35,36,40,41}. While job exposure matrices may be an efficient way of including a large study population, it does so at the expense of the specificity of the exposure \textsuperscript{33}. Occupational tasks can vary widely between workplaces as would perceptions of stress, entailing a considerable amount of non-differential misclassification and attenuating risk estimates. Secondly, a majority of the studies measured job strain only at baseline. This would require an assumption that job strain would remain constant but would seem unlikely over long follow-up periods. Most studies identified in prior reviews assessed job strain only at baseline and reported null findings. However, two which measured job strain several times during the follow-up period reported a positive association with CVD. Markovitz et al. measured a change in job strain between the beginning and end of follow-up and found a higher risk of hypertension among those who went from low-strain to high-strain in comparison
to those who remained in either a low-strain or high-strain job at both time points (OR 2.06, 95% CI: 1.01 – 4.26)\(^45\). Chandola et al. summarized frequency of high job strain at 2 time points to develop a cumulative score and found a dose-response relationship between frequency of job strain and CHD incidence (RR 1.33, 95% CI: 1.01 – 4.26)\(^58\).

I completed an additional search for additional prospective cohort studies published since 1977 using key terms identified in previous reviews such as “job strain” and “cardiovascular disease” or “heart disease” or “coronary disease” and “prospective”. I found three prospective cohort studies \(^52,56,57\) which are also summarized in Table 1.1.

Aboa-Éboulé et al. examined the risk of recurrent CHD among a group of 972 men and women after their first myocardial infarction \(^52\). Job strain was assessed at baseline (6 weeks after return to work) and again 2 years later. Results were consistent with findings in prior reviews: an increased risk was reported for recurrent CHD when accounting for job strain measured at 2 points in time (HR 2.00, 95% CI: 1.08 – 3.72), however, a null finding was reported when only accounting for job strain at baseline (HR 1.45, 95% CI: 0.82 – 2.58).

More recently, Netterstrom et al. conducted a study to test the validity of the Job Strain Model to measure job stress in the “current economy” but did not find a significant risk associated with CVD for men or women [(OR 1.6, 95% CI: 0.7 – 3.7) and (OR 1.1, 95% CI: 0.3 – 4.2), respectively]\(^56\). However, while the authors' intent was to study the effects of job strain during a 14 year follow-up “in period … characterized by relative wealth and increasing employment rates”\(^56\), subjects completed the job strain questionnaire only at baseline which may not have reflected working stress experienced during the lengthy follow-up period.
In a study using a national registry to identify disability pensions related to CVD, Mäntyniemi et al. found mixed results when comparing self-reported job strain to imputed scores using a job exposure matrix. The authors found that using imputed scores resulted in a significantly positive risk among men but not women [(HR 2.37, 95% CI: 1.10 – 5.10) vs. (HR 0.98, 95% CI: 0.39 – 2.47), respectively]. However when using self-reported scores, the reverse was true with a significantly positive result among women [(Men: HR 0.99, 95% CI: 0.63 – 1.56) vs. (Women: HR 1.65, 1.11 – 2.45)]. This is contradictory to limitations addressed in previous reviews which found that using job exposure matrices resulted in null findings. However, the use of disability pensions may not be a reliable outcome measure and may have biased risk estimates as a proportion of the population may not eligible to receive a pension.

In summary, findings from 3 current prospective cohort studies were mixed, but risk estimates were similar to those found in prior reviews suggesting a modest association between CVD and job strain. Further investigations should consider improving quantifying work-related stress over time. Recommendations future research identified in previous reviews included:

- **Identifying specific occupational stressors** to develop effective prevention strategies which may have a significant impact to maintain overall worker health. To do so, **standardized instruments expanding on existing stress model theories** should be used to assess subjective exposures. **Individual-level responses**, rather than aggregated approaches, are necessary to improve specificity in identifying stressors among differing work environments.

- Improving exposure measurements by **including temporal changes and evaluating the intensity and duration of exposure of psychosocial stressors**.
• Developing sophisticated assessment strategies to gain a better understanding of the role of work stress in the etiology of CVD. To determine if factors such as reduced HRV and early atherosclerosis are stress mediators, studies directly linking epidemiologic evidence with subsequent intermediate biological mechanisms with cardiovascular endpoints are needed.

1.3 Shift work: a physical and psychosocial stressor

While there is no agreement on an exact definition of shift work in the literature, it is generally considered to pertain to work outside of the “conventional 8 to 9 hour workday”, often into the night or with very early starting times. It can include permanently displaced work hours (e.g. regular night shifts), rotating-shifts (e.g. alternating shifts across the 24-hour clock) or any other irregularly scheduled working hours. This workplace stressor has been identified as a complex categorization with characteristics of both physical and psychosocial stressors and one which merits special consideration with respect to worker health.

In a broad sense, the need for shift work may reflect the increasing demands on the global economy which are transferred as an additional stressor on workers. In Canada alone, while the number of workers in daytime-only schedules increased by 23.0% between 1996 and 2008, more growth was observed in regular night - and evening- shifts (38.5%), rotating-shifts (25.8%) and irregular schedules (37.4%). Studies have shown that up to 80% of shift workers would prefer to work only during conventional daytime hours, but many have little choice in their working schedules and there are few opportunities to obtain a daytime-only schedule without extensive experience.
Biological functioning in humans follows a circadian rhythm which dictates being active during daylight hours and recovering when it is dark. However, shift work can lead to circadian disruption of normal biological and social functioning, contributing to an increased risk for disease. The pathway linking shift work and heart disease has been proposed as one that is multifaceted with disruptions in psychosocial, behavioural and physiological mechanisms. Added to the complexity of this association is the interrelatedness of the proposed mechanisms. Firstly, shift work can act as a psychosocial stressor when workers perceive a lack of control over a more desirable work schedule. Working during times when the general population socializes may also contribute to work-life imbalances with consequences on psychosocial well-being. Secondly, these psychosocial stressors combined with the effect of working at night can result in adverse health behaviours such as sleep disruption and poor dietary intake. Studies have shown that shift workers suffer from chronic sleep deprivation and fatigue; and sleep deprivation has been linked to decreasing levels of leptin, a hormonal appetite suppressor, which can result in unhealthy eating habits. Finally, the combined effects of psychosocial and behavioural stressors may lead to physiological stress such as dysregulation of neuroendocrine systems, contributing to permanent changes in cardiovascular functioning and increasing the risk for heart disease.

1.3.1 Evidence linking shift work and cardiovascular disease

While allostatic overload and neuroendocrine dysregulation have been investigated, the strongest evidence can be found in studies examining sleep disruption and sleep deprivation. Impairment of healthy neuroendocrine functioning resulting from sleep disruption can be attributed to two main factors: 1) sleep deprivation can impair brain function and lead to chronic psychological stress; and 2) exposure to light at night can alter normal circadian rhythmicity and
consequently, neuroendocrine hormone production\textsuperscript{70}. It could be deduced that because shift work is strongly associated with sleep disorders\textsuperscript{71}, that the resulting neuroendocrine dysregulation may increase the risk of heart disease among these types of workers. However, while most experimental research examining response of cardiovascular biomarkers to circadian misalignment have found altered neuroendocrine activity, the effects studied were only short-term and effects associated with chronic circadian desynchronization remain to be elucidated\textsuperscript{72}.

Despite evidence suggesting that shift work may contribute to a risk of heart disease through direct and indirect effects of disruptions in psychosocial, behavioural and physiological mechanisms (such as neuroendocrine activity), results of epidemiologic studies remain mixed. In an early review of English- and Swedish-language publications up to 1998, including conference reports and papers in-press, Boggild \textit{et al.} estimated that shift workers were at a 40\% increased risk of CVD incidence in comparison to daytime-only workers\textsuperscript{62}. However, in a recent systematic review of English-language, peer-reviewed publications, Frost \textit{et al.} reported the summary estimate was “closer to unity”\textsuperscript{73}. This difference between reviews may be attributed to the inclusion of different study types. Whereas Frost \textit{et al.} restricted their review to longitudinal studies, Boggild \textit{et al.} included cross-sectional studies and conference reports (RR range: 1.5 – 3.17) which may have biased their risk estimates upwards. However, despite the differences in types of studies summarized, summary risks by both reviews were based on crude, visual observations of point estimates which are not exact and may be subject to interpretation.

I completed an additional search of publications since 1972 using key words identified by Frost \textit{et al.} including terms such as “shift work” or “shift near work” or “night near work” and “cardiovascular disease” or “heart disease” or “coronary near disease” and identified 6 additional studies to update the epidemiological evidence investigating shift work and CVD (Table 1.2).
Two studies reported a significantly increased risk of hypertension associated with shift work. Morikawa et al. found an increased risk only among young workers between 18 to 29 years of age (RR 3.6, 95% CI: 1.41 – 9.1)\textsuperscript{74}; whereas Sakata et al. reported a smaller risk among male steelworkers of all ages (RR 1.1, 95% CI: 1.01 – 1.2)\textsuperscript{75}. In a follow-up study to Sakata, Oishi et al. found that among steelworkers with pre-existing mild hypertension (i.e. systolic blood pressure between 140 to 159 mmHg), shift workers were at a modestly elevated risk (OR 1.23, 95% CI: 1.05 -1.44) of developing clinical hypertension (i.e. World Health Organization definition: systolic blood pressure ≥ 160 mmHg) in comparison to those only working days. Ellingsen et al. and Pimenta et al. reported significant increased risks of CVD among shift workers, [(OR 1.65, 95% CI: 1.38 – 1.97) and (OR 1.67, 95% CI: 1.1 – 2.54)], but these 2 study designs did not allow for inference of causality (i.e. cross-sectional, case series) and neither adjusted for differences in occupations which may bias risk estimates. Contradictory to these findings, in a well-executed, large prospective cohort study that examined shift work status at the beginning and end of follow-up, Hublin et al. did not find a significantly increased risk of CVD associated with chronic shift work exposure (OR 1.06, 95% CI: 0.75 – 1.5)\textsuperscript{76}. 
### Table 1.2 Summary of shift work and heart disease studies

(see footnote for abbreviations)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design, Sample Size, Follow-up period</th>
<th>Exposure Assessment</th>
<th>Outcome Assessment</th>
<th>Risk Estimates for fully adjusted model (95 % Confidence Interval)</th>
<th>Adjustments</th>
<th>Notes</th>
<th>Reviews*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Taylor 1972</strong></td>
<td>Retrospective cohort N = 8,603</td>
<td>Work history records from 10 participating companies</td>
<td>Death certificates from company records and national registry for those who did not have company records</td>
<td>Evening shift RR 1.01 (0.66-1.52)</td>
<td>Age, calendar year</td>
<td>Selection bias in population • only included older workers because death rates among young workers was “too low” • companies volunteered to participate</td>
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<td></td>
<td>Multi-occupational, male factory labourers, UK FU 1956 - 1968</td>
<td>1. Day workers (10 yr continuous, &lt; 6 mo shift work prior to 1946)</td>
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<td>Night shift RR 0.64 (0.28-1.47)</td>
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<td>2. Shift workers (10 yr continuous shift work; interruption &lt; 6 months)</td>
<td>Mortality: CVD, Arteriosclerotic heart disease and hypertensive diseases</td>
<td>No significant effects. Trend shows that moving from evening/night to day might have a protective effect. This protective effect disappears when time on current shift increases</td>
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<td>3. Ex-shift (&gt; 6 months of shift work, then transfer to daytime)</td>
<td>ICD 7: 400-468</td>
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<td></td>
<td>Cases = 1,578</td>
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<td><strong>Angersbach 1980</strong></td>
<td>Retrospective cohort N = 640</td>
<td>Did not report how shift work information was ascertained</td>
<td>Sick records from company health insurance and occupational health centre</td>
<td>Reported incidence density = # people with CVD-related absences / 100 person-yrs</td>
<td>None</td>
<td>Limitations: Small study size, non-clinical case definition and unclear exposure assessment</td>
<td>1, 2</td>
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<tr>
<td></td>
<td>Chemical firm, men Germany</td>
<td>Shift work groups</td>
<td>CVD incidence defn = work absence &gt; 2 days</td>
<td>No difference between shift workers and daytime-only workers (p &gt; 0.05)</td>
<td></td>
<td>Subdivided day and night shift workers into further groups of people who stayed or changed work schedule during FU period</td>
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<td></td>
<td>FU 1966-1977</td>
<td>1. Dayshift workers</td>
<td>Cases: 60 CVD-related absences among shift workers</td>
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<td>Mentioned in systematic review by Frost et al⁷³, but did not include it in their overall summary because of the outcome data included hypertension and arrhythmia</td>
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<tr>
<td>Study</td>
<td>Study Design, Sample Size, Follow-up period</td>
<td>Exposure Assessment</td>
<td>Outcome Assessment</td>
<td>Risk Estimates for fully adjusted model (95 % Confidence Interval)</td>
<td>Adjustments</td>
<td>Notes</td>
<td>Reviews*</td>
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<td>Alfredsson 1982</td>
<td>Case-control N = 1216 Cases = 334 Controls = 882 Male manual workers Switzerland 13 yr FU</td>
<td>Census data; Baseline interview Shift work definition: “Continuously changing day and night work schedule” for at least 50% of the time at their occupation</td>
<td>Registry data and medical data Fatal or non-fatal MI ICD 410 – 410.99</td>
<td>RR 1.25 (0.97 – 1.62)</td>
<td>Age</td>
<td>Also asked about work pace, physical intensity of work, job strain, education, smoking, but did not control for any of these factors</td>
<td>1, 2</td>
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<tr>
<td>Knutsson 1986</td>
<td>Retrospective cohort N = 504</td>
<td>Self-report</td>
<td>Self-report or by proxy if subject had died: Cases: 43</td>
<td>RR 1.4, p &gt; 0.05</td>
<td>Smoking status and age</td>
<td>Did not account for duration or temporal changes of shift work</td>
<td>1, 2</td>
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<tr>
<td>Tüchsen 1993</td>
<td>Cross-sectional: N = 1,293,888, men, Denmark 4 yr FU</td>
<td>Census data: Used occupational groupings to define daytime only vs. shift work</td>
<td>Hospitalization records: ICD8 – 410-414 Total cases: 406,969 Shift work cases: 161,181</td>
<td>Standardized Hospitalization Ratios (SHR): Night/early morning SHR 193 (158.3–236.0) Later evening SHR 215 (192.4–240.1) 24-hour services SHR 168 (151.8–185.5) Irregular hours SHR 172 (166.4–182.1)</td>
<td>Age</td>
<td>Surrogate measures for exposure; baseline measures only linked census (1981) to national inpatient register (1981 – 84)</td>
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<td>Study</td>
<td>Study Design, Sample Size, Follow-up period</td>
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<td>Kawachi 1995</td>
<td>Prospective cohort Nurses Health Study Cohort</td>
<td>Questionnaire: what is total number of years during which you worked rotating night shifts (at least 3 nights per month in addition to days or evenings in that month)? • Categories of duration • Ever vs. never</td>
<td>Non-fatal MI and fatal CHD Reported non-fatal MI → reviewed medical records and used WHO defn Deaths from National Death Index for those who did not respond to questionnaire cycle Cases among shift workers: - 29 of Fatal CHD - 170 for non-fatal MI</td>
<td>RR 1.21 (0.92 – 1.59) among women with less than 6 years of shift work RR 1.51 (1.12 – 2.03) among women with 6 or more years of rotating night shift</td>
<td>Smoking, alcohol, BMI, hypertension, diabetes, hypercholesterolemia, menopausal status, current use of post-menopausal hormones, past use of oral contraceptives, levels of physical activity, Vitamin E intake, average aspirin use, parental history of MI before age 60</td>
<td>Partial use of self-reported non-fatal MI</td>
<td>1, 2</td>
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<tr>
<td>Steenland 1996</td>
<td>Nested Case-Control N = 944 Matched 5 controls per case on age, race and plant Men working at 4 heavy equipment plants, USA</td>
<td>Work history records: Day, evening or night shift; only accounted for shift type (and duration of) worked at time of case death, and if there was a shift change or interruption of more than 1 month in the work schedule, what the preceding shift type was Layoffs and disability leaves were also listed</td>
<td>IHD fatality (ICD9 410-414) while working or within 1 week of work Cases = 163 Not clear how cases were ascertained (i.e. registry?)</td>
<td>Evening shift OR 1.01 (0.66-1.52) Night shift OR 0.64 (0.28-1.47) Trend shows that moving from evening/night to day might have a protective effect. This protective effect disappears when time on current shift increases.</td>
<td>Age, race plant</td>
<td>Just a brief communication, not a very detailed study</td>
<td>1, 2</td>
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<tr>
<td>Study</td>
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<tr>
<td>McNamee 1996</td>
<td>Nested Case-Control (1:1 matching on age and year of starting work)</td>
<td>Shift work derived from personnel records (pay codes), dosimetry records and occupational health records</td>
<td>Fatal IHD (ICD 410-414) from death registries</td>
<td>OR 0.90 (0.68-1.21) Baseline measures: height, BMI, BP, smoking, duration of employment and job status</td>
<td>Almost a daily record of shift work exposure</td>
<td>Did not account for change of labour type (skilled/unskilled) during follow-up or shift work outside of the company</td>
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<tr>
<td>N = 934</td>
<td></td>
<td>Shift work = someone who did shift work for &gt; 1 month</td>
<td>Cases: 467</td>
<td></td>
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<td>Included a 10 year lag to account for survivor effect</td>
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<td>All male industrial workers, UK</td>
<td>FU 1950 - 1992</td>
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<tr>
<td>Tenkanen 1997</td>
<td>Prospective cohort study</td>
<td>Questionnaire assessment in 1987 – 1988 (established categories); retrospective report of shift work status</td>
<td>ICD9 410-414 in hospitalization and death records</td>
<td>RR 1.38 (p &lt; 0.05) Baseline at enrollment into study (1982): smoking habits, alcohol use, leisure time physical activity, BMI and BP measurement</td>
<td>Different types of occupation for daytime shifts (academic and clerical workers) and shift workers (industrial workers or machine operation) may not have adequately adjusted for occupational confounders</td>
<td>Middle aged men (40 – 55 years) upon entry into cohort selection bias?</td>
<td>1, 2</td>
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<tr>
<td>N = 1806 men working in industry (blue collar and white collar), Sweden</td>
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<td>Grouped different shift types together to form ‘Shift work’ variable</td>
<td>FU to 1993 after questionnaire assessment of shift work status</td>
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<td>6 years FU</td>
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<td>Unclear how many cases</td>
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<tr>
<td>Boggild 1999</td>
<td>Prospective cohort study</td>
<td>Exposure measured at 2 points in time 1970 and 1985 (interview, questionnaire, blood draw and medical exam)</td>
<td>Registry data – morbidity and mortality (hospitalization and death certificates) ICD 410-414</td>
<td>RR 0.9 (0.7-1.1) using 1975 baseline shift work exposure Social class, sleep, smoking, age, weight, height, fitness</td>
<td>Limitation: not specific about the amount of night work which may have differed between individuals attenuation of results</td>
<td>Only included older men survivor effect of those who have remained in shift work</td>
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<td>Study</td>
<td>Study Design, Sample Size, Follow-up period</td>
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<tr>
<td>Knutsson 1999</td>
<td>Case-control</td>
<td>N = 4648, Cases = 2006, Controls = 2642, matched on age, geographic region and gender</td>
<td>Collected by questionnaires and telephone interview</td>
<td>Fatal and non-fatal MI ICD9 410 or 412</td>
<td>Men shift work RR 1.3 (1.1-1.6)</td>
<td>Job strain, education level and smoking</td>
<td>No additive interaction between shift work and job strain</td>
</tr>
<tr>
<td></td>
<td>Men and women, Sweden</td>
<td></td>
<td>Question – did you undertake shift work during most recent 5 years? If yes, what type of schedule? What time did major part of work occur (reported in categories)?</td>
<td>3 sources of data: hospital discharge records, death certificates, coronary and intensive care units at emergency hospitals</td>
<td>Women shift work RR 1.3 (0.9-1.8)</td>
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<td>Shift work = work includes time outside daytime (6 am – 6 pm) • Subgroup: Night work defn as work often or always between 10 pm and 6 am</td>
<td>Specific diagnosis criteria by Swedish Association of Cardiologists</td>
<td>Men night-work RR 1.3 (0.9-1.8)</td>
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<td>Cases of MI = 2006</td>
<td>Women night-work RR 1.6 (0.8-3.1)</td>
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<td>Higher risk among younger age groups perhaps because they had worked shift work most recently. Older respondents may have been retired and not worked shift within the past 5 years</td>
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<td>Morikawa 1999</td>
<td>Cohort</td>
<td>N = 1551, Men, in zipper and aluminum sash factory, Japan</td>
<td>Self-report on questionnaires</td>
<td>Hypertension defn: SBP ≥ 140 mmHg or DBP ≥ 90 mmHg in annual medical examinations at least twice; or initiation of antihypertensive treatment</td>
<td>Examined 3 different age groups, compared shift work at beginning and end of FU with daytime-only at beginning and end of FU: 18 – 29 years RR 3.6 (1.41 - 9.1)</td>
<td>Baseline measures of age, BMI, SBP, drinking habits</td>
<td>Accounted for change in shift schedule at beginning and end of FU</td>
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<td>FU 1990 - 1995</td>
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<td>Continuous and non-continuous rotating 3-shift vs. daytime only</td>
<td>Cases: 109</td>
<td>30 – 39 years RR 0.4 (0.14 – 1.4)</td>
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<td>Reported shift work status at beginning and end of FU</td>
<td>40 – 49 years RR 1.2 (0.55 – 2.7)</td>
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<td>Study</td>
<td>Study Design, Sample Size, Follow-up period</td>
<td>Exposure Assessment</td>
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<tr>
<td>Virtanen 2002</td>
<td>Prospective cohort N = 507,000 Men, all occupations, excluding mining, military and agricultural work Finland FU 1981 – 1994</td>
<td>Census data collected every 5 years job exposure matrix to impute shift type</td>
<td>CVD mortality ascertained with registry data ICD9 390-459 Cases: 16,344</td>
<td>Two shift, evening RR 1.02 (0.96 – 1.08) Three shift, evening RR1.02 (0.94 – 1.10)</td>
<td>Confounders (e.g. age), SES, and job exposure variables (e.g. noise, diesel exhaust)</td>
<td>Only kept people who remained in the same occupation during between 1975 and 1980 as an indicator of a stable workforce</td>
<td>2</td>
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<tr>
<td>Sakata 2003</td>
<td>Cohort N = 5,338 Men employed in steel company Japan FU 1991 – 2001, avg FU period – 4.64 years</td>
<td>Payment ledger Shift workers vs. daytime -only</td>
<td>Blood pressure measured during annual health exams; and medical histories ascertained in interviews Defn of hypertension: SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg or taking antihypertensive medication</td>
<td>OR: 1.10 (1.01 – 1.20)</td>
<td>Age, BMI, alcohol and smoking habits, exercise, cholesterol, creatinine, hemoglobin</td>
<td>Treated each 1-year interval as an independent observation Case defn is not a medical diagnoses, and does not conform to any medical criteria (e.g. WHO), resulting in high number of hypertensive cases Not known how much shift work exposure individuals may have had prior to current job</td>
<td>none</td>
</tr>
<tr>
<td>Study</td>
<td>Study Design, Sample Size, Follow-up period</td>
<td>Exposure Assessment</td>
<td>Outcome Assessment</td>
<td>Risk Estimates for fully adjusted model (95 % Confidence Interval)</td>
<td>Adjustments</td>
<td>Notes</td>
<td>Reviews*</td>
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<tr>
<td>Karlsson 2005 88</td>
<td>Retrospective cohort</td>
<td>Used company registries to ascertain shift work exposure</td>
<td>Registry data – from Jan 1952 to Dec 2001</td>
<td>Mortality due to CHD was 11% higher among shift workers in comparison to daytime only workers.</td>
<td>Age, calendar period</td>
<td>Did 2 analyses – first with the entire cohort, then restrict to those under 68 years and within 4 years of quitting shift work</td>
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<tr>
<td>N = 5442</td>
<td>Shift workers (n=2,354), Daytime-only (n=3,088)</td>
<td>Used job title and workplace characteristics to classify shift work exposure</td>
<td>Total mortality and cause-specific mortality due to CHD, ischemic stroke, and diabetes</td>
<td>Standardized RR (to age) SRR 1.11 (0.95-1.30)</td>
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<td>Not clear if they took into account the change in shifts during this period</td>
<td></td>
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<tr>
<td>Male pulp and paper manufacturing workers</td>
<td>Sweden</td>
<td>Categories of shift work:</td>
<td>Shift work cases of CHD = 287</td>
<td>Increase of CHD mortality for shift workers who had worked shifts &gt; 30 years SRR 1.24 (1.04-1.49)</td>
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<tr>
<td>Oishi 2005 89</td>
<td>Prospective cohort</td>
<td>Payment ledger</td>
<td>BP measurements from annual health examinations. Outcome measures as defined by WHO criteria:</td>
<td>Severe hypertension: OR 1.23 (1.05 – 1.44)</td>
<td>Age, BMI, smoking and drinking habits, exercise, cholesterol, creatinine, uric acid, blood glucose</td>
<td>Each 1-yr interval was treated as an independent observation</td>
<td>none</td>
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<tr>
<td>N = 6,498</td>
<td>Men employed in steel company with mild hypertension (SBP between 140 – 159 mmHg and/or DBP between 90 - 99 mmHg) without use of antihypertensive medication</td>
<td>Shift work vs. daytime only</td>
<td>1) Severe hypertension (SBP ≥ 160mmHg and/or DBP ≥ 100mmHg) Cases: 695</td>
<td>Severe systolic hypertension: OR 1.13 (0.94 – 1.35)</td>
<td>Results indicate shift work is a risk factor for hypertension progression</td>
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<tr>
<td>Japan</td>
<td>FU: 1991 - 2001</td>
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<td>2) Severe systolic hypertension (SBP ≥ 160mmHg) Cases: 504</td>
<td>Severe diastolic hypertension: OR 1.28 (1.07 – 1.52)</td>
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<td>3) Severe diastolic hypertension (DBP ≥ 100mmHg) Cases: 559</td>
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<td>Study</td>
<td>Study Design, Sample Size, Follow-up period</td>
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| Fujino 2006  | Prospective cohort N = 17,649 Men from various occupations, Japan | Baseline Self-Admin Questionnaire: *during your working life, until the present, what shift (time of day) did you work most: mainly daytime, mainly night or alternate night and daytime)?* | 1) Fatal IHD  
(ICD10 I20-25)  
Cases: 86  
2) Self-reported hypertension  
Cases: 20 | IHD  
- Reg night worker RR 1.23 (0.49-3.10)  
- Rotating RR 2.32 (1.37-3.95)  
Hypertension RR 1.81 (1.07 – 3.06) | Smoking, alcohol, past medical history (hypertension, diabetes), education level, daily life stress, physical activity and type of job (office worker, manual worker, other) | Does not account for temporal patterns nor type of shift work at time of baseline measure.  
Only examined what was the most frequent type of shift work up to the time of baseline survey | 2 |
| Tüchsen 2006 | Prospective cohort N = 5,517 Men and women, Denmark FU1991- 2002 | Baseline Interview in 1991 *what kind of work schedule do you have?*  
Irregular working hours defn: anyone who did work 2 shift, 3 shift, fluctuating according to special schedule or rotation, permanent evening duty, permanent night duty, other | Registry data + hospitalization records  
ICD8 390-458  
ICD10 I00-I99  
Cases:  
Irregular work hours = 113  
Daytime-only = 449 | Irregular work hours: RR 1.31 (1.06-1.63)  
Aetiological fraction of circulatory disease due to shift work 5% | Smoking, prolonged standing or walking at work, cold/hot work environment, repetitive tasks, work conflict, ergonomic exposure, job insecurity, decision authority, social support, psychological demands, seniority | Limitation: Do not know how long people have worked in shift work | 2 |
<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design, Sample Size, Follow-up period</th>
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<th>Risk Estimates for fully adjusted model (95 % Confidence Interval)</th>
<th>Adjustments</th>
<th>Notes</th>
<th>Reviews*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ellingsen 2007</td>
<td>Case series N = 223 cases</td>
<td>Work history records Rotating-shift workers vs. daytime-only</td>
<td>Medical records; unclear how CVD cases were identified from medical records Cases: 223</td>
<td>RR 1.65 (1.38 – 1.97)</td>
<td>None</td>
<td>Simple comparison of prevalence of CVD among shift workers to daytime-only workers</td>
<td>none</td>
</tr>
<tr>
<td>Yadegarfar 2008</td>
<td>Nested Case Control N = 1270</td>
<td>Shift work derived from personnel records (pay codes), dosimetry records and occ health records Shift work = someone who did shift work for &gt; 1 month</td>
<td>Fatal IHD (ICD 410-414) from death registries Cases = 635</td>
<td>OR 1.04 (0.83 - 1.30)</td>
<td>Baseline measures: height, BMI, BP, smoking, duration of employment and job status; also included social class 10 year lag</td>
<td>Similar cohort to McNamee et al. and used same data sources 2</td>
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<tr>
<td>Hublin 2010</td>
<td>Prospective cohort N = 20,142</td>
<td>Self-report questionnaire at 2 time points 1975 and 1981 5 exposure groups 1) Day → Day (reference) 2) Night work in either 1975 or 1981 3) Shift → Day 4) Day → Shift 5) Shift → Shift</td>
<td>CVD mortality from national registry data (ICD10 I20 - I25) Cases: 857 Disability retirement due to CVD from national insurance corporation and national pension registry (ICD10 I00 – I99) Cases: 721 Hypertension defn: record of medical treatment from CHD mortality (Shift work at beginning and end of FU): Men: HR: 1.06 (0.75 - 1.50) Women:HR: 1.21 (0.75 – 1.93) CVD disability retirement (Shift work at beginning and end of FU): Men: HR: 0.70 (0.48 - 1.03) Women:HR: 0.79 (0.43 – 1.43)</td>
<td>Age, marital status, social class, education, smoking and drinking habits, BMI, physical activity, life satisfaction, diurnal type, sleep length, use of hypnotics or tranquilizers, physical workload, work pace</td>
<td>Examined shift work status at 2 points in time and accounted for change in work schedule over time</td>
<td>none</td>
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<tr>
<td>Study</td>
<td>Study Design, Sample Size, Follow-up period</td>
<td>Exposure Assessment</td>
<td>Outcome Assessment</td>
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<tr>
<td>Pimenta 2012 84</td>
<td>Cross-sectional N = 211 Men and women employed in Health Science department at a University Brazil</td>
<td>Interview Day shift: between 7 am to 7 pm Night shift: between 7 pm to 7 am</td>
<td>Cardiovascular risk as calculated using Framingham score (incorporates age, cholesterol, SBP, DBP, smoking and diabetes). Ascertained with biological measures and interview questions Low/medium score: &lt; 20% High: ≥ 20%</td>
<td>Hypertension (Shift work at beginning and end of FU): Men: HR: 1.07 (0.88 - 1.30) Women: HR: 1.00 (0.80 – 1.23)</td>
<td>Shift workers: PR 1.67 (1.10 – 2.54)</td>
<td>Job strain, social support, number of working hours, years of employment in current position, years of formal schooling, monthly income, physical activity during leisure time, waist circumference, plasma triglyceride levels</td>
<td>63% of population &lt; 40 years old</td>
</tr>
</tbody>
</table>

Abbreviations:
- BMI = Body Mass Index
- BP = Blood Pressure
- CHD = Coronary heart disease
- DSP = Diastolic Blood Pressure
- Defn = definition
- FU = follow-up
- HR = Hazard Ratio
- ICD = International Classification of Diseases
- IHD = Ischemic Heart Disease
- IR = Incidence Ratio
- MI = Myocardial Infarction
- N = number
- OR = Odds Ratio
- PR = Prevalence Ratio
- RR = Relative Risk
- SBP = Systolic Blood Pressure
- SES = Socio-economic status
- US = United States
- UK = United Kingdom
- Yr = year

* Reviews:
1 = Boggild et al. 62
2 = Frost et al. 73
To summarize, out of 22 English-language studies examining the risk of CVD with shift work (Table 1.2), 20 found a positive association, with 13 achieving statistical significance. Risk estimates ranged from 0.9 to 3.6, with most falling between 1 – 1.6. With the exception of 3 studies, all used a longitudinal design to examine evidence of a temporal relationship between shift work and heart disease. Five studies attempted to find a dose-response relationship: four reported an elevated risk of CVD associated with years of shift work with statistical significance achieved in 3. However, the existing evidence supporting an association between shift work and heart disease is still inconsistent.

Mixed findings could be partially attributed to the substantial differences in assessment of shift work exposure. Ten used self-reported exposure, 8 relied on employment records and 3 used census data and assigned shift work status using a job exposure matrix. Studies using retrospective interviews \(^{80,82,86}\) may result in differential misclassification bias when shift workers believe their work schedule has contributed to their illness; and the use of job exposure matrices to impute shift work exposure \(^{81,88}\) may not accurately reflect the true exposure among differing workplaces\(^{62}\). Baseline exposure assessments do not take into account temporal changes, and particularly among unstable labour populations, may also contribute to misclassification error and lead to null findings \(^{33}\).

While the use of broad study populations may allow for larger sample sizes and greater statistical power, there are some limitations which could result in mixed findings. It has been suggested that daytime-only workers differ from shift workers in terms of work tasks, workload and socioeconomic status; and results may be biased if these factors are not accounted for \(^{63}\). For example, although Pimenta et al. reported an increased risk of CVD among those working nights at a university health science department, descriptive findings revealed daytime workers
consisted of faculty members and administrative staff whereas shift workers were primarily health care professionals and technicians. However, not controlling for differences in job-related tasks between occupations (e.g. physical demands such as lifting patients) may have biased risk estimates. Pooling workers from across different workplaces can also lead to inconsistent definitions of shift work and may lead to non-differential exposure misclassification and bias risk estimates towards the null.

In summary, I support conclusions by Frost *et al.* that there is limited evidence to support a causal relationship between CVD and shift work. While the overall evidence of an association is weak, it still suggests there is an increased risk and that further investigation is warranted. I agree with recommendations made by Boggild *et al.* that future research should include:

- **Choosing suitable reference groups** to reduce the effects of confounding and provide valid comparisons. It has been proposed that “the ideal [comparison] group should resemble shift workers in all ways (at least regarding risk factors for CVD) than the worktime schedule”
- Incorporating knowledge on risk factors for CVD and **not controlling for factors that lie on the causal pathway**
- **Utilizing a more precise definition of shift work** (e.g. fast-forward rotating, regular night) to reduce non-differential exposure misclassification and contribute to the understanding of risks associated with different types of shift schedules
- **Including markers of both atherosclerosis and homeostasis, with particular attention to circadian rhythms of the biomarkers** to gain a better understanding of the pathophysiology of circadian misalignment with heart disease
• Identifying if shift work is associated with acute or chronic cardiovascular events
to gain a better understanding of the pathophysiology, shape future research
methodologies and aid in development of effective prevention strategies to negate the
adverse health effects associated with shift work

1.4 Paramedics and cardiovascular disease

Emergency service workers, such as police, firefighters and paramedics, can be considered to be
among the most stressful of occupations. Their work environment is one of extremes: periods of
inactivity and anticipation interspersed with peaks of physical activity and psychological strain
during emergency calls. They are routinely exposed to traumatic incidents involving human
suffering. In addition, they work long hours (often including nights) and can be subject to
hazardous conditions which compromise their personal health and safety. In a crude analysis of
shift work prevalence using a national survey of the Canadian workforce population, I found
that the majority of technical health service occupations such as paramedics (National
Occupational Classification Codes D211-D313), and those employed in protective services such
as police and firefighters (National Occupational Classification Codes G611-G631) reported
working in evening, night or rotating-shift schedules (56.4% and 64.4%, respectively). However, it should be noted that this may be an underestimation of the true shift work
prevalence because these occupational groupings include occupations which may only work
daytime shifts (e.g. dental hygienists, parole officers).

Shift work, psychological trauma and irregular physical exertion have been identified as
occupational risk factors that may elevate risk of cardiovascular morbidity and mortality among
firefighters and police officers. While paramedics may be exposed to similar types of
stressors, evidence has shown that they respond to more emergency calls than police and fire service combined and may suffer greater psychological distress, resulting in a greater risk of stress-related disorders and diseases. A descriptive study by Nirel et al. found that while 98% paramedics reported being in “good health”, 69% reported “at least one physical problem such as hypertension” and one third reported that recurring emotional problems interfered with their work to some extent. While it is unclear what how the authors defined their outcome measures, results of this study generally suggest that paramedics may believe that adverse physical and psychological effects are an acceptable part of their general health.

It has been estimated that cardiovascular disease events are the second leading cause of on-duty deaths (behind vehicle crashes) and account for approximately 11% annual fatalities among paramedics. Despite some basic similarities in occupational stressors among emergency service workers and the evidence supporting the association of shift work and psychosocial stress with CVD, studies of heart disease among paramedics are infrequent. Among studies referenced in a recent systematic review of health problems among paramedics, self-reported psychological outcomes such as post-traumatic stress disorder, depression and burnout were most frequently noted.

A search of literature investigating CVD exclusively among paramedics resulted in only 3 studies to date (Table 1.3). (Key search terms included: “paramedic” or “ambulance men” or “ambulance attendant” and “cardiovascular disease” or “heart disease” or “coronary disease”). Two studies examined cardiovascular mortality among paramedics and found an increased risk in comparison to the general population of the same sex and age range (SMR range: 101 to 116). The excess risk of CVD is somewhat surprising considering paramedics are required to pass a physical fitness exam upon entering the service and the general working population is
considered to be healthier than the general population which includes those who may be unable to work. Rodgers et al. examined cause of early retirement among health care workers and found that circulatory disorders were the second most common cause of early retirement among paramedics (behind musculoskeletal injuries). The authors also reported that paramedics were more likely to retire due to circulatory disorders than other health service workers including nurses, administrative workers and those employed in professional and technical medical services. However, this was only a descriptive study and the use of retirement records may not have accounted for those who may have left the paramedic profession due to health issues such as CVD.
### Table 1.3 Summary of paramedic and heart disease studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design, Sample Size, Follow-up period</th>
<th>Exposure Assessment</th>
<th>Outcome</th>
<th>Risk Estimates (Fully adjusted model)</th>
<th>Adjustments</th>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>Grainger 1985</td>
<td>Mortality study, Population based N = 334,321</td>
<td>Census data from UK</td>
<td>Census data to ascertain mortality</td>
<td>Deaths attributed to diseases of the circulatory system = 177</td>
<td>None reported</td>
<td>Short, descriptive study</td>
</tr>
<tr>
<td>Balarajan 1989</td>
<td>Mortality study, Population based N = 664 deaths attributed to cancer, IHD, cerebrovascular disease, asthma, cirrhosis of liver and suicide</td>
<td>Census data from England and Wales to identify “ambulance men”</td>
<td>IHD fatalities Not reported how outcome measures were ascertained ICD codes not identified</td>
<td>SMR116, p ≤ 0.05 Compared paramedic deaths with deaths among the general population of the same social class (social class IV)</td>
<td>None reported</td>
<td>Mortality rates were higher among porters, ambulance men and orderlies, collectively, than in general population of social class IV</td>
</tr>
<tr>
<td>Rodgers 1998</td>
<td>Cross-sectional study, Population based N = 39 male Paramedics</td>
<td>Health Services workers employed by Eastern Health and Social Services Board, Ireland</td>
<td>Retirement records; paramedics qualify for early retirement due to medical condition that prohibits them from performing their usual occupation -- assessed by physician Diseases of the circulatory system ICD 100 - 99</td>
<td>Musculoskeletal injuries most common reason for early retirement among male paramedics (41%), followed by circulatory disorders (31% male paramedics)</td>
<td>None reported</td>
<td>Low numbers of paramedics studied Descriptive analyses, No statistical testing for risk estimates More likely to retire due to hypertension and vascular diseases than IHD than other male health service workers</td>
</tr>
<tr>
<td>Study</td>
<td>Study Design, Sample Size, Follow-up period</td>
<td>Exposure Assessment</td>
<td>Outcome</td>
<td>Risk Estimates (Fully adjusted model)</td>
<td>Adjustments</td>
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<tr>
<td>Koehoorn 2011</td>
<td>Retrospective Cohort</td>
<td>Paramedic Cohort N = 5,567 total</td>
<td>Duration of employment as a paramedic ascertained through work history records</td>
<td>Vital statistics, hospitalization discharge records, physician billing information</td>
<td>Reference group: paramedics with &lt; 10 yrs employment</td>
<td>Adjusted for age, sex and calendar period</td>
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<td>ACS (n = 85):</td>
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<td>10 to 19 years, IRR 0.9 (0.6 – 1.5)</td>
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<td>Also included a survey of random sample of active and retired paramedics to ascertain prevalence of non-occupational risk factors for CVD. Results were compared to the BC working population.</td>
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<td>20 + years, IRR 1.4 (0.7 – 2.7)</td>
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<td>In comparison to BC working population, paramedics were:</td>
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<td>Ptrend= 0.5</td>
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<td>- at higher risk for obesity (BMI &gt; 30 kg/m²), M: OR 2.1; W: 1.5</td>
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<td></td>
<td>CCS (n = 103);</td>
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<td>- male paramedics were at similar levels of work stress; female paramedics reported lower work stress</td>
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<td>10 to 19 years, IRR 1.3 (0.8 – 2.0)</td>
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<td>- lower or similar prevalence of cardiovascular related co-morbidities; but higher BP among male paramedics</td>
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<td>20 + years, IRR 1.3 (0.7 – 2.5)</td>
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<td>Ptrend= 0.3</td>
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<td>HTN (n = 400):</td>
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<td></td>
<td>10 to 19 years, IRR 0.8 (0.6 – 1.2)</td>
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<td>20 + years, IRR 1.4 (0.6 – 3.1)</td>
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<td>Ptrend= 0.2</td>
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</tbody>
</table>

**Abbreviations:**

ACS = acute coronary syndrome  
BMI = Body Mass Index  
BP = Blood Pressure  
CCS = Chronic Coronary Syndrome  
FU = follow-up  
HTN = Hypertension  
ICD = International Classification of Diseases  
IHD = Ischemic Heart Disease  
IRR = Incidence Rate Ratio  
M = men  
N= number  
OR = Odds Ratio  
P = p-value for trend  
PTrend = p-value for trend  
SMR = Standard Mortality Ratio  
W= women  
US = United States  
UK = United Kingdom
I am aware of one more study, recently completed by Koehoorn et al.\textsuperscript{107}, which examined the incidence of chronic and acute heart disease among the same cohort of BC paramedics studied in this dissertation. In their retrospective cohort study, the authors hypothesized that exposure to CVD risk factors common to paramedic work (e.g. noise from sirens, diesel exhaust from ambulances, psychological and physical stressors associated with emergency runs) may increase the risk of CVD among this population.

To examine the association of cardiovascular morbidity and mortality with duration of paramedic work, the authors used employment records, which provided information including the start and end dates and description of each job held by employees of the British Columbia Ambulance Service. These records were linked with administrative databases from the British Columbia Linked Health Database which contains information regarding hospitalizations, physician visits and vital statistics for almost all residents of British Columbia\textsuperscript{109}. Hospitalization data included information such as admission and discharge date, principal diagnosis (i.e. ICD code for immediate reason for hospital visit) and primary diagnosis (i.e. ICD code for the condition requiring the most medical care). Information regarding physician visits included date and primary reason for visit (i.e. ICD code). Vital statistics included records from the provincial death registry regarding the dates and underlying cause of all deaths (i.e. ICD code) in the province.

The authors found a non-statistically significant increased risk of acute coronary syndrome (ACS), chronic coronary syndrome (CCS) and hypertension (HTN) associated with more than 20 years of employment in comparison to less than 10 years of employment in the ambulance service [Incidence Rate Ratios: ACS 1.4 (95% CI: 0.7 - 2.7), CCS 1.3 (95% CI: 0.7 - 2.5), HTN 1.4 (95% CI: 0.6 - 3.1)]\textsuperscript{107}. The risk of heart disease was attenuated among the small group of
paramedics working for over 30 years which the authors concluded may be due to a healthy worker survivor effect.

In summary, among the 4 studies investigating the risk of heart disease among paramedics, 2 earlier studies are of poor quality and only provide descriptive results\textsuperscript{106,108}. Of the two that provided risk estimates, one found a modest increased risk of CVD in comparison to the general population\textsuperscript{105} and the other reported a non-significant increased risk with duration of employment \textsuperscript{107}. Overall, there is a paucity of studies surrounding the risk of heart disease among paramedics and future studies are needed to support findings from previous research.

\subsection*{1.5 Dissertation objectives}

The purpose of this dissertation is to determine if exposure to shift work and psychosocial stress contributes to an increased risk of heart disease among paramedics. To address the gaps in literature and recommended directions for future studies mentioned in the previous sections, a multi-disciplinary approach was used incorporating health psychology, epidemiology, exercise physiology and occupational hygiene.

The basic foundations of this dissertation grew from principles gathered from health psychology regarding neuroendocrine systems and their role in the etiology of heart disease. Theories used in practical application of activation and recovery of neuroendocrine systems were garnered from studies in exercise physiology. Techniques used in occupational hygiene to derive exposure measurements and assess health effects were incorporated into field sampling. As a final step, epidemiologic methods were used to synthesize and apply theories to examine the association between specific stressors and forms of heart disease.
Studies completed for this dissertation was carried out among paramedics employed by the British Columbia Ambulance Service.

Specific objectives of this dissertation include:

1) To gain a better understanding of how exposure to shift work and job strain can affect the neuroendocrine systems by examining salivary biomarkers and subclinical heart disease indicators in the autonomic nervous system and hypothalamic-pituitary-adrenal axis (Chapter 2)

2) To determine if results and conclusions obtained in the convenience study sample used in Chapter 2 can be generalized to the larger population of paramedics (Chapter 3)

3) To examine if chronic exposure to shift work is associated with acute and chronic heart disease; and if the influence of recovery time from work at night would mitigate the risk (Chapter 4)

4) To explore if stress associated with emergency calls can trigger acute coronary events among paramedics (Chapter 5)

1.5.1 Dissertation structure

This dissertation builds upon a prior study and existing survey completed at the University of British Columbia, School of Population and Public Health by Koehoorn et al. 107. It consists of 6 chapters: the introduction, 4 research chapters which address the objectives listed above, and a concluding chapter. Although each chapter is independent of one another, they are interrelated and build upon one another.

The rationale and principal objective of each research chapter are described below.
**Chapter 2: Intermediate and chronic neuroendocrine effects related to shift work and stress**

While it is believed that the biological pathway linking stress and shift work with heart disease is a result of neuroendocrine dysfunction\(^2\), there are no studies to date which have simultaneously examined activity in both the autonomic nervous system and hypothalamic-pituitary-adrenal axis using biomarkers and subclinical CVD outcomes. To examine this combination of biological measures would help to provide a more complete picture of intermediate and long-term effects of neuroendocrine dysregulation. The primary objective of this chapter was to examine salivary biomarkers (i.e. alpha-amylase and cortisol) as intermediate neuroendocrine activity to stress and shift work; and subclinical heart disease indicators (i.e. heart rate variability and endothelial function) as long-term effects to chronic exposure. Effects of job stress and shift work were examined by comparing paramedic types (dispatchers vs. ambulance attendants) and shift types (daytime vs. rotating day/night). The secondary objective was to test the feasibility of collecting numerous samples from a busy workplace setting to inform protocol development for a future large-scale field study.

**Chapter 3: Is our convenience sample representative of the larger population?**

The study population in Chapter 2 consisted of a convenience sample of 21 paramedics from the busiest stations in south-western British Columbia. Because our sample consisted of volunteers, and not randomly sampled from a larger population, the possibility of selection bias was evident and may preclude the ability to generalize results to all paramedics. The purpose of Chapter 3 was to compare demographic (e.g. age, sex) and health information (e.g. prevalence of heart disease, physical activity) from the small convenience sample from Chapter 2 with a larger
random sample of currently employed paramedics. The random sample was provided by responses to previously administered mail survey of non-occupational risk factors for heart disease\textsuperscript{107}.

**Chapter 4: Risk of acute/chronic forms of heart disease with shift work, and the influence of recovery time**

Exposure to shift work may increase the risk of heart disease directly and indirectly through psychosocial, behavioural and physiological stressors\textsuperscript{16}. These interrelated mechanisms stimulate neuroendocrine activity, but with chronic activation and insufficient recovery, dysregulation of the neuroendocrine systems may occur and is believed to contribute to risk of CVD\textsuperscript{22}. However despite a belief in these hypothesized psychophysiological mechanisms, results from the existing body of knowledge have been mixed\textsuperscript{73}. One of the reasons for this could be attributed to broad definitions of shift work leading to non-differential exposure misclassification which may bias risk estimates towards the null.

Emergency run data provided from the BC Ambulance Service included information about daily exposure to shift work over several years of follow-up, thus allowing us to develop a more accurate exposure assessment than any other study of shift work and heart disease conducted to date. Building upon descriptive results from Chapter 2 which suggested neuroendocrine dysregulation among shift workers, this chapter formulated the hypotheses that (1) chronic exposure to shift work leads to neuroendocrine dysregulation and would be associated with heart disease; and (2) that time away from work at night would allow neuroendocrine systems to recover and return to normal functioning, thus reducing the risk of heart disease.
Chapter 5: Can stress related to emergency runs trigger acute coronary events?

It is believed that chronic exposure to stress without sufficient recovery can alter neuroendocrine functioning, damage blood vessels and accelerate arterial plaque buildup leading to chronic heart disease; and that the underlying cause of most acute coronary events is attributed to plaque rupture. This may occur when factors such as intense psychosocial stressors increase blood flow, resulting in added shear stress on vessel walls and plaque instability. While studies have found an association of long-term exposure to job stress with acute coronary events, this broad interpretation could be somewhat misleading. The pathologic processes of chronic diseases, such as CVD, can start with early-acting initiators but requires late-acting components with short induction times to complete sufficient cause for disease initiation. The purpose of this study was to examine if stress from emergency runs can be considered to be late-acting constructs in triggering acute coronary syndromes among paramedics.
2 JOB STRAIN AND SHIFT WORK INFLUENCES ON BIOMARKERS AND SUBCLINICAL HEART DISEASE INDICATORS: A PILOT STUDY

2.1 Synopsis

It is believed that shift work and stress may lead to heart disease through neuroendocrine dysregulation of the autonomic nervous system (ANS) and the hypothalamic-pituitary-adrenal axis (HPA). The aim of this study was to explore this hypothesized biological pathway by examining activity in the ANS and HPA axis using salivary stress biomarkers (alpha-amylase and cortisol) and subclinical heart disease indicators (heart rate variability and endothelial functioning). This study also tested the feasibility of a rigorous biological sampling protocol in a busy workplace setting.

Twenty-one full-time paramedics in south-western British Columbia volunteered to participate in this study. Participants self-collected 5 salivary samples per day over 3 days (1 rest day, followed by 2 working days), that were analyzed for diurnal slopes and daily production of both salivary alpha-amylase and cortisol. Heart rate variability was logged over 2 work days using wireless exercise heart rate monitors. Endothelial functioning was measured using fingertip peripheral arterial tonometry upon enrollment into the study. The effects of job stress and shift work were examined by comparing paramedic types (dispatchers vs. ambulance attendants) and 2 shift types (daytime vs. rotating day/night).

Over 90% of all expected samples were collected and fell within valid ranges as described in prior studies. In comparison to daytime-only workers, rotating-shift workers reported higher levels of job stress and exhibited dysregulation in ANS and HPA axis among all biological measures. In
comparison to ambulance paramedics, dispatchers reported higher job stress but differences in biological results were not as evident as among the shift work comparison.

The consistency of the overall trend in measures suggest that exposure to work stressors may lead to dysregulation in neuroendocrine activity and contribute to the development of heart disease. High compliance among paramedics to complete the intensive protocol suggests this study will be feasible in a larger population.

A version of this chapter has been published as: Wong, IS, Ostry, AS, Demers, PA, Davies, HW. Job Strain and Shift work influences on biomarkers and subclinical heart disease indicators: a pilot study. Journal of Occupational and Environmental Hygiene. 2012 Aug; 9(8): 467 – 4771.

### 2.2 Introduction

High job strain, defined as an individual’s perception of high demands and low control over their work situation 114, has been associated with approximately 50% excess risk of cardiovascular disease (CVD) 32,33,115. Karasek’s Stress Disequilibrium Theory, a recent extension to the Job Strain Model, hypothesizes insufficient control to maintain stability over dynamic work demands may lead to physiological deregulation 116. This is similar to the definition of allostasis, a dynamic function whereby the cardiovascular system is activated to prepare for threats and shut off once the threat has passed. But dysregulation of allostasis (i.e. allostatic load) can result in the system not shutting off when no longer needed and is believed to eventually lead to disease 22. Results from a recent study examining the Stress Disequilibrium Theory suggest that chronic exposure to high job strain may lead to symptoms of exhaustion and permanent deregulation of cardiovascular functioning 117. Prospective studies have found this change in cardiovascular functioning may be a factor
contributing to a doubling of risk in developing ischemic heart disease among those reporting high levels of exhaustion. 

Shift work, a workplace stressor, has been associated with up to twice the risk of CVD. Work at night has been hypothesized to disrupt circadian rhythms, affecting normal biological patterns of growth and maintenance. These changes can be permanent and increase CVD risk with cumulative years of shift work.

The paramedic profession is considered to be a high stress occupation due to the frequent exposure to trauma and human suffering. Furthermore, the nature of emergency services requires working long hours or at night which may sensitize psychosocial responses to other stressors, increasing the risk of adverse health effects. Studies have found that paramedics have significantly higher blood pressure (p < 0.05) and increased risk of death attributed to ischemic heart disease in comparison to the general population (SMR = 116, p < 0.05).

Potential pathways linking psychosocial workplace stressors and CVD involve neuroendocrine activity of the autonomic nervous system (ANS) and the hypothalamus-pituitary-adrenal (HPA) axis. The ANS reacts to stress by immediately increasing peripheral responses such as heart rate and blood pressure as preparation for imminent danger. Reaction of the HPA axis may follow by releasing cortisol to prepare for further threats. It is believed that long-term repeated stress system reactivity without sufficient recovery can lead to permanent changes in normal cardiovascular functioning and eventually to frank disease.

Despite evidence for a biological pathway linking chronic work stress with CVD, there are no field studies to date which have simultaneously examined effects of psychosocial work-related stressors with biomarkers and subclinical CVD outcomes in both the ANS and HPA axis. In this study, we
used easy to administer, non-invasive measures to gain a better understanding of the innervation of salivary biomarkers (i.e. alpha-amylase and cortisol) as neuroendocrine hormonal responses to current psychosocial work stress and subclinical CVD indicators (i.e. heart rate variability and endothelial dysfunction) as cumulative effects of chronic psychosocial stress. Salivary alpha-amylase has been associated with heart rate variability, and both provide information about ANS 131,132; and salivary cortisol has been linked to endothelial functioning, both representing HPA activity 133,134.

The main objective of this pilot study was to obtain descriptive results of neuroendocrine activity and subjective responses to the effects of job strain and shift work. Rotating-shift work and dispatch work have been identified as occupational groups in stressful situations which may increase their risk of adverse health effects 13. To examine this hypothesis, we compared shift work types (i.e. rotating-shift vs. daytime-only) and paramedic types (i.e. dispatch vs. ambulance). A secondary objective was to test the feasibility of a rigorous sampling protocol using non-invasive techniques with minimal researcher supervision in a busy workplace environment, and determine full-scale study power parameters.

We assumed that paramedics in rotating-shift work and dispatch job categories would be more chronically stressed in comparison to daytime-only workers and ambulance paramedics. Thus we hypothesized that in respective comparisons with daytime-only workers and ambulance paramedics, shift workers and dispatch paramedics would have: (i) higher levels of reported self-perceived job strain; (ii) flattening of biomarker diurnal slopes on both rest and work days, indicating neuroendocrine systems remain taxed despite time away from work; (iii) reduced daily production of salivary alpha-amylase, indicating exhaustive functioning of the ANS; and (iv) elevated daily production of salivary cortisol as a preventative measure to mobilize the HPA axis as needed. We also hypothesized that dysregulation of diurnal slopes and daily production of biomarkers on rest
and work days without sufficient recovery may also result in reduced levels of subclinical CVD measures.

2.3 Methods

2.3.1 Study population and recruitment

In British Columbia, Canada, paramedics may work on ambulances or dispatch units. Dispatch paramedics work in call centers and are the first point of contact when people telephone to report a medical emergency. They verbally assess the situation, assign an ambulance paramedic team and relay details to prepare the team when they arrive on scene. Ambulance paramedics attend the emergency at the scene, administer appropriate medical care and may transport patients to hospitals for further treatment. Paramedics can be scheduled in either forward rotating-shifts (i.e. 2 days from 0600h to 1800h followed by 2 nights from 1800h to 0600h) or daytime-only schedules (i.e. ending before midnight).

We recruited volunteers from the sole dispatch unit and the nine busiest ambulance stations in south-western British Columbia (population = 4.4 million). Information about the study was provided in brochures and internal communication. Recruitment was restricted to paramedics in non-administrative positions who did not self-report (a) having circulatory disorders which may affect peripheral blood flow (e.g. Raynaud’s phenomenon); (b) taking heart medication or blood thinners; (c) diabetes; or (d) having physician-diagnosed irregular sinus arrhythmia, or an ischemic episode, within the past 3 months.

2.3.2 Study protocol

Data was collected between November 2008 and January 2009. The investigator met with participants one week prior to starting their next work block to provide verbal and written
instructions of all sampling procedures, distribute study materials and to conduct endothelial functioning testing. All volunteers were informed that their participation was completely voluntary and they would be free to withdraw at any time.

Salivary samples were self-collected over 3 consecutive days (1 rest day, immediately followed by the first 2 work days from 0600 to 1800 hrs). To capture basal cardiovascular functioning that was least influenced by work-stress “spillover”, salivary sampling was performed on the last rest day prior to returning to work. Heart-rate variability was logged on both work days. Table 2.1 shows the sampling protocol for all study measures.
| **Table 2.1 Sampling protocol for salivary alpha-amylase, salivary cortisol, heart rate variability and endothelial functioning** |
|---|---|---|---|
| **Day 0 (1 week prior to enrolment): Orientation and distribution of materials** | **Day 1: Rest day (last day of 4 to 6 days off work before returning to work)** | **Day 2: Workday 1** | **Day 3: Workday 2** |
| Questionnaire | Distributed following orientation | | |
| Endothelial Functioning Test | Subjects were tested following orientation | | |
| Salivary Samples analyzed for cortisol and alpha-amylase. | Subjects collect own salivary samples at 0.5 hr, 1 hr, 6 hr and 12 hr after waking, and before bed * | Subjects collected own saliva samples to measure at 0.5 hr after waking, beginning of shift (6:00am), mid-shift (noon), end of shift (6:00pm) and just before bed ** | |
| Heart rate variability logging over full 12 hour shift (0600 to 1800) | | Researcher started monitors at 0600, and returned at 1800 to download logged information | Subjects started their own heart rate monitors at 0600, and researcher met subjects at 1800 to collect study materials |

*Saliva sample collection times on the rest day were chosen to approximate the same collection time points on work days after waking, to allow for more accurate comparison of cortisol and alpha-amylase levels.

**Saliva sample collection times on work days were chosen to coincide with significant time-related event to allow for ease of collection and complete representation of diurnal slope.
2.3.3 Study measures

2.3.3.1 Perceived job strain and general health

The Sources of Occupational Stress survey, a standardized and validated questionnaire was used to quantify paramedic-specific workplace stressors. This survey was developed following a review of stressors identified in existing literature and further developed in consultation with several firefighter/paramedic organizations. (In Washington State, where this survey development was conducted, firefighters also work as paramedics and thus are considered one occupational group). The survey was pilot tested in focus groups on a sample of firefighter/paramedics (n=30), and items that were not endorsed as occupational stressors and which had not been observed by at least 40% of the participants as occurring within their past 10 shifts were removed.

The final Sources of Occupational Stress instrument consisted of 57 items mainly focused on occupational stressors specific to paramedic employment with a few questions pertaining to carry-over stress from family problems or from a second job. Validation of the questionnaire was completed by administering the survey to a large sample of firefighter/paramedics (n = 2,050). Additional questions from Edward’s Social Desirability were included to control for test-taking bias which has been shown to account for up to 50% of the variance of self-reported measures of health. A factor analyses was conducted from responses, resulting in 14 main clusters of paramedic-specific stressors which consisted of 41 of the original 57 survey items. The overall Cronbach’s α of this questionnaire was 0.95. This is the only validated questionnaire that we are aware of that identifies occupational stressors specific to paramedic work.

To calibrate this survey with Job Strain Model theories, a psychologist, an expert in the health and stress domain, and an occupational hygienist categorized a subset of the 41 questions identified in
the factor analysis into “demand” and “control” components using classic definitions \(^{13}\) and Karasek’s Stress Disequilibrium Theory \(^{13,116}\). Psychological demands included situational work pressures external to the worker. A worker’s job control was defined as their self-efficacy (e.g. skills and freedom to make decisions) to manage dynamic work situations. Only questions which had consensus from three raters were kept in the analysis. In the end, 13 questions (8 “demand”, 5 “control”) of the original 57-items remained. Job strain was calculated as the ratio of demand and control. Full validation of the new scale of 8 demand and 5 control questions was not undertaken as part of this pilot study, however.

The questionnaire also included items regarding demographic variables, work history, general health and non-occupational risk factors for CVD. Questions from the Canadian Community Health Survey were used to ascertain self-reported general health and well-being \(^{138}\). Body Mass Index (BMI) was calculated as body weight (kg) divided by the square of height (m).

2.3.3.2 Biological markers of stress: salivary cortisol and alpha-amylase

Cortisol is considered to be a reliable indicator of physiological reactions to stressful stimulation. It is a necessary biological response to mobilize defense mechanisms for action and also contributes to recovery from it. While beneficial in the short-term, excessive levels over prolonged periods can lead to permanent biological system changes associated with increased risk of cardiovascular morbidity and mortality \(^{19}\).

Salivary cortisol has long been recognized as a convenient and reliable marker of the HPA axis \(^{139,140}\). However, it has been measured in many different ways making it difficult to compare results. A recent meta-analysis of over 100 studies identified several characteristics of chronic stressors which can influence cortisol activity: temporality (e.g. time since first onset), type of stressor (e.g. traumatic
vs. non-traumatic), emotions elicited by the situation (e.g. shame), perceived control of the stressor, and the individual psychological consequences of the stressor (e.g. depression). The general findings of this study indicated that exposure to chronic stressors lowers the morning peak and elevates evening nadir in salivary measures of cortisol. This may flatten the diurnal profile and result in elevated daily production to prepare for further threats. Studies on cortisol responses among shift workers had similar findings.

Autonomic activity has been assessed in prior studies by measuring epinephrine or norepinephrine levels, but these are short acting and short lived. While these can be collected in urine or serum samples, these methods can be cumbersome and difficult to collect in field studies. Recent evidence has shown that salivary alpha-amylase is a promising enzymatic marker of the ANS and has a positive correlation with norepinephrine. This correlation can be attributed to the innervation of salivary glands by the sympathetic and parasympathetic branches of ANS.

A normal diurnal alpha-amylase profile is upward sloping following a dip after waking. This suggests that the body produces more epinephrine and norepinephrine as needed throughout the day to combat threats and returns to normal levels after a resting state. While alpha-amylase has not been studied as extensively as cortisol, recent evidence has shown that exposure to chronic stress is associated with flatter diurnal slopes and decreased daily production. Flattened diurnal slopes may indicate the body is unable to produce needed amounts of epinephrine and norepinephrine through the day; and decreased daily production may suggest that the system is in an exhaustive phase.

To delineate diurnal slope, participants collected their own saliva samples using Salivettes (Sarstedt, Canada) at 5 predetermined times over 24 hours (Table 2.1). Collection times on work days coincided with significant time-related events to allow for ease of collection (0.5 hr after waking,
beginning of shift (6:00am), mid-shift (noon), end of shift (6:00pm) and just before bed). Collection
times during the rest day were similar to work days relative to waking to aid comparison of results
(0.5, 1, 6 and 12 hours after waking). Subjects transferred samples to the investigator at the end of
shift or mailed samples through regular post (salivary alpha-amylase and cortisol samples are not
temperature sensitive). Samples less than the limit of detection or higher than normal limits
were removed from analyses (i.e. salivary cortisol: 0.6 to 50 nmol/L; and salivary alpha-amylase:
2.0 to 900 U/mL).

If more than 3 samples were missing from a single day, analyses were not completed. Two variables
were created for each of cortisol and alpha-amylase (using log-transformed values over collection
times): (1) Diurnal slope, estimated with linear regression, provided information about
neuroendocrine dysregulation; (2) Area under the curve, indicating total daily production, was
calculated with a trapezoidal method using log-transformed cortisol and alpha-amylase values over
collection times.

2.3.3.3 Heart rate variability

Heart Rate Variability (HRV) has been considered to be a marker of the dynamic and cumulative
load on the cardiovascular system. It represents variations of intervals between peaks of cardiac
sinus rhythms influenced by the balance of sympathetic nervous system (SNS) and parasympathetic
nervous system (PNS) activity. SNS mobilizes the body to prepare for action and is associated
with shortening of time in between interbeat intervals, thus causing a rise in heart rate. PNS activity
represents vagal tone and indicates the recovery of the body to daily activity by slowing down heart
rate and lengthening time between beats. Measurement of the SNS and PNS influences are
quantified with statistical time-domain methods or spectral frequency methods.
Decreased HRV is attributed to relative dominant SNS hyperactivity over inadequate PNS hypoactivity and is a reliable predictor of cardiovascular morbidity and mortality. It believed that when the SNS branch dominates for a prolonged period of time, the energy requirements of the organism to maintain stability is exhausted and may contribute to adverse health outcomes such as heart disease.

To measures HRV, participants wore wireless Polar® RS 800 Heart Rate monitors over their 12-hour shifts to capture typical work activity levels and stressors. These monitors are commonly worn by people during exercise and are less cumbersome than Holter monitors, especially during physically demanding work. Studies validating the Polar technology report a correlation of 0.93 to 1.00 with electrocardiogram readings and a bias ranging from 1.7 to 1.5 ms.

On the first work day, a study investigator demonstrated use of the monitors pre-shift and returned at the end of shift to download logged data. On the following work day, participants activated and stopped the monitors on their own. Following methods reviewed by Berardi et al. heart rate measures below 30 bpm or above 190 bpm were eliminated. HRV was extracted and processed with Kubios HRV software (v 2.0, Biomedical Signal Analysis Group, Finland).

The following parasympathetic measures were reported as an indication of rest and recovery to maintain allostasis: pNN50 (the percentage of intervals >50ms different from the preceding interval), rMSSD (the square root of the mean of the squares of successive NN interval differences) and HF (high frequency 0.15 to 0.40 Hz). These measures have been shown to be all highly correlated. Any measures that did not fall within normal expected ranges by age were eliminated from analysis.
2.3.3.4  **Endothelial dysfunction**

Endothelial functioning is a measure of nitric oxide production in the small to medium arteries and is a marker of vasodilation properties. However, excessive cortisol and cytokine production can damage the endothelial layer, resulting in loss of regular blood vessel tone and atheroprotective properties\textsuperscript{134,169,170}. This has been termed ‘endothelial dysfunction’, and is considered to be an early predictor of atherosclerosis \textsuperscript{171,172}.

To assess endothelial functioning, we used an Endo-PAT2000 (Itamar Medical Ltd, Caesarea, Israel) to measure reactive hyperemia peripheral arterial tone (PAT) via pneumatic fingertip probes. This portable instrument allows for measurements to be taken in field studies more easily than traditional ultrasound methods. Studies have shown there is good correlation between these instruments ($r = 0.55$) \textsuperscript{173}.

We followed the testing protocol as described in prior studies \textsuperscript{174,175}. Testing was conducted in a dark, noise- and climate-controlled (22$^\circ$C - 24$^\circ$C) room. Blood pressure measurements were taken as reference. Participants were seated in a chair with their arms placed at heart level on support pads to avoid muscular interference of the arms and fingers. Pneumatic probes were placed on index fingers of both hands. Following a 10 minute resting period, baseline recordings were obtained for 5 minutes. To induce reactive hyperemia, a blood pressure cuff placed on the participant’s non-dominant arm was inflated rapidly to 60 mmHg above their systolic pressure. After a 5 minute occlusion period, the cuff was rapidly deflated and recording continued to measure the ability of the endothelium to return to normal functioning. A computer algorithm was used to measure Reactive Hyperemia Index (RHI) \textsuperscript{173} as a ratio of the pre- and post-occlusion signal, normalized to the non-occluded arm. Higher ratios indicate greater dilatation in the finger arteries and thus better endothelial function. Values below 1.35 are considered to indicate abnormal coronary functioning\textsuperscript{176}.
2.3.3.5 Statistical analysis

Descriptive analyses were completed and tests of normality were conducted for all continuous variables. Mean results were reported for normally distributed measures and median results were reported for non-normally distributed measures. Two sample student t-tests, Mann-Whitney tests and chi-squared tests were used to determine if measures were different in shift type and paramedic type comparisons. Measures taken on both workdays were averaged if correlation was greater than 0.50 otherwise, they were treated as separate values.

All analyses were completed using Stata 11.2 (StataCorp, College Station, Texas).

The effect size, represented by Cohen’s $d$, was used to indicate the standardized difference in various measures of interest when comparing chronically stressed groups to those who are not. Cohen’s $d$ is calculated by the absolute difference in group means divided by the pooled standard deviation. Between-subject differences were calculated using parameters in group comparisons and within-subject differences were calculated using measures taken on rest and working days. A small effect size is defined as 0.2, medium as 0.5 and large as 0.8. Effect and sample size calculations were completed using G*Power (Version 3.1.2, Germany).

2.4 Results

2.4.1 Study feasibility

Of 25 paramedics who volunteered, four dropped out of the study before any measures were collected due to change in work assignment (n=2) or leave for disability (n=2). Twenty-one paramedics (14 men, 7 women) participated though 2 did not complete the full sampling protocol due to illness or change in work schedule. Demographic characteristics of the participants in the
sample are provided in Table 2.2. There were 7 daytime-only workers (2 dispatch, 5 ambulance) and
14 rotating-shift workers (5 dispatch, 9 ambulance).

The average age of participants was 41.3 years with an average of 13.7 years of service (Table 2.3).
Mean age of ambulance paramedics was 43.1 years who worked for an average of 15.7 years;
whereas mean age of dispatchers was 37.6 years with an average of 10.3 years service. In the shift
type comparison, mean age of daytime-only workers was 43.1 who worked for an average of 16.2
years; compared to rotating-shift workers who had a mean age of 40.4 years and 12.4 years of
service.
Table 2.2 Demographic characteristics and survey responses by shift and paramedic type comparisons

<table>
<thead>
<tr>
<th></th>
<th>Shift Type*</th>
<th>Paramedic Type*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day only (n = 7)</td>
<td>Rotating (n = 14)</td>
</tr>
<tr>
<td>Dispatch, n (%)</td>
<td>2 (28.6%)</td>
<td>5 (35.7%)</td>
</tr>
<tr>
<td>Ambulance</td>
<td>5 (71.4%)</td>
<td>9 (64.3%)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6 (85.7%)</td>
<td>8 (57.1%)</td>
</tr>
<tr>
<td>Female</td>
<td>1 (14.3%)</td>
<td>6 (42.9%)</td>
</tr>
<tr>
<td>Age, mean ± standard deviation</td>
<td>43.14 ± 6.57</td>
<td>40.35 ± 7.88</td>
</tr>
<tr>
<td>Years as paramedic</td>
<td>16.24 ± 6.55</td>
<td>12.39 ± 8.33</td>
</tr>
<tr>
<td>Body Mass Index (BMI)</td>
<td>27.8 ± 4.48</td>
<td>29.4 ± 7.66</td>
</tr>
<tr>
<td>Physical Activity outside work**</td>
<td></td>
<td></td>
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<tr>
<td>Active</td>
<td>2 (28.6%)</td>
<td>4 (33.3%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>1 (14.3%)</td>
<td>5 (41.7%)</td>
</tr>
<tr>
<td>Inactive</td>
<td>4 (57.1%)</td>
<td>3 (25.9%)</td>
</tr>
<tr>
<td>Health now***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td>2 (28.6%)</td>
<td>3 (25.0%)</td>
</tr>
<tr>
<td>Good</td>
<td>2 (28.6%)</td>
<td>2 (16.7%)</td>
</tr>
<tr>
<td>Very Good / Excellent</td>
<td>3 (42.9%)</td>
<td>7 (58.3%)</td>
</tr>
<tr>
<td>Health now vs. one year ago***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Much worse/ Somewhat worse</td>
<td>1 (14.3%)</td>
<td>4 (33.3%)</td>
</tr>
<tr>
<td>Same</td>
<td>3 (42.9%)</td>
<td>6 (50.0%)</td>
</tr>
<tr>
<td>Somewhat better / Much better</td>
<td>3 (42.9%)</td>
<td>2 (16.6%)</td>
</tr>
<tr>
<td>Reclassified Demand and Control Scores</td>
<td></td>
<td></td>
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<tr>
<td>Demand (1= low, 5 = high)</td>
<td>1.75 ± 0.27</td>
<td>2.15 ± 0.91</td>
</tr>
<tr>
<td>Control (1= low, 5 = high)</td>
<td>4.10 ± 0.57</td>
<td>3.86 ± 0.92</td>
</tr>
<tr>
<td>Job strain (demand / control)</td>
<td>0.43 ± 0.10</td>
<td>0.63 ± 0.92</td>
</tr>
</tbody>
</table>

* Differences in shift type and paramedic type group comparisons are not statistically significant. All p-values > 0.05, not shown

** Canadian Community Health Survey categories based on number of times exercised over a 3 month period and amount of energy expenditure

*** Number of responses may not add up to number of subjects due to non-response to questions
Despite the numerous requirements of this study, participants fulfilled the majority of the required protocols. All questionnaires were completed and returned. All subjects attended orientation and were tested for endothelial functioning. Of the 315 diurnal salivary samples expected from all participants, only 6.7% were missing. Of the received samples, 96.2% of the cortisol samples and 97.3% of alpha-amylase fell in normal ranges and were retained for analysis. HRV was logged for all participants on the first work day; and only one recording on the second work day was lost due to a monitor malfunction. All recorded 12-hour measures fell into expected ranges by age for a healthy population measured using gold standard 24-hour Holter recordings.

Table 2.3 shows correlation of (i) work day 1 and 2 samples; and (ii) work day average with rest day salivary samples. Samples taken on work days 1 and 2 were correlated ($p \leq 0.05$), but averaged workday results were not significantly correlated with rest day samples. Tests for differences all subjective and biological measures between shift type and paramedic type comparisons did not yield any statistically significant results.

<table>
<thead>
<tr>
<th>Table 2.3 Correlation of working day and rest day measurements</th>
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<tbody>
<tr>
<td><strong>Salivary alpha-amylase</strong></td>
</tr>
<tr>
<td><strong>Diurnal slope</strong></td>
</tr>
<tr>
<td>Work day 1 and 2: 0.51 0.05</td>
</tr>
<tr>
<td><strong>Daily Production</strong></td>
</tr>
<tr>
<td>Work day 1 and 2: 0.55 0.05</td>
</tr>
<tr>
<td><strong>Salivary Cortisol</strong></td>
</tr>
<tr>
<td><strong>Diurnal slope</strong></td>
</tr>
<tr>
<td>Work day 1 and 2: 0.56 0.02</td>
</tr>
<tr>
<td><strong>Daily Production</strong></td>
</tr>
<tr>
<td>Work day 1 and 2: 0.60 0.006</td>
</tr>
<tr>
<td><strong>Heart Rate Variability</strong></td>
</tr>
<tr>
<td><strong>rMSSD (msec)</strong></td>
</tr>
<tr>
<td>Work day 1 and 2: 0.85 &lt; 0.001</td>
</tr>
<tr>
<td><strong>pNN50</strong></td>
</tr>
<tr>
<td>Work day 1 and 2: 0.86 &lt; 0.001</td>
</tr>
<tr>
<td><strong>HF (msec²)</strong></td>
</tr>
<tr>
<td>Work day 1 and 2: 0.89 &lt; 0.001</td>
</tr>
</tbody>
</table>

$r$MSSD = root mean squared standard deviation successive difference  
$p$NN50 = percentage of intervals >50ms different from the preceding interval  
HF = high frequency measures (0.15 – 0.4 Hz)
2.4.2 Job strain, autonomic nervous system and hypothalamus-pituitary-adrenal activity

Results of the questionnaire are reported in Table 2.3. Mean job strain scores among dispatchers was 2.05 (SD 0.77) and ambulance paramedics was 1.99 (SD 0.81) (Cohen’s $d = 0.18$). A larger standardized difference ($d = 0.68$) between mean job strain scores was observed between rotating-shift workers (mean: 2.15, SD: 0.91) and daytime-only workers (mean: 1.75 , SD: 0.27).

ANS activity is represented in Figure 2.1 (alpha-amylase measures) and Table 2.4 (heart rate variability measures). Figures 2.1a) and 2.1b) represent diurnal slope results by shift type and paramedic type comparisons on work and rest days. Flatter slopes indicate a dysregulation in normal functioning. Figures 2.1c) and 2.1d) represent daily production of amylase, with lower daily production associated with chronic stress. Mean heart rate variability measures are presented in Table 2.4. Reduced heart rate variability has been an indicator of an increased cardiovascular disease risk.
Figure 2.1 Alpha-amylase slope and calculated daily production for shift and paramedic type comparisons

Geometric mean line is labeled within box; Interquartile range is depicted by the box; 95% CI is outlined by whiskers; Outliers are represented by dots.

* Differences in shift type and paramedic type group comparisons are not statistically significant. All p-values > 0.05, not shown

Cohen’s $d$ is the effect size comparing day to rotating-shift workers; and ambulance to dispatch paramedics. A small effect size is defined as 0.2, medium as 0.5 and large as 0.8.

Figures a) and b) represent diurnal slope results by shift type and paramedic type comparisons. Flatter slopes indicate a dysregulation in normal functioning. Linear regression is used to calculate slopes of log-transformed values over collection times. Units are not reported.

Figures c) and d) represent calculated total daily production by shift type and paramedic type. Larger values indicate higher production. Daily production is represented as area under the curve calculations of log-transformed values over collection times. Units are not reported.

Non-shaded boxes represent high job strain groups in each group comparison. (i.e. Rotating-shift workers in shift type comparisons; and Dispatch paramedics in paramedic type comparisons)
<table>
<thead>
<tr>
<th></th>
<th>Shift Type *</th>
<th></th>
<th></th>
<th>Paramedic Type *</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day (n = 7)</td>
<td>Rotating (n = 14)</td>
<td></td>
<td>Ambulance (n = 14)</td>
</tr>
<tr>
<td>rMSSD (msec), mean ± standard deviation</td>
<td>28.63 ± 12.97</td>
<td>26.25 ±12.20</td>
<td>0.75</td>
<td>27.15 ± 12.82</td>
</tr>
<tr>
<td>pNN50</td>
<td>8.17 ± 7.67</td>
<td>7.59 ± 7.83</td>
<td>0.07</td>
<td>7.55 ± 7.07</td>
</tr>
<tr>
<td>HF (msec²)</td>
<td>289.92 ± 225.66</td>
<td>257.47 ± 217.12</td>
<td>0.15</td>
<td>293.96 ± 225.19</td>
</tr>
</tbody>
</table>

rMSSD = root mean squared standard deviation successive difference
pNN50 = percentage of intervals >50ms different from the preceding interval
HF = high frequency measures (0.15 – 0.4 Hz)

* Differences in shift type and paramedic type group comparisons are not statistically significant. All p-values > 0.05, not shown
HPA axis results are represented by cortisol measurements and results of tests for endothelial functioning. Figures 2.2a) and 2.2b) show results of diurnal cortisol slopes and Figures 2.2c) and 2.2d) show daily cortisol production. As with alpha-amylase, flatter diurnal slopes indicate a dysregulation in normal functioning. However, unlike alpha-amylase, elevated daily cortisol production has been associated with exposure to chronic stress. Figure 2.3 shows median levels and distribution of endothelial functioning. Lower values indicate a reduction in normal functioning.

![Cortisol Slope](image1)

![Cortisol Daily Production](image2)

**Figure 2.2** Cortisol slope and calculated daily production for shift and paramedic type comparisons
See figure 2.1 for explanation of abbreviations and symbols.
Figure 2.3  Endothelial functioning by shift and paramedic type comparisons

Geometric mean line is labeled within box; Interquartile range is depicted by the box; 95% CI is outlined by whiskers; Outliers are represented by dots.

* Differences in shift type and paramedic type group comparisons are not statistically significant. All p-values > 0.05, not shown.

Cohen’s $d$ is the effect size comparing day to rotating-shift workers; and ambulance to dispatch paramedics. A small effect size is defined as 0.2, medium as 0.5 and large as 0.8.

Figures a) and b) represent results by shift type and paramedic type comparisons. The dashed line delineates healthy and unhealthy endothelial functioning as marked by a Reactive Hyperemia Index (RHI) cut-point of 1.35.

Non-shaded boxes represent high job strain groups in each group comparison. (i.e. Rotating-shift workers in shift type comparisons; and Dispatch paramedics in paramedic type comparisons)
2.5 Discussion

The purpose of this pilot study was to examine the feasibility of collecting several biological measurements at busy paramedic stations and to examine any trends in job strain, salivary biomarker levels and early heart disease indicators by job and shift work categories. Our study is one of the first field studies to concurrently examine psychological, physiological and subclinical pathology measures of stress and disease using salivary biomarkers and subclinical CVD indicators in both the ANS and HPA axis. Results from the study will be used to help design future, larger-scaled studies.

2.5.1 Study compliance and feasibility

This study required collecting 15 salivary samples in a busy occupational setting over a rest day followed by two work days. In addition, heart rate variability was logged over both work days. Subjects in our study were able follow a strict protocol and obtain reliable results with minimal researcher interaction; over 90% of all expected samples were collected and fell within expected normal ranges. Measurements taken on both workdays were highly correlated with each other, but not with measures taken on a rest day. This suggests that on top of other daily stressors, paramedic work stress may have an additional effect on neuroendocrine activity.

Karasek first identified rotating-shift workers and dispatchers as high job strain groups which may be at risk of “oppressed stress-related problems” \(^{114}\). Later reviews reported shift work and psychosocial stress may have the same effects on neuroendocrine activity linked with cardiovascular pathogenesis \(^{16,179}\). Although our study population was small, our findings were generally consistent with trends found in studies among larger populations that examined separate portions of the neuroendocrine systems linking stress or shift work with
CVD\textsuperscript{150,180-182}. The small sample size for our observational study inhibited our ability to determine statistically significant differences between groups. However, the main message of our study does not lie in statistical significance of individual measures, but rather in the consistency of the overall trend in findings.

### 2.5.2 Dispatch vs. ambulance paramedic comparisons

In the paramedic type (dispatch vs. ambulance) comparison, two of the three hypothesized trends (job strain and HPA activity) were observed. However, effect sizes were small ($d < 0.20$); thus to test for significant differences with sufficient power might require such a large population size that it would not be economically feasible. To find statistical significance in a feasible population size would require a larger effect size. This could be achieved by comparing dispatchers to a group with more contrast. For example, to examine if it is the nature of the emergency call that elicits a stress response, a comparison of dispatchers to non-emergency call centers, could be completed.

### 2.5.3 Neuroendocrine responses among shift workers

In comparing rotating-shift workers and daytime-only workers, all three hypothesized trends (job strain, ANS and HPA activity) were observed. Effect sizes among measures were large enough that differences could be detected with at least 80% power and a 5% significance level (2-sided) in a study population of 250 paramedics for (a) between-subjects for job strain and workday salivary cortisol, alpha-amylase and heart rate variability as measured by rMSSD; and (b) within-subjects for salivary cortisol and alpha-amylase on work and rest days. Only differences in endothelial functioning may not be detected in the proposed study size due as suggested by the small effect size found in this pilot study ($d = 0.22$). However, the small effect size may have resulted from not accounting for the time of endothelial
testing and diurnal variations may have attenuated effect sizes. A recent study which restricted testing between 8:00 am and 12 noon found a difference in endothelial functioning when comparing shift workers to non-shift workers (RHI = 1.73 vs. 1.94, p = 0.03)\textsuperscript{183}, suggesting that restricting the time of endothelial testing should be considered to control for diurnal effects.

### 2.5.4 Strengths and limitations

There are several limitations in our study. Our participants were volunteers that may result in selection bias and skew results. However, subjects were not informed to which questions would be used to calculate job strain and should not have influenced biological measures. The post-hoc recalibration of a validated questionnaire into domains of job demands and control is also problematic because it has not been validated with standard psychometric approaches (i.e. pilot testing, measuring validity, factor analyses) and thus may not accurately reflect paramedics’ perception of job strain. Therefore results from the job strain comparison can only be considered to be preliminary and further work is necessary to validate this scale using rigorous psychometric techniques.

Although we used non-clinical methods to capture HRV and ED, these methods have been shown to have high correlation with gold-standard measures\textsuperscript{164,176}. In addition, the standard long-term recording time for HRV is 24 hours, our 12 hour results were comparable to normal ranges expected for 24 hour measurements\textsuperscript{168}. The small sample size prohibited our ability to show statistically significant differences and account for covariates which might have influenced biological measures (e.g. age and sex). However, the purpose of this pilot study was to examine descriptive trends obtained by our proposed methodology to develop a larger-scaled study. Finally, our cross-sectional design prohibits conclusions about causality.
Strengths of the study include the use of non-invasive methods which allowed us to explore more biological markers representing the hypothesized biological pathway linking work stress and heart disease in a busy occupational population. This provided a more complete picture of how the ANS and HPA axis work together to prepare the body to threatening situations. Because these measures were easy to use and not cumbersome, we were able to measure subjects under true workplace exposures, thereby limiting the possibility of misclassification bias. We also completed our study on only one occupation which reduced the influence of external occupational and socio-economic factors that can arise with multi-occupational studies and may confound the relationship between exposure and outcome.

2.6 Conclusion

Our study showed that it is feasible for participants to collect many viable samples in a busy occupational setting with limited researcher supervision. We built upon previous studies examining various components of the pathway linking stress and heart disease by examining intermediate and subclinical ANS and HPA components using non-invasive and easy to use measures. Descriptive trends in our study suggest that exposure to stressors at work may lead to dysregulation in daily neuroendocrine hormone production and over the long-term, lead to early signs of heart disease. Future studies should include larger study numbers and a prospective study design to confirm our findings.
3 COMPARING A CONVENIENCE SAMPLE WITH LARGER POPULATIONS OF PARAMEDICS

3.1 Synopsis

Although convenience samples are commonly used in research, the sample obtained may often not be representative of the general population, precluding the ability to make inferences from results. Random sampling is preferred to reduce biases (e.g. selection), however, it can be costly, time consuming, complicated and may produce other biases (e.g. non-compliance).

The purpose of this chapter is to determine if a convenience sample of paramedics from Chapter 2 is representative of the larger, randomly selected population of paramedics. A semi-quantitative analysis was used to compare participants in 2 studies independently completed between 2007 and 2008. One was a field-sampling study conducted on a small convenience sample of full-time paramedics (n = 21), working in south-western BC (described in Chapter 2). The second was a mail survey of randomly sampled full- and part-time paramedics living across all areas of BC (n = 460). Three groups were compared: (1) the convenience sample of full-time paramedics (n = 21), (2) a random sample full-time paramedics (n = 291), and (3) a random sample of full- and part-time paramedics to account for the large proportion of part-time paramedics employed by the BC Ambulance Service (n = 417).

Results showed that heart disease prevalence and most demographic, anthropometric and health behaviour measures were similar between the convenience and both random samples. Similarities between the sample groups might be attributed to the homogenous BC paramedic workforce population, which has resulted from a limited number of new hires and retirees between 1989 and 2002. However, the low response rate among the randomly sampled population may have resulted in
a response bias and prohibits our ability to conclude that the convenience sample is a good representation of the larger population of paramedics.

3.2 Introduction

Although study recruitment techniques such as convenience sampling may be cost-efficient and pragmatic, the sample obtained rarely represents the larger population\(^\text{184}\). Studies have shown volunteers are more likely to be women, younger, practice a healthier lifestyle, be actively involved in their communities and have higher levels of education than randomly selected participants\(^\text{185}\). These biases complicate the ability to generalize findings to the larger population.

Random sampling is generally preferred because it reduces biases inherent with convenience sampling\(^\text{186}\), but is usually more complex in design and can be more costly, for example, if the study requires traveling to different locations. Random samples are generally rare among research that requires frequent biological monitoring (e.g. salivary samples), because of the costs and other logistical concerns such as compliance\(^\text{187}\).

The purpose of this chapter is to determine if the small study population from a convenience sample recruited for the neuroendocrine study described in Chapter 2, is representative of the larger population of BC paramedics.

3.3 Methods

Two independent studies were conducted between 2007 and 2008 on paramedics working for BC Ambulance Service: one examined neuroendocrine activity in a small convenience sample and is described in detail in Chapter 2, the second examined non-occupational risk factors for heart disease on a large cohort of paramedics\(^\text{107}\).
3.3.1 Recruitment protocols used for convenience sampling and random sampling

3.3.1.1 Convenience sample

Volunteers for the neuroendocrine sampling study were recruited from the sole dispatch unit and the nine busiest ambulance stations in south-western British Columbia and were restricted to full-time dispatch and ambulance paramedics. Information about the study was communicated to paramedics with the assistance of the BCAS through brochures, flyers and internal communication. The self-administered survey was provided to subjects upon enrollment and returned upon completion to study researchers by mail.

3.3.1.2 Random sample

Respondents to the non-occupational risk survey were randomly chosen with the assistance of the BCAS and use of their personnel files. One-thousand self-administered surveys were mailed to a sample of current and retired BCAS employees who have worked in various locations across the province of British Columbia.

3.3.2 Survey measures

Information regarding age, sex, employment history, anthropometric measures and health behaviours were ascertained. To assess health behaviours (e.g. smoking status, physical activity level) both surveys used identical wording as questions from the Canadian Community Health Survey (CCHS) 188, a national survey administered by Statistics Canada to gather information about health status of Canadians. This allowed for consistency between the surveys to compare study populations. Categories of Body Mass Index (BMI), smoking status and level of physical activity were derived using the following CCHS guidelines 189. Body mass index (BMI) was calculated as kilograms per squared-metre using self-reported height and weight. BMI categories were defined
using classifications for adults aged 18 and older: normal weight (BMI: 18.50 - 24.99 kg/m²),
overweight (BMI: 25.00 - 29.99 kg/m²) and obese (BMI ≥ 30.00 kg/m²).

Smoking status was derived from the question “at the present time do you smoke cigarettes daily,
occasionally or not at all?” Three categories of smokers were defined: current smokers, former
smokers and never smokers.

To identify physical activity levels, participants were asked to identify any activities they had
participated in over the past 3 months from a list of specified leisure time activities. A category of
“Other activity” was also provided for activities not listed. For positive responses to any activity,
participants were further asked to provide frequency and duration for each. From this information,
a respondent’s total daily energy expenditure over the past year was calculated using the following
formula:

\[
\sum_{\text{all activities}} \frac{N \times D \times \text{METvalue}}{365}
\]

Where  
N = number of times a respondent engaged in an activity over the past 12 months

D = average duration of activity, in hours

METvalue = metabolic equivalent of task provided in the CCHS and defined as the energy
cost of physical activity; expressed as kilocalories expended per kilogram of body weight per
hour of activity (kcal/kg per hour)

Following CCHS guidelines, levels of physical activity was categorized as “active” if total daily
energy expenditure was 3 or more, “inactive” if it was less than 1.5 and “moderate if it fell in
between.
Heart disease prevalence was ascertained differently in each study. Among the convenience sample, heart disease was defined as a positive response to the question “Have you ever been diagnosed with heart disease (e.g. high blood pressure, hypertension)?” Among the randomly sampled population, heart disease prevalence was ascertained with questions from the Canadian Community Health Survey and defined as a positive response to any of the following conditions: currently have high blood pressure, heart disease, angina, congestive heart failure, ever had a heart attack or suffer from the effects of a stroke.

3.3.3 Comparing the convenience sample to the random sample

A semi-quantitative approach was used to compare demographic variables, anthropometric measures and health behaviour categories between the convenience sample and the random sample of paramedics.

Because recruitment for the convenience sample was restricted to full-time dispatch and ambulance paramedics, to allow for a comparison of study populations we applied this same restriction to the randomly sampled population. However, in a preliminary analysis of BCAS work history files, I discovered that a large portion of the paramedics (60%) employed by the BCAS work in part-time positions. Thus including only those who work full-time hours may not accurately represent the entire working population of dispatch or ambulance paramedics. Therefore, a second comparison was completed which included those employed in part-time positions.

3.4 Results

3.4.1 Response rates and populations

From the 21 volunteers in the convenience sample, 20 completed and returned the surveys.
Of the 1000 surveys mailed out to a random selection of paramedics, 460 were completed and returned. We excluded those who were retired, on sick leave or missing responses regarding current job status (n = 32); and those employed as supervisors or trainers or were in-training (n = 10). The final population consisted of 291 paramedics who worked full-time hours (279 ambulance, 12 dispatch) and 126 who worked less than full-time hours (124 paramedics, 2 dispatch).

3.4.2 Comparing demographic variables, anthropometric measures and health behaviours

A descriptive comparison of the study populations is reported in Table 3.1. The convenience sample was predominantly male (66.7%) with an average age of 42.1 years and 15.6 years of service with the BCAS. The majority of randomly sampled full-time paramedics were also male (76.3%) with an average age of 43.1 years and 16.7 years of service. Inclusion of randomly sampled part-time paramedics resulted in similar descriptive characteristics (i.e. 69.8% men, average age 43.4 years and 16.2 years of service).

There was little difference between the random sample of part-time and full-time workers with the random sample of only full-time workers. Therefore, in further descriptions the term “random sample” will include the group of full-time and part-time workers, as well as the group of only full-time workers.

Prevalence of heart disease was similar for men in the convenience and random samples (21.4% vs. 23.0%, respectively). The majority of men in both sample populations were “overweight”, as defined by BMI criteria (convenience: 71.4% vs. random: 51.7 – 52.9%), and almost a third were categorized as “obese” (convenience: 21.4% vs. random: 28.2 – 29.4%).

Average age and years of service among women in the convenience sample were similar to those who were randomly sampled [(age range: convenience: 39.6, random: 39.4 – 39.5 years); (years of
service: convenience: 9.8, random: 9.9 - 10.8 years}). While no women in the convenience sample reported prevalence of heart disease, prevalence reported among those randomly sampled ranged from 9.5 - 10.1%. BMI metrics were also similar: among women just over half (convenience: 66.6%, random: 50.4 – 54.4%) were in the “normal range” (BMI 18.5 – 24.9 kg/m²).
Table 3.1  A comparison of demographic information, heart disease prevalence and non-occupational risk factors of heart disease between the convenience sample population used in the neuroendocrine sampling study and a random sample of the larger paramedic population

<table>
<thead>
<tr>
<th>CONVENIENCE SAMPLE</th>
<th>RANDOM SAMPLE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neuroendocrine Sampling Study¹,</strong></td>
<td><strong>Non-Occupational Risk Survey²</strong></td>
</tr>
<tr>
<td>all full-time dispatch and</td>
<td>Full-time, dispatch and ambulance</td>
</tr>
<tr>
<td>ambulance paramedics</td>
<td>paramedics</td>
</tr>
<tr>
<td>Male (n=14)</td>
<td>Male (n = 222)</td>
</tr>
<tr>
<td>Female (n=7)</td>
<td>Female (n = 69)</td>
</tr>
<tr>
<td>% of population</td>
<td>66.7 %</td>
</tr>
<tr>
<td></td>
<td>33.3 %</td>
</tr>
<tr>
<td>Average Age, yrs (SD)</td>
<td>42.1 (7.4)</td>
</tr>
<tr>
<td></td>
<td>39.6 (7.7)</td>
</tr>
<tr>
<td>Yrs of employment with BCAS³</td>
<td>15.6 (8.0)</td>
</tr>
<tr>
<td></td>
<td>9.8 (6.1)</td>
</tr>
<tr>
<td>Prevalence of heart disease, n (%)</td>
<td>3 (21.4%)</td>
</tr>
<tr>
<td></td>
<td>--</td>
</tr>
<tr>
<td>Smoking Status⁴, n (%)</td>
<td></td>
</tr>
<tr>
<td>Current Smoker</td>
<td>2 (15.3%)</td>
</tr>
<tr>
<td></td>
<td>1 (14.3%)</td>
</tr>
<tr>
<td>Former Smoker</td>
<td>2 (15.3%)</td>
</tr>
<tr>
<td></td>
<td>3 (42.9%)</td>
</tr>
<tr>
<td>Never Smoker</td>
<td>9 (69.2%)</td>
</tr>
<tr>
<td></td>
<td>3 (42.9%)</td>
</tr>
<tr>
<td>Body Mass Index⁴, n (%)</td>
<td></td>
</tr>
<tr>
<td>Normal (18.5 - 24.9 kg/m²)</td>
<td>1 (7.1%)</td>
</tr>
<tr>
<td></td>
<td>4 (66.7%)</td>
</tr>
<tr>
<td>Overweight (25.0 - 29.9 kg/m²)</td>
<td>10 (71.4%)</td>
</tr>
<tr>
<td></td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>Obese (30+ kg/m²)</td>
<td>3 (21.4%)</td>
</tr>
<tr>
<td></td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>Physical Activity⁴, n (%)</td>
<td></td>
</tr>
<tr>
<td>Active</td>
<td>4 (28.6%)</td>
</tr>
<tr>
<td></td>
<td>2 (28.6%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>3 (21.4%)</td>
</tr>
<tr>
<td></td>
<td>3 (42.9%)</td>
</tr>
<tr>
<td>Inactive</td>
<td>7 (50.0%)</td>
</tr>
<tr>
<td></td>
<td>2 (28.6%)</td>
</tr>
</tbody>
</table>

¹ Wong et al. ¹
² Koehoorn et al. ¹⁰⁷
³ BCAS = British Columbia Ambulance Service
⁴ Categories derived using Canadian Community Health Survey guidelines
Physical activity levels were similar for men in the convenience sample in comparison to those randomly sampled, (active range: 28.6 vs. 31.5 - 32.0%; moderate range: 21.4 vs. 26.1%); inactive range: 50.0 vs. 41.9 – 42.3%, respectively). However, the differences were more substantial among women in both groups (active range: 28.6 – 40.5%; moderate range: 23.2 – 42.9%; inactive range: 28.6 – 40.5%). Smoking behaviours (i.e. current, former and never smokers) were also noticeably different for both men and women when comparing the convenience sample to the random sample.

3.5 Discussion

Although study recruitment techniques, such as convenience sampling, may be cost-efficient and pragmatic, the populations sampled rarely represent the larger population and preclude the ability to generalize results. While random sampling techniques are considered to reduce sampling bias and improve generalizability, the use of this recruitment method may introduce a non-compliance bias in studies with strict protocols such as those requiring collection of biological samples. Because randomly selected participants may not be as interested in the study as volunteer participants, they may not follow instructions as precisely as volunteers and unwittingly spoil collection samples.

Results of this chapter suggest that demographic information, anthropometric measures and categories of health behaviours were similar between a convenience and random samples of dispatch and ambulance paramedics. However, noticeable differences were observed for responses reporting physical activity levels among women and smoking behaviours among both sexes. These differences may have been attributed to the small number of participants in the convenience sample, particularly among women. For example, each woman represents 14% of the total population of women in the convenience sample (n = 7). Therefore, small differences in numbers may result in drastic changes in proportions.
While it may be surprising that our convenience and random samples are similar given the contrary evidence among other studies\textsuperscript{185-187}, it may be explained by the recruitment history of the BC Ambulance Service. After the inception of the BCAS in 1974, the number of new recruits increased steadily and peaked from 1988 to 1991 when the BCAS workforce reached a steady state of approximately 3,600 workers (Figure 3.1). A significant decline in new recruits coupled with a low number of retirees resulted in a workforce largely consisting of the same workers thereafter. In addition, the paramedic population has generally been male-dominated\textsuperscript{190} and all must obtain similar levels of education to serve in the BCAS. These series of factors has contributed in creating a homogenous workforce during the time when both studies described in this chapter were conducted. As such, it would be possible that there would be little difference between the convenience and randomly sampled populations.

![Figure 3.1 BC Ambulance Service new hires, retirees and working population by year](Source: BC Ambulance Service employment records)
It is also worthwhile noting the surprising prevalence of obesity and sedentary behavior among the men in this population, given the requirements of good physical fitness upon entering the paramedic service. Our anthropometric and health behaviour results are similar to other studies which found that among male police, firefighters and paramedics approximately 30% were obese (BMI 30+ kg/m²) and two-thirds of workers in emergency services were of low to moderate fitness as defined by a standardized cardiovascular fitness test ⁹⁶,¹⁹¹,¹⁹².

The major limitation to this chapter is the low response rate (46%) in the randomly sampled population. As such, this may have lead to a response bias and may have reflected the same biases that arise with convenience samples. Ambulance paramedics who have an interest in research may have participated in the neuroendocrine study and survey thus resulted in similar demographic characteristics and health behaviours between both groups. Paramedics who did not respond may have been hesitant to do so because of uncertainty if the information provided may be obtained by employers and could be used against them. No information was available about non-respondents; however, if I had information regarding paramedics contacted, I could follow-up with non-responders to identify reasons for non-response, encourage participation, or at least to obtain demographic information for comparative purposes.

To help understand how the study groups compared with the full cohort of paramedics, I analyzed employment records from 2002 (n = 3,517) and compared them to the convenience sample (n=21) and the random sample (n=416). This revealed similar distribution of sex (men: 70.9%, women: 28.9%) and average age [men: 41.8 years (SD 10.2), women: 39.7 years (SD 10.2)] in comparison to our study populations. While this does provide limited evidence of a homogenous workforce, caution is still required in interpreting findings in this chapter.
In conclusion, while similarities were observed for demographic characteristics, health behaviours and anthropometric measures, the low response rate among the randomly sampled survey population may have resulted in a response bias, preventing us definitively concluding that the small convenience sample is a good representation of the larger population of paramedics.
4 RISK OF ACUTE AND CHRONIC FORMS OF HEART DISEASE WITH SHIFT WORK, AND THE INFLUENCE OF RECOVERY TIME

4.1 Synopsis

The pathway linking shift work and heart disease has been proposed as one with disruptions in psychosocial, behavioural and physiological mechanisms. While shift work may result in neuroendocrine dysregulation and lead to an increased risk of heart disease, time away from shift work may provide opportunity for recovery and mitigation of risk. However, most longitudinal studies have not accounted for periods when shift workers may not be working at night. This could have resulted in misclassification of their exposure and lead to biases towards null risk estimates.

The aim of this study was to examine the association of shift work with the risk of acute and chronic forms of heart disease, and to determine if recovery time from shift work might reduce the risk. A nested case-control study was used to examine heart disease risk among 5,604 British Columbia paramedics. Incidence of acute and chronic coronary syndromes and hypertension were ascertained through hospitalization, physician billing and death registry records between 1991 and 2002 available through the BC Linked Health Database. Information regarding paramedics’ daily shift work status was ascertained from emergency run records provided by the BC Ambulance Service. We examined recovery periods in 2 ways: (1) the number of times a paramedic switched between a shift work and non-shift work schedule; and (2) a ratio of average length of a shift work period to a non-shift work period. Cumulative exposure was included as a comparison to our new measures.

We found indications that the risks of chronic coronary syndrome (CCS) and hypertension (HTN) may be elevated with increasing number of changes between shift work and recovery periods. In the tertile with the highest number of changes between shift work and recovery periods, odds ratios
were 1.10 (95% CI: 0.39-3.08) for CCS and 1.25 (95% CI: 0.71–2.20) for HTN. We also found an elevated risk of CCS and HTN with shorter periods of recovery in comparison to shift work. Elevated risks were not found for ACS, nor with cumulative exposure to shift work.

Overall results were non-significant and no dose-response effects were evident. However, we consider this to be an exploratory study using new shift work metrics by incorporating periods of neuroendocrine dysregulation and recovery. This is also the first study, we are aware of, which examines the association of shift work with separate heart disease outcomes to gain a better understanding of the role shift work may play in the progression of heart disease.

A version of this chapter has been submitted to the Scandinavian Journal of Work, Environment and Health and is currently under review.

4.2 Introduction

Basic biological functioning in humans depends on the coordination of circadian rhythms by the hypothalamic suprachiasmatic nucleus (SCN) – the ‘master’ internal clock located in the brain which coordinates physiologic functions such as the neuroendocrine system \(^{193}\). Exposure to light at night and sleep deprivation, common in shift work, may lead to decreased SCN activity and changes in neuroendocrine function affecting the hypothalamic-pituitary-adrenal axis and autonomic nervous system \(^{194}\). Chronic activation of these neuroendocrine systems can interfere with other physiological functions, resulting in adverse consequences such as heart disease \(^{195}\). While activation of these systems is normal, periods of rest and recovery are crucial to maintain allostasis \(^{130}\). This dynamic has been studied extensively in the fields of stress and sports research \(^{3,196}\), but has rarely been investigated in occupational research and never examined in shift work studies.
Evidence has shown that neuroendocrine functioning among shift workers is altered in comparison to daytime only workers \(^{182,197}\). It is believed that chronic neuroendocrine dysregulation may damage blood vessels and accelerate coronary plaque build-up and leading to \textit{chronic} coronary events, while \textit{acute} coronary events are associated with intense cardiovascular reactivity and plaque rupture \(^{111}\). However, a recent review of 14 studies concluded that there is limited epidemiologic evidence of an association between shift work and cardiovascular disease (CVD) \(^{73}\). If shift work is associated with only one specific category of heart disease, pooling all forms of CVD as one general outcome measure may dilute effects and attenuate risk estimates.

It is thought that workplace exposures have a relatively small effect on human health in comparison to non-occupational risks and therefore, may be difficult to detect \(^{198}\). Because random error in occupational exposure measures may reduce study power, it has been suggested that improving accuracy in exposure assessment, such as including temporal changes, should be considered \(^{33,198}\). Using broad classifications of shift work exposure (e.g. ‘ever’ versus ‘never’), may not account for periods when shift workers may temporarily not be working at night (e.g. vacations) or alter work schedules to accommodate changes in their lives (e.g. providing childcare). This may contribute to non-differential misclassification bias. Many prior shift work studies have used questionnaires to identify shift work exposure which may be subject to recall bias \(^{73}\). Eleven out of 14 studies in a recent review included workers from various occupations and did not control for different job-related exposures which may contribute to the risk for heart disease (e.g. noise) \(^{73}\). Pooling workers from across different workplaces can also lead to inconsistent definitions of shift work and may lead to non-differential exposure misclassification and bias risk estimates towards the null.

Our study identified an individual’s daily shift work schedule using daily work activity records over several years to provide a more accurate exposure assessment than any other study of shift work and
heart disease conducted to date. The primary objective of this study was to determine if increased exposure to shift work involving work at night was associated with an increased risk of heart disease, and if periods of non-shift work reduced the risk. The secondary objective was to examine the association of shift work with separate acute and chronic heart disease outcomes to gain a better understanding of the role of shift work may play in the etiology of heart disease.

Our hypotheses were:

1) Shift work may be associated with chronic heart disease which may be attributed through the chronic effects of neuroendocrine dysregulation. However, shift work may not be associated with acute heart disease because resulting neuroendocrine disruption may not have enough intensity to rupture coronary plaques

2) Frequent changes between shift and non-shift work periods may not allow workers to adapt to a regular schedule, sustaining neuroendocrine activity and increasing risk of heart disease

3) Those with the longest recovery times from shift work may negate the effects of circadian disruption and will have a lower risk of heart disease

4.3 Methods

4.3.1 Study population and data sources

This was a retrospective study of a cohort of all ambulance paramedics employed by the British Columbia Ambulance Service (BCAS). Paramedics were included if they (1) worked as an ambulance paramedic and attended emergencies between April 1991 to March 2002; (2) worked at least one year with the BCAS prior to 2002; (3) were registered for provincial medical insurance for at least
one year after start of employment; and (4) were between the ages of 17 to 65 on commencement of employment.

Employment history records provided by the BCAS were used to enumerate the cohort, and included information about changes in employment status (i.e. regular, irregular or part-time position) and occupation type (e.g. ambulance paramedic, dispatcher, administrator). Emergency run data compiled by the BCAS for every emergency attended by paramedics during the study period provided information regarding occupational exposures.

The province of British Columbia (BC) provides a medical insurance program for virtually all BC residents that pays for health care services such as hospitalizations and physician visits\textsuperscript{199}. These administrative health data plus death registry records between April 1991 and March 2002 were provided by the BC Ministry of Health and linked to cohort employment history records and emergency run data by Population Data BC\textsuperscript{107}. All personal information was removed from this data and replaced with anonymous study identifiers prior to receipt by study researchers.

4.3.2 Study design, case definition and selection of controls

Our cardiovascular morbidity and mortality outcome measures were: Acute Coronary Syndrome (ACS) (ICD9 410 - 411), Chronic Coronary Syndrome (CCS) (ICD9 413 - 414, 429.2) and Hypertension (HTN) (ICD9 401 - 405). ACS (n=49) and CCS (n=54) cases were defined by the underlying cause of death on death certificates, or principal or primary diagnosis from hospitalization records. The principal diagnosis is the immediate condition for the hospital visit, whereas the primary diagnosis is the most resource intensive condition influencing length of stay\textsuperscript{200}. In addition to underlying cause of death and hospitalization diagnosis, we also defined hypertension following Canadian Medical Association clinical practice guidelines of 3 physician visits within 70 days\textsuperscript{201}, with the last physician visit as case date (n=197). Where multiple cases may have occurred
per individual (e.g. several hospitalizations), we only used the first to define case incidence and removed subsequent cases from the analyses.

This study used a nested case-control study design with incident density sampling. Three controls were matched to each case on age (in 10 year groups), sex and year of first employment (in 5 year age groups). The start of follow-up for each subject was the later of April 1, 1991 (start of physician billing records) or one year following the start of work as a paramedic. The end of follow-up was the earliest of end of employment, end of registration in the BC medical system, disease incidence or death, or March 31, 2002.

4.3.3 Shift work exposure assessment

Information including the date, identification numbers of attending paramedics and type of ambulance were recorded by the attending paramedics on BCAS forms during each emergency run. Time of emergency was not provided in our dataset; therefore, ambulance type was used as a surrogate measure to categorize subjects’ shift work exposures. There were two primary classifications of ambulance type: daytime-only cars and 24-hour cars. Shifts on daytime-only cars started between 0600 and 1200; and ended between 1800 and 2400. Shifts on 24-hour cars followed a clockwise rotating-shift pattern [i.e. two day shifts (0600 to 1800), two night shifts (1800 to 0600), followed by 4 rest days].

Although we knew a paramedic was working a rotating-shift on a 24-hour car, we did not know if it was the day or night shift. To reduce the possibility of exposure misclassification, we systematically identified as many day shifts as possible within a rotating-shift pattern. To do so, we used a BCAS policy which required paramedics to have at least 8 hours rest between shifts. If a paramedic worked a rotating-shift, followed by a dayshift on the next day, the rotating-shift must have ended before 0400 to allow 8 hours of rest before the start of the day shift, which can start as late as 1200.
Therefore, the rotating-shift could only be a day shift since a night shift would have ended at 0600 and not provide the required 8 hours of rest before the start of the next day shift. In these incidences, we reclassified the rotating-shift as a day shift.

Most of our sample (80%) had been employed in part-time or irregular schedules at some point during the follow-up period. These employment types frequently change shift schedules (i.e. rotating or daytime-only) to fill in for regularly scheduled paramedics as needed and could have periods when they were not actively attending emergencies. Days that were not recorded in the emergency run data could include times when a paramedic was (a) not working or (b) working but did not attend any emergencies. We assumed on days where no emergencies were recorded, workers continued with normal daily activities and remained awake during daytime hours and slept during the night.

We considered rotating-shift work as a period of circadian disruption which may result in augmentation of neuroendocrine activity, and periods of normal wake-sleep cycles as recovery from circadian disruption. To construct periods of exposure, we first categorized each month during a paramedic’s exposure window as rotating-shift or recovery (i.e. daytime only shifts combined with days with no emergency runs) based on how a paramedic spent >50% of their time. This followed a definition used in a prior study to categorize shift workers among a cohort which also did not have a regular work schedule. We defined a rotating-shift period as the number of consecutive months categorized as “rotating-shift”, and recovery period as the number of consecutive months categorized as “recovery”.

To test our hypotheses, we developed 3 shift work exposure measures:
1) Frequency of changes between shift work and recovery. Using our derived periods of shift work and recovery periods, we defined the frequency of changes as the number of times a paramedic switched between the two.

2) Ratio of average length of shift work to recovery period. Using our derived periods of shift work and recovery, we applied an exercise physiology metric which examines the effects of exercise (i.e. neuroendocrine activation) relative to periods of rest to define a measure of shift work relative to recovery:

\[
\frac{\text{average length of shift work period (in days)}}{\text{average length of recovery period (in days)}}
\]

3) Cumulative exposure. As a comparison to our two derived shift work exposures, we also included a broad definition of cumulative exposure as identified by a recent review. This was defined as a count of the number of rotating-shifts during the follow-up period.

4.3.4 Potential covariates

Three occupational exposures (i.e. workload, noise and social instability) were considered as potential confounders in the relationship between shift work and heart disease.

Workload has been described in terms of occupational physical and psychosocial demands, and excessive workload has been associated with an increased risk of CVD. Workload in this study was defined as the number of emergency runs per paramedic during study follow-up.

Ambulance paramedics do not wear hearing protection during emergency runs and can be exposed to sirens previously measured at a range of 80 – 90 dB(A). Studies have shown that cumulative exposure at these noise levels are associated with hypertension and acute myocardial infarction. To capture exposure to noise, we included the number of emergency runs made with sirens.
Lack of social support also has strong links to myocardial infarction \(^{51}\). The most compelling evidence of this can be seen in animal studies which have shown that monkeys subjected to social instability for only 21 months, in comparison to those housed in stable environments, had more extensive coronary artery atherosclerosis as determined in post-mortem examinations immediately following termination of the experiment \(^{208}\). In high stress situations like emergencies, coherent teamwork is crucial for the delivery of effective patient care\(^{209}\). But frequent changes in partners may create a socially stressful situation and augment neuroendocrine activity, increasing the risk for heart disease. To account for this potential confounder, we developed a variable to include the frequency of partner changes during the follow-up period.

### 4.3.5 Statistical analysis

Correlations between potential confounders were examined using Spearman’s rank correlation analysis. We used conditional logistic regression to estimate odds ratios (OR) with 95% confidence intervals to estimate the association between shift work exposure and heart disease risk. Continuous variables were categorized into low, medium and high exposures using tertile cutpoints. Separate analyses were completed for each shift work variable and heart disease outcome. Because all covariates were based upon the number of emergency runs, we assumed this would have the most influence and introduced workload into the model first, followed by noise, then changes in partners. Models were assessed using changes in the magnitude and direction of coefficients and confidence intervals; and Akaike’s Information Criterion. Tests for trends were completed treating shift work variables as continuous variables in conditional logistic regression.

All statistical analyses were performed using Stata 11.2 (StataCorp LP, College Station, Texas, USA).
4.4 Results

4.4.1 Cohort description

A total of 5,604 paramedics were employed by the BC Ambulance Service between April 1991 to March 2002. We excluded: 143 paramedics who never worked as attending paramedics, 355 who were employed for less than one year, 26 who were registered for the BC medical insurance program for less than one year and 7 who were not between the ages of 17 – 65 years at the start of employment. Our final cohort consisted of 5,073 ambulance paramedics (69.5% men, 30.5% women).

A total of 49 cases of Acute Coronary Syndrome (ACS), 54 Chronic Coronary Syndrome (CCS) and 197 Hypertension (HTN) cases were identified (Table 1). Among ACS cases, this represents 1 death and 48 hospitalized. All CCS cases were hospitalizations. A majority of HTN cases (94%) were ascertained from physician visits and the rest from hospitalizations.

Table 4.1 shows descriptive characteristics of cases and controls for each heart disease outcome.

Duration of follow-up ranged from 4.8 years to 6.4 years. During this period, paramedics attended emergencies approximately 25% of the time. While emergencies happened more frequently in urban settings than in rural settings (81% vs. 46% of study period, chi-squared: 40.4, p < 0.001); there was no difference in location between cases and controls.

Hypertensive cases were generally younger (mean age: 46.9 years; SD 9.1) than those diagnosed with ACS (mean age: 53.0 years; SD 7.9) or CCS (mean age: 52.6 years; SD 8.2).
# Table 4.1 Descriptive characteristics of cases and controls for acute coronary syndrome, chronic coronary syndrome and hypertension

<table>
<thead>
<tr>
<th></th>
<th>ACUTE CORONARY SYNDROME (ACS)</th>
<th></th>
<th>CHRONIC CORONARY SYNDROME (CCS)</th>
<th></th>
<th>HYPERTENSION (HTN)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Cases (n=49)</td>
<td>Controls (n=134)</td>
<td>Cases (n=54)</td>
<td>Controls (n=155)</td>
<td>Cases (n=197)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Age at start of employment (yrs)</td>
<td>35.3 (9.3)</td>
<td>34.8 (9.4)</td>
<td>34.4 (9.3)</td>
<td>33.4 (10.6)</td>
<td>33.5 (9.2)</td>
</tr>
<tr>
<td>Duration of employment (yrs)</td>
<td>21.9 (8.1)</td>
<td>21.1 (7.9)</td>
<td>21.8 (8.4)</td>
<td>21.8 (8.6)</td>
<td>17.7 (8.5)</td>
</tr>
<tr>
<td>Duration of follow up (yrs)</td>
<td>5.8 (3.0)</td>
<td>6.0 (3.0)</td>
<td>6.3 (3.2)</td>
<td>6.4 (3.2)</td>
<td>4.8 (3.2)</td>
</tr>
<tr>
<td>Number of days with emergency runs</td>
<td>438.6 (563.3)</td>
<td>455.0 (489.1)</td>
<td>535.7 (548.6)</td>
<td>471.3 (539.4)</td>
<td>352.7 (456.9)</td>
</tr>
<tr>
<td>Age at incidence</td>
<td>53.0 (7.9)</td>
<td>--</td>
<td>52.6 (8.2)</td>
<td>--</td>
<td>46.9 (9.1)</td>
</tr>
<tr>
<td><strong>SHIFT WORK VARIABLES</strong></td>
<td></td>
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<tr>
<td>Cumulative exposure (days)¹</td>
<td>284.3 (468.5)</td>
<td>359.7 (443.5)</td>
<td>357.8 (454.3)</td>
<td>353.5 (464.0)</td>
<td>293.7 (424.0)</td>
</tr>
<tr>
<td>Frequency of changes between shift work and recovery ²</td>
<td>6.5 (12.9)</td>
<td>8.5 (14.24)</td>
<td>7.7 (12.3)</td>
<td>7.8 (14.2)</td>
<td>6.4 (12.1)</td>
</tr>
<tr>
<td>Ratio of average shift work period to average recovery period ³</td>
<td>0.57 (0.54)</td>
<td>0.48 (0.74)</td>
<td>0.41 (0.49)</td>
<td>0.49 (0.84)</td>
<td>0.54 (1.17)</td>
</tr>
<tr>
<td><strong>COVARIATES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Workload (number of runs)</td>
<td>1619.9 (2442.2)</td>
<td>1446.7 (1887.0)</td>
<td>1889.6 (2309.5)</td>
<td>1538.0 (2154.8)</td>
<td>1146.8 (1730.2)</td>
</tr>
<tr>
<td>Noise (number of runs with sirens)</td>
<td>698.6 (1234.7)</td>
<td>685.8 (1074.8)</td>
<td>734.0 (976.3)</td>
<td>714.4 (1131.3)</td>
<td>489.9 (815.3)</td>
</tr>
<tr>
<td>Social Instability (number of partners)</td>
<td>51.04 (69.16)</td>
<td>48.8 (53.3)</td>
<td>62.2 (73.1)</td>
<td>52.5 (65.9)</td>
<td>43.9 (54.8)</td>
</tr>
</tbody>
</table>

SD = Standard Deviation  
¹ Number of days with logged runs on a 24 hr ambulance  
² Switches between rotating-shift period and recovery period  
³ Average length of rotating-shift work / average length of recovery
4.4.2 Risk of acute coronary syndrome, chronic coronary syndrome and hypertension

Cumulative exposure and covariates (i.e. workload, noise and social instability) were all highly correlated ($r > 0.80$) reflecting that they were derived from the frequency of emergency runs (Table 4.2). Inclusion of highly correlated variables resulted in unstable risk estimates; and Akaike’s Information Criterion analyses suggested the best fit for each shift work model did not include any covariates, therefore none were considered in the final models.

<table>
<thead>
<tr>
<th>Table 4.2 Correlation of shift work variables and covariates</th>
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<tbody>
<tr>
<td><strong>Correlation Coefficient</strong></td>
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<tr>
<td><strong>Shift work variables</strong></td>
</tr>
<tr>
<td>Cumulative exposure (days)$^1$</td>
</tr>
<tr>
<td>Frequency of changes between shift work and recovery$^2$</td>
</tr>
<tr>
<td>Ratio of average shift work period to average recovery period $^3$</td>
</tr>
<tr>
<td><strong>Covariates</strong></td>
</tr>
<tr>
<td>Workload$^4$</td>
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<tr>
<td>Noise$^5$</td>
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<tr>
<td>Social Instability$^6$</td>
</tr>
</tbody>
</table>

* $p < 0.001$ for all correlation coefficients

$^1$ Number of days with logged runs on a 24 hr ambulance

$^2$ Switches between rotating-shift period and recovery period

$^3$ Average length of rotating-shift work / average length of recovery

$^4$ Number of emergency runs

$^5$ Number of emergency runs with sirens

$^6$ Number of changes in partners
Table 4.3 provides the results of the risk estimates for all shift work variables and heart disease outcomes. No elevated risks were associated ACS among any of the shift work variables. Elevated risks of CCS and HTN were observed only in the group with the highest cumulative exposure to shift work (CCS: OR 1.11, 95% CI: 0.48 -2.61; HTN: OR 1.10, 95% CI: 0.65 - 1.56). A consistent elevated risk associated with increasing frequency of changes between periods of shift work and recovery; and increasing average length of shift work combined with decreasing length of recovery periods. However, all confidence intervals included unity suggesting that there may be no difference between exposure and reference categories. Results of tests for linear trend did not show statistical significance in any relation.
Table 4.3  Risk of heart disease outcomes associated with shift work variable and covariates

<table>
<thead>
<tr>
<th>SHIFT WORK MEASURES</th>
<th>ACUTE CORONARY SYNDROME (n = 183)</th>
<th>CHRONIC CORONARY SYNDROME (n = 209)</th>
<th>HYPERTENSION (n = 732)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N cases (n= 49) OR (95% CI) Trend p-value</td>
<td>N cases (n= 54) OR (95% CI) Trend p-value</td>
<td>N cases (n= 197) OR (95% CI) Trend p-value</td>
</tr>
<tr>
<td>Cumulative Exposure (days)¹</td>
<td></td>
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<td></td>
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<tr>
<td>Low</td>
<td>61 20 ref</td>
<td>70 19 ref</td>
<td>249 73 ref</td>
</tr>
<tr>
<td>Medium</td>
<td>61 17 0.83 (0.37, 1.85)</td>
<td>70 16 0.82 (0.36, 1.84)</td>
<td>246 55 0.69 (0.45, 1.06)</td>
</tr>
<tr>
<td>High</td>
<td>61 12 0.44 (0.17, 1.15)</td>
<td>69 19 1.11 (0.48, 2.61)</td>
<td>247 69 1.01 (0.65, 1.56)</td>
</tr>
<tr>
<td>Frequency of changes between</td>
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<tr>
<td>Shift work and Recovery ²</td>
<td></td>
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</tr>
<tr>
<td>No changes</td>
<td>105 32 ref</td>
<td>113 26 ref</td>
<td>429 109 ref</td>
</tr>
<tr>
<td>Low</td>
<td>27 6 0.64 (0.24, 1.71)</td>
<td>32 10 1.54 (0.63, 3.75)</td>
<td>113 30 1.11 (0.69, 1.78)</td>
</tr>
<tr>
<td>Medium</td>
<td>25 6 0.75 (0.27, 2.08)</td>
<td>34 11 1.79 (0.72, 4.46)</td>
<td>102 30 1.28 (0.77, 2.12)</td>
</tr>
<tr>
<td>High</td>
<td>26 5 0.49 (0.16, 1.52)</td>
<td>30 7 1.10 (0.39, 3.08)</td>
<td>98 27 1.25 (0.71, 2.20)</td>
</tr>
<tr>
<td>Ratio of average length of shift</td>
<td></td>
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<tr>
<td>work to recovery period ³</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No shift work exposure</td>
<td>95 31 ref</td>
<td>105 25 ref</td>
<td>394 99 ref</td>
</tr>
<tr>
<td>Low</td>
<td>26 5 0.48 (0.17, 1.35)</td>
<td>32 10 1.48 (0.61, 3.58)</td>
<td>105 28 1.05 (0.64, 1.72)</td>
</tr>
<tr>
<td>Medium</td>
<td>26 3 0.25 (0.07, 0.96)</td>
<td>32 8 1.38 (0.50, 3.81)</td>
<td>104 32 1.37 (0.83, 2.26)</td>
</tr>
<tr>
<td>High</td>
<td>26 9 0.88 (0.32, 2.43)</td>
<td>32 10 1.74 (0.62, 4.90)</td>
<td>104 28 1.17 (0.68, 1.99)</td>
</tr>
<tr>
<td>COVARIATES</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Workload*</td>
<td>0.46</td>
<td>0.07</td>
<td>0.86</td>
</tr>
<tr>
<td>Low</td>
<td>62 17 ref</td>
<td>70 15 ref</td>
<td>250 72 ref</td>
</tr>
<tr>
<td>Medium</td>
<td>60 15 0.95 (0.41, 2.22)</td>
<td>70 17 1.24 (0.53, 2.91)</td>
<td>245 59 0.79 (0.52, 1.20)</td>
</tr>
<tr>
<td>High</td>
<td>61 17 1.20 (0.46, 3.15)</td>
<td>69 22 2.35 (0.93, 5.97)</td>
<td>247 66 1.01 (0.64, 1.62)</td>
</tr>
</tbody>
</table>
|                      | ACUTE CORONARY SYNDROME  
|                      | (n = 183)                   | CHRONIC CORONARY SYNDROME  
|                      | (n = 209)                   | HYPERTENSION  
|                      | (n = 732)                   |
|----------------------|-----------------------------|-----------------------------|-----------------------------|
| N cases              | OR (95% CI) Trend p-value   | N cases                     | OR (95% CI) Trend p-value   | N cases                     | OR (95% CI) Trend p-value   |
| Noise<sup>a</sup>    |                             |                             |                             |                             |                             |
| Low                  | 61                          | 18                          | ref                         | 70                          | 17                          | ref                         | 254                          | 69                          | ref                         | 0.84 0.26 0.38                |
| Medium               | 61                          | 15                          | 0.82 (0.35, 1.91)           | 70                          | 16                          | 1.00 (0.44, 2.23)           | 241                          | 61                          | 0.95 (0.63, 1.43)           | 0.61 0.21 0.37                |
| High                 | 61                          | 16                          | 0.92 (0.37, 2.83)           | 69                          | 21                          | 1.74 (0.69, 4.37)           | 241                          | 61                          | 1.15 (0.72, 1.83)           | 0.63 0.21 0.37                |
| Social Instability<sup>b</sup> |                       |                             |                             |                             |                             |                             |                             |                             |                             | 0.63 0.21 0.37                |
| Low                  | 62                          | 18                          | ref                         | 71                          | 17                          | ref                         | 253                          | 70                          | ref                         | 0.63 0.21 0.37                |
| Medium               | 60                          | 15                          | 0.89 (0.39, 2.07)           | 69                          | 17                          | 1.10 (0.49, 2.45)           | 249                          | 62                          | 0.92 (0.61, 1.39)           | 0.63 0.21 0.37                |
| High                 | 61                          | 16                          | 0.95 (0.36, 2.50)           | 69                          | 20                          | 1.59 (0.66, 3.84)           | 240                          | 65                          | 1.11 (0.70, 1.78)           | 0.63 0.21 0.37                |

OR = Odds Ratio obtained with conditional logistic regression; All controls are matched to cases by year of birth, sex and first year of employment
Ref = reference group

<sup>1</sup>Number of days with logged runs on a 24 hr ambulance
<sup>2</sup>Switches between rotating-shift period and recovery period; where recovery = dayshifts + days without emergency runs
<sup>3</sup>Average length of rotating-shift work / average length of recovery; where recovery = dayshifts + days without emergency runs
<sup>4</sup>Number of emergency runs
<sup>5</sup>Number of emergency runs with sirens
<sup>6</sup>Number of changes in partners
Increased workload also showed a consistent elevated risk with CCS and HTN. Tests for additive interaction of workload with (1) ratios and (2) frequency of changes between shift work and recovery periods were negative and did not show any significant effects (Table 4.4).

### Table 4.4 Additive interaction effects of workload and (1) number of shift changes between shift work and non-shift work; and (2) ratio of average length of shift work to recovery, for chronic coronary syndrome and hypertension outcomes

#### Chronic Coronary Syndrome

<table>
<thead>
<tr>
<th>Workload</th>
<th>Frequency of changes between shift work and recovery</th>
<th>Ratio of average length of shift work to recovery period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Changes</td>
<td>Shift work and recovery periods</td>
</tr>
<tr>
<td>OR(N)</td>
<td>OR(N)</td>
<td>OR(N)</td>
</tr>
<tr>
<td>Low</td>
<td>1 (90)</td>
<td>1.97 (15)</td>
</tr>
<tr>
<td>High</td>
<td>2.64 (23)</td>
<td>2.02 (81)</td>
</tr>
</tbody>
</table>

#### Hypertension

<table>
<thead>
<tr>
<th>Workload</th>
<th>Frequency of changes between shift work and recovery</th>
<th>Ratio of average length of shift work to recovery period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Changes</td>
<td>Shift work and recovery periods</td>
</tr>
<tr>
<td>OR(N)</td>
<td>OR(N)</td>
<td>OR(N)</td>
</tr>
<tr>
<td>Low</td>
<td>1 (320)</td>
<td>1.7 (51)</td>
</tr>
<tr>
<td>High</td>
<td>1.22 (109)</td>
<td>1.17 (262)</td>
</tr>
</tbody>
</table>

OR = Odds Ratio obtained with conditional logistic regression, matching cases to controls by sex, age and year of first employment

N = number of observations

1 Switches between rotating-shift period and recovery period; where recovery = dayshifts + days without emergency runs

2 Average length of rotating-shift work / average length of recovery; where recovery = dayshifts + days without emergency runs

a) Combined effects of workload with frequency of shift changes between shift work and recovery, for chronic coronary syndrome outcome. Exposure groups were dichotomized into Low and High categories for workload measure, and Exposed and Not Exposed for shift work variable.

b) Combined effects of workload with ratio of average length of shift work to recovery period, for chronic coronary syndrome outcome. Exposure groups were dichotomized into Low and High categories for workload measure, and Exposed and Not Exposed for shift work variable.

c) Combined effects of workload with frequency of shift changes between shift work and recovery, for hypertension outcome. Exposure groups were dichotomized into Low and High categories for workload measure, and Exposed and Not Exposed for shift work variable.

d) Combined effects of workload with ratio of average length of shift work to recovery period, for hypertension outcome. Exposure groups were dichotomized into Low and High categories for workload measure, and Exposed and Not Exposed for shift work variable.
4.5 Discussion

The purpose of this study was to examine the association of shift work with acute coronary syndrome, chronic coronary syndrome and hypertension. Studies have shown that work at night may result in neuroendocrine dysregulation; and it has been speculated that chronic neuroendocrine augmentation without sufficient recovery may result in permanent changes in cardiovascular functioning, and may, in turn, lead to heart disease. We hypothesized that shift work may be associated with chronic and not acute heart disease.

Two of our three shift work exposure measures showed a positive, but not significant, association with chronic forms of heart disease. Risk of ACS was not associated with any shift work exposure; in fact, results suggested that there may be a protective effect for ACS with cumulative duration of shift work (p > 0.05). This pattern of results follows what is generally believed about the progression of heart disease: chronic heart disease may be associated with neuroendocrine dysregulation and accelerate coronary plaque development; whereas acute coronary events may be attributed to increased cardiovascular reactivity resulting in plaque ruptures. It could be speculated that alterations of neuroendocrine activity attributed to shift work may not be sufficient enough to increase blood flow to dislodge coronary plaques leading to thrombosis. However, confidence intervals were wide and did not conclusively support this hypothesis.

Studies identified in a systematic review by Frost et al., have grouped acute and chronic coronary syndromes as one outcome (OR range: 0.9 to 2.32). Our risk estimates for chronic coronary syndrome (OR range: 1.10 to 1.79) were similar to these findings, but our acute coronary syndrome risk estimates (OR range: 0.25 to 0.88) fell below this range. This could suggest that an elevated risk may be associated for chronic but not for acute outcomes, but has not been examined until this present study. Our hypertension risk estimates (OR range: 0.69 – 1.37) were not significant,
however, they were similar to those reported in 3 longitudinal studies that found rotating-shift work was significantly associated with an increased risk of hypertension (OR range: 1.10 to 1.81)\(^{75,76,90}\). Future studies should also consider examining ACS, CCS and HTN separately to explore the hypothesis that shift work may be closely related to chronic heart disease, but not acute coronary events.

We also explored the role that recovery time may play in mitigating the risk of CVD. To improve on prior measures of shift work exposure, 2 novel metrics were developed which incorporated recovery from work at night: (1) the number of times a paramedic switched between shift work and recovery periods; and (2) the length of the average length of shift work and the average length of recovery. Cumulative duration of shift work was also included as a comparative measure to assess if our new metrics improved upon exposure assessment. We hypothesized that increasing risk of CVD would be observed with: (1) increasing frequency of changes between shift work and recovery periods would result in increased risk of chronic CVD; and (2) increasing length of shift work periods in conjunction with shorter periods of recovery. We also hypothesized that the broad category of cumulative duration would result in misclassification error, and bias risk estimates towards the null.

Elevated risks of chronic coronary syndrome and hypertension were observed with both shift work variables that included recovery periods but not with cumulative duration of shift work. However, the confidence intervals were wide and included 1, and neither showed clear exposure-response trends. This limits support for our hypotheses. In addition, the high correlation between the two variables that included recovery periods prohibited our ability to determine whether recovery length or number of recovery periods may be more beneficial to worker health. Results may be have been spurious, but are intriguing, and we hope that There are several limitations in this study. Secondary analysis of administrative data did not allow us to control for modifiable non-occupational
individual-level attributes that may be important risk factors for heart disease such as psychosocial factors, diet, physical fitness, smoking and alcohol consumption. We were also unable to assess the use of antithrombotic agents, such as aspirin, which may act as protective factors against CVD. Exclusion of these potential confounders, if they are correlated with exposure, may result in over- or under-inflated risk estimates. Due to the multi-factorial nature of CVD, it is difficult to control for all potential confounders, however, the matched case-control design did account for two important CVD risk factors (i.e. age and sex).

It is thought that shift work may be associated with lower socioeconomic status and adverse lifestyle factors. However, because our study was an internal comparison that examined: (i) only one occupational group which required the same level of certified training; and (ii) employees working for the same employer, all our workers are presumed to have similar education and income levels. This may suggest that education and income may not be confounding the relationship between shift work and heart disease among this study cohort.

Three major mechanisms have been identified linking shift work with heart disease: behavioural influences (e.g. diet), psychosocial stress (e.g. work stress) and physiological dysregulation (e.g. neuroendocrine activity). We were not able to assess dietary differences between groups, but at least one study has found no dietary differences between night and day workers. It is suggested that it is not the nutritional consumption, but rather the timing of meals that may lead to circadian desynchronization of metabolism and contribute to increased cholesterol levels among shift workers. Measures of psychosocial stress, such as those in the workplace, were also not available. Workplace stress is considered to be a strong risk factor for heart disease and it is hypothesized that people who work at night are subject to higher psychosocial stress than those who work during the day. This may be attributed to different work environments and tasks at night in comparison to
day. However, our study population was restricted to paramedics whose primary task was to attend emergencies irrespective of time of day. Those who work at night are most likely to be sleep deprived which can lead to sensitization of stress perception and eventually to stress-related disorders. This suggests that in comparison to those who work only during the day, those who work at night may perceive the same situation as being more stressful, leading to overactivation of the neuroendocrine systems. However, while many factors, such as diet and job strain, have been identified as lying on the causal pathway between shift work and CVD; adjustments for these factors may result in biased estimates.

We did not have any baseline measures of workers and it is possible that people with adverse health behaviours self-selected into shift work. However, bias attributed to primary selection into shift work may be diminished because paramedics entering the British Columbia Ambulance Service must pass a physical exam and are required to be in good health. By matching cases to controls on year of first employment, we compared paramedics with similar seniority level and choice of shift schedule. Those with more seniority have higher priority to choose their schedule and it is possible that secondary selection may occur among those with health problems who give up shift work. This would attenuate any association and the actual risk may be greater than what we found.

Finally, it was also unknown if a paramedic characterized as working a rotating-shift schedule was active on the day or night shift. However, two previous studies showed altered neuroendocrine functioning among rotating-shift workers during a day shift, even after 4 days off work. This suggests that our general characterization of rotating-shift work periods should be sufficient to capture periods of circadian disruption.

The main strength in our study is the quality of data used to derive shift work exposure. Most previous studies have used either self-reports of exposure which may be subject to recall bias; or
baseline measures of shift work that do not account for time away from work at night, which may negate adverse effects of circadian disruption. Our emergency run data provided a daily record of activity over 11 years of follow-up and may be the most accurate record of temporal pattern of shift work to date.

Most prior studies investigating shift work and CVD have been multi-occupational making it difficult to control for all occupational confounders. Restricting our study population to one job type minimized the influence of occupational confounders that have been associated with shift work and heart disease. In addition, there were only 2 primary shift types (i.e. rotating and daytime only), reducing the possibility of exposure misclassification and biasing risk estimates towards the null.

Overall, study results were non-significant and no dose-response effects were evident; therefore results should be interpreted cautiously. However, this present study provides several unique contributions to the current body of knowledge. We developed novel shift work metrics incorporating the underlying theories of neuroendocrine dysregulation and cycles of recovery. Including recovery periods may refine long-term exposure assessments and provide a better risk estimate than broad categories. In addition, this is the first study we are aware of that examined shift work with separate forms of heart disease to gain a better understanding of the role shift work may play in the progression of heart disease. We consider our analyses to be exploratory and encourage more research to consider using these novel approaches to examine the risk of CVD associated with shift work.
5 EMERGENCY RUNS AS TRIGGERS OF ACUTE CORONARY EVENTS AMONG PARAMEDICS

5.1 Synopsis

The purpose of this chapter is to examine whether exposure to emergency runs can trigger acute coronary events among paramedics. Survey responses and previous literature were used to categorize perceived levels of stress associated with different types of emergencies. Detailed exposure information concerning emergency runs was ascertained with data provided by the BC Ambulance Service. Information regarding hospitalizations for, and underlying causes of death attributed to, acute coronary syndrome (ACS) was obtained through hospitalization discharge records and death registry information provided by the BC provincial government.

We hypothesized busier-than-normal work days, high-stress emergencies and discrepancies between dispatched information with actual diagnoses by paramedics at the scene may trigger ACS similarly as anger, negative emotions, physical exertion and working under pressure. We also hypothesized secondary traumatic stress may delay onset of ACS after exposure to emergency run stressors.

Results suggested that attending emergency runs and discrepancies between dispatched information and diagnosis of emergency at the scene posed an increased, but non-statistically significant, risk of acute coronary syndrome; and there may be a delay in disease onset following exposure. We also found the greatest risk of ACS occurred 3 days after experiencing high-stress emergencies. This finding suggests that current post-hoc stress debriefing sessions may not be effective at combating mental distress. Recommendations to develop more comprehensive, on-going organizational and educational programs to help paramedics develop long-term coping skills to reduce psychological strain should be considered. While it may be speculated that negative emotions, anger or work-
related time pressures associated with emergency runs may be the underlying triggers of acute coronary events, future research should be considered to explore this hypothesis.

A version of this chapter is in preparation for submission to Annals of Emergency Medicine.

5.2 Introduction

Paramedic work has been identified as a highly stressful occupation, due to its regular exposure to trauma and human tragedy. Their work environment has also been described as one of extremes: periods of inactivity while waiting at an ambulance station or hospital, punctuated with peaks of physical activity and psychological strain during emergency runs. Attending to life-threatening situations often requires paramedics to work under extreme time pressures, and as a consequence of dealing with traumatic emergencies, paramedics have reported experiencing feelings of depression, anger and negativity.

Secondary traumatic stress has been reported to be prevalent among paramedics after exposure to critical incidents such as large-scale motor vehicle accidents and disasters. While at the scene of an emergency, paramedics’ expertise and training may “take over” allowing them to perform effectively, and it is not until they have had time to ruminate about the incident that an elevated stress response occurs. It has been estimated that this delayed response occurs in approximately 50% of ambulance paramedics after they have had time to think about their experience following administration of medical treatment to patients.

Discrepancies in information dispatched to ambulance paramedics may also contribute to feelings of stress. Emergencies requiring an ambulance are telephoned to dispatch centers that assess the situation and relay information to paramedics who attend the scene. Receiving accurate emergency information prior to arrival is crucial to helping paramedics prepare physically and psychologically.
While anticipation of future stress may be associated with increased risk of myocardial ischemia through activation of neuroendocrine systems \(^{220}\), it has also been shown that those who are not adequately prepared mentally or physically for a stressor may not be able to effectively cope and recover \(^{221}\). In a recent qualitative study exploring the consequences of interactions between health care providers, at-home caregivers reported that receiving misinformation from health professionals limited their ability to provide appropriate medical care to their patients and contributed to their feelings of frustration and anger \(^{222}\).

Exposure to emotionally upsetting events, feelings of anger, working under time pressures or short bursts of physical exertion have been shown to produce adrenergic surges and may trigger the onset of myocardial infarction \(^{223-227}\). It is believed that chronic exposure to stress without sufficient recovery can alter neuroendocrine functioning, damage blood vessels and accelerate arterial plaque buildup leading to chronic heart disease \(^{22,110}\); and that the underlying cause of most acute coronary events is attributed to plaque rupture. This may occur when external factors, such as intense psychosocial stressors increase, blood flow and shear stress on vessel walls, resulting in plaque instability \(^{111}\).

In this study, our primary question was “Can emergency runs trigger acute coronary syndrome among paramedics?”. Our secondary question was “Is there a delayed acute coronary onset after experiencing stressful emergencies?”

### 5.3 Methods

#### 5.3.1 Study population and case definition

This case-crossover study draws its cases from a retrospective cohort of all ambulance paramedics employed by the British Columbia Ambulance Service (BCAS) between 1990 and 2002. Paramedics
were included in the cohort if they (1) worked as an ambulance paramedic and attended emergencies between April 1990 to March 2002; (2) were employed by the BCAS for at least one year prior to 2002; (3) were registered for provincial medical insurance for at least one year after start of employment; and (4) were between the ages of 17 to 65 on commencing employment.

Cases of acute coronary syndrome (ICD9: 410-411) during the study follow-up (1990 – 2002) were identified from hospitalization and death registry records provided by the British Columbia (BC) Linked Health Database. These records include information such as dates of deaths or hospitalizations for almost all BC residents, the medical reasons for hospitalizations and underlying causes of death recorded on death certificates. Multiple incidences of acute coronary syndrome (ACS) per paramedic were included in the analyses and treated as independent events if they were at least 6 months apart. For incidents less than 6 months apart, the first incident was used for analyses and subsequent incidents within 6 months were not included.

5.3.2 Exposure variables: potential triggers of acute coronary syndrome

Two main sources of information were used to derive exposures related to emergency runs which may act as triggers of ACS:

(i) a mail survey to a random sample of paramedics (n= 460) employed by the BCAS. This survey asked paramedics to rank their perceptions of stress related to 13 ambulance-specific tasks and emergencies on a 5-point Likert Scale. These specific tasks and emergency types were developed in consultation with BC Ambulance management and union representatives

(ii) emergency run data provided by the BCAS. This included information about every run attended by paramedics during the study period, including: the date the emergency occurred, the type of emergency as it was defined by the dispatcher initially to paramedics (i.e.
anticipated stressors), and the type of emergency it was diagnosed at the scene by paramedics (i.e. experienced stressors). The dispatched and diagnosed emergencies were recorded using identical BCAS-designated codes by paramedics who attended the scene.

We hypothesized 3 types of emergency-run related stressors that may trigger acute coronary events:

1) Frequency of emergencies. On days with emergency runs recorded, paramedics on average, attended 1 to 2 emergencies. Based on this finding, we considered days with 3 or more emergencies as ones that were busier than normal and may act as triggers of ACS. Attending 1 or 2 runs was considered as an average day and “days with no emergency runs” was the reference category.

2) Differences between dispatched and diagnosed emergencies. We hypothesized that discrepancies between information provided about the emergency and the actual emergency would be associated with ACS onset. Two categories of discrepancies were identified:

   • No patient care: defined as frequency of emergencies that do not require any patient care. This was defined as emergencies with a dispatch code, but no diagnostic code following BCAS definitions. This includes emergencies that are terminated on the way to the scene, or is designated by the paramedic at the scene that no care is required

   • Patient care required: defined as the frequency of emergencies where medical diagnoses at the scene differed from what was dispatched

2) Severity of emergency. We hypothesized that witnessing high-stress emergencies, would elicit a strong stress response to trigger ACS onset. Exposure to low-stress emergencies was also explored. The reference group was defined as days without any emergencies.
A series of steps were taken using different data sources to identify emergency types as high-, medium- and low-level stressors (Figure 5.1):
Figure 5.1 Steps taken to categorize emergencies into high, medium and low stressors using survey responses, existing literature, dispatch and diagnostic codes and patient care codes. Step 1: rank survey responses of typical emergency types from most to least stressful. Step 2: Use existing literature to group survey responses into categories of High, Medium and Low levels stressors. Step 3: Use patient care codes to match dispatch and diagnostic codes of emergency types to survey responses. Step 4: Apply categories of High, Medium and Low stressors from survey responses to dispatch and diagnostic codes.
Step 1) Survey responses to perceived stress of paramedic tasks were ranked by mean scores of severity.

Step 2) To group survey responses into categories of high-, medium- and low-level stressors, we used existing studies in which paramedics ranked serious operational tasks (e.g. taking care of seriously injured or dying patients) as being high-level stressors and non-emergency tasks (e.g. patient-transfers) as being the lowest-level stressors related to ambulance work.  

Step 3) To align the detailed categories of dispatched and diagnosed emergencies from the emergency run data with the broad categories of stressors from the survey, we used BCAS-designated patient care codes which included broad categories of emergencies with detailed descriptions.

Step 4) Categories of high-, medium- and low-stress runs from the survey responses were applied to the emergency run data dispatch and diagnostic codes (Table 5.1).
Table 5.1 Summary of survey rankings, primary care codes and dispatched and diagnosed codes grouped into categories of high, medium and low-stress emergencies; and frequency of dispatched and diagnosed emergencies

<table>
<thead>
<tr>
<th>Categories of Perceived Stress¹</th>
<th>Survey Rankings</th>
<th>Primary Care Codes (major categories and detailed descriptions)</th>
<th>Dispatch and Diagnosis Categories</th>
<th>Dispatch Frequency</th>
<th>Diagnosis Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Items</td>
<td>Mean Score²</td>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>High</td>
<td>Multiple Casualties</td>
<td>3.61</td>
<td>Major Trauma - e.g. pulseless (traumatic, with and without resuscitation), motor vehicle accident, gunshot, stabbing, falls, assault, other major trauma</td>
<td>Cardiac Arrest 682</td>
<td>0.6% 788 0.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chest Pain - Myocardial Infarction 6,127</td>
<td>5.1% 2,586 2.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Congestive Failure 218</td>
<td>0.2% 426 0.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dead on Arrival 259</td>
<td>0.2% 360 0.3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Drowning 60</td>
<td>0.0% 19 0.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Head Injury 592</td>
<td>0.5% 835 0.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hemorrhage 540</td>
<td>0.4% 484 0.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Interpersonal violence 1,623</td>
<td>1.4% 427 0.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Motor Vehicle Accident 10,570</td>
<td>8.8% 1,905 1.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Spinal Trauma 443</td>
<td>0.4% 1,336 1.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Trauma - Major 660</td>
<td>0.5% 629 0.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Burns 237</td>
<td>0.2% 202 0.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Fracture 1,396</td>
<td>1.2% 3,244 2.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Trauma Minor Cuts 1,827</td>
<td>1.5% 5,070 4.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Collapse Found Down 9,547</td>
<td>7.9% 2,016 1.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Coma 34</td>
<td>0.0% 19 0.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Neuro / Cerebrovascular Accident 2,048</td>
<td>1.7% 2,209 1.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Seizure 2,838</td>
<td>2.4% 1,788 1.5%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Drug Alcohol Overdose 2,423</td>
<td>2.0% 1,913 1.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Altered Level of Consciousness - e.g. seizures, hypoglycemia, persyncope, syncope, cerebrovascular accidents</td>
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<tr>
<td></td>
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<td></td>
<td>Minor Trauma – e.g. burns (greater than or less than 20% body surface area), dislocation of hip or extremities, soft tissue injury (lacerations, wounds, pain), other minor trauma</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Overdose / Poisoning – e.g. narcotics,</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>Motor Vehicle Accidents</td>
<td>2.91</td>
<td>Altered Level of Consciousness – e.g. seizures, hypoglycemia, persyncope, syncope, cerebrovascular accidents</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>Fatalities</td>
<td>2.87</td>
<td>Minor Trauma – e.g. burns (greater than or less than 20% body surface area), dislocation of hip or extremities, soft tissue injury (lacerations, wounds, pain), other minor trauma</td>
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<tr>
<td></td>
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<td></td>
<td>Fracture</td>
<td>1,396</td>
<td>1.2% 3,244 2.7%</td>
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<td></td>
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<td></td>
<td>Burns 237</td>
<td>0.2% 202 0.2%</td>
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<td></td>
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<td>0.0% 19 0.0%</td>
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<td></td>
<td></td>
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<td>Neuro / Cerebrovascular Accident 2,048</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Altered Level of Consciousness – e.g. seizures, hypoglycemia, persyncope, syncope, cerebrovascular accidents</td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Minor Trauma – e.g. burns (greater than or less than 20% body surface area), dislocation of hip or extremities, soft tissue injury (lacerations, wounds, pain), other minor trauma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Categories of Perceived Stress</td>
<td>Survey Rankings</td>
<td>Primary Care Codes</td>
<td>Dispatch and Diagnosis Categories</td>
<td>Dispatch Frequency</td>
<td>Diagnosis Frequency</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>----------------</td>
<td>-------------------</td>
<td>-----------------------------------</td>
<td>--------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td></td>
<td>Items</td>
<td>Mean Score</td>
<td>(major categories and detailed descriptions)</td>
<td></td>
<td>n</td>
</tr>
<tr>
<td>5. Medical</td>
<td>2.66</td>
<td>tricyclic, overdose/poisoning with altered level of consciousness, carbon monoxide poisoning, smoke inhalation</td>
<td>Arrhythmia</td>
<td>162</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cardiac / Dysrhythmia – e.g. Ischemic chest pain, non-cardiac chest pain, symptomatic bradycardia</td>
<td>Chest Pain - Other</td>
<td>2,727</td>
<td>2.3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dyspnea – e.g. upper airway obstruction, asthma, respiratory arrest</td>
<td>Airway Obstruction</td>
<td>201</td>
<td>0.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gastrointestinal Illness (GI) – e.g. GI bleed, nausea, other GI</td>
<td>Respiratory / Short of Breath</td>
<td>7,694</td>
<td>6.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obstetrics / Gynecology – e.g. first, second, third trimester</td>
<td>GI / Abdominal Pain</td>
<td>3,450</td>
<td>2.9%</td>
</tr>
<tr>
<td>Low (non-emergency)</td>
<td>1.97</td>
<td>Miscellaneous – e.g. psychological, transfer, headache, back pain (non-traumatic)</td>
<td>Obstetrics / Maternity</td>
<td>547</td>
<td>0.5%</td>
</tr>
<tr>
<td>6. Non-emergency</td>
<td></td>
<td>Chronic Disorder</td>
<td>Diabetes</td>
<td>943</td>
<td>0.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infectious Disease</td>
<td>1,252</td>
<td>1.0%</td>
<td>878</td>
</tr>
<tr>
<td>7. Patient Transfers</td>
<td>1.37</td>
<td>Psychiatric Behaviour</td>
<td>1,889</td>
<td>1.6%</td>
<td>1,767</td>
</tr>
<tr>
<td>8. Interhospital Transfers</td>
<td>1.37</td>
<td>Transfer</td>
<td>27,810</td>
<td>23.2%</td>
<td>15,660</td>
</tr>
<tr>
<td>Other (not specified)</td>
<td></td>
<td>Other (not specified)</td>
<td>Error in Coding</td>
<td>23,341</td>
<td>19.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Missing</td>
<td>7,849</td>
<td>6.5%</td>
<td>717</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TOTAL NUMBER OF EMERGENCIES</td>
<td>12,616</td>
<td>10.5%</td>
<td>120,093</td>
</tr>
</tbody>
</table>

1 Derived from existing literature 229,230
2 Responses from mail survey sent to a random sample of paramedics (n=1000), with a 46% response rate. Respondents were asked to rank typical paramedic situations and emergencies on a 5-point Likert Scale (1=low, 5 = high).
5.3.3 Statistical analysis

A case-crossover design was used to explore the transient effects of stress from emergency runs on the risk of acute coronary syndrome. In this design, each paramedic served as his or her own control thus eliminating important between-person confounders for coronary heart disease such as age, sex and health behaviours (that are unlikely to change over the short study period). It also controls for past experiences such as exposure to traumatic events and each person's inherent ability to cope with stressors. Exposures during a “hazard period” were compared with “control periods” to identify if the increased probability of an “unusual” exposure occurring during the hazard period triggered an acute coronary event.\(^{231}\)

To determine the length of hazard period, we used existing literature which reported that other acute work-related anger, negative emotions and physical exertion could trigger an acute coronary event within 1-2 hours of exposure\(^ {227,232}\) and that work-related time pressures could trigger an acute coronary event within 24 hours\(^ {223}\). Because our exposure and health outcome records were recorded by date of occurrence, “day” was the smallest time unit in our data and was chosen as the unit of hazard period. Single-lag modeling was then used to identify the potential delayed effects of secondary traumatic stress. This type of modeling is common among air pollution studies using a case-crossover design to explore delayed effects of air pollution associated with cardiac mortality\(^ {233,234}\). We lagged exposures by 1 to 4 days prior to ACS onset, allowing for several induction times (i.e. time from exposure to disease onset)\(^ {113}\) to be investigated. A parsimonious multiple intervals approach\(^ {235}\) was used to compare risk during hazard periods to 4 randomly chosen control days, outside of the lag period, in the month prior to acute coronary onset.

We also considered if position on the paramedic team (i.e. driving paramedic or attending-only paramedic) would have an influence on risk estimates. Prior studies have shown increased
neuroendocrine activity among drivers in comparison to attending-only paramedics\textsuperscript{112}. This may be attributed to additional stress associated with driving, particularly at high-speeds during emergencies\textsuperscript{190}.

Conditional logistic regression was used to account for the matched design by individual. Separate analyses were conducted for each exposure variable. All statistical analyses were performed using Stata 11.2 (StataCorp LP, College Station, Texas, USA).

5.4 Results

5.4.1 Cohort description

A total of 5,873 paramedics were employed by the BC Ambulance Service between April 1990 to March 2002 and met the inclusion criteria. From this cohort, 95 were hospitalized for, or whose deaths were attributed to, ACS as the underlying cause. We excluded 42 paramedics who were hospitalized or died outside of the study period because we would not be able to ascertain their immediate exposure histories prior to ACS onset. The final cases consisted of 65 separate hospitalizations at least 6 months apart and 2 deaths among 53 paramedics (48 men, 5 women). Each event was treated independently. A majority of the subjects (n = 43) only had 1 hospitalization for ACS and 10 paramedics had multiple incidents of ACS onset (9 had 2 events and 1 had 4 events) during the study follow-up period.

The mean age of all cases at ACS onset was 52.9 years (SD 7.7 yrs), with mean length of employment of 22.1 years (SD 8.7 yrs) and mean follow-up of 6.4 years (SD 3.2 yrs). During the follow-up period, paramedics attended emergencies approximately 25% of the time. Just over 120,090 emergencies were dispatched during between 1990 - 2002. Over half (57.2%) were dispatched as a different type of emergency than what was diagnosed at the scene, and almost 40%
of dispatched emergencies did not require any patient care. High-stress emergencies accounted for almost 18% of all emergencies dispatched but only represented 8% of emergencies diagnosed by attending paramedics.

5.4.2 Emergency run-related triggers of acute coronary syndrome (ACS)

Overall, no significant results were found (Table 5.2). Confidence intervals were wide and included unity, suggesting that the true risk of ACS may not have differed from days with no emergency runs. However, a consistent pattern of elevated risks of ACS were observed 1 to 4 days following exposure to all emergency types examined in this study. It appeared that there may not be any increased risk for ACS on the day of disease onset.

There was little difference between ACS risk for days with 1 or 2 emergencies (OR range: 1.30 - 1.70) and those with 3 or more (OR range: 0.99 - 1.65). The risks associated with differences between dispatched and diagnosed emergencies, were also non-significantly elevated. Risk of ACS associated with emergencies that did not require patient care ranged from 1.20 to 1.89 for 1 to 4 days after exposure, in comparison to days without any emergencies. The risk of ACS associated with differences between dispatched and diagnosed emergencies requiring patient care was similar but only elevated 1 to 3 days following exposure (OR range: 1.18 to 1.83) and not elevated on the 4th day (OR 0.57, 95% CI: 0.15 – 2.19).
Table 5.2 Odds ratios for acute coronary syndrome associated with emergency run-related exposures

<table>
<thead>
<tr>
<th>Induction time¹</th>
<th>Day of ACS onset ²</th>
<th>1 day after exposure²</th>
<th>2 days after exposure²</th>
<th>3 days after exposure²</th>
<th>4 days after exposure²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure</td>
<td>Cases exposed</td>
<td>OR (95% CI)</td>
<td>Cases exposed</td>
<td>OR (95% CI)</td>
<td>Cases exposed</td>
</tr>
<tr>
<td>Frequency of Emergency Runs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No emergency runs (reference)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1 or 2 runs / day³</td>
<td>2</td>
<td>0.55 (0.12 – 2.66)</td>
<td>5</td>
<td>1.70 (0.52 – 5.51)</td>
<td>2</td>
</tr>
<tr>
<td>3 + runs / day³</td>
<td>4</td>
<td>0.62 (0.16 – 2.39)</td>
<td>5</td>
<td>0.99 (0.30 – 3.26)</td>
<td>8</td>
</tr>
<tr>
<td>Severity of Diagnosed Emergencies (no emergencies = reference)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-level stressors³,⁴</td>
<td>0</td>
<td>–</td>
<td>1</td>
<td>1.40 (0.14 – 13.6)</td>
<td>1</td>
</tr>
<tr>
<td>Low-level stressors³,⁵</td>
<td>2</td>
<td>0.86 (0.16 – 4.68)</td>
<td>2</td>
<td>1.08 (0.19 – 5.98)</td>
<td>3</td>
</tr>
<tr>
<td>Difference between Dispatched and Diagnosed (no emergencies = reference)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No patient care³,⁶</td>
<td>5</td>
<td>0.69 (0.21 – 2.31)</td>
<td>7</td>
<td>1.20 (0.42 – 3.46)</td>
<td>8</td>
</tr>
<tr>
<td>Patient Care required³</td>
<td>2</td>
<td>0.31 (0.07 – 1.46)</td>
<td>6</td>
<td>1.18 (0.41 – 3.46)</td>
<td>7</td>
</tr>
</tbody>
</table>

¹ time from exposure to ACS onset
² 4 randomly chosen control days from Days 5 to 30 after date of onset of Acute Coronary Syndrome
³ Reference group = no emergencies
⁴ High stressors = multiple casualties, fatalities, motor vehicle accidents
⁵ Low stressors = non-emergency tasks, transfers
⁶ Emergency was dispatched, but no medical care was administered (i.e. no diagnostic code)
Experiencing high-stress emergencies such as fatalities or multiple casualties was associated with non-significant increased risk for ACS, on days 1, 2, 3, and 4 following exposure (OR range: 1.40 – 5.29). The greatest risk of an acute coronary event (OR: 5.29, 95% CI: 0.84 – 33.12) was observed 3 days after experiencing a high-stress emergency. No high-stress emergencies occurred on day of ACS onset. Exposure to low-stress emergencies such as patient transfers resulted in non-significant increased risks 1 to 4 days following exposure (OR range: 1.08 – 1.72), but not on the day of ACS onset (OR 0.86; 95% CI: 0.16 – 4.68). A sensitivity analyses was completed using different time frames to choose control periods (i.e. 2 weeks vs. 1 month prior to ACS onset) and different number of control periods (i.e. 4 randomly chosen days vs. all days in the remainder of the month). Using shorter time frames to choose control periods resulted in increased elevated risks and larger confidence intervals. Increasing the number of controls resulted in slight attenuation of risk estimates and narrower confidence intervals. However, the pattern in risk estimates with each exposure variable remained the same.

Examination of a subject’s position within the paramedic team during hazard and control periods showed equal frequency of drivers and attending-only paramedics. This could be expected since paramedics may switch team positions frequently to share in different responsibilities. However, the additional stress of driving may be considered as being on the causal pathway between emergency run stress and acute coronary events; therefore, it was not considered as a potential confounder.

5.5 Discussion

The purpose of this study was to examine if stress related to emergency runs was associated with ACS onset. We hypothesized that stressful situations, such attending 3 or more emergencies per day, high-stress emergencies, and discrepancies between information obtained from dispatcher and the actual emergency, may trigger acute coronary events among paramedics. We also considered that a
delay in ACS onset may occur after exposure to stressful events as a result of secondary traumatic stress. However, all results were non-significant making it difficult to draw conclusions on our hypotheses.

Borderline significance was observed following 3 days after exposure to a high-stress emergency, where the risk for triggering ACS was almost 5-fold in comparison to days without emergencies. This risk estimate is similar in range to those found in previous studies for negative emotions as a trigger of acute coronary events (RR range: 3.0 – 14.0)\textsuperscript{225,232}. Our findings suggest that there may be a delayed onset of a neuroendocrine response to stressors which could be attributed to secondary traumatic stress after attending emergencies. While the BCAS does provide post-hoc Critical Incidence Stress Debriefing sessions in the days following traumatic events\textsuperscript{236}, it has been shown that these psychological debriefing sessions are not effective and may even be harmful\textsuperscript{236,237}. Results from our current study also support these concerns that ad-hoc debriefing sessions may not be effective at treating psychological strain among paramedics.

There are several limitations to our study. The multi-step method used to group emergencies into high, medium and low-stress categories provided possibilities for non-differential misclassification exposure. However, the majority of emergencies dispatched and diagnosed were transfers (23.2% and 13.0%, respectively) and other not specified (19.4% and 10.5%, respectively). The frequency of other individual categories of emergencies was very low (< 8%) and would have little impact on overall exposure assessment.

In our emergency run data, we did not have information to distinguish between days when paramedics were not working and days they were working but did not attend any emergency runs. However, we grouped both situations together as the reference category. Studies have shown that some paramedics find work days with few or no emergency runs more stressful than days with
frequent emergencies. A study of merchant marine engineers found that on nights they were allowed to sleep on duty, but were not wakened by an alarm to repair malfunctioning machinery, they exhibited physiological responses of anticipatory stress (i.e. reduction of deep sleep), in comparison to nights when they were not working. Therefore, our use of days without emergency runs as a reference category may not have been a suitable comparison group for our exposure measures and have resulted in an underestimation of the true risk. Future studies should also separately examine days when paramedics were working but did not have any emergency runs.

Both exposure and health data used in this study was recorded by date only, which prohibited our ability to obtain an exact measure of time between trigger and ACS onset. Instead, our use of ‘date’ of trigger and ACS onset resulted in overlapping ranges in induction times and reduced precision in risk estimates.

The definition of “no patient care” may have been problematic. This variable was defined as one with a dispatch code but no corresponding diagnostic code. While no diagnostic code may have indicated that the dispatched call was terminated or did not require medical at the scene, it could have also been attributed to clerical error and non-completion of the reporting form. This may have resulted in exposure misclassification and biased estimates.

The major strength of this study is the case-crossover design. Self-matching eliminates between-subject confounding such as important individual-level confounders for heart disease. It also reduces the effects of past experiences, chronic exposures and accounts for each person’s inherent coping mechanisms.

While it is often said that chronic diseases such heart disease have long induction periods, this statement can be misleading. The pathologic process of chronic diseases can start with early-acting
initiators but requires late-acting components with short induction times to complete sufficient cause for disease initiation. Without consideration of the appropriate induction period for the disease of interest can lead to attenuation of effect estimates. This suggests that using long-term exposures to work place stressors may underestimate the risk associated with acute forms of heart disease. Our study tries to address this by examining late-acting constructs related to work place stressors as triggers of acute coronary syndrome.

The use of daily work records to ascertain exposures reduced the possibility of selection bias because all cases were enrolled into the study. It also reduced information bias, considered to be of special concern in case-crossover studies, because it eliminated the reliance on participants to recall exposures (and thus recall bias) prior to disease onset. While the use of administrative data precluded our ability to ask subjects about what specific constructs related to emergency runs may have triggered ACS onset, we were able to identify perceived high-stress emergency types using survey responses.

Our study is among the first, to our knowledge, to examine if differences between anticipated and experienced stressors could trigger ACS onset. While results were not statistically significant and should be interpreted with caution, they suggest that discrepancies between how emergencies are dispatched and diagnosed may take a toll on paramedic health. Further research is needed to examine the effects related to direction or magnitude of differences between anticipated and experienced stressors may trigger ACS onset.

While it is generally agreed that paramedics work in a very stressful environment, results of this study found that the frequency of traumatic events is somewhat rare. However, the resulting psychological impact can have lasting effects that may contribute to onset of acute coronary
syndrome. Improvements to mental health programs are needed to ensure effectiveness in reducing carryover effects of traumatic events among this population.
6 CONCLUSIONS, IMPLICATIONS AND FUTURE DIRECTIONS

The three main content chapters in this dissertation were written for discrete publications in peer-reviewed journals and thus specific conclusions, policy implications and future studies were described separately in each. The purpose of this chapter is to synthesize the overall findings, highlight unique contributions to the existing body of knowledge and identify potential avenues for future research.

6.1 Objectives and key findings

The dissertation examined shift work and psychosocial stress as risk factors that may potentially increase the risk of heart disease among ambulance paramedics. The specific objectives of this dissertation were to: 1) gain an understanding of how shift work and job strain influence neuroendocrine systems and may potentially manifest into heart disease; 2) determine if results and conclusions derived from the convenience sample in Chapter 2 could be generalized to the larger population of paramedics; 3) examine if long-term shift work exposure is associated chronic and not acute heart disease; and if the influence of recovery time from work at night would mitigate the risk; and 4) examine if stress related to attending emergencies is associated with acute coronary events among paramedics.

In summary, we found that shift work and job strain adversely affected neuroendocrine systems (Chapter 2). However, further work is needed to validate job strain measures derived in this study in accordance to psychometric standards. In comparing volunteers from this study with a randomly sampled population from a prior survey, a low response rate in the survey population inhibited our ability to determine if the convenience sample in Chapter 2 is representative of the larger study population. Special concern was noted of the high prevalence of non-occupational risk factors for heart disease (i.e. obesity and sedentary behaviour) among this occupational group despite physical
and health screenings to enter the profession (Chapter 3). We hypothesized that shift work may be associated with chronic heart disease but may not create a high enough demand on the cardiovascular system to trigger an acute coronary event; and that recovery time from shift work may reduce the risk. However, while some individual results were suggestive of an association between shift work with chronic coronary syndrome and hypertension, findings were non-significant and no dose-response trends were evident; therefore, results did not conclusively support our hypotheses (Chapter 4).

We hypothesized that acute coronary events may be triggered by the frequency of emergency runs, high-stress emergencies, and discrepancies between dispatched information with diagnosis at the scene. Results suggested that the highest risk of acute coronary onset might be delayed up to 3 days after a experiencing a traumatic event (Chapter 5). However, again wide confidence intervals and non-significant results were observed, and thus results should be interpreted with caution.

6.2 Scientific contributions

6.2.1 Influences of shift work and job strain on neuroendocrine activity (Chapter 2)

This chapter examined salivary biomarkers (i.e. alpha-amylase and cortisol) and subclinical heart disease indicators (i.e. heart rate variability and endothelial functioning) in the ANS and HPA as intermediate and long-term effects of shift work and job strain. We found that shift workers and dispatch paramedics reported higher job strain than daytime-only workers and ambulance paramedics, respectively. Both high-strain groups also exhibited neuroendocrine activity on both working and rest days that are predictive of higher risk of heart disease: flatter diurnal slopes, suppressed daily production of alpha-amylase, elevated daily production of cortisol, reduced HRV, and reduced endothelial function. These results suggest that neuroendocrine dysregulation among shift workers might be activated through 2 pathways: circadian disruption and psychosocial stress
and supported theories suggested in prior reviews. Given a high study protocol compliance rate among this population (>90%) we recommend this study should be replicated in a larger population of paramedics. Further work is needed to validate the derived job strain measures using standard psychometric measures.

Our cortisol measures supported findings from a recent meta-analysis of over 100 studies which reported flatter diurnal slopes and elevated daily production with increased stress\(^{21}\). While alpha-amylase has not been studied as extensively as cortisol, our alpha-amylase findings were similar to recent studies which found flatter diurnal slopes among a group of PTSD patients (in comparison to healthy controls)\(^{241}\); and reduced alpha-amylase daily production among a cohort of children assessed as being chronically stressed using a validated interview protocol\(^{150}\).

We also found that in comparison to daytime-only workers, shift workers exhibited reduced HRV and endothelial functioning. While we used non-clinical methods to measure HRV and endothelial functioning, our results supported findings from a recent study which used gold-standard measures (i.e. electrocardiogram monitoring and ultrasound assessment of flow-mediated dilatation)\(^{182}\) and supports validation studies confirming good correlation between methods\(^{152, 153, 162}\).

Our sample size precluded the ability to observe statistically significant findings. Further studies on a larger study population (n = 250) will provide adequate study power to support the hypothesized biological pathway linking shift work and job strain to early indicators of heart disease.

### 6.2.2 Risk of acute/chronic forms of heart disease with shift work, and the influence of recovery time (Chapter 4)

Although the current evidence supporting an association between shift work and heart disease is weak, results have been mixed\(^{73}\) and may be due to quality of data (e.g. self-reported data vs.
administrative records), broad definitions of shift work (e.g. cumulative exposure), and/or combining all forms of heart disease as one outcome. Our study utilized work history information and medical records to reduce recall bias that may occur with self-reported data.

Overall, results were non-significant and no dose-response effects were observed. However, this study provides several unique contributions to the current body of knowledge. Novel shift work metrics were developed using theories of neuroendocrine dysregulation and recovery to examine if time away from shift work may reduce risk of CVD. In addition, this is the first study I am aware of that examined shift work with separate forms of heart disease to gain a better understanding of the role shift work may have in the progression of heart disease. I consider these analyses to be exploratory and hope that future studies will consider using these novel approaches to examine the risk of CVD associated with shift work.

6.2.3 Emergency runs as triggers of acute coronary events among paramedics (Chapter 5)

This is the first study to my knowledge that used administrative data in a case-crossover design to ascertain if stress experienced during emergency runs could trigger acute coronary onset among paramedics. Potential triggers such as frequency of emergencies, high-stress emergencies and discrepancies between dispatched and diagnosed emergency types posed a non-significant increased risk of ACS on days following exposure, but not on the day of ACS onset. The greatest risk was observed 3 days after exposure to the most stressful types of emergencies and may be attributed to a delayed effect of secondary traumatic stress.

What remains unknown is specifically what psychological or physical factors associated with emergency runs may trigger onset of acute coronary events. While it may be speculated that negative emotions or anger may act as triggers, future studies are needed to examine this more fully.
6.3 Synthesizing results to address gaps in previous research

The novel contributions of this dissertation have been described in detail in the preceding chapters. However, as a collective body of work, this dissertation addressed several gaps in the body of knowledge identified from previous systematic reviews (Chapter 1).

6.3.1 Developing occupation-specific standardized surveys

It has been noted that while the Job Strain Model contains language generic enough to allow for use across a variety of occupations, this approach may not be effective to help identify intervention strategies to improve worker health because the “questions are more ‘remote from actual work experiences’” 242. Therefore, the marriage of occupational-specific questionnaires with established work-stress models will improve the validity of the measures 33 and provide a sophisticated approach in developing a more complete picture of the role of work stress in the etiology of CVD 32. Our restructuring of a paramedic-specific stress questionnaire into domains of job strain categories was an exploration in providing the specificity to assess variability in job strain responses between paramedic group comparisons. I would like to encourage further psychometric validation of this scale in future studies (Chapter 2).

6.3.2 Linking epidemiologic evidence with biological markers

Kivimaki et al. suggested that to determine whether markers of early-stage atherosclerosis, such as reduced HRV, behave as mediators between the stress response and CVD, “studies directly linking epidemiologic evidence with subsequent intermediate biological mechanisms with cardiovascular endpoints are needed” 32. With respect to shift work research, Boggild et al. also noted that including markers of both atherosclerosis and homeostasis, with particular attention to circadian rhythms of
the biomarkers, should be considered to gain a better understanding of the pathophysiology of circadian misalignment with heart disease 62.

The combination of these studies in this dissertation addressed these recommendations. The study described in Chapter 2 examined neuroendocrine activity associated with shift work and job strain through salivary biomarkers representing intermediate effects of psychosocial stress, and subclinical heart disease as indicators of long-term effects of chronic exposure. We extended this further by applying these theories of underlying neuroendocrine mechanisms leading to CVD, to develop exposure variables in Chapters 4 and 5 using epidemiologic approaches to examine shift work and job stress with clinical CVD endpoints.

### 6.3.3 Reducing misclassification biases by improving exposure assessment and refining outcome measures

One of the primary limitations in previous shift work research can be attributed to use of broad exposure definitions which may include regular nights, various forms of rotating-days and nights, and irregular schedules62. While our use of one study population allowed for comparisons of only two types of shift schedules (i.e. fast-forwarding rotating vs. daytime-only) in Chapters 2 and 4, the precise shift work definition may have improved upon exposure measurements in comparison to most previous studies and may have also greatly reduced the effects of confounding that may arise with multi-occupational studies.

In a recent systematic review, Eller et al. noted that neglecting changes in exposure during long follow-up periods may result in inaccurate exposure assessments and bias results33. We examined temporal changes in shift work exposure (Chapter 4) and discovered that including periods of shift work and non-shift work in our exposure measures resulted in noticeable and consistent differences in risk estimates.
With respect to epidemiological analyses, it has been suggested that factors which are part of the causal pathway should not be controlled for in analyses. To do so may underestimate the strength of the effect of the exposure on the outcome. While hypertension is considered to be related to shift work and a precursor for CVD, in Chapter 4, hypertension was treated as a separate outcome along with acute coronary syndrome and chronic coronary syndrome, allowing us to examine the effect of shift work exposure on various stages of CVD.

6.4 Challenges and limitations

While the findings in this dissertation are unique and provide a novel contribution to the body of knowledge, as with any study, challenges were present and need to be identified to strengthen future studies.

6.4.1 Lack of statistical significance and precision in risk estimates

The small sample size and effect sizes in our pilot study described in Chapter 2 limited our ability to observe statistically significant differences between comparison groups. Wide confidence intervals reported in Chapters 4 and 5 indicated a lack of precision in risk estimates and inhibited the ability to support our hypotheses. In case-control studies, odds ratios are defined as a ratio of the odds that cases were exposed with the odds that controls were exposed. A lack of precision in our exposure variables (e.g. shift work periods, high-stress emergencies) could be attributed to the use of surrogate measures and multi-step methods to derive variables. Case definitions could also be considered to be imprecise because they combined several types of heart disease. For example, acute coronary syndromes included cases of acute myocardial infarction (ICD9 410) and unstable angina (ICD9 411). If the exposure of interest is associated with one disease definition, but not the other, it may result in a broad range in risk estimates. In addition, the limited medical records we obtained did not allow us to conclusively identify first incidence of disease. Therefore, it is possible some controls
may have actually been cases prior to study follow-up and may have contributed to imprecise case definitions. Small numbers of cases may result in spurious results because the inclusion or exclusion of one case in exposure categories resulting from small changes in cut points could contribute to drastic changes in risk estimates. The combination of lack of precision in exposure measures and case definitions may have contributed to wide confidence intervals and non-significant findings in our studies.

6.4.2 Data quality

The secondary analysis of administrative data can be beneficial because it provides a rich source of readily available information that may be free of certain biases, such as recall, which may occur in primary data. However, one major drawback is that secondary data is usually not collected for purposes which suit the research question and the validity of the data may be compromised.

One limitation to this dissertation was the quality of measures recorded in the emergency run data used in epidemiologic analyses in Chapters 4 and 5. This information was compiled from data recorded by paramedics for every emergency to which they were dispatched. While attending emergencies, BCAS paramedics manually record details using a crew report form (Appendix A): a paper-based document with 96 sections to capture different aspects of the emergency (e.g. time the call was received, use of sirens, medical procedures). Some of these sections require recollection of numerous BCAS codes while others require detailed, written responses. While this data provided a record of daily activity for each paramedic, the complexity of the form in combination with limited memory of BCAS codes could result in incomplete or inaccurate information. For example, in preliminary analyses of the data we received, out of 4.7 million emergencies between 1989 and 2002, 95% were missing information regarding the type of procedure administered at the scene (e.g. cardio-pulmonary resuscitation, obstetrical delivery). Inclusion of this data may have provided
additional information on the level of severity associated with the emergency and could have been used to investigate the associated physical or psychological strain which may have triggered an acute coronary event (Chapter 5).

We found approximately 18% of emergency run data were missing codes used to identify the paramedics dispatched to attend each emergency. We discovered a strong correlation of missing paramedic identification codes by year ($r = -0.83$). The largest proportion of missing paramedic-identifier codes (23%) occurred at the beginning of our emergency run records (1989) and may have been because of a labour dispute or job action. As a result, we excluded data from the year 1989 to reduce bias that may have occurred with missing data from this year.

In addition, while time of emergency run was recorded by paramedics, we did not receive this information as part of our data. This resulted in the use of surrogate measures for shift work (Chapter 4) that may have introduced misclassification error in our exposure estimates. Future studies examining shift work may consider requesting this information to obtain more accurate exposure information with regards to activity by time of day.

As a suggestion to improve the quality of data to provide a better understanding of the types of emergencies that occur in paramedic work, the BCAS may consider implementing a more streamlined reporting form by eliminating some which are repetitive, and expanding on vague categories (e.g. “other”) which currently constitute a large proportion of emergency types (Chapter 5). Implementation of handheld electronic devices such as smart phones could also improve data quality and efficiency of data collection. Studies examining the use of digital technology found that the information gathered in digital forms was more complete and written responses were more detailed in comparison to paper-based forms.
6.4.3 Deriving the metric “exposure to stressful emergencies”

In case-crossover studies, retrospective self-report of exposures during hazard and control periods may result in recall bias and has been identified as potentially being the greatest threat to the internal validity of this type of study design\textsuperscript{240}. While our use of administrative data (i.e. emergency run data) to ascertain exposure to stressful emergencies may have reduced recall bias, some uncertainty may have been introduced in the multi-step method to derive rankings of stressful emergencies described in Chapter 5. The use of survey responses allowed us to incorporate individual-level measures into analyses (e.g. perceived levels of stress), but difficulties arose because the initial purpose of the survey was to identify paramedic-specific stressors and was not intended to be used in conjunction with the emergency data to identify frequency of exposure. The result was that survey questions relating to stressors in paramedic work did not directly correspond with categories of emergencies in the emergency run data. Some of the questions did not apply to all respondents (e.g. working at special events or on an air ambulance crew), and others were vague and subject to interpretation (e.g. “medical” vs. “emergency”). The combination of these effects may have contributed to non-differential exposure misclassification and lead to null findings.

In addition to the survey questions which asked paramedics to rank their level of perceived stress, two open-ended questions were provided for elaboration on the injury and patient type that paramedics felt were the most stressful. We were unable to incorporate findings from these questions because of the low response rate (~ 70%) and the lack of a baseline measure to reference degree of stressfulness.
6.5 Policy implications

Findings from this dissertation have identified areas for intervention and results can be used to develop health and safety programs in mitigating the risk of heart disease associated with shift work and work-related stress. Suggestions are described below.

6.5.1 Mitigating the adverse health effects associated with shift work

Shift workers who exhibit excessive sleepiness and / or clinically disturbed sleep resulting in “social or occupational impairment” may be at risk for shift work disorder (ICD10: G47.26), a class of circadian rhythm sleep disorder that is defined as a “persistent pattern of sleep disturbance resulting from exogenous and endogenous factors leading to misalignment between the timing of internal circadian rhythms and the desired or required time for sleep”\(^{246}\). Studies have shown the prevalence of shift work sleep disorder is estimated to be 10 to 23\% among rotating and night shift workers\(^{247}\) and has been associated with increased risk of health problems such as heart disease\(^{248}\). Despite the adverse health effects associated with shift work, for many occupations which attend to emergencies, such as the paramedics, work at night is necessary. However, there are organizational and individual-level measures that can be taken to reduce the associated risks.

Results from Chapter 4 suggested recovery time from shift work may mitigate the risk of chronic heart disease. The implications of these findings may affect long-term schedule design for shift workers to lessen the impact of circadian misalignment. For example, increasing years of shift work could correspond with increasing length of recovery time, either in terms of time off or daytime-only work. Other organizational approaches include: shorter work hours at night, at least 11 hours of rest between shifts, fast-forwarding rotations, restricting secondary employment and limiting shift work among older workers and pregnant women\(^{247,249-251}\). The feasibility of these recommendations
will require an integrated joint effort by employers and employees to develop policies that are suitable.

The first step to reducing the potentially harmful effects of circadian misalignment is public and self-awareness. In the United States, campaigns have been targeted to improve sleep behaviours among children and teens, but less emphasis has focused on adults even though sleep is a modifiable health-related behaviour. CIRCADIAN, a company created from Harvard Medical School that specializes in shift work health and safety programs, recently surveyed 600 shift work facilities in the United States and found that 78% do not offer training for employees to adapt for a shift work lifestyle, 17% provide training for their employees, and 5% offer training to the families of shift workers as well. Companies such as CIRCADIAN and Fatigue Management Solutions have been effective at developing educational programs for employees and their families to learn about managing a “shift work lifestyle” (e.g. improving sleep hygiene); and planning optimal shift work schedules in consultation with employers and employees to reduce fatigue. These types of initiatives have been shown to result in fewer employee work absences and better employee health in comparison to facilities that do not offer any preventative programs. Health professionals may also benefit from education and training in recognition and diagnoses.

6.5.2 Reducing emergency-related stressors

Results from Chapter 5 suggested that the frequency and severity of emergencies, and discrepancies between information dispatched to paramedics and the actual events occurring at the emergency scene may result in a stress response that could trigger acute coronary events. While exposure to emergencies cannot be eliminated from the paramedic occupation, organizational policies and programs may help to reduce residual psychological strain.
6.5.2.1 Coping with traumatic events

Our finding that the greatest risk for an acute coronary event occurred 3 days after exposure to high-stress emergencies (Chapter 5) corresponds with recommendations that to effectively assist emergency responders in coping with after-effects of traumatic situations, Critical Incidence Stress Debriefings (CISD) should be provided 24 to 72 hours after a critical incident to allow time for paramedics to move beyond the initial stages of professional detachment. While the International Critical Incident Stress Foundation provides recommended guidelines surrounding these debriefings sessions, their use and administration vary widely among organizations. Details of the BCAS-administered psychological debriefing sessions have been outlined by Macnab et al. The authors reported that after a fatal air ambulance accident, “defusing sessions” were available to medical transport staff (i.e. physicians and paramedics) on the same day, a “spousal debriefing” was provided the following day for paramedics and their spouses, and a “formal debriefing” was provided 2 days later for “all who sought assistance” including those from the ambulance service, hospital and aircraft company. These findings suggest that while BCAS debriefing sessions were available soon after a critical incident, it included members other than paramedics. Inclusion of other occupational groups, members of the general public or family members may create additional barriers to deter paramedics from participating.

These post-hoc debriefing sessions are intended to be part of a comprehensive Critical Incident Stress Management program; however, they are often administered as voluntary one-time sessions for groups to express their thoughts about trauma following an event. While this approach is used among those who have experienced traumatic events, there is little evidence of its effectiveness and its continued used has been criticized. Reviews of this psychological debriefing method suggest that revisiting traumatic events may be harmful not only to participants but also to the administrators of these sessions.
Exposure to traumatic events has been linked with Post-Traumatic Stress Disorder (PTSD), which may lead to changes in neuroendocrine functioning and behaviour (e.g. smoking and alcohol abuse) and increase risk of CVD. Studies have found that the prevalence of PTSD symptoms is frequent among paramedics (range: 15-20%) and prevalence of clinical-level PTSD among rescue workers has been reported to be as high as 10% as defined by DSM-IV-TR criteria. In comparison, the incidence of PTSD among the general population of U.S. adults is approximately 3.6%. However, it has been reported that among those who frequently witness traumatic events as a regular part of their job, such as paramedics, and who could be classified as clinical-level PTSD using standardized measures, approximately 30–40% do not seek professional mental health care. A lack in mental health treatment may result in reduced ability for paramedics to cope with stress in daily work and may lead to a progression of more severe forms of mental illness such as PTSD.

The effectiveness of BCAS-administered psychological debriefing sessions has also been explored by Macnab et al. Six months after a fatal air ambulance crash, BCAS paramedics who received CISD reported they were not self-aware of any PTSD symptoms and were “back to normal” after 6 months. However, after a 2 year follow-up, 16% were still negatively impacted by the event as measured with the Impact of Events Scale and General Health Questionnaire. This discrepancy between subjective self-reports of stress and those measured using validated, standardized questionnaires suggests that the BCAS debriefings were not effective and that denial may be a coping mechanism among paramedics. These findings suggest a prevalence of untreated psychological strain among paramedics and may result in chronic neuroendocrine dysregulation leading to increased risk of CVD. Our finding that the greatest risk of ACS may occur several days following high-stress emergencies suggests there may be residual psychological distress among paramedics and supports evidence that CISD may not be effective.
While exposure to traumatic events may be a part of the paramedic profession, studies have shown that paramedics with pre-existing stress management routines had less severe PTSD symptoms, in comparison to those without, six months following witnessing a traumatic incident \( (p = 0.07) \).

Suggestions for other avenues of on-going psychological counseling or educational programs should be pursued. Implementation of regular, career-long, occupation-specific mental health training, such as the Badge of Life Psychological Survival Program utilized among law enforcement officers, may be warranted to provide on-going education in reducing psychological strain.

6.5.2.2 Reducing discrepancies between dispatched information and actual emergency on scene

Discrepancies between information dispatched to paramedics and the actual emergency at the scene were also identified as potential triggers of ACS (Chapter 5). It has been reported that these discrepancies may lead to feelings of anger or frustration among paramedics resulting in heightened cardiovascular responses and onset of acute coronary events. We found that discrepancies occurred in over half of all emergencies dispatched. High prevalence of inappropriate use of ambulance services (42%) as defined by differences between dispatched information and hospital admission records have also been reported in prior studies. Therefore, reduction in these discrepancies may have a significant impact on reducing work-related stress and potential ACS onset among paramedics.

Discrepancies between how emergencies are dispatched and diagnosed at the scene can be attributed to 2 main reasons: misinformation provided by those requesting emergency medical services and misinterpretation of the type of emergency by the dispatch centre. Most ambulance dispatch systems use an automated computer-assisted program that helps dispatch paramedics categorize the level and type of emergency based on a series of responses provided by the person calling in. I am aware of only one study, to date, which examines the reliability of this system. Clawson et al. found the
automated, protocol-based approach to be more effective in correctly diagnosing the type of emergency in comparison to a non-structured subjective approach by individual dispatchers\textsuperscript{265}. However, this study only examined critical emergencies and cardiac arrests. Future studies are warranted to examine the effectiveness of an automated approach with a wider range of emergency types. Consultations with dispatchers and ambulance paramedics should also be considered to identify areas for improvement.

Studies have shown that patients’ perceptions of required medical care is a strong predictor of ambulance requests\textsuperscript{266}, but often times there is a discrepancy of perceived level of urgency between the patient and health care provider. Gardner et al. found in an observational study that 22\% of patients transported to hospital emergency departments did not require any medical treatment as diagnosed by hospital staff\textsuperscript{267}. The economic burden, increased hospital wait times and lack of ambulance availability associated with inefficient use of paramedic resources have been discussed in previous studies\textsuperscript{268-270}, but a solution to this problem has not yet been identified. Developing programs to improving public awareness of ambulance overuse and providing alternate transportation solutions for non-critical emergencies should be explored.

6.5.3 Maintaining healthy workers

Despite mandatory physical fitness requirements to enter the paramedic profession, we found over 50\% of the male paramedics in our study population were overweight (BMI: 25.0 – 29.9 kg/m\textsuperscript{2}), approximately 30\% were obese (BMI $\geq$ 30+ kg/m\textsuperscript{2}) and 40 – 50\% reported no leisure-time physical activity (Chapter 3). High prevalence of obesity and sedentary activity have also been reported by studies among other paramedic cohorts which also found that increasing BMI scores were significantly associated with higher blood pressure (SBP > 120mmHg), worse metabolic profiles (e.g. high total cholesterol), and inability to achieve minimum fitness requirements for paramedic
work. A study of the same population of BCAS paramedics examined in this dissertation reported that paramedics were more likely to be obese in comparison to the general working population [Men: OR 2.1, 95% CI: 1.6-2.7; Women: OR 1.5, 95% CI: 0.9-2.3].

These findings suggest that surveillance programs should be considered for this group to gain a better understanding of what occupational factors may be contributing to an increase in obesity and sedentary behaviour. Interdisciplinary occupational health programs, such as Kaiser Permanente’s “HealthWorks,” may be developed in consultation with employers and employees to maintain worker health. Examples of services and solutions include: education about developing a healthy lifestyle through nutrition and exercise, identification of occupational barriers to healthy living and intervention strategies to reduce psychosocial factors which can influence the course of cardiovascular disease. It has been reported that the most effective programs are those which provide a comprehensive format in combination with long duration of contact and follow-up. A randomized control trial found that after 2 years of follow-up, individuals enrolled into an interdisciplinary intervention lifestyle program showed a significant reduction of cardiovascular risk factors and improvement in self-reported mental health in comparison to those who received treatment from a general practitioner or physician specializing in cardiovascular prevention (p < 0.05). The Public Health Agency of Canada has reported that since the implementation of the “Lifestyles Program” at BC Hydro in 1988, annual sick-leave costs were reduced by $1.2 million by 2000.

Periodic assessment of worker health with provision of preventative health programs, particularly in potentially physically and mentally demanding jobs such as paramedic work, may lead to reduction of early onset of CVD. Ensuring the health of those employed to keep the general population safe and healthy may ultimately have a significant impact on overall public health.
6.6 Future research directions

The studies described in this dissertation raised many questions and opportunities that should be considered in future research. Several study ideas are discussed below.

6.6.1 Extending studies of shift work, job strain and neuroendocrine dysregulation

Findings from Chapter 2 were consistent with studies which examined separate portions of the neuroendocrine systems linking stress or shift work with CVD \cite{142,182,202}. However, ours was the first study, to my knowledge, which concurrently examined biomarkers and subclinical heart disease indicators in both the ANS and HPA axis to gain a better understanding of intermediate and potential long-term effects of chronic exposure to job strain and shift work. We were able to determine that by using innovative, non-invasive techniques, it was feasible to collect numerous samples among this study population. More field studies using the described study protocol are needed to support findings from this pilot study.

Interest from the BCAS suggests that opportunities to replicate this pilot study among a larger cohort of BC paramedics may be viable. Path analyses\cite{275} could be completed to examine the mediating effects of salivary biomarkers between shift work, job strain and subclinical heart disease indicators.

All participants in the pilot study have indicated an interest in being a part of a larger study, thus providing a potential longitudinal component. While study power would still be a limitation, results from this longitudinal portion could help inform (1) if biomarker activity and subclinical heart disease markers indicate a decline in cardiovascular health with time as we have hypothesized; (2) what the associated effects sizes are to complete sample-size power calculations for future longitudinal studies; and (3) if follow-up is feasible among this cohort.
6.6.2 Dispatcher studies

In addition to our study of paramedic dispatchers (Chapter 2), there is only one other study among paramedic dispatchers that I am aware of. Weibel et al. examined cortisol responses among 8 volunteers during a working day in comparison to volunteers from the authors’ laboratory on a rest day\textsuperscript{276}. The authors reported cortisol levels among dispatchers were higher than the controls over all 6 time points during the day, but did not provide any further details on diurnal slope or daily production, making it difficult to compare neuroendocrine dysregulation to studies of other populations. In addition, the comparison of dispatchers during a working day to laboratory staff on a non-working day makes it difficult to disentangle occupational and workday influences. However, our study (Chapter 2) found significant differences in cortisol responses between working and rest days, but the effect sizes found in neuroendocrine measures of dispatchers in comparison with ambulance paramedics were small. This suggests that comparing occupational groups with similar training and exposures may result in little variability in biological responses.

While dispatchers have been identified as a group with limited opportunities for growth and may suffer from related psychosocial strain\textsuperscript{13}, little is known about what occupation-specific factors may contribute to work-related stress among this group (e.g. long hours sitting at a desk). Qualitative research with focus groups should be considered to identify these stressors for future quantitative studies and to determine a suitable reference group for comparison.

6.6.3 Recovery from shift work: biomarker studies and epidemiologic evidence

The study described in Chapter 4 is the first, to my knowledge, that examines the effect of recovery periods from exposure to work at night. Future longitudinal studies which include recovery periods are necessary to support our findings.
What remains unknown are the long-term consequences of shift work and if the associated neuroendocrine impairment is reversible? If so, how much recovery is needed for neuroendocrine functioning in shift workers to return to patterns similar to daytime-only workers?

I am only aware of two studies to date that have examined periods of neuroendocrine recovery following work at night. One examined catecholamine and cortisol diurnal profiles in shift workers over 2 rest days following 2 night shifts and found neuroendocrine functioning did not return to baseline levels. Another supported our findings in the neuroendocrine study described in Chapter 2 which found that that even after 4 days off work, diurnal cortisol patterns among shift workers were still flatter in comparison to daytime only workers, suggesting that neuroendocrine disruption persisted on even on rest days. However, neither study examined baseline measures of these shift workers with daytime-only workers, leaving the question “If shift workers stopped working nights, would their risk of CVD be the same as among daytime-only workers?”

Opportunities for intervention studies could compare neuroendocrine responses of shift workers who are reassigned to daytime-only schedules with those who have only worked daytime-only shifts and those who remain in shift work. The research question could address if “After switching out of shift work, is neuroendocrine activity among the intervention group similar to those who have only worked daytime shifts; does it remain the same as those who remain in shift work; or does it falls somewhere in between?” Additional longitudinal epidemiologic studies could examine trends in CVD risk among all groups over several years of follow up to see if the risk decreases over time among those who move out of shift work.

Natural experiments could also be conducted among nurses or interns who rotate through hospital wards requiring shift work or daytime-only schedules in between their classroom work. A planned crossover design could be used where each person would act as their own control. Neuroendocrine
activity during daytime classroom work prior to hospital ward rotation would be taken as baseline measures; activity during shift work during hospital rotations would indicate the degree of neuroendocrine dysregulation; and the following daytime classroom work as period could be considered as the period of neuroendocrine recovery.

6.6.4 Identifying constructs related to emergency runs that may act as triggers of acute coronary events

While it can be speculated that feelings of anger, negative emotion or work-related time pressures associated with emergency runs may behave as triggers of ACS\(^{190}\) (Chapter 5), studies are needed to validate this hypothesis and our identification of stressful emergencies. A traditional case-crossover approach may be necessary with self-reported exposures to identify constructs related to specific emergency types that may trigger acute coronary events. However, the low prevalence of ACS cases among our study population, despite having 13 years of work history and medical records (Chapter 4 and 5), suggest that this would not be a feasible approach. Increasing the study population to include paramedics employed by other jurisdictions and inclusion of other occupations with similar exposure to traumatic events, such police, firefighters, health care workers in emergency departments, may need to be considered.

From a prevention perspective, what also should be explored is if risk of subsequent ACS increases with each acute coronary event? If so, it might imply that those in emergency work should be reassigned to other, non-emergency related duties following an acute coronary event. To address this study question, a case-crossover approach can be used in a pooled cohort of emergency workers as described above, following our methodology by linking emergency run exposures to medical history records. The use of administrative data would be more efficient and require fewer resources than
following subjects over many years. Risk estimates could be compared for first and subsequent coronary events in the follow-up period and tested for trend.

**6.6.5 Progression of risk factors for heart disease**

Our findings of high prevalence of obesity and sedentary behaviour (Chapter 3) support prior studies which report an “epidemic of overweight and obese paramedics” ¹⁹² and suggest that these known risk factors for CVD may contribute to a higher risk of CVD among paramedics. Similarly among other emergency service workers (i.e. firefighters and police), studies have found an increase of weight and obesity, clustering of CVD risk factors (e.g. hypertension, glucose levels) with duration of employment that persisted even after retirement ⁹⁶,⁹⁷.

It has been estimated that 27% of American adults do not engage in any leisure time physical activity ²⁷⁸; however, we found 40 – 50% of male paramedics were inactive during their leisure time. In addition, we found a high prevalence of obesity among paramedics (~30%), similar to those reported in prior studies ¹⁹². While it could be argued that the prevalence of obesity among paramedics may reflect the prevalence among the general population (35%) ²⁷⁹, a prior study found that paramedics are twice as likely to be obese in comparison to the working population ¹⁰⁷. This suggests that there may be factors inherent in emergency medical services that may contribute to a more sedentary lifestyle and thus an increased risk for heart disease (e.g. lack of time for exercise due to long or irregular working hours). A prospective study among firefighters found that over a 5 year period, the prevalence of obesity increased by 5% and was associated with an increased prevalence of hypertension but the underlying cause of deterioration in physical health was unknown ¹⁹¹. It has also been shown that obesity may increase the risk of total cardiovascular morbidity and mortality by 1.3 times in men who are overweight or obese ²⁸⁰ and may be a predictor of CHD retirement among firefighters (OR 1.4, 95% CI: 0.96 - 1.93) ²⁸¹.
These findings among those employed to ensure public health and safety suggest occupational health and medical surveillance programs may be warranted. Future studies should examine what factors may lead to these CVD risk factors (i.e. obesity and sedentary behaviour) among paramedics and the effectiveness of intervention programs.

What remains to be explored is the potential mediating role of obesity and sedentary behaviour between shift work, job strain and CVD among paramedics. Prospective studies could be implemented to survey paramedics annually about occupational factors (e.g. shift work, job strain), health behaviours and anthropometric measurements. Additional efforts could be made to measure early heart disease indicators (e.g. endothelial functioning) annually as biological markers of CVD progression. Path analyses can be used to examine the strength and direction of the mediating effects of obesity and sedentary activity between shift work and job strain with subclinical indicators of heart disease. To examine growth trends in obesity, sedentary behaviour and early heart disease indicators associated with exposure to shift work and job strain, multilevel regression growth modeling could be completed to account for repeated measures per individual over time. Results from these studies can be used to inform occupational health and safety programs specific to the paramedic population.

6.7 Conclusion

While shift work and work-related stress have been identified as potential risk factors for heart disease and are common in paramedic work, there are few studies examining the risk of heart disease among this population. The purpose of this dissertation was to address this research gap. Results from my studies suggest that shift work and stress related to emergency runs may play different roles in the etiology of heart disease. Neuroendocrine dysregulation resulting from chronic exposure to shift work may damage blood vessels, accelerate coronary plaque buildup and contribute to chronic
forms of heart disease; whereas secondary traumatic stress associated with emergency runs may result in adrenergic surges and trigger acute coronary events. High prevalence of obesity and sedentary behaviour among this population, despite strict physical fitness requirements to enter the service, may act as mediating factors between shift work, occupational stress and heart disease, and warrants further investigation.

In addition to the scientific contributions of this dissertation, findings were intended to identify several avenues to improve current practices and suggest future topics of research.

Suggested policy implications include:

- Developing educational programs to recognize and improve sleep hygiene
- Reducing discrepancies between dispatched information and emergency at the scene through public awareness of ambulance misuse and by examining effectiveness of computer-assisted diagnostic programs used at dispatch centers
- Incorporating health surveillance programs to monitor worker health and providing interdisciplinary lifestyle preventative health programs

Suggested future research areas include:

- Validation of the paramedic-specific job strain scale developed in Chapter 2
- Comparing a variety of long-term shift work and recovery schedules to identify ones that may mitigate the risk of heart disease
- Examining if neuroendocrine dysregulation associated with shift work is permanent or reversible with intervention studies
• Identifying the constructs related to emergency runs (e.g. anger, negative emotion) which may act as triggers of acute coronary events, to help in the development of targeted occupational health and safety programs

• Investigating if the risk of subsequent acute coronary events is increases with each incident. Results from this study may provide evidence for duty reassignment following a coronary event

• Exploring if shift work and occupational stress contribute to obesity and sedentary behaviour among paramedics and if this has a significant contribution to an increased risk for CVD

Although the study population in this dissertation focused solely on paramedics, portions of this dissertation may be generalizable to other groups of shift workers, emergency health care workers and first responders because of similarities in the nature of their work.
REFERENCES


(201) British Columbia Health Services. Medical association guidelines and protocols. Detection and Diagnostic of Hypertension.


APPENDIX A  PARAMEDIC CREW REPORT

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**RESULTS**

<table>
<thead>
<tr>
<th>74. RESPIRATORY</th>
<th>75. PULSE</th>
<th>76. SYMPTOMS</th>
<th>77. CARDIAC RHYTHM</th>
<th>78. RESULT</th>
<th>79. INITIAL CODE</th>
</tr>
</thead>
<tbody>
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</tbody>
</table>
68. RELEASE FROM RESPONSIBILITY WHEN PATIENT REFUSES TRANSPORT/TREATMENT

This is to certify that ___________________________ is refusing ___________________________.

_________________________  ____________________________
Signature  Phone #

I acknowledge that I have been informed of the possible risks involved and hereby release the
ambulance attendants, the Emergency Health Services Commission's physician
consultant, and the attending hospital from all responsibility for any illness which may
result from this action.

_________________________
Signature

69. PATIENT MOVES

| # | ACTION | CAUSE FOR MOVE
|---|--------|----------------|
| 1 | STANDING | SUGGEST (MEDICATION)
| 2 | SITTING | PATIENT REQUEST
| 3 | STANDING AND SITTING | PATIENT REQUEST
| 4 | SITTING | PATIENT REQUEST
| 5 | SITTING | HOSPITAL DIRECTIONS
| 6 | STANDING | OVERWHELMED

69. PATIENT DIES

69. ROTATION

70. PROCEDURE

<table>
<thead>
<tr>
<th>#</th>
<th>ACTION</th>
<th>CAUSE FOR MOVE</th>
</tr>
</thead>
</table>
| 1 | ANOREXIA | NOT　
| 2 | CARDIO-PULMONARY | NOT　 |
| 3 | PAIN | NOT　 |
| 4 | CHEST PAIN | NOT　 |
| 5 | CHEST PAIN IN INCORPORATION | NOT　 |
| 6 | CONGESTIVE HEART FAILURE | NOT　 |
| 7 | PAIN | NOT　 |
| 8 | PYKODERMA | NOT　 |
| 9 | OSTEOMALACIA | NOT　 |
| 10 | PAIN | NOT　 |
| 11 | UREMIA | NOT　 |
| 12 | SEIZURE | NOT　 |
| 13 | OTHER | NOT　 |

70. PROCEDURE

<table>
<thead>
<tr>
<th>#</th>
<th>ACTION</th>
<th>CAUSE FOR MOVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ANOREXIA</td>
<td>N/A</td>
</tr>
<tr>
<td>2</td>
<td>CARDIO-PULMONARY</td>
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</tr>
<tr>
<td>3</td>
<td>PAIN</td>
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</tr>
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<td>6</td>
<td>CONGESTIVE HEART FAILURE</td>
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<tr>
<td>7</td>
<td>PAIN</td>
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<td>8</td>
<td>PYKODERMA</td>
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<tr>
<td>9</td>
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<td>10</td>
<td>PAIN</td>
<td>N/A</td>
</tr>
<tr>
<td>11</td>
<td>UREMIA</td>
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</tr>
<tr>
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<td>SEIZURE</td>
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</tr>
<tr>
<td>13</td>
<td>OTHER</td>
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</table>