AN INVESTIGATION INTO ATHEROSCLEROTIC INDICATORS AMONG CURRENT SHIFT AND NON-SHIFT WORKING FEMALE HOSPITAL EMPLOYEES: AN EXPLORATORY STUDY

by

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Abstract

**Background:** Shift work has been suggested to be associated with early adverse atherosclerotic changes. Endothelial function, intima-media thickness (IMT), and arterial stiffness are preclinical predictors of atherosclerotic changes, which may suggest a specific pathway through which shift work exposure contributes to cardiovascular disease (CVD). The aims of this exploratory study were: 1) to describe and compare early atherosclerotic indicators between current shift workers [SW] with at least 6 years of shift working experience and current non-shift workers [NSW] with at least 6 years of work experience; 2) to describe the potential for a dose-response relationship between length of shift work exposure and early atherosclerotic indicators; and 3) to explore and compare the associations between psychological stress and vascular changes in SW and NSW.

**Methods:** Female current shift (n = 20) and non-shift work employees (n = 19) visited a lab on one occasion to complete vascular function testing. These included reactive hyperemia flow mediated dilation, pulse wave velocity (PWV), and structural examination of intima-media thickness (IMT). Self-report validated measures of psychological job stress, life stress and other personal and demographic information were collected.

**Results:** Within this sample, there was no significant difference between groups regarding atherosclerotic indicators. The SW participants reported a higher effort-reward imbalance (p = 0.003) and greater physical job demands (p < 0.001). Skill discretion, decision authority, and decision latitude were negatively correlated with peripheral PWV ($r = -0.623$, $p < 0.001$; $r = -0.338$, $p = 0.044$; $r = -0.346$, $p = 0.039$, respectively). IMT was positively correlated with psychological job demands ($r = 0.413$, $p = 0.029$). There was no dose-response relationship between years of shift work experience and atherosclerotic indicators after controlling for age.

**Conclusion:** Women working in a shift work position did not significantly differ in their atherosclerotic development when compared to non-shift working women. However, women employed in a shift work position did report greater psychological work stress and physical
demands, which may play a role in CVD. Individuals exposed to shift work may be prompted to engage in healthy behaviours and employers may benefit from implementing practices to reduce workplace-related stress.
Co-Authorship

This thesis represents the work of Morgan Batson in collaboration with her colleague, Ira Carson, supervisors, Joan Tranmer and Kyra Pyke, and committee member, Joan Almost. Morgan Batson, along with Ira Carson, were responsible for the conceptualization of this thesis project, along with data collection, data analysis, statistical analysis, interpretation of the results, and writing of the manuscript with the supervision of Joan Tranmer, Kyra Pyke, and feedback from Joan Almost.
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Student Contributions

To complete this thesis project, I became familiar with the Cardiovascular Stress Response Lab in which all the data were collected. I learned how to use the equipment, learned how to troubleshoot errors, as well as function as part of a collaborative team with Ira Carson. Together, with the assistance of our supervisors, we developed a protocol for data collection and completed pilot testing to ensure proper implementation of the protocol. Over several months, I recruited participants via email and by visiting each site. I circulated flyers throughout the hospital. Data collection occurred over 9 months, with ongoing data analysis and recruitment. I learned how to analyze the signals (e.g. clean the data) and compute values for key variables (i.e. PWV, IMT, and FMD).
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List of Abbreviations

Body mass index (BMI)
Cardiovascular disease (CVD)
Coronary heart disease (CHD)
Derogatis Stress Profile (DSP)
Effort Reward Imbalance (ERI)
Flow mediated dilation (FMD)
Global Physical Activity Questionnaire (GPAQ)
Hazard ratio (HR)
Intima-media thickness (IMT)
Ischemic heart disease (IHD)
Job Content Questionnaire (JCQ)
Male shift worker (MSW)
Male non-shift workers (MNSW)
Myocardial Infarction (MI)
Nitrate mediated dilation (NMD)
Nitric oxide (NO)
Non-shift work (NSW)
Odds Ratio (OR)
Central pulse wave velocity (cPWV)
Pulse wave (PW)
Pulse wave velocity (PWV)
Peripheral pulse wave velocity (pPWV)
Relative risk (RR)
Shift work (SW)
Chapter 1

Introduction

1.1 Background and Rationale

Cardiovascular disease (CVD) and its underlying risk factors are an increasing burden to the healthcare system worldwide. CVD is one of the leading causes of death in Canada and estimates suggest that an individual dies from CVD related events every seven minutes (Statistics Canada, 2011). In 2008, heart disease was the number one cause for hospitalizations in Canada (Statistics Canada, 2011). An estimated $20.9 billion is spent each year in Canada on hospital and physician services, lost work wages, and decreased productivity due to CVD (Conference Board of Canada, 2010).

Several non-modifiable and modifiable risk factors contribute to CVD development. Non-modifiable factors include factors such as age, genetic predisposition and family history of early heart disease. Traditional modifiable factors include physical inactivity, obesity, diabetes mellitus, hypertension, and dyslipidemia. More recently, other important factors such as psychological stress and work environment have emerged as attributable risk factors to CVD (Bosma, Peter, Siegrist, & Marmot, 1998).

Many epidemiologic studies have suggested an association between shift work and CVD (Bøggild & Knutsson, 1999; Ellingsen, Bener, & Gehani, 2007; Frost, Kolstad, & Bonde, 2009; Fujino et al., 2006; Karlsson, Alfredsson, Knutsson, Andersson, & Torén, 2005; Knutsson, Akerstedt, Jonsson, & Orth-Gomer, 1986; Tenkanen, Sjöblom, Kalimo, Alikoski, & Härmä, 1997; Tüchsen, Hannerz, & Burr, 2006; Vyas et al., 2012; Yadegarfar & McNamee, 2007). Puttonen, Härmä, and Hublin (2010) developed a framework summarizing the potential
mechanisms through which shift work, resulting in circadian-related stress, may lead to CVD. They hypothesize that these pathways (i.e. physiological, biological, and psychosocial stressors) influence CVD development, either independently or synergistically. Such sub-pathways may also influence preceding conditions, such as atherosclerosis, which may also influence CVD development. Previous epidemiological and clinical research has suggested that shift work may be associated with atherosclerotic changes and, as a result, may contribute to the risk for CVD development (Amir et al., 2004; Chen et al., 2010; Haupt et al., 2008; Kim et al., 2011; Puttonen et al., 2009; Suessenbacher et al., 2011; Tarzia et al., 2011). Since atherosclerotic indicators (e.g. endothelial function, intima-media thickness and arterial stiffness) are early, preclinical predictors of atherosclerosis, they may provide an opportunity to explore the specific pathway through which shift work exposure may lead to future CVD.

The research supporting the aforementioned pathways is growing and has predominantly focused on the relationship between SW and end-stage CVD, and not preclinical markers, such as the atherosclerotic indicators previously mentioned. Moreover, fewer studies have explored early CVD development in women which is concerning, as overt CVD develops at a later age in women. To the best of our knowledge, no research has explicitly investigated all three atherosclerotic measures in women concurrently. Given the increase in prevalence of women employed in SW positions, especially within the health care system, and the inconsistent findings within the literature, research focused on the specific health of women is important and relevant. Thus this thesis aims to contribute much needed information regarding the relationship between female shift workers and overall adverse cardiovascular changes.
1.2 Purpose and Objectives

The purpose of this study was to determine whether atherosclerotic indicators were different for women employed in SW positions in comparison to those employed in NSW positions. The specific research objectives were:

1. To describe and compare early atherosclerotic indicators (i.e., endothelial function, intima-media thickness, arterial stiffness) between two groups of age and menopause-matched female hospital employees (current shift workers [SW] with at least 6 years of shift working experience and current non-shift workers [NSW] with at least 6 years of work experience), while controlling for significant covariates (to be addressed further).

2. To explore whether a dose-response relationship exists between length of shift work exposure and early atherosclerotic indicators (endothelial function, intima-media thickness, and arterial stiffness).

3. To explore and compare the associations between psychological stress and vascular changes in SW and NSW.

1.3 Overview of Study

This project used a descriptive comparative between-participant design to explore atherosclerotic indicators in shift and non-shift working females. Participants were female hospital employees who worked at local area inpatient and outpatient hospital. Participants were inpatient staff (e.g. Registered Nurses’, Registered Practical Nurses, Registered Dietarians, etc.) and laboratory, diagnostic, and treatment staff (e.g. Pharmacy Technicians, Radiation Therapists, administrators, etc.). A total of 39 participants were included for this study: 20 shift workers and 19 non-shift workers. Shift workers were classified based on their self-reported schedules and required overnight work (i.e. having worked between the hours of midnight and 5 a.m.).
Participants visited the Cardiovascular Stress Response Lab for a one-time anthropometric measures and vascular function testing. Self-reported questionnaires were also completed in order to describe the sample and control for potential confounding variables.

1.4 Thesis Organization

Following this introduction, Chapter 2 provides a thorough review of the literature, including key concepts, a conceptual framework, and summary of the existing evidence providing the rational for the thesis project and the included manuscript. Current research evidence in regard to the associations between shift work and CVD will be explored. This is followed by a detail discussion of the associations between shift work and atherosclerosis. As atherosclerosis development has been measured using three key vascular properties (i.e. endothelial function, intima-media thickness, arterial stiffness), each will be described as they relate to shift work; a rationale for the study will also be provided. Chapter 3 is the manuscript, “The effect of shift work on vascular structure and function in female hospital workers: an exploratory study”, which will be submitted to Vascular Medicine. The manuscript will provide a description of the background, methods used to complete the study (i.e. study design and experimental procedure), data analysis, and statistical analysis. The final chapter, Chapter 4, will include a discussion of the overall thesis project, including the relevance of the research, nursing implications, strengths, limitation, future direction, and concluding remarks.
1.5 References


Chapter 2

Background

2.1 Introduction

Shift work refers to work patterns outside the usual “9 to 5, 8-hour workday” (Kawachi et al., 1995; Williams, 2008). It is comprised of various types of schedules such as regular night schedules, irregular schedules, rotating work schedules (alternating through the 24-hour day), split shifts, and/or other non-day schedules (Williams, 2008; Vyas et al., 2012). Conversely, non-shift work refers to any regular daytime work schedule (Williams, 2008). Rotating shifts and irregular schedules are among the most common shift type (Williams, 2008). In today’s globalized economy, there is significant pressure for “24/7” service in several occupational sectors, such as manufacturing, protective services (e.g. police), and healthcare services (Williams, 2008). Approximately 28% of the Canadian working population is employed in a shift work position (Williams, 2008). This proportion is higher amongst health care professionals, increasing to 45%, with a higher percentage of women working in the health care sector as compared to men (Canadian Centre for Occupational Health and Safety, 2010).

While shift work may allow for potentially more employment opportunities, greater flexibility among employee schedules, and around the clock delivery of services, it has been associated, in some cases, with several health effects, potentially causing a decreased efficiency and loss in productivity (Rajaratnam & Arendt, 2001). Shift work has been adversely associated with various health disorders, including psychological and mental health, social problems, gastrointestinal disorders, cancer, metabolic disorders, and reproductive disorders (Costa, 2010). In addition, epidemiological evidence has suggested shift work is associated with an increased risk of CVD (Costa, 2010).
Despite advances in modern medicine, CVD remains to be a serious health concern among female Canadians. Heart disease and stroke are the second and third leading cause of mortality in females, respectively (Statistics Canada, 2014). Given the increased number of women working in the healthcare sector, there is a need to investigate shift work as an environmental factor contributing to CVD development.

2.2 Cardiovascular Disease

Commonly known as heart disease, CVD is an all-encompassing term used to describe any disease process that affects the heart and blood vessels (American Heart Association [AHA], 2014). This includes, but is not limited to: angina, heart block, ischemic stroke, heart attack, heart failure, pericarditis, rheumatic heart disease, valve disorders, and cardiac arrest (AHA, 2014; Heart & Stroke Foundation [HSF], 2009a). Atherosclerosis, a narrowing of the artery due to plaque formation, is an additional disease process under the CVD umbrella, which precipitates many of the aforementioned diseases (AHA, 2014). In Canada, coronary artery disease (CAD) is the most common cardiovascular condition, whereby the blood vessels supplying the heart become narrow or occluded by atherosclerotic development, thus preventing efficient blood flow to the tissue and muscle of the heart (HSF, 2009a). Ischemic stroke may also occur as a result of atherosclerotic development in the cerebral arteries (HSF, 2009a). In comparison to hemorrhagic stroke (where bleeding into the brain tissue occurs), ischemic strokes are responsible for 80% of the total number of strokes in Canada (HSF, 2009a). Therefore, preventing the occurrence of atherosclerosis may be beneficial in lessening such devastating downstream affects.

There are many recognized risk factors that influence CVD development (HSF, 2009a). Traditional non-modifiable risk factors include age, gender, family history, and ethnicity. Traditional modifiable risk factors include hypertension, high cholesterol, diabetes, obesity, smoking, and physical inactivity. In this study, these factors have been controlled using exclusion
criteria and questionnaires, which will be described further. In addition to the aforementioned factors, chronic elevated levels of psychological stress may potentially influence CVD development (Government of Canada, 2013). Stress is used as a general term and can include the following components (Bunker et al., 2003): depression, social isolation, acute and chronic life events, work characteristics, and hostility. Due to the lack of evidence and inconsistencies in the literature, it is unknown if stress is an independent risk factor for CVD or whether it influences traditional risk factors (Bunker et al., 2003). In this thesis, stress has been accounted for as a potential covariate by using both life and job stress questionnaires to investigate their effect on atherosclerotic indicators.

2.3 Epidemiology of Shift Work and CVD

A growing body of evidence suggests that shift work is a risk factor for CVD development (Ellingsen, Bener, & Gehani, 2007; Fujino et al., 2006; Karlsson, Alfredsson, Knutsson, Andersson, & Torén, 2005; Knutsson, Akerstedt, Jonsson, & Orth-Gomer, 1986; Tenkanen, Sjöblom, Kalimo, Alikoski, & Härmä, 1997; Tüchsen, Hannerz, & Burr, 2006); however, inconsistencies do exist. A systematic review investigated the link between shift work and CVD using approximately 2,380,000 individuals (Bøggild & Knutsson, 1999). Various studies were included if they compared shift workers to day workers (or followed shift workers after a change in schedule) and if they reported CVD risk factors or CVD end points (Bøggild & Knutsson, 1999). The authors did not describe the definition of CVD used. Using cross-sectional, case-referent, and cohort studies, results indicated varying risk ratios among 17 studies, ranging from 0.4 to 3.6. Four studies failed to find any relationship, despite having comparable research quality. Based on the most convincing study by Knutsson et al. (1986), it was suggested that shift workers are at 40% increased risk of CVD compared to non-shift working individuals. Several limitations were identified in this review to which Bøggild and Knutsson (1999) stated
contributed to the lack of consistency among studies. Many of the studies used varying research designs, making comparisons between studies difficult. The definition of “shift work” varied between studies and many studies did not include a description of this exposure variable. Similarly, the outcome variable (i.e. CVD) was defined differently among studies; some studies included a broad definition (including hypotension and varicosis), while others used only ischemic heart disease or mortality figures on myocardial infarctions (MI). Furthermore, Bøggild and Knutsson (1999) recommended that atherosclerotic markers may be useful outcome indicators in future research on CVD risk among shift workers.

In a systematic review of 14 studies, Frost, Kolstad, and Bonde (2009) examined the causal relationship between shift work and ischemic heart disease (IHD). Studies were included if they used a prospective design and explicit information regarding shift work exposure was presented along with estimates regarding the risk of IHD. Approximately 600,000 individuals were included in the review and most of the studies included male populations only. Seven studies used mortality rates, six used incidence data, and one used both. Among these studies, the relative risk (RR) estimates varied from 0.6 (95% CI [0.28, 1.47]) to 2.35 (95% CI [1.37, 3.95]). While two studies demonstrated significant associations, Frost et al. (2009) concluded no or weak associations within the mortality studies and minor positive associations within the incidence studies. In addition, they cautioned interpretation of these findings due to methodological issues, insufficient confounder control, as well as exposure definitions used. Overall, Frost et al. (2009) determined there is little evidence for a causal relationship between shift work and IHD.

Alternatively, a recent review and meta-analysis presented by Vyas et al. (2012) suggested an association between shift work and vascular events. A sample of 2,011,935 individuals among 34 studies was used, including prospective cohorts, retrospective cohorts, and case-control studies. Shift schedules varied among studies and the majority of studies used day workers (non-shift working) as the control group. Results indicated an association between shift work and the following vascular outcomes: MI (risk ratio (RR) = 1.23, 95% CI [1.15, 1.31])
coronary events (RR = 1.24, 95% CI [1.10, 1.39]); and ischemic stroke (RR = 1.05, 95% CI [1.01, 1.09]). Similar limitations existed, including varied outcome definitions and varied control over confounders (Vyas et al., 2012).

Thus there remains some uncertainty with regards to the associations between shift work and risk for CVD. It has been suggested that in order to better understand and elucidate the relationships one must understand the psychophysiological pathways through which shift work may influence CVD development (Puttonen, Härmä, & Hublin, 2010). These pathways that facilitate disease development, however, are not as well understood. In addition, there are several gaps within the literature that required further exploration. For example, in previous studies, measured outcomes often include only end-stage CVD and mortality; this is problematic as CVD develops over time and CVD events occur later in life for women. Indications of premature disease development may be evident prior to clinical manifestation (Poredos, 2004; Puttonen et al., 2010). Secondly, limited studies have examined CVD risk in females specifically (Kawachi et al., 1995; Brown et al., 2009). Lastly, few studies have examined the cumulative effect of shift work exposure (Tüchsen et al., 2006; Yadegarfar & McNamee, 2007).

Therefore, this thesis addressed these gaps by examining the effects of shift work exposure on early atherosclerotic indicators in a female-specific cohort. The presence of a dose-response relationship between length of shift work exposure and the manifestation of early atherosclerotic indicators has been explored as Objective 2.

### 2.3.1 Shift work and CVD in men

A Swedish retrospective study by Karlsson et a. (2005) followed a historical cohort of male paper-pulp manufacturers to investigate the relationship between shift work and mortality due to coronary heart disease (CHD). The population included males, aged 10 to 59, who had been employed from 1940 to 1998. The shift workers (n = 2354) and day workers (n = 3088) were classified into the following six categories: never having worked shift work (i.e. day
workers); shift work < 5 years, shift work 5 to 9 years; shift work 10 to 19 years; shift work 20 to
29 years; and shift work > 30 years. While shift work schedules varied over the years as a result
of legislation changes, shift work was consistent with rotating schedules over the years. Company
files were obtained to determine employment position and mortality was determined through
registration databases. Measured outcomes included coronary and stroke related mortalities. The
results suggested that the duration of shift working exposure was associated with increased risk of
CHD; mortality due to CHD was 11% higher among shift workers (RR = 1.11, 95% CI [0.95,
1.30]). In addition, risk for CHD was highest in those with greater than 30 years of shift working
exposure (RR = 1.24, 95% CI [1.04, 1.49]).

Fujino and colleagues (2006) examined the association of shift work and risk for IHD
among Japanese male workers using a prospective cohort study. A national survey was
administered from 1988 to 1990 to collect information regarding work history, current working
schedules, lifestyle choices and health history. Follow up data regarding deaths attributed to
circulatory disease, IHD and cerebrovascular disease were collected until 2003. The selected
cohort consisted of 17,649 men (aged 40 to 59) who had completed the survey section regarding
patterns of shift work (day [n = 14,774], fixed-night [n = 864], and rotating [n = 2011]).
Measured outcomes included coronary, cardiovascular, and cerebrovascular mortalities. Results
of the study found that fixed night work was not associated with any cause of death. However,
rotating shift work was associated with a 59% increased risk of circulatory disease development
(RR = 1.59; 95% CI [1.16, 2.18]; p = 0.004) and higher risk of death due to IHD when compared
to day workers (RR = 2.32, CI [1.37, 3.95]; p = 0.002).

Using a case-control design, Yadegarfar and McNamee (2007) investigated this similar
association of shift work and IHD. The sample included male industrial workers employed at a
nuclear producing plant from 1950 to 1998. Work status information was obtained from personal
records and occupational health records. Shift workers (cases) were defined as having worked
shift positions for at least 30 or more days and shift patterns varied among workers. Any workers
who had never done shift work (i.e. any pattern of shift work) were classified as day workers (control). The measured outcome included coronary mortality. Death certificates were extracted using the UK Office of National Statistics (period of 1950 to 1998, aged 75 or under) to obtain case information of cohort members having died of IHD. Cases (n = 635) and controls (n = 635) were matched based on age and year of starting work; variables such as smoking, blood pressure, and social class were also controlled. After adjustment of risk factors, duration of employment and survival to at least 10 years after hire, shift workers had 11% increased risk of death from IHD, in comparison to day workers (OR = 1.11, 90% CI [0.9, 1.37]). This risk was decreased to 4% once adjusted for social class (OR = 1.04, 90% CI [0.83, 1.30]).

A major concern within the aforementioned studies is that no females were used within the participant pool; however, as discussed in the following sections more recent epidemiological studies have addressed this limitation. Regardless, these studies provide epidemiological evidence for the association between shift work and CVD development.

2.3.2 Shift work and CVD in men and women

A Danish prospective cohort study by Tüchsen et al. (2006) used a large cohort (n = 5517) of men and women to investigate the risk of circulatory disease among shift and non-shift workers. The information and samples were drawn from the 1990 Danish Work Environment Cohort survey: participants, aged 20 to 59 years, were included if they answered a question about their work schedule and defined as employees by the national employment registry. Eighty-three percent were permanent day workers (males [n = 2371] and females [n = 2208]); the remaining 17% were classified as male (n = 482) and female (n = 456) non-day workers with schedules varying between those working two shifts, three shifts, rotational, and permanent hours (evening, night, and morning). Information regarding disease was gathered using the national patient registry for all treatments in Danish hospitals, outpatient courses, and emergency room visits. The study also controlled for several known or suspected confounding factors, such as smoking and
psychological job demands and stressors. Measured outcomes included coronary and cardiovascular events. Researchers concluded that shift workers had a 36% greater risk for circulatory disease development (RR = 1.36, 95% CI [1.10, 1.68]), in comparison to day workers. Once adjusted for confounding variables, this risk decreased to 31% (RR = 1.31, 95% CI [1.06, 1.63]). An identified limitation was that no information was obtained regarding the length of time exposed to shift work. The aforementioned study by Yadegarfar and McNamee (2007) also echoed this discrepancy as no significant evidence was generated to indicate a dose-response relationship between duration of shift work and IHD.

Since both studies were unable to address the cumulative effects of shift work exposure, the aim of this thesis is to address this knowledge gap by examining if the presence of a dose-response relationship exists within the group of female shift workers.

### 2.3.3 Shift work and CVD in women

An important component of a large prospective cohort study, the Nurses’ Health Study, determined the effect of shift work on CVD development among female nurses (n = 79,109) (Kawachi et al., 1995). Participants completed mail-in surveys and follow-up questionnaires regarding their overall health and information in regard to how long they had worked rotating night shifts, in addition to day or evening shifts. Measured outcomes included MI, coronary, and cardiovascular events. The results showed that women who self-reported shift work were at 38% greater risk for CHD, in comparison to those never working shift work (age-adjusted RR =1.38, 95% CI [1.08, 1.76]). The researchers also found that individuals with longer durations of shift work experience had significantly higher risk for CHD (p = 0.04). When compared to those who had never done shift work, workers with at least six years of shift working experience had a 51% increased CHD risk (RR = 1.51, 95% CI [1.12, 2.03]), while those with less than six years shift work experience had 21% increased CHD risk (RR = 1.21, 95% CI [0.92, 1.59]). Additional findings from the Nurses’ Health Study further illustrated the harms associated with shift work
and vascular disease (Brown et al., 2009). Based on confirmed cases of ischemic stroke and consideration of confounding variables, the results suggested a significant association between ischemic stroke and shift work among women with 15 to 19 years of exposure (hazard ratio [HR] = 1.42, 95% CI [1.07, 1.89]). Furthermore, a dose-response relationship was suggested; with every five years of having worked shift work resulting in a 4% increased risk for ischemic stroke (HR = 1.04, 95% CI [1.01, 1.07]). An important gap, highlighted by Kawachi et al. (1995), was that no information was gathered to determine current shift working status.

This thesis built upon this Kawachi et al epidemiological study. A minimum of six years of shift work experience was required to participate in the study and current shift work status was explored.

2.4 Conceptual Framework

This thesis project conceptually built upon a framework presented by Puttonen et al. (2010). Based on the existing literature and findings, they hypothesized three mechanistic pathways linking shift work to CVD development: psychological stress, behavioural stress, and physiological stress. In accordance with the framework, shift work is defined as either work patterns at rotating hours of the day (i.e. day, evening or night shift) or work at consistent but unusual hours (i.e. consistent night shifts). These shift-working patterns result in a circadian stress, which contributes to psychological, physical, and behavioural consequences as a result of the sleep/wake cycle disruption (Puttonen et al., 2010). These three pathways produced by circadian disruption may offer possible mechanistic explanations for the link between shift work and CVD development.

2.4.1 Psychological stress pathway
Evidence has suggested that psychological stress in the workplace is an independent risk factor for atherosclerosis and IHD (Eller et al., 2009). Kivimäki and colleagues (2002) used a prospective cohort design to investigate psychological job stress within 812 employees without existing CVD. Employees who experienced high job strain had 2.2-fold increased risk for cardiovascular mortality (95% CI 1.16 to 4.17). Similarly, those who experienced an Effort Reward Imbalance (ERI) had 2.4-fold increased risk for cardiovascular mortality (95% CI 1.26 to 4.42). Kivimäki et al. (2006) also conducted a systematic review of 14 prospective cohort studies (n = 83,014) that utilized similar measures, including job strain and ERI. After controlling for potential covariates, high job strain was associated with 16% (95% CI 0.94 to 1.43) increased risk for CHD and a high ERI was associated with 58% (95% CI 0.84 to 2.97) increased risk for CHD. Therefore, psychological job stress was associated with adverse CVD changes. In addition, Albertsen and colleagues reviewed 88 studies to investigate the negative impact between shift work and work life balance. They advised that shift work increases stress as a result of the inflexibility of shifts, therefore limiting the possibilities for employees to self-manage working hours (Albertsen, Rafnsdóttir, Grimsmo, Tomasson, & Kauppinen, 2008). Employees may be subjected to irregular leisure time and social activity outside of work, as a result of shift work (Albertsen et al., 2008).

**2.4.2 Behavioural stress pathway**

Shift work is associated with behavioural changes as a result of circadian stress (Puttonen et al., 2010). The behavioural stress sub-pathway most notably addresses sleep quality and length, which may be associated with increased risk for CVD (Åkerstedt, 2003; Ayas et al., 2003). Since a regular sleep pattern is displaced, shift workers experience acute impacts on sleep and alertness that can also affect days off (Åkerstedt, 2003). It has been noted that insufficient sleep causes activation of the sympathetic nervous system resulting in increased heart rate and blood pressure (Lusardi et al., 1999). Shift work may also have an influence on other behaviours such as poor
dietary habits, smoking, and physical inactivity, therefore facilitating CVD (Frost et al., 2009). In addition, shift workers may participate in such behaviours in order to cope with the stresses of shift work (Puttonen et al., 2010).

2.4.3 Physiological stress pathway

The physiological stress pathway addresses the biological mechanisms that influence CVD development as a result of circadian stress. Several mechanisms have been suggested to independently influence CVD development: inflammation (Sookian et al., 2007); blood coagulation (Peternel et al., 1990); physiological and biochemical stress mediators (including cortisol and catecholamine regulation) (Munakata et al., 2001); and, cardiac autonomic function (Chung et al., 2009). Such mechanisms may also influence preceding disease conditions, such as atherosclerosis, type II diabetes, and metabolic syndrome, which may influence CVD development. Furthermore, Puttonen et al. (2010) suggest that both psychological and behavioural stresses could trigger physiological stress reactions, therefore influencing the development of preceding conditions and CVD itself.

This thesis utilized this organizing framework and focused specifically on early atherosclerotic indicators in shift working women, as indicated by gaps within the literature. Psychological stress was also included within this pathway as it may alter individual behaviour (e.g. engaging in poor lifestyle choices and diet) as well as alter autonomic and hormonal disruption, which can influence endothelial function resulting in increased risk for CVD (Das & O’Keefe, 2006). Figure 1 (below) represents a modified framework based on Puttonen et al. (2010). Since atherosclerosis may be influenced by various confounding factors as illustrated in the organizing framework, these were controlled for in the study design.
2.5 The Relationship Between Shift Work and Atherosclerosis

2.5.1 Atherosclerosis

Atherosclerosis is a complex arterial disease involving injury, formation of arterial plaques and chronic inflammation (Libby, Ridker, & Maseri, 2002; Sima, Stancu, & Simionescu, 2009). Based on the “response-to-injury” hypothesis, atherosclerosis begins with damage to the endothelium (Cullen, Rauterberg, & Lorkowski, 2005). As a single layer of endothelial cells that separate blood from the vessel wall, they act as a semi-permeable barrier separating blood and interstitium and are also responsible for critical vascular homeostatic responses (Celermajer, 1997). Physiologically, endothelial cells monitor and regulate vascular tone, growth, thrombosis, thrombolysis, as well as platelet formation (Celermajer, 1997; Libby et al., 2002; Sima et al., 2009). Endothelial cells respond specifically to an increase in shear stress. When blood flow increases, a potent vasodilator, nitric oxide (NO) is released, facilitating an increased flow through the vasculature (Cullen et al., 2005). The healthy endothelium also limits thrombosis by secreting anticoagulants and ensures little expression of pro-inflammatory factors (Cullen et al., 2005).
The major pathologic process of atherosclerosis is injury or damage of arterial endothelial function (Duprez & Cohn, 2007). Such dysfunction is primarily characterized by a reduction in bioavailability of vasodilators, resulting in reduced endothelial-derived vasodilation (Cullen et al., 2005). Endothelial dysfunction creates a pro-inflammatory state, along with the increased proliferation of smooth muscle and increased clot formation (Anderson, 1999). Atherosclerotic lesions (atheroma) progress through extensive structural remodeling and thickening of the intima by smooth muscle cells (Cullen et al., 2005). Macrophages and foam cells accumulate, which facilitate inflammation, plaque formation and calcification (Cullen et al., 2005). The arterial wall thickens as a result of plaque deposits and remodeling, leading to decreased blood flow through the vasculature (Choy, Siow, Mymin, & O, 2004). Thrombi formation may also occur at the plaque site, which can ultimately present a serious risk for MI, stroke, or death (Cullen et al., 2005).

### 2.5.2 Measures of atherosclerosis

Changes in arterial function and structure can identify early atherosclerotic risk and potential risk for future CVD. Functional and anatomic changes in arterial structure can be described using endothelial function, intima-media thickness, and arterial stiffness (Poredos, 2004).

#### 2.5.2.1 Endothelial function

The arterial endothelium plays a critical role in the development and clinical course of atherosclerosis (Verma, Buchanan, & Anderson, 2003). Endothelial dysfunction is the earliest incident in the atherosclerotic process and thus may serve as a useful prognostic measure of disease formation (Verma et al., 2003). An important function of the endothelium is the release of nitrous oxide (NO) (Verma et al., 2003). NO plays a critical role in maintaining vascular tone: when shear stress is applied to the endothelium (such as increased blood flow), NO is released
thus causing flow-mediated dilation (FMD) (Verma et al., 2003). Vasculature with healthy endothelial cells will dilate with increased flow; individuals with endothelial dysfunction, as in atherosclerosis, will have a reduced FMD response (Celermajer et al., 1992). In order to examine endothelial function, the brachial artery is imaged using ultrasound and FMD is induced using the reactive hyperemia technique. FMD using the brachial artery is an accepted technique used to identify those with endothelial dysfunction by measuring and quantifying the amount of vasodilation that occurs in response to increased blood flow (Celermajer et al., 1992). While the brachial artery is ultrasound-imaged, a pneumatic cuff is applied to the participant’s forearm and inflated to 260 mmHg for 4 to 5 minutes (Celermajer et al., 1992). Blood flow increases, shear stress is stimulated, and FMD is produced as the cuff is deflated (Anderson, 1999; Celermajer et al., 1992). Ultrasound and FMD measurements are both reliable and valid indicators of endothelial function (Anderson, 1999; Sorensen et al., 1995).

2.5.2.2 Intima-media thickness

Intima-media thickness (IMT) is used to assess atherosclerotic development and CVD risk by determining the extent of anatomical changes in arterial structure (Poredos, 2004). IMT is measured using standard ultrasound techniques to capture images that highlight the thickness of the artery wall. The common carotid artery is most suitable for assessment as it is close to the surface, large in size, and limited in movement (Poredos, 2004). This non-invasive technique illustrates atherosclerotic wall changes that cannot be obtained by more invasive counterparts, such as contrast angiography or Magnetic Resonance Imaging (Poredos, 2004). IMT measurement using ultrasound has been established in the literature as being both reliable and valid (Poredos, 2004). In addition, carotid artery ultrasound offers a safe, accurate, and cost-efficient measure to assess atherosclerotic development and its progression (Aminbakhsh & Mancini, 1999). To obtain IMT, ultrasound is applied to the common carotid artery (see Appendix B for example image). The outer line corresponds to the media-adventitial wall of the
carotid artery; the inner line corresponds to the lumen-intima wall, which separates the lumen from the endothelium (the single cells that line the inside of the artery) (Gutierrez, Higa, Pilon, de Sá Rebelo, & Lage, 2013). The distance between these two lines represents the thickness of the arterial wall (Gutierrez et al., 2013). Results from The Atherosclerosis Risk in Communities (ARIC) Study, where the association between arterial wall thickness and the prevalence of CVD in was investigated, show IMT measurements to range from 0.70 to 0.83 in middle-aged US women (Burke et al., 1995).

2.5.2.3 Arterial stiffness

Arterial stiffening is a key feature of atherosclerosis (Zieman, Melenovsky, & Kass, 2005). Calcification of the innermost part of the arterial wall (intima) occurs as a result of inflammation, plaque formation, and lipid accumulation (Mackey, Venkitachalam, Sutton-Tyrrell, 2007). This hardening is associated with an increase in arterial stiffness (Mackey et al., 2007). As stiffer arteries are unable to accommodate fluctuations in blood flow, arterial stiffness may perpetuate atherosclerotic development (Mackey et al., 2007). Consequently, such increased arterial strain can result in further injury to the intima and prolonging vascular damage (Mackey et al., 2007). Arterial stiffness can be measured via pulse wave velocity (PWV) (Laurent et al., 2007).

PWV is a non-invasive technique used to reflect arterial wall stiffness (Duprez & Cohn, 2007) and is an independent predictor of cardiovascular events (Oliver & Webb, 2003). PWV refers to “the speed with which the pulse wave travels along a length of artery” (Oliver & Webb, 2003, p. 556). A pulse wave (PW) is detected when a small probe, called a tonometer, is applied to the artery; the pressure within the tonometer is equivalent to the pressure inside the artery, thus PW can be accurately detected (Oliver & Webb, 2003). PW is recorded at two sites: a proximal site (such as the common carotid artery) and a distal site (such as the femoral artery) (Oliver & Webb, 2003). Both the carotid and femoral arteries are superficial in location, making them ideal
for non-invasive assessment (Oliver & Webb, 2003). A more notable consideration for selection of these sites is that the aorta, an artery known to be particularly vulnerable to atherosclerotic development, is located between these two sites (Oliver & Webb, 2003). Therefore, the PW must travel through the aorta to get to both proximal and distal sites (Oliver & Webb, 2003). A final PW is taken at a third point (typically the foot) and the time is noted between its arrival from the proximal and distal points (Oliver & Webb, 2003). The total distance traveled is measured over the body surface and the final PWV can then be calculated by dividing distance by time (Oliver & Webb, 2003). With increased stiffness of the artery, there is an increase in velocity, as the artery does not have the elasticity to diminish the speed. Increased arterial stiffness, as reflected through an elevated PWV, has been associated with increased risk for cardiovascular events and mortality (Chen et al., 2010). In addition, arterial stiffness may augment atherosclerotic development by increasing shear stress against the arterial wall (Chen et al., 2010).

2.6 Epidemiology of Shift Work and Atherosclerosis

As previously discussed, the relationship between shift work and an increased risk of CVD is generally well supported in the literature; however, the specific mechanistic pathways are not (Tarzia et al., 2011). For the purpose of this project, the pathway of atherosclerotic changes (potentially leading to CVD) in relation to shift work exposure was investigated. Surrogate markers (i.e. endothelial function, IMT, and arterial stiffness) were used to identify early atherosclerotic development in shift working populations (Poredos, 2004).

2.6.1 Shift work and endothelial function

Recent studies have attempted to objectively determine pre-clinical atherosclerotic development in shift workers through measurement of endothelial function (Amir et al., 2004; Kim et al., 2011; Suessenbacher et al., 2011; Tarzia et al., 2011). Amir et al. (2004) examined endothelial function in healthy male (n = 23) and female (n = 7) physicians who worked a
continuous 24-hour workday. Shift work experience ranged from 0.5 years to 15 years, with an average of 5 years night shift experience. Endothelial function was measured twice in each participant with brachial artery FMD: one, a baseline measure on a regular workday (no previous or subsequent night shift); and the second, a post-night shift measure (taken after working a continuous 24-hour shift). Questionnaires addressing the number of hours slept on shift, difficulty of shift, and amount of coffee consumption, were also completed after the 24-hour shift. Smoking was not quantified, as it was not permitted on the facility; however, 6 physicians were known smokers. Researchers found that endothelial function significantly decreased after having worked night shifts, in comparison to the baseline measure (p < 0.0001). FMD was independently related to length of shift work exposure; endothelial function was significantly reduced in those who had longer (> 3 years) shift work history (p = 0.0008). The potential confounding effects of age were a significant consideration in this study; subjects who had been in shift work longer were also older. Despite sleep being independently related to a decrease in FMD (p = 0.03), it was unclear as to whether sleep deprivation or mental stress caused the decrease in endothelial function.

Tarzia et al. (2011) conducted a similar study to assess the acute effects of shift work on endothelial function in a group of cardiology residents. Nine males and 11 females took part in this study; all participants were non-smokers, non-diabetic, within normal Body Mass Index (BMI), free from hypertension and dyslipidemia, free from CVD, and had no history of acute or chronic inflammatory disease. The average age was 27 years, while the average shift working experience was 2 years. Shift work experience varied from 3 to 4 nights a month, along with 1 to 2 weekends a month. As previously discussed, vascular testing was done at 2 points: once at baseline (after a restful sleep and no night work in the last 7 days); and once post-shift (after night shift). Endothelial function was measured via 2 methods: brachial artery reactive hyperemia FMD to assess endothelial-dependent vasodilation and nitrate mediated dilation (NMD) to assess endothelial-independent vasodilation. To induce NMD, sublingual glycerin trinitrate was administered and then calculated as the percent change in diameter of the brachial artery from
baseline. Using reactive hyperemia FMD, researchers found a reduced endothelial function after a night shift in comparison to baseline (p = 0.025). However, when compared to baseline, no differences were noted in NMD after the night shift (p = 0.48).

Kim et al. (2011) examined the effect of sequential night shifts on endothelial function in healthy female nurses (n = 22). The participants were free from arterial disease, diabetes, as well as hypertension. Similar to the aforementioned studies, endothelial function was measured twice in each subject using brachial artery FMD: one, a baseline measure on a regular workday (no previous or subsequent night shift) and another, taken after working three consecutive night shifts. Bioavailability of the endothelium-derived vasodilator, NO, was also measured. Concentrations of nitrate (NO$_3^-$) and nitrite (NO$_2^-$) were obtained through blood sampling and processed via NO-analyzer. Questionnaires were administered after the night shifts to address number of hours slept on shift, amount of coffee consumed, and number of cigarettes smoked. Researchers found endothelial function to be significantly decreased after working three consecutive night shifts, in comparison to the participants’ baseline measurements (p < 0.001). Nitric oxide was also significantly decreased after working three consecutive night shifts, in comparison to the participants’ baseline measurements (p < 0.033). However, no correlations were noted between changes in NO and FMD at baseline and after night shift work. Researchers proposed that oxidative stress, resulting from night shift work, may be the cause of the decreased endothelial function as oxidation causes a reduction in available NO.

Using a cross-sectional study design, Suessenbacher et al. (2011) compared peripheral endothelial function in men working rotating shifts (MSWs) to those working non-rotating shift (MNSW). Forty-seven male glass factory workers were categorized as MNSW (employed from 8 a.m. to 6 p.m.) and 48 males were categorized as MSW (having rotated among 3 shift times). The employees were matched based on several potential confounding variables: age (35-55 years), BMI, smoking, hyperlipidemia, hypertension, family history of CVD, and work place. Peripheral endothelial function was assessed using reactive hyperemia and measured using the
EndoPAT plethysmograph device, an instrument that records arterial pulse wave amplitude using pneumatic probes. Researchers found MSWs had reduced endothelial function in comparison to MNSWs ($p = 0.03$).

While these studies support an acute association between shift work and reduced endothelial function, several gaps can be identified: only one study used a strictly female population; no studies included other valuable atherosclerotic indicators concurrently; and few studies investigated a dose-response relationship based on cumulative shift work or the presence of early atherosclerosis. This project addressed these gaps by examining the effect of shift work exposure on several atherosclerotic indicators within a female specific population, while exploring a potential dose-response relationship.

2.6.2 Shift work and IMT

A few research studies have explored the effect of shift work on intima-media thickness (IMT), despite it being a validated indicator of atherosclerosis and predictor of cardiovascular events (Puttonen et al., 2009). Haupt et al. (2008) investigated the association between shift work with subclinical atherosclerosis and MI by measuring IMT in a sample of the general population. 2510 participants (1242 female, 1268 male; aged > 45 years) were recruited for the study; of the sample, 508 males and 190 females were former shift workers. Blood samples, BMI, and waist-to-hip ratios were obtained and analyzed; IMT was measured using ultrasound of the common carotid artery. Interviews were conducted to gather information regarding shift work exposure, CVD risk factors, and socioeconomic variables. Years of shift work exposure were categorized into the following: 0 years, 1-5 years, 6-10 years, 11-20 years, and > 20 years. MI history was defined using self-reported physician’s diagnosis. Approximately 30% of the sample was former shift workers with an average shift work duration of 13.2 years. Exposure to shift work was associated with increased atherosclerotic risk; IMT was greater in those exposed to shift work ($p < 0.05$). The number of years exposed to shift work was significantly related to atherosclerosis ($p$
Those exposed to 1-5 years of shift work had significantly higher averages of IMT; maximum IMT values were found in those whose shift working exposure was greater than 20 years. In addition, shift work was identified as an independent risk factor for MI at younger ages (HR = 1.53, 95% CI 1.06 – 2.22).

Using a similar method, Puttonen et al. (2009) examined potential associations between shift work and pre-clinical atherosclerosis as indicated by carotid IMT in a young adult population. Participants for the study were selected from a prospective epidemiological study known as the Cardiovascular Risk in Young Finns study. Beginning in 1980, the original sample consisted of healthy Finnish children (ages 3 to 18 years). Puttonen et al. (2009) derived their sample from respondents over a 21-year follow-up in 2001, at which the participants reached 24 to 39 years of age. Carotid intima-media ultrasound data were obtained in 2001 for 2265 participants; however, only 1543 subjects (712 male and 831 female) were selected for the study as these subjects had data regarding their working schedule. Subjects were asked about their work experience over the last 12 months: regular day work, 2 or 3 shifts, solely evening or night shift, irregular shift, or not working. The “irregular shift” and “not working groups” were excluded allowing for working schedules to be categorized as either day work or shift work.

Cardiovascular risk factors, such as serum biomarkers, obesity, smoking, physical activity, job stress, family history, and diet were taken into account within the analysis. While controlling for age, the results showed that male shift workers had an increased risk of pre-clinical atherosclerosis as indicated by higher carotid IMT mean and maximum values (odds ratio [OR] = 1.03, p = 0.021; OR = 1.03, p = 0.028). There were no significant results female participants (p = 0.843; p = 0.789), likely related to the young age of the cohort. Additional research needs to further examine potential associations between shift work and atherosclerotic processes within exclusively female groups. This was addressed within this thesis.

2.6.3 Shift work and arterial stiffness
Similar to endothelial function and IMT, arterial stiffness can be non-invasively evaluated to assess the extent of pre-clinical artherosclerosis (Chen et al., 2010). However, few studies have utilized this measure when assessing atherosclerotic processes within a shift working population (Chen et al., 2010). A Taiwanese study investigated arterial stiffness in shift and non-shift professional bus drivers (Chen et al., 2010). Researchers hypothesized that long-term shift work would be positively associated with atherosclerotic severity. A total of 184 male bus drivers were included in the study; 135 were shift workers (including night-shift work), while the remaining 49 were regular day workers (control group). Arterial stiffness was measured using pulse wave velocity (PWV) of arm and ankle. Age, blood pressure, anthropometric data (including years in shift work), and fasting blood samples (i.e. glucose, insulin, total cholesterol, triglyceride, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol levels) were also collected. For analysis, shift work exposure was categorized into long-term exposure (>10 years) and short-term exposure (<10 years). In this study, male participants exposed to long-term shift work had significantly higher PWV (p < 0.01), thus an increased atherosclerotic risk when compared to those not working shift work or short-term shift workers. After controlling for confounding factors, a dose-response relationship was found to exist between number of years in shift work and increased PWV (Regression Coefficient= 5.7; p = 0.01).

Using similar measures, Kantermann et al. (2013) recently investigated atherosclerotic risk using PWV in steel workers. The aim of the study was to determine an association between social jet lag (representative of circadian rhythm disruption as a result of shift schedules) and atherosclerotic risk. Participants included 77 male workers employed in 3 types of work schedules: 1) a rapid rotating schedule with less consecutive days on the same shift (fast clockwise group); 2) a slower reverse schedule with more consecutive days on the same shift (slow counterclockwise group); and 3) exclusively day shifts (control group). The number of days off each year was the same for each worker and despite group allotment, and all participants had at least 5 years of work experience in their current work schedule. Participants completed
questionnaires regarding demographics, health, sleep, social life, work life and social jet lag (measured by the difference between sleep timing on workdays and work free days). PWV, BP, and HR were also measured in a controlled environment. As expected, shift workers experienced more social jet lag, representing more circadian disruption. Both shift working groups reported increased GI symptoms (i.e. stomach upset, digestion problems, and weight fluctuations). There was a positive correlation between HR and average amount of social jet lag experienced in all workers combined (while adjusting for age). Despite finding that PWV was not significantly different in the fast clockwise group when compared to the other two groups, the three highest velocities were seen in the fast clockwise group. In other words, this increase in velocity represented stiffer vessels as the arteries demonstrated inelasticity (unable to expand and retract depending on blood flow). PWV was significantly positively correlated (p = 0.005) with individual shift-work load, a measure that takes in account the account social jet lag and the speed of shift rotation (i.e. faster rotation having fewer days per shift cycle). Therefore, the researchers suggested that fast rotating shift work may impose more physiological stress, and consequently, increased CVD risk.

While the aforementioned studies suggest that both long-term and fast rotational shift work could increase atherosclerotic risk, further evidence is needed regarding the effects of shift work on arterial stiffness as determined by PWV. This project addressed this gap by investigating PWV as an indicator of atherosclerotic risk.

### 2.6.4 Summary of strengths and limitations

Within the aforementioned studies, there were some notable study strengths. This included the use of validated physiological measurement techniques, such as ultrasound and reactive hyperemia flow-mediated dilation, to collect data. In addition, these studies also accounted for various potential confounders, including age and metabolic measures, which are thought to influence atherosclerotic development. However, some limitations do exist; firstly, few
studies used a strictly female population. As previously mentioned, no studies include all three
atherosclerotic measures concurrently within the same study. In addition, many studies addressed
the “acute” effects of shift work, rather than investigating the cumulative effect of shift work on
the presence of atherosclerotic development. This exploratory study is aimed to addresses these
limitations.

2.7 Confounding Factors of Atherosclerotic Development

As previously mentioned, there are many factors that can contribute to CVD
development. Therefore, in order to accurately investigate shift work exposure and its relation to
atherosclerotic indicators, potential confounders thought to influence atherosclerotic development
must be controlled for. A confounder is defined as: 1) a variable that potentially effects the
outcome variable (i.e. atherosclerosis); 2) is associated with the exposure variable and; 3) is not
on the casual pathway. It has been observed that shift workers may adopt an unhealthy lifestyle in
order to cope with the stressors of shift work (Bøggild & Knutsson, 1999). Therefore, some of the
following factors may present potential causal mechanism(s) of CVD development instead of
being potentially confounding factors.

2.7.1 Biological factors

Age is an important factor when considering CVD development. As an individual ages,
the risk for CVD increases (HSF, 2014a). Thus, controlling for this variable is of great
importance.

Menopause is an additional biological factor that can greatly influence CVD development
as females aged 12 to 50 are innately protected from CVD when they are menstruating due to
estrogen secretion (HSF, 2014b). However, when menopause begins (i.e. menstruation stops for
12 consecutive months), estrogen production ceases and CVD risk increases (HSF, 2014b). The
profound effect of estrogen, as well as the utilization of female participants for this project, requires strict control over this confounding variable.

An increase in cholesterol has been associated with increased CVD (HSF, 2014c). Despite high-density lipoproteins (HDL) being higher in women than men, low-density lipoproteins (LDL) and triglycerides increase after menopause, and are higher in women above the age of 65 (Eastwood & Doering, 2005). Furthermore, the presence of increased triglycerides may lower HDLs and increase LDLs, thus increasing CVD risk (Eastwood & Doering, 2005; HSF, 2014c). Therefore, cholesterol and blood lipids were considered as potential covariates.

2.7.2 Lifestyle factors

CVD health can be greatly influenced by varying lifestyle factors and therefore, it is important to consider these within this specific population. Diet, physical activity, and alcohol consumption are important factors when examining CVD risk as shift work may result in changes in these behaviours in order to cope with circadian stress; thus they may be considered as causal factors or potential mediators (Bøggild & Knuttson, 1999).

Cigarette smoking highly influences in the development of CVD, resulting in increased risk for blood clots, reduced oxygen supply, and an overall increased workload on the heart (HSF, 2013). A large scale epidemiological study found that women who smoked were at an 88% increased risk for congestive heart failure in comparison to 45% in men (He et al., 2001). In addition, smoking has also been implicated with increased risk for atherosclerotic development (Zieske et al., 2005). Due to its overwhelming influence on CVD risk, individuals who smoke were excluded from the study.
2.8 Rationale

Researchers and clinicians have recognized an increased risk of CVD in the female population, specifically women entering their adulthood and middle-aged women (HSF, 2014b). Not only do the clinical signs and symptoms of CVD appear eight to 10 years later in women compared to men, but women also experience a greater risk of death as well as an increased risk of re-infarction during the first year following a cardiac event (Eastwood & Doering, 2005). Similarly, more Canadian women die from heart disease and stroke per year than all types of cancer combined (HSF, 2014b). These realities present a desperate need for early disease recognition and disease prevention.

The 2009 Canadian Heart Health Strategy and Action Plan recommends creating heart-healthy environments in order to prevent the onset of heart disease and stroke (HSF, 2009b). Given the rather recent acknowledgment of shift work as a potential environmental risk factor, the high proportion of females employed in health care settings, as well as the limited understanding of early subclinical pathways leading to CVD development, an opportunity to address this potential, and poorly understood occupational health hazard has been presented. Findings from this study may provide information to female employees and employers and create an opportunity to develop workplace policies and strategies for the prevention of CVD in both SW and NSW female employees.

Overall, the aim of this thesis is to contribute information regarding the hypothesized relationships between shift work and adverse cardiovascular changes in current female shift workers. The effect of shift work exposure on early CVD development in a female-specific group was addressed using three known atherosclerotic indicators: endothelial function, arterial stiffness, and intima-media thickness. A dose-response relationship was also investigated to determine if longer exposure to shift work resulted in greater disease risk.
2.9 References


Chapter 3

The effect of shift work on vascular structure and function in female hospital employees: an exploratory study
3.1 Abstract

**Background:** Recent epidemiological and clinical research suggests that shift work may be associated with adverse atherosclerotic changes. Endothelial dysfunction, elevated intima-media thickness (IMT), and arterial stiffening are early, preclinical predictors of atherosclerosis and may offer an opportunity to explore the specific pathway through which shift work exposure contributes to CVD development. The aims of this exploratory study were to describe and compare early atherosclerotic indicators between two groups of female hospital employees (current shift workers [SW] with at least 6 years of shift working experience and current non-shift workers [NSW] with at least 6 years of work experience and no shift work exposure); to describe the potential for a dose-response relationship between length of shift work exposure and early atherosclerotic indicators; and to explore and compare the associations between psychological stress and vascular changes in SW and NSW.

**Methods:** A comparative descriptive study was conducted using 2 groups of participants: SW (n= 20) and NSW (n= 19). Endothelial function was assessed using reactive hyperemia flow mediated dilation (FMD), arterial stiffness was assessed using pulse wave velocity (PWV), and IMT was assessed via ultrasound of the common carotid artery. Self-report measures of psychological job stress, life stress, and other personal and demographic information were collected.

**Results:** Within the sample, there were no significant difference between groups regarding atherosclerotic indicators and mean atherosclerotic values were within normal range. Based on the Effort-Reward Ratio (p = 0.003), the SW group reported a higher effort-reward imbalance as well as greater physical job demands (p < 0.001). After controlling for significant covariates, skill discretion, decision authority, and decision latitude were negatively correlated with peripheral PWV (r = -0.623, p < 0.001; r = -0.338, p = 0.044; r = -0.346, p = 0.039, respectively). IMT was positively correlated with psychological job demands (r = 0.413, p = 0.029). There was no dose-
response relationship between years of shift work experience and atherosclerotic indicators after controlling for age.

**Conclusion:** Within this sample, women working in a shift work position did not demonstrate significantly greater atherosclerotic development when compared to non-shift working women. However, women working in a shift work position reported greater psychological work stress and physical demands, and aspects of psychological job stress were associated with selected vascular indicators. Further investigation is warranted to determine the contribution of shift work related versus non-shift work related stress to vascular changes.

### 3.2 Introduction

Atherosclerosis is a complex arterial disease involving vessel injury, plaque formation, and chronic inflammation. Consequently, changes in arterial function and structure may be used to investigate early atherosclerotic development, which may allude to potential risk for future cardiovascular disease (CVD) development. Three investigative properties are known to suggest atherosclerotic development: endothelial function, arterial stiffness, and intima-media thickness (IMT). Arterial endothelium (i.e. the single layer of cells lining the vasculature) plays a critical role in hemodynamic processes as it releases nitrous oxide (NO), a potent dilator (Verma, Buchanan, & Anderson, 2003). This release of NO causes results in vascular tone changes; therefore, when there is an increase in blood flow, there is an increase in a frictional force or shear stress that causes NO to be released, subsequently causing flow-mediated dilation (FMD) (Verma et al., 2003). Vasculature with healthy endothelial cells will dilate when there is an increase in blood flow, however, individuals with endothelial **dysfunction**, will have a reduced FMD response (Celermajer et al., 1992). Endothelial dysfunction is the earliest indicator in the atherosclerotic process and can serve as a useful prognostic measure of disease formation (Verma et al., 2003). Arterial stiffening is an additional notable feature of atherosclerosis (Zieman,
Melenovsky, & Kass, 2005). As a result of inflammation, plaque formation, and lipid accumulation, arterial calcification and stiffness occurs (Mackey, Venkitachalam, & Sutton-Tyrrell, 2007). Structural changes can be measured via intima-media thickness (IMT) as this allows examination into the extent of anatomical changes within an arterial wall (Poredos, 2004). In addition to being known indicators of atherosclerotic development, the aforementioned functional and structural properties can be non-invasively measured using reactive hyperemia flow-mediated dilation (FMD), pulse-wave velocity (PWV), and ultrasound techniques.

Shift work has been associated with early atherosclerotic changes (Amir et al., 2004; Chen et al., 2010; Haupt et al., 2008; Kim et al., 2011; Puttonen et al., 2009; Suessenbacher et al., 2011; Tarzia et al., 2011). Despite this evidence, several gaps can be identified that warrant further investigation: 1) few studies have used a strictly female population; 2) no studies have investigated all three aforementioned atherosclerotic indicators concurrently; and 3) few studies investigated a dose-response relationship based on cumulative shift work or the presence of early atherosclerosis. In addition, evidence has suggested that psychological stress in the workplace may be a risk factor for atherosclerotic development (Eller et al., 2009). Acute episodes of mental stress have resulted in attenuated endothelial response, arterial stiffness, and greater IMT (Ghiadoni et al., 2000; Matthews et al., 1998; Vlachopoulos et al., 2006). In addition, workplace demands have been associated with increased arterial thickness (Lynch, Krause, Kaplan, Salonen, & Salonen, 1997). This may present an important link between repeated or chronic exposure and atherosclerotic development (Ghiadoni et al., 2000). Since shift work involves several workplace stressors (e.g. inflexible shifts, limited self-management of working hours, irregular leisure time), it may be a potential source of occupational stress that may or may not be related early atherosclerotic changes.

Given the increase in prevalence of women who work shift work and the gender-specific risk within the female population, specifically women entering adulthood and middle-aged women (Heart and Stroke Foundation, 2014), there is reason for further investigation into this
health concern. With this as a background, the objectives of this study were: 1) to describe and compare early atherosclerotic indicators (i.e., endothelial function, intima-media thickness, and arterial stiffness) between two groups of female hospital employees (female current shift workers [SW] and female current non-shift workers [NSW]) while controlling for significant covariates; 2) to explore whether a dose-response relationship exists between the length of shift work exposure and the presence of early atherosclerotic indicators; and 3) to explore and compare the associations between psychological stress and vascular changes in this population.

3.3 Materials and Methods

3.3.1 Ethics approval

The study protocol was approved by the Health Sciences Research Ethics Board (HSREB) at Queen’s University. Prior to participation, all participants provided written informed consent.

3.3.2 Participants

Thirty-nine non-pregnant women (20 SW and 19 NSW) between the ages of 23 and 65 years participated in the study. To be included in the study, participants were required to be: 1) female; 2) able to communicate in both verbal and written English; 3) employed (regular part time or full time employment) at a local Southeastern Ontario acute care hospital; 4) currently working shift work (SW group) with at least six years experience or currently working non-shift work (NSW group) with at least six years experience; and 5) have an acceptable pass of medical history questionnaire as described below (administered prior to data collection during telephone recruitment session). The women were non-smokers or previous smokers who had quit at least 5 years ago and free from diabetes (either type 1 or type 2) or cardiovascular disease (i.e. angina, cardiomyopathy, coronary artery disease, peripheral artery disease, myocardial infarction,
congenital heart disease, rheumatic heart disease, and heart failure) (Heart and Stroke Foundation, 2009). Participants who were being treated for hypertension and hyperlipidemia were included; however, those taking beta or alpha-blockers, and/or ACE inhibitors, were excluded. Lastly, morbidly obese women (body mass index [BMI] > 35) and those diagnosed with other chronic cardiovascular or metabolic illness were excluded.

3.3.2.1 Sample size considerations

Based on an *a priori* G-power calculation to allow for the detection of moderate associations between shift work exposure and FMD with 80% power (α = 0.05), a sample size of 134 participants (67 participants per group) was found to be appropriate (GPower 3.1.5 Software, Universitat Kiel, Germany). However, due to the exploratory nature of this study and feasibility considerations, this sample size was reduced to 39 participants (20 SW and 19 NSW).

3.3.3 Experimental procedure

Participants were recruited via email and telephone from two local area acute and ambulatory hospitals. Participants completed a medical screening questionnaire to ensure they met eligibility criteria prior to being accepted into the study. Once this was determined they attended the laboratory on one occasion for approximately 3.5 hours to complete the study protocol (Figure 1). They abstained from consuming any food or drink (with the exception of water) for 8 hours prior to each testing session. Each testing session began between 0800 and 1000 h, with the exception of one participant (NSW) who began testing at 1615 h. To avoid the potential acute impact of shift work on vascular function, each SW participant was tested at least 12 hours post night shift (Suessenbacher et al., 2011). Data collection sessions were performed in a quiet, temperature-controlled room (~20- 23°C).
Upon arrival at the laboratory, participants’ anthropometric measures were obtained. Waist circumference was measured by wrapping a measuring tape around the participant’s bare waist, above the iliac crest (De Michele et al., 2002). Height and weight were also obtained using the same scale throughout the data collection phase. Blood pressure was obtained prior to experimental testing using a BpTRU™ device (BpTRU Medical Devices, BC, Canada) and an average of three consecutive readings was obtained. Participants were then placed in a supine position and an IV catheter (BD Nexiva™ Closed IV Catheter System, Franklin Lakes, New Jersey, USA) was inserted for baseline and repeated blood sampling. Repeated samples were obtained as part of a longer protocol. A 30-minute rest followed. Once the rest period was completed, intima-media thickness (IMT) and pulse wave velocity (PWV) measurements were obtained followed by two flow-mediated dilation (FMD) tests, each separated by 10-minute rest period. Each participant was monitored throughout the study using an electrocardiogram (ECG) (see Appendix A).

3.3.3.1 Blood samples
Prior to the initial 30-minute rest period, baseline blood samples were obtained to quantify triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol (TC), fasting glucose (FG) and blood viscosity.

3.3.3.2 Intima-media thickness

IMT was measured using ultrasound of the common carotid artery. A 12-MHz ultrasound probe (Vivid i2 GE Medical Systems, Milwaukee, WI, USA) operating in B mode was applied to the participant’s left common carotid artery. Once a satisfactory image was obtained (i.e. a clear lumen-arterial wall boundary on the far wall), the image was recorded for 10 seconds. Acquired images were recorded as .avi files using a separate computer (Camtasia Studio, TechSmith, Okemos, MI, USA) with a VGA to USB frame grabber (Epiphan Systems Inc., Ottawa, ON, Canada).

3.3.3.3 Pulse wave velocity

Three separate pulse waves were measured simultaneously using two separate tonometers (Millar® Instruments, Houston, TX, USA) and a photoplethysmography (PPG) sensor Plethysmograph (AD Instruments, Colorado Springs, CO, USA). The tonometers were applied to the right common carotid artery and the right femoral artery, while the IR probe was secured above the dorsalis pedis, positioned dorsally on the right foot. A 20-second recording of the pulse waves was obtained using Lab Chart (Powerlab, AD Instruments, Colorado Springs, CO, USA). Once completed, straight line distances between pulse wave recording sites were measured as follows: carotid tonometer site to sternal notch, sternal notch to femoral tonometer site, and femoral tonometer site to dorsalis pedis PPG site.

3.3.3.4 Brachial artery blood velocity and diameter

Endothelial function was tested using reactive hyperemia flow-mediated dilation (FMD) of the brachial artery (Celermajer et al., 1992). A 12-MHz ultrasound probe (Vivid i2 GE
A pneumatic cuff was applied to the participant’s left forearm. One minute of baseline artery diameter and blood velocity was recorded. The cuff was then inflated to 260 mmHg for five minutes. Arterial diameter and blood velocity were recorded for the last minute of occlusion and for three minutes following cuff release. Four participants had a third trial completed, as the signal and image quality was deemed unacceptable in both of the first two trials. The mean of two trials was calculated for 12 participants, giving a mean FMD measurement. The remaining 27 participants only had one acceptable FMD measurement. This method was also used for shear stress stimulus calculations (i.e. mean of two trials for 12 participants and one trial for 27 participants).

3.3.4 Psychological stress measures

Work stress was measured with the Job Content Questionnaire (JCQ), developed by Karasek et al. (1998), and the Effort Reward Imbalance (ERI) questionnaire, developed by Siegrist (1996). The JCQ consists of 56-items, including subscale measurements for decision latitude (9 items), decision authority (3 items), skill discretion (6 items), psychological demands
(5 items), and physical demands (5 items). For each question, the participant rated on a scale – 1 - strongly disagree, to 4 - strongly agree – how she felt the statement described her job and job environment. As per guidelines, items contributed to the calculation of the selected subscale. The ERI provided an additional measure of psychological workplace stress. This index focuses on reciprocity in one’s occupational life, such that high-efforts and low-rewards conditions result in a state of emotional stress, which may lead to cardiovascular risk (de Jonge, Bosma, Peter, & Siegrist, 2000; Siegrist, 1996). Efforts include both extrinsic (e.g. demands, obligations) and intrinsic factors (e.g. critical coping), and rewards include money, esteem, and status control (Siegrist, 1996). This tool consists of 52-items, including six effort and 11 reward subscales. In order to calculate the degree of imbalance, the following formula was used:

\[
\text{Effort-reward Ratio} = \frac{e}{r * c}
\]

where \(e\) is the sum of the effort score, \(r\) is the sum of the reward score, and \(c\) is the correlational factor (number of items in the numerator divided by the number of items in the denominator) (Peter et al., 1998). Ratio values close to zero suggest favorable conditions (i.e. low effort and high rewards) while values over one indicate unfavorable conditions (i.e. high effort and low rewards) (Peter et al., 1998).

Life stress was measured using the Derogatis Stress Profile (DSP) (Helmers, Danoff, Steinert, Leyton, & Young, 1997). This 77-item self-report questionnaire examines area of life that precipitates psychological stress and includes the following domains and subscales: environmental factors (domestic, vocational, and health); personality mediators (time pressure, driven behaviour, attitude posture, relaxation potential, and role definition); and emotional responses (hostility, anxiety, and depression) (D’Zurilla & Sheedy, 1991). Each question was rated on a five-point scale – 0 - not at all true of me, to 4 - extremely true of me. Participant responses were tallied, and then standardized with original DSP data, to give a total stress score
A t-score of 50 is defined as the mean for the general population, with a standard deviation of 10 (Helmers et al., 1997). A higher t-score is suggestive of more stress (Helmers et al., 1997).

### 3.3.5 Covariates

Variables potentially associated with vascular outcomes were identified a priori. These included age, menstruation status, weight, BMI, waist circumference, total cholesterol (TC), triglycerides (TG), fasting glucose (FG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and blood pressure.

Since physical activity has been suggested to decrease CVD risk (Oguma & Shinoda-Tagawa, 2004), physical activity was included as a potential covariate. The Global Physical Activity Questionnaire (GPAQ) (World Health Organization [WHO], 2013) was administered to measure participants’ overall level physical activity in the following domains: activity at work, travel to and from places, and recreational activities. A total physical activity score (i.e. sum of activity per week) was determined using all activity domains (WHO, 2013).

### 3.3.6 Data analysis

#### 3.3.6.1 Blood sample analysis

Blood samples were analyzed for TC, TG, FG, LDL, and HDL using the Alere Cholestech LDX® System (Ottawa, ON, Canada). Whole blood viscosity was measured using a viscometer at a shear rate of 225 s\(^{-1}\) at 37 ± 2 °C (DV-II + Pro, Brookfield Viscometer, Middleboro, MA, USA). Blood viscosity was obtained for all participants, with the exception of three participants (1 SW, 2 NSW) whose blood viscosity was substituted with the mean of that group. TG and LDL levels were not obtained in 11 participants (5 SW; 6 NSW) whose levels were beyond the detectable range of the Cholestech system and therefore excluded from the mean calculation (King, Slattery, & Pyke, 2013). One participant (SW) was excluded for FG as the
value was below the detectable range.

3.3.6.2 IMT analysis

IMT boundaries were identified using .avi files (as previously described) and edge
detection software (Carotid Analyzer for Research, Version 5.7.4, Medical Imaging Applications
LLC, Coralville, IA, USA). The operator manually calibrated the image; the M-line (the media-
adventitial wall of the carotid artery) was then automatically detected using the software program.
This was subject to approval by the operator and altered if needed, in order to reflect proper wall
representation. Once selected, the I-line was automatically detected using the M-line as a guide
(Davis, Dawson, Blecha, Mastbergen, & Sonka, 2010). Approximately 75 frames were generated
per file and each frame was reviewed to ensure accurate border wall recognition. The frame was
rejected if wall tracking was not accurate and the tracking could not be manually altered to
accurately represent wall location (i.e. border not clearly identified). An average far wall IMT
measurement was generated using all frames in the image clip. Rejected frames were not included
in the calculation. Variability in IMT measurements in the Cardiovascular Stress Response
Laboratory ([CVSRL] Kingston, Ontario, Canada) was recently established as follows: intra-
observer (same participant assessed by the same operator on two occasions) coefficient of
variation (CV) (CV=SD/mean*100) of 6.4%; and inter-observer (same participant, same session,
two different operators) CV of 4.5%.

3.3.6.3 PWV analysis

PWV was analyzed offline using LabChart (Powerlab, AD Instruments, Colorado
Springs, CO, USA). Each tonometer and PPG signal was band-pass filtered at five to 30 Hz. Since
this filter removed higher (>30 Hz) and lower (<5 Hz) frequencies, the point of steepest incline
on each wave was more easily detected (Martin, Cotie, Timmons, Gorter, & MacDonald, 2012).
Pulse transit times were determined within a 10-beat period using two separate measures: 1)
central transit time, using the time delay between the carotid pulse wave and the femoral pulse wave; and 2) peripheral transit time, using the time delay between the femoral pulse wave and the dorsalis pedis pulse wave. Distances between measurement sites were calculated, as follows (Martin et al., 2012): 1) central distance: sternal notch to femoral tonometer measurement site minus carotid tonometer measurement site to sternal notch; and 2) peripheral distance (femoral tonometer measurement site to dorsalis pedis PPG measurement site). Both central and peripheral PWV were determined using the following formula:

\[ \text{PWV} = \frac{D}{\Delta t} \]

where \( D \) was the distance (in meters) between measurement sites and \( \Delta t \) was the pulse transit time (in seconds). The transit time was represented as mean central and peripheral time calculated separately for each heart cycle; all subjects had a minimum of eight heart cycles included in the calculation for average transit time (up to 2 outlier cycles omitted from 10 beat sample). The variability of central pulse wave velocity measurements in the CVSRL was recently established as follows: intra-observer CV of 3.16% and inter-observer CV of 2.9%.

3.3.6.4 Brachial artery blood velocity

As previously described by Pyke, Poitras, and Tschakovsky (2008), blood flow velocity was calculated offline using 3-second average time bins using the software program LabChart (Powerlab, AD Instruments, Colorado Springs, CO, USA).

3.3.6.5 Brachial artery diameter

As previously described by Woodman and colleagues (2001), brachial artery vessel diameter was analyzed using an automated edge-detection software program (Encoder FMD & Bloodflow, Reed Electronics). The user identified the clearest arterial wall border and then manually selected this as the region of interest (ROI). Once selected, the program automatically
processed the video file, tracking the intensity of wall of the artery versus the lumen of the vessel. One diameter was generated for every pixel column in the ROI and the median diameter was used as a diameter measurement for that particular frame. Erroneous diameter measures (due to vessel wall tracking issues) were reviewed and removed. The diameter measures were then compiled into 3-second time bins. Missing data as a result of diameter removal for poor tracking were interpolated. The percent change in diameter (%FMD) was calculated as the change in diameter from baseline prior to cuff occlusion, to the peak post-cuff release. This was applied for each FMD Trial with the exception of seven subjects (4 SW; 3 NSW), where the diameter in the last minute of occlusion was utilized for the baseline diameter in the calculation. This was done in these cases due to substantially superior tracking during occlusion, compared to the data during the pre-occlusion period. The user was blinded to whether the participant was a SW or NSW. Within the CVSRL, the stability of FMD measurements was recently established (Szijgyarto et al., 2013) using both within (intraobserver intraclass correlation coefficient: FMD 0.98) and between (interobserver intraclass correlation coefficient: RH-FMD 0.96) observers.

3.3.6.6 Shear stress

Brachial artery shear stress (dynes per square centimeter) was used to quantify the stimulus for FMD. It was calculated using the following formula (Gnasso et al., 2001):

\[ \text{Shear stress} = \frac{4\eta v}{D} \]

where \( \eta \) is blood viscosity (measured in Poise), \( v \) is the mean blood velocity (measured in centimeters per second in 3-second time bins), and \( D \) is the brachial artery diameter (measured in centimeters). The shear stress during FMD was expressed using the area under the curve (AUC). AUC was calculated using SigmaPlot (San Jose, CA, USA) from time of cuff release until time of peak diameter (Pyke & Tschakovsky, 2007; Thijssen et al., 2011). One participant (1 SW)
demonstrated a very small dilatory response; subsequently, it was unknown if the time to peak
diameter was representative of a physiologic response. Therefore, the shear stress for this
participant was expressed using the AUC for the first 30 seconds following cuff release (Poitras
et al., 2014) in order to capture an accurate shear stress value.

3.3.6.7 FMD- normalization

Based on the recommendations of Pyke and Tschakovsky (2005), the magnitude of the
FMD response was also considered in the context of the stimulus imposed. Known as FMD-
normalization, this variable was calculated by dividing % FMD by the corresponding magnitude
of the stimulus achieved (Pyke & Tschakovsky, 2005). Since the degree of dilation has been
shown to depend on the respective stimulus, this calculation allowed for consideration of both the
functionality of the endothelium resulting in a dilatory response as well as the magnitude of the
stimulus imposed on the vessel wall (Pyke & Tschakovsky, 2005; Rakobowchuk et al., 2005).

3.3.7 Statistical analysis

Baseline characteristics, outcome variables (i.e. FMD, IMT, pPWV, and cPWV), and data
from the questionnaires were statistically analyzed using SPSS Statistics version 22 (IBM,
Armonk, NY, USA). Each variable was initially analyzed using Kolmogorov-Smirnov Test for
normality. To compare differences between groups, continuous variables were analyzed using
independent t-tests (for normally distributed data) and Mann Whitney tests (non-normally
distributed data). Chi-square test and Fisher’s Exact Test were used to analyze categorical data. In
order to control for the effects of significant covariates, bivariate correlational analysis was used
to determine the effect of covariates on vascular indicators and psychological stress scores.
Significant covariates were then included within the partial correlational analysis to determine the
associations between atherosclerotic indicators and psychological stress. In addition, partial
correlation was used to determine the presence of a dose-response relationship between shift
work and the various atherosclerotic indicators while controlling for age. Statistical significance for all analyses was set at \( p \leq 0.05 \).

### 3.4 Results

Demographic characteristics are presented in Table 1. Women of the SW group were more likely to be employed in a nursing position \(( p < 0.01 \)) , have more children \(( p = 0.03 \) ), and work longer shifts in comparison to the NSW group \(( p < 0.01 \) ). As expected, the SW group worked exclusively mixed shifts while the NSW working group worked exclusively day shifts \(( p < 0.01 \) ). There were no differences in marital status, education, household income, menstrual phase, family history of heart attack, personal history of blood pressure or cholesterol and employment status.

Baseline characteristics are presented in Table 2. There were no significant differences between groups regarding baseline characteristics, with the exception of blood viscosity, which was higher in the SW group \(( p = 0.007 \) ). The average age of all participants was 41 years, ranging from 23 to 61 years of age. Approximately 56% of all participants (12 SW; 10 NSW) were overweight (BMI > 25).

Atherosclerotic indicators are presented in Table 3. There was no significant difference between groups regarding FMD, shear stress, IMT, cPWV, or pPWV.

Psychological stress scores (JCQ, ERI and DSP) are presented in Table 4. SW, in comparison to NSW reported significantly higher Effort-Reward Ratio scores \(( 1.68 \pm 1.20 \text{ versus } 0.90 \pm 0.37, p = 0.003 \) ), lower reward \(( 3.10 \pm 1.21 \text{ versus } 4.53 \pm 1.78, p = 0.016 \) ) and higher physical job demands \(( 13.6 \pm 1.82 \text{ versus } 7.79 \pm 3.37, p < 0.001 \) ). While not significant, SW also reported lower levels of skill discretion \(( 34.6 \pm 4.45 \text{ versus } 36.3 \pm 5.09, p = 0.176 \) ), decisional authority \(( 31.4 \pm 5.84 \text{ versus } 35.4 \pm 6.83, p = 0.076 \) ), decisional latitude \(( 66.0 \pm 8.99 \text{ versus } 71.7 \)
± 10.2, p = 0.072), and psychological job demands (21.1 ± 4.46 versus 17.7 ± 5.43, p = 0.061). There were no significant differences in the remaining subscale measures.

Correlations between psychological stress scale measures and atherosclerotic indicators are presented in Table 5. After controlling for significant covariates (Table 7), three JCQ subscales were significantly negatively correlated with pPWV: skill discretion (r = -0.62, p < 0.001); decision authority (r = -0.34, p = 0.04); and decision latitude (r = -0.35, p = 0.04). Psychological job demands was positively correlated with IMT (r = 0.41, p = 0.03) and shear stress, as represented by AUC, was positively correlated with physical job demands (r = 0.42, p = 0.03). FMD-normalized was positively correlated with status control (r = 0.46, p = 0.03).

Correlations between years of shift work experience and atherosclerotic indicators are presented in Table 6. Years of shift work experience did not significantly correlate with atherosclerotic indicators after controlling for age.

3.5 Discussion

To the best of our knowledge, this study was the first of its kind, comparing both vascular function and structure within a female population. The key findings from this exploratory study are: 1) there was no difference in selected atherosclerotic indicators between SW and NSW; 2) SW reported higher effort-reward imbalance and physical job demands as well as a trend towards higher levels of psychological job stress; 3) among all workers, selected aspects of psychological job stress were associated with some indicators related to atherosclerotic development (i.e. negative aspects of work were associated with increased IMT and positive aspects of work were associated with peripheral PWV). Based on these exploratory findings, it can be postulated that the combination of psychological job stress in a shift work position may influence atherosclerotic changes. This preliminary evidence suggests that some workplace characteristics may be protective, while others may be deleterious.
The observed %FMD, IMT, and PWV values were comparable to those found in within the literature. In healthy individuals, the percentage of FMD reported is 7 to 10% from baseline arterial diameter (Moens, Goovaerts, Claeys, & Vrints, 2005). In Caucasian women aged 45 to 64 years of age without CVD disease, the mean IMT is 0.69 mm (Folsom et al., 1994). The reported central PWV range in a healthy population (n = 1455), aged 30 to 59 with 59% women, is 6.5 to 8.3 cm/s (Reference Values for Arterial Stiffness' Collaboration, 2010). Since peripheral arteries do not exhibit the same pulsatile changes in comparison to central arteries (Miyatani et al., 2009), the peripheral PWV values tend to be higher.

Based on these “normal” values, our study population as a whole did not exhibit signs of early atherosclerotic disease development. Within this sample, shift workers did not reveal greater atherosclerotic development in comparison to the NSW group. However, when individual cases were examined, 5 SW and 3 NSW exhibited percentage FMD values between zero and 5%, a range associated with CVD (Moens et al., 2005). Three NSW participants (aged 45 to 61) demonstrated greater than normal IMT (0.7, 0.7, and 0.74 respectively); two NSW participants exhibited greater than normal age-appropriate velocities (10.2 cm/s and 9.9 cm/s). It is noteworthy that one NSW participant demonstrated both increased IMT as well as increased central PWV, which may indicate early atherosclerotic development. As expected, peripheral PWV was higher when compared to central PWV in each group. However, 13 participants (6 SW; 7 NSW) had greater central PWV in comparison to their peripheral values; this may have been due to instrumentation and measurement errors (e.g. errors in measuring location of probe placement). Further investigation regarding peripheral PWV in this population is needed.

An evaluation of traditional risk factors suggests that the SW group may be more at risk for CVD development. While not statistically significant, the SW group tended to have greater waist circumference, higher TC, and increased LDL values – all of which are influential factors of vascular health (Moens et al., 2005). However, the SW group also reported greater physical activity. Since physical activity is beneficial in cardiovascular health (Oguma & Shinoda-
Tagawa, 2004), this may have offset any the influence of these factors on vascular changes, making it difficult to detect atherosclerotic changes in this group.

Our finding of no difference in atherosclerotic indicators between SW and NSW may be explained by several factors. It is possible that the shift-working group was well adjusted to the stresses of shift work; therefore, it is possible that they were not experiencing the circadian stress as predicted. Also, given the aforementioned protective effect of physical activity on vascular health, it is possible that the GPAQ did not capture all physical activity due to self-reporting error (i.e. the participants did not accurately report the level of physical activity experienced). Therefore, it is possible that participants were more physically fit than reported, which may protect vascular health. An additional factor may be due to the age of the sample; the mean age of the sample was 41, with a large portion of these women actively menstruating. Due to the presence of estrogen, this may have created a protective vascular effect for these women, potentially influencing atherosclerotic changes. In the case where participants had been older and pre-menopausal/menopausal, it is possible that we would have observed attenuated arterial function. In addition, participant sample size could have been a factor. Despite being unable to obtain our predetermined sample size, our original calculation was similar to Chen et al. (2010), who explored arterial stiffness in 184 participants. Compared to a short-term (less than 10 years) SW group (n = 99) and a control group (n= 49), they found increased arterial stiffness among a long-term (greater than 10 years) SW group (n = 36). Since our exploratory study only included 39 participants total, it is possible that with a larger sample size, differences may have been more easily detected between groups.

While atherosclerotic indicators were not significantly different between groups, there were differences in self-reported psychological stress in the workplace. Shift working women reported significantly greater effort reward imbalance as well as significantly lower rewards in the workplace, suggesting increased psychological job stress. While not significant, they also reported lower levels of skill discretion, decisional authority, and decisional latitude, further
suggesting a trend of increased psychological job stress. These findings are consistent within existing literature (Bøggild, Burr, Tüchsen, & Jeppesen, 2001; Golubic, Milosevic, Knezevic, & Mustajbegovic, 2010; Harada et al., 2005; Jamal, 2004). A recent unpublished study (Tennant, 2014) compared psychological job stress using female shift and non-shift working hospital employees from the same site as this exploratory study. Similar to the current study’s findings and trends, those in a shift work position reported greater effort reward imbalance and greater psychological job demands.

Shift working women also reported greater physical job demands, as measured using the JCQ. This result was expected, given the high physical requirements needed within the nursing profession (e.g. transferring patients, walking the floors, standing long hours) and the large majority of individuals within the SW group employed in a nursing field. Tennant (2014) also reported similar findings, suggesting that shift work employees in a hospital setting experience greater physical job demands.

We found significant correlations with selected psychological job stress scales and atherosclerotic indicators. Skill discretion, decision authority, and decision latitude were all negatively correlated with pPWV. These components of the JCQ address control over job performance as well as highlight creativity and autonomy over job decisions (Karasek et al., 1998); thus, they may be considered desirable workplace qualities. This may account for the decrease in pPWV as an increase in these positive workplace characteristics may result in a slower pPWV, suggesting healthier arterial structure (e.g. decreased arterial stiffness). Our results are consistent with Utsugi et al. (2009), as they investigated the association of work-related psychological stress and arterial stiffness in male (n = 3,412) and female (n = 854) government employees. Within the female population, they concluded that high job strain (representative of low control) was significantly associated with increased brachial-ankle PWV, indicative of increased aortic stiffness. The current exploratory study may complement this existing study, suggesting that such positive workplace characteristics may provide vascular protection. The
existing literature has focused on central PWV and its associated risk; however, the degree of influence regarding CVD risk factors on central versus peripheral arteries remains unclear (Choo et al., 2014). Therefore, additional research regarding peripheral PWV is warranted.

Normalized FMD was positively correlated with status control; as status control increased, endothelial function also increased. Sense of control could be considered desirable within the workplace (Bakker, Killmer, Siegrist, & Schaufeli, 2000). Therefore, it may be initially interpreted that this occupational feature has a protective effect towards endothelial function. Vasculature with healthy endothelial cells will dilate with increase flow whereas individuals with endothelial dysfunction, as in atherosclerosis, will have a reduced FMD response (Celermajer et al., 1992). However, this result should be considered with caution, as there are some inconsistencies between stress subscales and endothelial function indicators. For example, if an increase in “positive” workplace qualities resulted in increased endothelial function, it may be predicted that an increase in extrinsic effort or ERI ratio (i.e. greater effort-reward imbalance) should have a reduced FMD or FMD-norm. However, no significant relationships were detected. These inconsistencies may be due to the nature of the self-report questionnaires (e.g. social desirability, negative versus positive response sets, etc.) (Elovainio, Kuusio, Aalto, Sinervo, & Heponiemi, 2010).

Physical job demands were positively correlated with brachial artery shear stress (represented as AUC). A shear stress stimulus is created with cuff release and allows for flow-mediated dilation of the brachial artery. This stimulus is reflective of resistance vessel function and/or brachial arterial diameter versus forearm size. For example, in the instance where an individual has a large forearm with a small brachial artery diameter, there may be a larger brachial artery shear stress. Exercise, or being physically active at work, could have altered the forearm musculature and forearm resistance vessel structure and tone (Niebaurer & Cooke, 1996), creating a larger forearm with increased metabolic needs.
Psychological job demands were positively correlated with IMT. This suggests that an increase in psychological job demands is associated with an increased thickness of the arterial wall (Fujishiro et al., 2010; Xu et al., 2010). However, Hintsanen et al. (2005) reported contradictory results in young women (n = 542). It was found that overall job strain, and its respective components, was not associated with increase in IMT. Hintsanen et al. (2005) attributed these results to the youth of the population, given that participants were aged 24 to 39 and atherosclerosis develops later in the female life. Rosvall et al. (2002) found that women (n = 1550), aged 45 to 65, occupied in psychologically demanding jobs (i.e. high demands, low control) had increased IMT when compared to women who reported low demands and high control. Our study contributes to these findings as we found increased psychological job demands in women over a wide range of ages (23 to 61 years of age) correlated with increased IMT. This may suggest that younger women are also subject to adverse atherosclerotic changes as IMT is a surrogate marker for cardiac health and is related to the extent of disease processes (Burke et al., 1995; Simon, Megnien, Chironi, 2009; Xu et al., 2010).

The specific mechanisms linking psychological stress to vascular changes have been questioned in previous literature: it is unknown whether the presence of stressors causes an increase in cortisol production and/or increased activation of the sympathetic nervous system resulting in adverse cardiovascular changes (Puttonen et al., 2009). In addition, changes in behavioural habits (e.g., dietary consumption, physical activity, smoking) to cope with such psychological stressors could also be a precipitating factor influencing changes in vascular structure. Further investigation into the specific mechanism is needed for verification.

The vascular indicators used for this study are all surrogate markers for atherosclerotic development; however, there exists an interrelationship between them (Moens et al., 2005). The dilatory response (FMD) represents the mechanics and functionality of the endothelial lining (e.g. shear stress and NO release causing endothelial-dependent dilation); similarly, PWV reflects mechanical distensibility of the arterial wall (Moens et al., 2005). Alternatively, morphological
changes are captured using IMT (Moens et al., 2005). The findings of this study indicate that job
stress was associated with both functional and structural atherosclerotic changes (i.e. IMT and
peripheral PWV). The association between central PWV and IMT is well noted in the literature;
van Popele et al. (2001) concluded that central arterial stiffness is strongly associated with IMT
within the carotid artery. There are some possible explanations for this association: the thickening
and plaque formation within arteries may cause the arterial walls to stiffen, resulting in an
increase in PWV (van Popele et al. 2001). Alternatively, arterial stiffening may cause vessel wall
damage, which then may stimulate progression of atherosclerosis (e.g. smooth muscle cell
proliferation) resulting in increased IMT (van Popele et al. 2001). Lastly, it is possible that
arterial stiffness and increased arterial thickness occur at similar sites by chance (van Popele et al.
2001). Regardless, the use of all three vascular indicators is recommended; individuals who
demonstrate reduced functionality and structural changes have higher atherosclerotic disease risk
(Moens et al., 2005). Therefore, the use of all three indicators provides a more accurate profile
than measurement alone (Moens et al., 2005).

This study possesses several limitations and strengths. Firstly, this study consisted of a
small sample size. While adequate for this exploratory study, increasing sample size may allow
for smaller detection of atherosclerotic differences between groups. In addition, a larger sample
size may allow for increased generalizability to populations. As previously mentioned, our
sample included young women who were menstruating, which may have added a protective
benefit, making it difficult to detect atherosclerotic changes.

Second, the quantification of SW presents a study limitation – since it introduces
increased variability into the SW group. Work experience was quantified by the number of years
worked, rather than the total number of hours worked. Therefore, each group contained both full-
time and part-time employees. However, this likely presents minimal influence as most part-time
employees in the SW group worked full-time hours (e.g. taking on additional shifts, working
over-time, etc.). Three NSW participants were included in the NSW group despite having shift
work history. This may present a limitation regarding the homogeneity of the groups; however, this is unlikely as these individuals participated in SW greater than 10 years prior (Bøggild & Knutsson, 1999; McNamee et al., 1996; Taylor & Pocock, 1972).

An additional study limitation relates to the menstrual stage classification. Each participant was asked to recall when her LMP occurred. This may present a self-reporting error as participant may inaccurately report when LMP occurred. Consequently, this could have influenced our ability to detect differences between shift and non-shift workers. For example, if more erroneous reports of menstruation occurred in the shift work group, this could have augmented FMD responses (e.g. increased FMD values in SW group). Therefore, when compared to the NSW, this may have disguised any atherosclerotic differences between groups. For future research, determining hormone levels may be a more accurate method for controlling for the effect of estrogen on arterial function.

Despite these limitations, this study demonstrated notable strengths. To our knowledge, this study is the first to examine and report on three concurrent atherosclerotic indicators within a female-specific population. This study followed a strict research methodology by using widely accepted techniques to investigate vascular structure and function known to be independent predictors of CVD risk (Skilton & Celemajer, 2014). Since this study was exploratory in nature, we have presented a well-designed protocol that may be used for a future large-scale study.

Overall, this study explored the atherosclerotic health of both shift and non-shift workers. While shift workers within this sample do not show indications of early atherosclerotic disease in regards to shift working status, shift workers do experience increased psychological and physical job demands, which is associated with vascular changes. These workplace factors may be protective in regards to vascular function, while others may be deleterious. Findings from this study highlight the need from individuals and employers to address stress as an occupational health concern. At an individual level, shift workers need to be aware of the unseen hazards within the workplace in order to develop healthy habits and facilitate stress release. Managers,
employers, and executives need to recognize these stressors and offer ways to facilitate healthier workplaces (e.g. offering team building exercises to facilitate unity among employees and decrease stress, applying new technologies to decreases physical stress in the workplace, etc.)

By investigating three known atherosclerotic indicators in a female-specific cohort, several gaps have been addressed within the context of this study. For future work, a longitudinal study investigating the effects of shift work over many years may show atherosclerotic changes over time. Since job stress was identified as a factor impacting the health of shift workers, it may be beneficial to explore this relationship further (i.e., investigating how an individual copes and manages stress). Furthermore, investigation into whether long periods of shift work result in decreased stress, suggesting that shift workers become accustomed to such workplace stressors, may be of interest. Lastly, using other female shift working groups, such as police officers and prison guards, may also help to describe the effect of shift work in other areas.
3.6 References


healthy middle-aged men: a cross-sectional population-based study. *BMC Cardiovascular Disorders, 14*(1), 5.


Folsom, A. R., Eckfeldt, J. H., Weitzman, S., Ma, J., Chambless, L. E., Barnes, R. W., ... & Hutchinson, R. G. (1994). Relation of carotid artery wall thickness to diabetes mellitus,


Heart and Stroke Foundation of Canada. 2009. Heart disease- heart disease conditions. Retrieved from
http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.3483923/k.FCD0/Heart_disease__Heart_Disease_Conditions.htm

http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.3484041/k.D80A/Heart_disease__Women_and_heart_disease_and_stroke.htm


Tennant, J. (2014). A comparative analysis of work and life stress in female shift work and non-shift work hospital employees. Unpublished manuscript, School of Nursing, Queen’s University, Kingston, Canada.


Table 1. Demographic characteristics of study population.

<table>
<thead>
<tr>
<th></th>
<th>All Workers (n = 39); n (%)</th>
<th>Shift workers (n = 20); n (%)</th>
<th>Non-shift workers (n = 19); n (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martial Status (^a)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married or common law</td>
<td>21 (55%)</td>
<td>12 (60.0%)</td>
<td>9 (50.0%)</td>
<td>0.812(^*)</td>
</tr>
<tr>
<td>Widowed, separated, Divorced</td>
<td>6 (16%)</td>
<td>3 (15.0%)</td>
<td>3 (16.7%)</td>
<td></td>
</tr>
<tr>
<td>Single, never married</td>
<td>11 (29%)</td>
<td>5 (25.0%)</td>
<td>6 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>Number of Children</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>21 (54%)</td>
<td>7 (35.0%)</td>
<td>14 (73.7%)</td>
<td>0.031(^*)</td>
</tr>
<tr>
<td>1-2</td>
<td>15 (38%)</td>
<td>10 (50.0%)</td>
<td>5 (26.3%)</td>
<td></td>
</tr>
<tr>
<td>≥3</td>
<td>3 (8%)</td>
<td>3 (15.0%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-secondary (cert./diploma)</td>
<td>23 (59%)</td>
<td>13 (65.0%)</td>
<td>10 (52.6%)</td>
<td>0.095(^*)</td>
</tr>
<tr>
<td>University Undergraduate</td>
<td>12 (31%)</td>
<td>7 (35.0%)</td>
<td>5 (26.3%)</td>
<td></td>
</tr>
<tr>
<td>Graduate</td>
<td>4 (10%)</td>
<td>0</td>
<td>4 (21.1%)</td>
<td></td>
</tr>
<tr>
<td>Household Income (^b)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;$49,999</td>
<td>3 (8%)</td>
<td>1 (5.0%)</td>
<td>2 (11.8%)</td>
<td>0.298(^*)</td>
</tr>
<tr>
<td>$50,000-$99,999</td>
<td>23 (62%)</td>
<td>11 (55.0%)</td>
<td>12 (70.6%)</td>
<td></td>
</tr>
<tr>
<td>&gt;$100,000</td>
<td>11 (30%)</td>
<td>8 (40.0%)</td>
<td>3 (17.6%)</td>
<td></td>
</tr>
<tr>
<td>Menstrual Phase (at time of collection) (^c)</td>
<td></td>
<td></td>
<td></td>
<td>0.173(^*)</td>
</tr>
<tr>
<td>Menopausal</td>
<td>10 (26%)</td>
<td>5 (26.3%)</td>
<td>5 (26.3%)</td>
<td></td>
</tr>
<tr>
<td>Menstruation</td>
<td>7 (18%)</td>
<td>3 (15.8%)</td>
<td>4 (21.1%)</td>
<td></td>
</tr>
<tr>
<td>Follicular</td>
<td>7 (18%)</td>
<td>1 (5.3%)</td>
<td>6 (31.6%)</td>
<td></td>
</tr>
<tr>
<td>Early Luteal</td>
<td>8 (21%)</td>
<td>6 (31.6%)</td>
<td>2 (10.5%)</td>
<td></td>
</tr>
<tr>
<td>Late Luteal</td>
<td>4 (11%)</td>
<td>2 (10.5%)</td>
<td>2 (10.5%)</td>
<td></td>
</tr>
<tr>
<td>Aphasic (^d)</td>
<td>2 (6%)</td>
<td>2 (10.5%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Family history of heart attack before age 60</td>
<td></td>
<td></td>
<td></td>
<td>0.605(^*)</td>
</tr>
<tr>
<td>History of/current medication for:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High blood pressure</td>
<td>2 (5%)</td>
<td>0</td>
<td>2 (10.5%)</td>
<td>0.136(^*)</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>2 (5%)</td>
<td>1 (5.0%)</td>
<td>1 (5.3%)</td>
<td>0.970(^*)</td>
</tr>
<tr>
<td>Employment category</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nursing</td>
<td>20 (51%)</td>
<td>18 (90.0%)</td>
<td>2 (10.5)</td>
<td>&lt;0.01(^*)</td>
</tr>
<tr>
<td>Allied Health</td>
<td>4 (10%)</td>
<td>0</td>
<td>4 (21.1%)</td>
<td></td>
</tr>
<tr>
<td>Administrative Services</td>
<td>9 (23%)</td>
<td>0</td>
<td>9 (47.4%)</td>
<td></td>
</tr>
<tr>
<td>(research, management)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supportive Services</td>
<td>2 (6%)</td>
<td>0</td>
<td>2 (10.5%)</td>
<td></td>
</tr>
<tr>
<td>(occupational health, facilities)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laboratory Services</td>
<td>4 (10%)</td>
<td>2 (10.0%)</td>
<td>2 (10.5)</td>
<td></td>
</tr>
<tr>
<td>Full time vs. Part time?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full-time</td>
<td>32 (82%)</td>
<td>17 (85.0%)</td>
<td>15 (78.9%)</td>
<td>0.695(^*)</td>
</tr>
<tr>
<td>Part-time</td>
<td>7 (18%)</td>
<td>3 (15.0%)</td>
<td>4 (21.1%)</td>
<td></td>
</tr>
<tr>
<td>Duration of shift/work day</td>
<td>8 hours</td>
<td>12 hours</td>
<td>Various (mix)</td>
<td>Other c</td>
</tr>
<tr>
<td>---------------------------</td>
<td>---------</td>
<td>----------</td>
<td>---------------</td>
<td>---------</td>
</tr>
<tr>
<td></td>
<td>19 (49%)</td>
<td>16 (41%)</td>
<td>1 (3%)</td>
<td>3 (7%)</td>
</tr>
<tr>
<td></td>
<td>4 (20.0%)</td>
<td>16 (80.0%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>15 (78.9%)</td>
<td>0</td>
<td>1 (5.3%)</td>
<td>3 (15.8%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Days vs. Mixed Shifts f</th>
<th>Days</th>
<th>Mixed (days, evenings, nights)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>19 (50%)</td>
<td>19 (50%)</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>19 (100%)</td>
</tr>
<tr>
<td></td>
<td>19 (100%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&lt;0.01^</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Years of Shift Work Experience g</th>
<th>0 to &lt;10</th>
<th>≥10 to &lt;20</th>
<th>≥20+</th>
<th>Not applicable (NSW)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8 (20%)</td>
<td>5 (13%)</td>
<td>10 (26%)</td>
<td>16 (41%)</td>
</tr>
<tr>
<td></td>
<td>7 (35.0%)</td>
<td>4 (20.0%)</td>
<td>9 (45.0%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>1 (5.3%)</td>
<td>1 (5.3%)</td>
<td>1 (5.3%)</td>
<td>16 (84.2%)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.01^</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Chi-Square test  ^ Fisher’s Exact Test.

a Missing 1 data point (NSW).
b Missing 2 data points (2 NSW).
c Missing 1 data point (SW).
d Two participants has intra-uterine devices and did not experience monthly menses. Therefore, classified as “aphasic”.
e 3 NSW reported working 7.5 hour shifts.
f Missing 1 data point (SW).
g 3 NSW had shift work experience at least 10 years prior.
Table 2. Baseline characteristics of study population.

<table>
<thead>
<tr>
<th>Variable Measure</th>
<th>All (n = 39)</th>
<th>Shift Workers (n = 20)</th>
<th>Non-shift workers (n = 19)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>41 ± 11</td>
<td>41 ± 11</td>
<td>42 ± 11</td>
<td>0.885*</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.0 ± 12.4</td>
<td>68.8 ± 10.1</td>
<td>67.1 ± 14.6</td>
<td>0.679*</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>90.6 ± 10.4</td>
<td>91.7 ± 8.3</td>
<td>89.5 ± 12.3</td>
<td>0.516*</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.6 ±4.08</td>
<td>25.7 ± 3.5</td>
<td>25.5 ± 4.7</td>
<td>0.935*</td>
</tr>
<tr>
<td>Blood Viscosity (Poise)</td>
<td>0.0403 ±</td>
<td>0.0416 ±</td>
<td>0.0389 ±</td>
<td>0.007*</td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>185 ± 33.1</td>
<td>189 ± 36.2</td>
<td>181 ± 29.9</td>
<td>0.450*</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>62.6 ± 13.0</td>
<td>62 ± 15.3</td>
<td>63 ± 10.3</td>
<td>0.736*</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>109.5 ± 33.4</td>
<td>115 ± 34.9</td>
<td>103 ± 32.8</td>
<td>0.380*</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>95.6 ± 40.1</td>
<td>92 ± 39.8</td>
<td>100 ± 41.7</td>
<td>0.599*</td>
</tr>
<tr>
<td>FG (mg/dL)</td>
<td>87.3 ± 9.8</td>
<td>87 ± 8.7</td>
<td>88 ± 11</td>
<td>0.807*</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>114 ± 11</td>
<td>112 ± 8.0</td>
<td>117 ± 13</td>
<td>0.221*</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>77 ± 7.0</td>
<td>76 ± 6.0</td>
<td>78 ± 8.0</td>
<td>0.390*</td>
</tr>
<tr>
<td>GPAQ score (total minutes/week)</td>
<td>1666 ± 1867</td>
<td>2301 ± 2400</td>
<td>1030 ± 758.1</td>
<td>0.593*</td>
</tr>
</tbody>
</table>

* Mann Whitney Rank Sum Test; * t-test

a LDL in non-shift workers (n = 13) and shift workers (n = 15) as the Cholestech reported undetected values in 11 participants.

b TG in non-shift workers (n = 13) and shift workers (n = 15) as the Cholestech reported undetected values in 11 participants.

c FG in shift workers (n = 19) as the Cholestech reported undetected values in 1 participant.

d Missing 5 data points (2 NSW and 3 SW).

BMI, body mass index; TC, total cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; FG, fasting glucose; GPAQ, Global Physical Activity Questionnaire.
Table 3. Atherosclerotic indicators comparing SW and NSW groups.

<table>
<thead>
<tr>
<th></th>
<th>All (n = 39)</th>
<th>Shift workers (n = 20)</th>
<th>Non-shift workers (n = 19)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RH-FMD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>7.60 ± 3.10</td>
<td>7.34 ± 2.78</td>
<td>7.86 ± 3.46</td>
<td>0.610*</td>
</tr>
<tr>
<td>Median</td>
<td>7.18</td>
<td>7.44</td>
<td>6.92</td>
<td></td>
</tr>
<tr>
<td>Range (MIN)</td>
<td>3.21</td>
<td>3.21</td>
<td>3.28</td>
<td></td>
</tr>
<tr>
<td>Range (MAX)</td>
<td>15.81</td>
<td>13.36</td>
<td>15.8</td>
<td></td>
</tr>
<tr>
<td><strong>AUC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>747.63 ± 285.97</td>
<td>787.62 ± 287.29</td>
<td>707.64 ± 286.67</td>
<td>0.396*</td>
</tr>
<tr>
<td>Median</td>
<td>705.43</td>
<td>810.33</td>
<td>691.18</td>
<td></td>
</tr>
<tr>
<td>Range (MIN)</td>
<td>312.85</td>
<td>312.85</td>
<td>318.84</td>
<td></td>
</tr>
<tr>
<td>Range (MAX)</td>
<td>1412.48</td>
<td>1324.75</td>
<td>1412.48</td>
<td></td>
</tr>
<tr>
<td><strong>IMT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>0.47 ± 0.11</td>
<td>0.45 ± 0.09</td>
<td>0.48 ± 0.12</td>
<td>0.578†</td>
</tr>
<tr>
<td>Median</td>
<td>0.44</td>
<td>0.43</td>
<td>0.45</td>
<td></td>
</tr>
<tr>
<td>Range (MIN)</td>
<td>0.34</td>
<td>0.34</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Range (MAX)</td>
<td>0.74</td>
<td>0.63</td>
<td>0.74</td>
<td></td>
</tr>
<tr>
<td><strong>Central PWV</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>6.62 ± 1.31</td>
<td>6.51 ± 1.31</td>
<td>6.73 ± 1.34</td>
<td>0.615*</td>
</tr>
<tr>
<td>Median</td>
<td>6.54</td>
<td>6.54</td>
<td>6.51</td>
<td></td>
</tr>
<tr>
<td>Range (MIN)</td>
<td>4.37</td>
<td>4.60</td>
<td>4.37</td>
<td></td>
</tr>
<tr>
<td>Range (MAX)</td>
<td>10.15</td>
<td>9.94</td>
<td>10.15</td>
<td></td>
</tr>
<tr>
<td><strong>Peripheral PWV</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>6.91 ± 0.90</td>
<td>7.05 ± 0.67</td>
<td>6.71 ± 1.17</td>
<td>0.350*</td>
</tr>
<tr>
<td>Median</td>
<td>6.80</td>
<td>6.91</td>
<td>6.91</td>
<td></td>
</tr>
<tr>
<td>Range (MIN)</td>
<td>5.53</td>
<td>5.98</td>
<td>5.53</td>
<td></td>
</tr>
<tr>
<td>Range (MAX)</td>
<td>10.43</td>
<td>8.68</td>
<td>10.43</td>
<td></td>
</tr>
</tbody>
</table>

† Mann-Whitney Rank Sum Test, * t-test.

* Missing 1 data point (1 SW)
† Missing 1 data point (1 NSW)
* Missing 2 data points (1 SW and 1 NSW)
* Missing 3 data points (1 SW and 2 NSW)

RH-FMD, reactive hyperemia flow-mediated dilation; AUC, area under the curve; IMT, intima-media thickness; PWV, pulse wave velocity.
Table 4. Stress scores and subscales for SW and NSW groups.

<table>
<thead>
<tr>
<th></th>
<th>All (n = 39) Mean ± SD</th>
<th>Shift Workers (n = 20) Mean ± SD</th>
<th>Non-shift workers (n = 19) Mean ± SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ERI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extrinsic effort</td>
<td>2.28 ± 1.09</td>
<td>2.40 ± 1.19</td>
<td>2.16 ± 1.02</td>
<td>0.597°F</td>
</tr>
<tr>
<td>Esteem reward</td>
<td>2.03 ± 0.99</td>
<td>1.75 ± 0.79</td>
<td>2.32 ± 1.11</td>
<td>0.100°F</td>
</tr>
<tr>
<td>Monetary Gratification</td>
<td>0.28 ± 0.46</td>
<td>0.15 ± 0.37</td>
<td>0.42 ± 0.51</td>
<td>0.063°F</td>
</tr>
<tr>
<td>Status control</td>
<td>1.49 ± 1.05</td>
<td>1.20 ± 0.95</td>
<td>1.79 ± 1.08</td>
<td>0.066°F</td>
</tr>
<tr>
<td>Reward</td>
<td>3.79 ± 1.66</td>
<td>3.10 ± 1.21</td>
<td>4.53 ± 1.78</td>
<td>0.016°F</td>
</tr>
<tr>
<td>Effort Reward Ratio</td>
<td>1.30 ± 0.97</td>
<td>1.68 ± 1.20</td>
<td>0.90 ± 0.37</td>
<td>0.003°F</td>
</tr>
<tr>
<td><strong>JCQ</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skill Discretion</td>
<td>35.44 ± 4.79</td>
<td>34.60 ± 4.45</td>
<td>36.32 ± 5.09</td>
<td>0.176°F</td>
</tr>
<tr>
<td>Decision Authority</td>
<td>33.33 ± 6.57</td>
<td>31.40 ± 5.84</td>
<td>35.37 ± 6.83</td>
<td>0.076°F</td>
</tr>
<tr>
<td>Decision Latitude</td>
<td>68.77 ± 9.88</td>
<td>66.00 ± 8.99</td>
<td>71.68 ± 10.16</td>
<td>0.072*</td>
</tr>
<tr>
<td>Psychological Job Demands</td>
<td>19.44 ± 5.19</td>
<td>21.10 ± 4.46</td>
<td>17.68 ± 5.43</td>
<td>0.061°F</td>
</tr>
<tr>
<td>Physical Job Demands</td>
<td>10.82 ± 3.88</td>
<td>13.55 ± 1.82</td>
<td>7.94 ± 3.37</td>
<td>&lt;0.001°F</td>
</tr>
<tr>
<td><strong>DSP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-Score</td>
<td>108 ± 25.9</td>
<td>110 ± 20.5</td>
<td>107 ± 31.4</td>
<td>0.684*</td>
</tr>
</tbody>
</table>

°F Mann Whitney Rank Sum Test; * t-test

*Missing 1 data point (1 NSW).

ERI, Effort Reward Imbalance; JCQ, Job Content Questionnaire; DSP, Derogatis Stress Profile
Table 5a. Correlations between scores/subscales and atherosclerotic indicators while controlling for significant covariates.

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>% FMD</th>
<th>p-value</th>
<th>Shear Stress&lt;sup&gt;a&lt;/sup&gt;</th>
<th>p-value</th>
<th>FMD-NORM&lt;sup&gt;b&lt;/sup&gt;</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ERI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extrinsic effort</td>
<td>39</td>
<td>-0.075&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.650</td>
<td>-0.084</td>
<td>0.677</td>
<td>-0.063</td>
<td>0.779</td>
</tr>
<tr>
<td>Esteem reward</td>
<td></td>
<td>0.172&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.296</td>
<td>-0.066</td>
<td>0.744</td>
<td>-0.099</td>
<td>0.662</td>
</tr>
<tr>
<td>Monetary gratification</td>
<td></td>
<td>-0.248&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.128</td>
<td>-0.153</td>
<td>0.446</td>
<td>-0.110</td>
<td>0.625</td>
</tr>
<tr>
<td>Status control</td>
<td></td>
<td>0.246&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.131</td>
<td>-0.162</td>
<td>0.420</td>
<td>0.462</td>
<td>0.031</td>
</tr>
<tr>
<td>Reward</td>
<td></td>
<td>0.168&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.308</td>
<td>-0.208</td>
<td>0.299</td>
<td>0.164</td>
<td>0.465</td>
</tr>
<tr>
<td>Effort Reward Ratio</td>
<td></td>
<td>-0.175&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.287</td>
<td>0.148</td>
<td>0.460</td>
<td>-0.187</td>
<td>0.405</td>
</tr>
<tr>
<td><strong>JCQ</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skill Discretion</td>
<td>39</td>
<td>-0.182&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.268</td>
<td>-0.054</td>
<td>0.787</td>
<td>0.070</td>
<td>0.757</td>
</tr>
<tr>
<td>Decision Authority</td>
<td></td>
<td>0.013&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.936</td>
<td>-0.296</td>
<td>0.134</td>
<td>0.117</td>
<td>0.603</td>
</tr>
<tr>
<td>Decision Latitude</td>
<td></td>
<td>-0.082&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.618</td>
<td>-0.234</td>
<td>0.239</td>
<td>0.113</td>
<td>0.617</td>
</tr>
<tr>
<td>Psychological Job Demands</td>
<td></td>
<td>-0.161&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.329</td>
<td>-0.179</td>
<td>0.373</td>
<td>0.032</td>
<td>0.887</td>
</tr>
<tr>
<td>Physical Job Demands</td>
<td></td>
<td>-0.055&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.739</td>
<td>0.418</td>
<td>0.030</td>
<td>-0.037</td>
<td>0.871</td>
</tr>
<tr>
<td><strong>DSP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-Score</td>
<td>38</td>
<td>0.113&lt;sup&gt;+&lt;/sup&gt;</td>
<td>0.498</td>
<td>0.245</td>
<td>0.902</td>
<td>-0.057</td>
<td>0.800</td>
</tr>
</tbody>
</table>

<sup>T</sup> Pearson’s rho; <sup>*</sup> Spearman’s rho.

Correlations between atherosclerotic indicators and anthropometric measures are presented in Table 7.

<sup>a</sup> Analysis controlling for age, menopause, and FG.

<sup>b</sup> Analysis controlling for BV, TG, and FG.

FMD, flow-mediated dilation; NORM, normalized; ERI, Effort Reward Imbalance; JCQ, Job Content Questionnaire; DSP, Derogatis Stress Profile
Table 5b. Correlations between scores/subscales and atherosclerotic indicators while controlling for significant covariates.

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>IMT&lt;sup&gt;c&lt;/sup&gt;</th>
<th>p-value</th>
<th>cPWV&lt;sup&gt;d&lt;/sup&gt;</th>
<th>p-value</th>
<th>pPWV</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ERI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extrinsic effort</td>
<td>39</td>
<td>-0.345</td>
<td>0.072</td>
<td>-0.249</td>
<td>0.319</td>
<td>0.131&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.446</td>
</tr>
<tr>
<td>Esteem reward</td>
<td></td>
<td>-0.266</td>
<td>0.171</td>
<td>-0.304</td>
<td>0.221</td>
<td>-0.029&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.867</td>
</tr>
<tr>
<td>Monetary gratification</td>
<td>39</td>
<td>-0.202</td>
<td>0.302</td>
<td>0.032</td>
<td>0.898</td>
<td>-0.161&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.348</td>
</tr>
<tr>
<td>Status control</td>
<td></td>
<td>-0.244</td>
<td>0.210</td>
<td>-0.015</td>
<td>0.952</td>
<td>-0.098&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.568</td>
</tr>
<tr>
<td>Reward</td>
<td></td>
<td>-0.366</td>
<td>0.055</td>
<td>-0.184</td>
<td>0.464</td>
<td>-0.112&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.515</td>
</tr>
<tr>
<td>Effort Reward Ratio</td>
<td>39</td>
<td>-0.124</td>
<td>0.529</td>
<td>-0.128</td>
<td>0.613</td>
<td>0.230&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.177</td>
</tr>
<tr>
<td><strong>JCQ</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skill Discretion</td>
<td>39</td>
<td>0.055</td>
<td>0.882</td>
<td>0.152</td>
<td>0.547</td>
<td>-0.623&lt;sup&gt;T&lt;/sup&gt;</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Decision Authority</td>
<td>39</td>
<td>0.162</td>
<td>0.409</td>
<td>0.034</td>
<td>0.895</td>
<td>-0.338&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.044</td>
</tr>
<tr>
<td>Decision Latitude</td>
<td>39</td>
<td>0.142</td>
<td>0.471</td>
<td>0.093</td>
<td>0.715</td>
<td>-0.346&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.039</td>
</tr>
<tr>
<td>Psychological Job Demands</td>
<td>39</td>
<td>0.413</td>
<td>0.029</td>
<td>-0.257</td>
<td>0.303</td>
<td>-0.215&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.209</td>
</tr>
<tr>
<td>Physical Job Demands</td>
<td>39</td>
<td>-0.176</td>
<td>0.370</td>
<td>-0.221</td>
<td>0.377</td>
<td>-0.010&lt;sup&gt;T&lt;/sup&gt;</td>
<td>0.952</td>
</tr>
<tr>
<td><strong>DSP</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-Score</td>
<td>38</td>
<td>-0.235</td>
<td>0.228</td>
<td>-0.039</td>
<td>0.879</td>
<td>0.119&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.495</td>
</tr>
</tbody>
</table>

<sup>T</sup> Pearson’s rho; <sup>*</sup> Spearman’s rho.

Correlations between atherosclerotic indicators and anthropometric measures are presented in Table 7.
<sup>c</sup> Analysis controlling for age, systolic BP, and menstruation status.
<sup>d</sup> Analysis controlling for age, menopause, systolic BP, LDL, and FG.

IMT, intima-media thickness; cPWV, central pulse wave velocity; and pPWV, peripheral pulse wave velocity; ERI, Effort Reward Imbalance; JCQ, Job Content Questionnaire; DSP, Derogatis Stress Profile.
Table 6. Dose-response relationship between years of shift work experience and atherosclerotic indicators among SW group while controlling for age.

<table>
<thead>
<tr>
<th>Atherosclerotic Indicator</th>
<th>n</th>
<th>Years of shift work experience Pearson’s rho (r)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% FMD</td>
<td>20</td>
<td>-0.055</td>
<td>0.835</td>
</tr>
<tr>
<td>AUC&lt;sup&gt;a&lt;/sup&gt;</td>
<td>19</td>
<td>-0.011</td>
<td>0.967</td>
</tr>
<tr>
<td>IMT</td>
<td>20</td>
<td>0.188</td>
<td>0.469</td>
</tr>
<tr>
<td>cPWV&lt;sup&gt;a&lt;/sup&gt;</td>
<td>19</td>
<td>0.223</td>
<td>0.390</td>
</tr>
<tr>
<td>pPWV&lt;sup&gt;a&lt;/sup&gt;</td>
<td>19</td>
<td>0.180</td>
<td>0.489</td>
</tr>
</tbody>
</table>

SW, female shift worker; FMD, flow-mediated dilation; IMT, intima-media thickness; cPWV, central pulse wave velocity; pPWV, peripheral pulse wave velocity.
Table 7a. Correlations between atherosclerotic indicators and anthropometric measures.

<table>
<thead>
<tr>
<th>Anthropometric Measures</th>
<th>FMD</th>
<th>p-value</th>
<th>AUC</th>
<th>p-value</th>
<th>FMD-norm</th>
<th>p-value</th>
<th>IMT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.146</td>
<td>0.375</td>
<td>0.383</td>
<td>0.017</td>
<td>-0.228</td>
<td>0.163</td>
<td>0.682</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>-0.035</td>
<td>0.831</td>
<td>0.045</td>
<td>0.788</td>
<td>-0.155</td>
<td>0.347</td>
<td>0.015</td>
<td>0.929</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>0.031</td>
<td>0.850</td>
<td>0.099</td>
<td>0.553</td>
<td>-0.109</td>
<td>0.510</td>
<td>-0.021</td>
<td>0.902</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.005</td>
<td>0.978</td>
<td>0.064</td>
<td>0.704</td>
<td>-0.123</td>
<td>0.457</td>
<td>0.003</td>
<td>0.987</td>
</tr>
<tr>
<td>Blood Viscosity (Poise)</td>
<td>-0.105</td>
<td>0.524</td>
<td>0.272</td>
<td>0.098</td>
<td>-0.376</td>
<td>0.018</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>-0.165</td>
<td>0.317</td>
<td>0.137</td>
<td>0.411</td>
<td>-0.245</td>
<td>0.133</td>
<td>0.275</td>
<td>0.095</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>-0.143</td>
<td>0.386</td>
<td>0.283</td>
<td>0.085</td>
<td>-0.282</td>
<td>0.081</td>
<td>0.101</td>
<td>0.548</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>-0.118</td>
<td>0.551</td>
<td>-0.157</td>
<td>0.435</td>
<td>0.403</td>
<td>0.479</td>
<td>0.360</td>
<td>0.060</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>0.287</td>
<td>0.139</td>
<td>-0.169</td>
<td>0.398</td>
<td>0.403</td>
<td>0.034</td>
<td>0.092</td>
<td>0.642</td>
</tr>
<tr>
<td>FG (mg/dL)</td>
<td>0.125</td>
<td>0.455</td>
<td>0.329</td>
<td>0.047</td>
<td>-0.333</td>
<td>0.041</td>
<td>-0.076</td>
<td>0.653</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>0.191</td>
<td>0.244</td>
<td>0.122</td>
<td>0.464</td>
<td>0.070</td>
<td>0.672</td>
<td>0.600</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>0.187</td>
<td>0.255</td>
<td>0.101</td>
<td>0.544</td>
<td>0.087</td>
<td>0.597</td>
<td>0.294</td>
<td>0.073</td>
</tr>
<tr>
<td>Menstruation status</td>
<td>-0.029</td>
<td>0.864</td>
<td>-0.356</td>
<td>0.031</td>
<td>0.118</td>
<td>0.480</td>
<td>-0.355</td>
<td>0.031</td>
</tr>
<tr>
<td>GPAQ score (total minutes/week)</td>
<td>-0.137</td>
<td>0.440</td>
<td>0.071</td>
<td>0.696</td>
<td>0.029</td>
<td>0.871</td>
<td>-0.186</td>
<td>0.299</td>
</tr>
</tbody>
</table>

Pearson’s rho; * Spearman’s rho.

* LDL in non-shift workers (n = 13) and shift workers (n = 15) as the Cholestech reported undetected values in 11 participants.
* TG in non-shift workers (n = 13) and shift workers (n = 15) as the Cholestech reported undetected values in 11 participants.
* FG in shift workers (n = 19) as the Cholestech reported undetected values in 1 participant.

BMI, body mass index; TC, total cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; FG, fasting glucose; GPAQ, Global Physical Activity Questionnaire.
Table 7b. Correlations between atherosclerotic indicators and anthropometric measures.

<table>
<thead>
<tr>
<th>Anthropometric Measures</th>
<th>cPWV</th>
<th>p-value</th>
<th>pPWV</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.797f</td>
<td>0.000</td>
<td>-0.180f</td>
<td>0.293</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>0.182f</td>
<td>0.282</td>
<td>-0.087f</td>
<td>0.615</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>0.165f</td>
<td>0.328</td>
<td>-0.141f</td>
<td>0.413</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.201f</td>
<td>0.234</td>
<td>-0.165f</td>
<td>0.337</td>
</tr>
<tr>
<td>Blood Viscosity (Poise)</td>
<td>0.043f</td>
<td>0.799</td>
<td>-0.144f</td>
<td>0.401</td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>0.500f</td>
<td>0.002</td>
<td>-0.283f</td>
<td>0.094</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>0.164f</td>
<td>0.333</td>
<td>0.078f</td>
<td>0.652</td>
</tr>
<tr>
<td>LDL (mg/dL)(^a)</td>
<td>0.418f</td>
<td>0.030</td>
<td>-0.189f</td>
<td>0.345</td>
</tr>
<tr>
<td>TG (mg/dL)(^b)</td>
<td>-0.064f</td>
<td>0.750</td>
<td>-0.049f</td>
<td>0.809</td>
</tr>
<tr>
<td>FG (mg/dL)(^c)</td>
<td>0.267f</td>
<td>0.116</td>
<td>-0.081f</td>
<td>0.643</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>0.519f</td>
<td>0.001</td>
<td>-0.112f</td>
<td>0.517</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>0.248f</td>
<td>0.139</td>
<td>0.044f</td>
<td>0.797</td>
</tr>
<tr>
<td>Menstruation status</td>
<td>-0.459f</td>
<td>0.005</td>
<td>0.162f</td>
<td>0.352</td>
</tr>
<tr>
<td>GPAQ score (total minutes/week)</td>
<td>-0.227f</td>
<td>0.212</td>
<td>-0.125f</td>
<td>0.496</td>
</tr>
</tbody>
</table>

\(^f\) Pearson’s rho; \(^*\) Spearman’s rho.

\(^a\) LDL in non-shift workers (n = 13) and shift workers (n = 15) as the Cholestech reported undetected values in 11 participants.

\(^b\) TG in non-shift workers (n = 13) and shift workers (n = 15) as the Cholestech reported undetected values in 11 participants.

\(^c\) FG in shift workers (n = 19) as the Cholestech reported undetected values in 1 participant.

BMI, body mass index; TC, total cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; FG, fasting glucose; GPAQ, Global Physical Activity Questionnaire.
Chapter 4

General Discussion

4.1 Summary of Findings

The purpose of this thesis was to investigate the effect of shift work on atherosclerotic indicators, early indicators of CVD. Shift work status was the primary exposure variable of interest and was represented using the following two groups: 1) female shift workers with at least 6 years of shift working experience; and 2) female non-shift workers with at least 6 years of non-shift working experience. The primary outcome variables of interest were endothelial function (e.g., % FMD), IMT, and arterial stiffness (e.g., cPWV and pPWV). Psychological workplace stress and life stress were considered as potential factors that may influence endothelial function and were measured using the Job Content Questionnaire, Effort-Reward Imbalance scale, and Derogatis Stress Profile.

The manuscript presented in Chapter 3 addressed the thesis objectives as previously described. No differences in atherosclerotic indicators were detected between groups and there was no evidence to suggest the presence of a dose-response relationship between years of shift work and atherosclerotic development. However, additional further exploratory analyses showed that shift workers experienced increased psychological and physical job-related stress. Further analysis into the stress subscales suggested that those who reported increased psychological job demands have increased IMT (i.e., increased atherosclerotic development). Conversely, those who reported higher levels of skill discretion, decision authority, and decision latitude also had decreased pPWV (i.e., decreased peripheral arterial stiffness). Thus our findings partially
supported the associations between aspects of occupational stress and increased atherosclerotic risk, regardless of SW status.

### 4.2 Psychological Stress Pathway Linking Shift Work to CVD

The findings from this study, and others (Elovainio, Kuusio, Aalto, Sinervo, & Heponiemi, 2010; Jamal, 2004) support positive correlations between SW and psychological job stress. Jamal (2004) suggested that employees who work beyond normal working hours experience higher levels of emotional exhaustion, job stress, and various health problems, when compared to day-workers. Similarly, Elovainio et al. (2010) found shift work to be related to psychological stress, low job involvement, and low work ability. We found psychological job stress, regardless of shift work status, to be associated with greater atherosclerotic development. Therefore, if shift workers are more prone to psychological job stress, then psychological job stress may act as a potential mechanistic pathway linking shift work to CVD. Figure 2 summarizes the significant (solid line) and non-significant (dotted line) findings found within this thesis:
Figure 3. Summary of thesis findings.

This exploratory study was designed to elucidate the potential associations between shift work and vascular indicators, while including potential covariates. Therefore, this thesis may inform further hypothesis and propose future analytical studies.

4.3 Nursing Implications

Nurses are an invaluable resource to the health care system. The nursing profession makes up one third of those working within the Canadian health care workforce (Canadian Federation of Nurses Unions, 2013). In 2011, approximately 62% of Registered Nurses were employed within the hospital sector, a sector characterized by shift work schedules (Canadian Federation of Nurses Unions, 2013). However, nurses have higher rates of absence due to illness or disability, a rate nearly doubled that of other occupations, at a cost of $711 million/year in 2010 (Canadian Federation of Nurses Unions, 2013). There is also an increase in age of nurses working, highlighting the importance of addressing this concern. In 2005, Canada had more RNs aged 50 to 54 years old in comparison to any other age group (Health Canada, 2007). In addition, the average age of an RN is increasing: 44.7 years in 2005 and in 2011, 46 years (Canadian
Federation of Nurses Unions, 2013; Health Canada, 2007). Given the large portion of employed female shift workers, as well as the aging population of nurses themselves, it is important that the health and wellness of such employees be considered.

This study suggests that aspects of psychological job stress are associated with indicators of atherosclerotic development; some of these psychological job stress factors were more common in shift workers. At an individual level, shift workers should be aware of the potential hazards within the workplace so that they are able to develop appropriate stress managing skills. Managers and employers also need to recognize these stressors to actively facilitate a positive work environment. Kluska, Laschinger, and Kerr (2004) investigated the association between nurses’ empowerment and Effort Reward Imbalances. They reported an average ERI value of 0.82, a value lower than reported in our exploratory study. Nonetheless, Kluska et al. (2004) suggested having access to support, resources, and opportunity in the workplace, reduced imbalance between self-appraised efforts and rewards. By identifying this modifiable risk factor, employers may identify and implement various healthy workplace strategies in order to increase empowerment. These may include: workload management systems; staffing initiatives (i.e. ensuring enough staff to cover patient load); providing appropriate technologies to assist with care and workload; designing ergonomically efficient workplaces (e.g. to alleviate physiological strain on backs, legs, etc.); and promoting autonomy within the context of nursing practice (Canadian Federation of Nurses Unions, 2013). Kluska et al. (2004) suggest implementing organizational empowerment as a useful strategy in reducing psychological job stress. In addition, it has been suggested that when management is focused on increasing employee control and rewards, adverse health outcomes may be avoided (Laschinger, Finegan, Shamian, & Wilk, 2001).

To foster a positive work environment, individuals and employers need to be given the resources to do so. Many nurses are working in hospital environments, where they are required to
provide a greater volume of care than they are able to deliver; however they are still responsible within the standards of the nursing profession (Laschinger et al., 2001). Furthermore, there are changes in the workplace that alter the autonomy of nurses, such as restricting aspects of patient care and increasing employment of less-qualified health care providers (Laschinger et al., 2001). This ultimately may affect patient care quality (Laschinger et al., 2001). To protect the health of all, it is imperative that nurses and managers alike be given a supportive environment (Laschinger et al., 2001). This may be through proper governmental policy (e.g. limiting cuts to nursing employment) as well as through educational programs (e.g. providing additional training for nurses to become leaders within their units). Additional programs, including implementing screening for early indicators of atherosclerotic development, should also be considered.

4.4 Strengths and Limitations

Most importantly, this study was novel in nature by examining three atherosclerotic indicators within a female population. Limited evidence has been generated regarding a female-only cohort. As previously mentioned in Chapter 3, there are additional strengths including a well-developed study protocol based strongly on findings and evidence reported in the literature, control over potential confounders, and the use of validated questionnaires. Despite these important strengths, several limitations were identified (as reported in Chapter 3). These include: a small sample size; limited by the population of eligible participants within city-limits; quantification of work experience as both part and full time employees in the same group; and menstrual stage classification limited by self-report.

An additional limitation was the potential for measurement error. For example, despite completing two trials for every participant, in some cases, only one FMD trial was valid. Therefore, only one %FMD was used to represent endothelial function. This was due to study
time constraints as well as resources available. Given the appropriate time and resources, it may be argued that using at least three valid trials may more representative of the variable of interest. In addition, as previously reported in Chapter 3, some of the metabolic measures were excluded as a result of being outside the detectable range. This may be due to measurement error within the equipment used. For future work, obtaining an entire vial of blood (which could be processed at an off-site laboratory) may be more valuable in detecting out of range metabolic values. As well, an additional limitation could include the lack of control over other medications, which could potentially alter atherosclerotic development (e.g. prostaglandins). In the event that a large-scale study is completed, further investigation into all interacting medications would be warranted.

### 4.5 Future Research Direction

There are several opportunities for improvements, including further mechanistic studies that investigate how shift work leads to atherosclerosis. Another future direction could include the use of a prospective cohort study design; a longitudinal study investigating the effects of shift work over many years may indicate changes in atherosclerotic structure and function over time. In addition, sampling metabolic measures at various time points (e.g. over years of shift work) may offer further explanation into the specific mechanism that may facilitate CVD development. Since psychological job stress was identified as a potential factor impacting the health of shift workers, it may be beneficial to explore this relationship further (i.e., investigating how an individual copes and manages stress). Another area of investigation regarding whether long periods of shift work result in decreased stress, suggesting that shift workers become accustomed to such workplace stressors may be of interest. Further investigation into other female shift working groups, such as police officers and prison guards, may also help to describe this potential pathway.
4.6 Conclusion

Overall, this study explored atherosclerotic indicators in shift and non-shift workers. While shift workers do not show indications of early atherosclerotic disease in regards to shift working status, shift workers do experience increased psychological and physical job demands, which is associated with vascular changes. Given the large portion of women exposed to shift work, it is important that we continue to explore this area to mitigate risk, if it exists. All shift working personnel may benefit from occupational health programs that focus on stress management and support.
4.7 References


Appendix A: Protocol Information

Venipuncture

Each participant was instructed to extend both arms out to the side in a T position. A tourniquet was applied just above the antecubital fossa of the participant’s right arm; the skin was sanitized (70% isopropyl swab) in preparation for intravenous catheter insertion. A BD Nexiva™ Closed IV Catheter System was inserted using standard techniques. To obtain the initial blood sample, a 10 ml syringe was luer-locked to the end. Once the initial blood sample was obtained, a primed septum was applied to the end and the IV catheter was flushed with 4 mL of saline in order to maintain patency. When a blood sample was taken, 4 mL of blood was first discarded and then was ready for sampling. Saline was then re-infused.

Participant Monitoring

After IV insertion and prior to vascular testing, each participant completed a 30-minute supine rest period and remained supine for the duration experimental visit. The participant was attached to a 3-lead ECG, to obtain heart rate. Three electrodes were placed on the trunk of the participant: at the right upper body (under the clavicle); at the lower left abdomen (laterally); and superiorly placed in relation to the black lead.

Menstruation Categorization

During the data collection session, each participant reported the first day of her last menstrual period (LMP). Each participant also reported the duration of each cycle; participants that deviated from this were noted. Using a pregnancy wheel calculator, the date of LMP was compared to when the data collection session took place to determine where each participant was
in her cycle. The following categories were used to classify participant’s menstruation stage based on LMP: 1) currently menstruating (day 1 to 7); 2) early luteal phase (day 8 to 14); 3) late luteal (15 to 21); 4) follicular phase (22 to ~28); 5) menopausal (no menses for 12 consecutive months); and 6) aphasic. Participants who had intrauterine devices (n=2) were unable to recall their LMP as visible menses had ceased. Therefore, they were classified as aphasic. Few participants reported that they were pre-menopausal with very irregular menses every 3-4 months. These participants (n=2) were classified as menopausal.

Sample Area Under the Curve (AUC)

![Image of Sample Area Under the Curve](figure4.png)

**Figure 4.** Example area under the curve.
Appendix B: Participant Questionnaires

Stress reactivity and vascular health in women who perform shift work

Faculty Investigators:
Dr. Kyra Pyke and Dr. Joan Tranmer

Graduate Student Investigators
Morgan Batson and Ira Carson
BACKGROUND INFORMATION

1. What is your marital status?
   - Married
   - Living common-law
   - Widowed
   - Separated
   - Divorced
   - Single, never married

2. How many children do you have? __________

3. What is the highest level of education you have obtained?
   - High School
   - Post Secondary (certificate/diploma)
   - University Undergraduate Degree
   - Graduate Degree (Master, PhD, etc)
   - Physician or Resident
   - Other __________________________

GENERAL HEALTH
The next few questions relate to your general health and well-being.

1. Do you currently use any form of oral contraception?
   a. Yes
   b. No

2. Have your natural menstrual periods ceased?
   a. Yes
   b. No

3. If Yes for question 2: For what reason has your periods ceased?
   a. Natural menopause (Periods have ceased for 12 consecutive months)
   b. Surgical
   c. Other (radiation/condition): __________________________

4. Are you currently taking Hormone Replacement Therapy to treat menopausal symptoms?
   a. Yes
   b. No

5. How many times have you been pregnant? (This would include any losses as well) __________
6. How many full-term births have you had? __________
7. How many pre-term births have you had? __________
8. How many spontaneous or therapeutic losses have you experienced? __________
9. Please fill in the below table regarding any pregnancy related conditions you may have experienced during all of your pregnancies.

Please state the date of birth (DOB) as Year/Month/Date (i.e. 75/08/26)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>DOB</td>
</tr>
<tr>
<td></td>
<td>(please indicate # of pregnancy in 2nd column)</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td></td>
</tr>
<tr>
<td>Gestational Hypertension (hypertension during pregnancy)</td>
<td></td>
</tr>
<tr>
<td>Gestational Diabetes or Gestational Impaired Glucose Tolerance</td>
<td></td>
</tr>
<tr>
<td>Placental Abruption</td>
<td></td>
</tr>
<tr>
<td>Pre-term Birth (&lt; 37 weeks)</td>
<td></td>
</tr>
<tr>
<td>Intrauterine growth restriction (your baby weighed much less than expected for their gestational age. i.e., &lt; 2500 gms for a term birth)</td>
<td></td>
</tr>
</tbody>
</table>
10. Please fill in the below table indicating any of the long term conditions listed that have lasted or been expected to last 6 months or more and were diagnosed by a Health Care Professional.

Please indicate the date of first diagnosis (Year/Month/Date - 75/08/26).

<table>
<thead>
<tr>
<th>Long Term Conditions</th>
<th>Date of Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergies</td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td></td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td></td>
</tr>
<tr>
<td>Arthritis or osteoporosis (excluding fibromyalgia)</td>
<td></td>
</tr>
<tr>
<td>Back problems, excluding fibromyalgia and arthritis</td>
<td></td>
</tr>
<tr>
<td>Migraine headaches</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td></td>
</tr>
<tr>
<td>Stomach or intestinal ulcers</td>
<td></td>
</tr>
<tr>
<td>A sleep disorder (such as sleep apnea)</td>
<td></td>
</tr>
<tr>
<td>A bowel disorder (such as Crohn’s Disease or colitis)</td>
<td></td>
</tr>
<tr>
<td>A thyroid condition</td>
<td></td>
</tr>
<tr>
<td>Chronic fatigue syndrome</td>
<td></td>
</tr>
<tr>
<td>Neurological disease</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>Anxiety or Panic Disorder</td>
<td></td>
</tr>
<tr>
<td>Lung Disease</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

11. Do you have a history of and/or take medication for any of the following? Please indicate the date of diagnosis on the space provided.
   a. High blood pressure _______________
   b. High cholesterol levels _______________
   c. Diabetes _______________
   d. Dyslipidemia _______________

12. Do you have a family history of premature heart disease or any of the following conditions?
   a. High blood pressure   Yes  No
   b. High cholesterol levels Yes  No
   c. Diabetes   Yes  No
   d. Dyslipidemia Yes  No

13. Did either of your parents have a heart attack before the age of 60?
   a. Yes
   b. No
14. What is your smoking status?
   a. Currently smoke
   b. Quit recently (4 weeks to 5 years ago)
   c. Quit remotely (over 5 years ago)
   d. Never smoked.

15. Does anyone in your household smoke regularly inside the house?
   a. Yes
   b. No

16. During the past 12 months, how often did you drink alcoholic beverages?
   a. Never / Do not Drink
   b. Less than once a month
   c. Once a month
   d. 2-3 times a month
   e. Once a week
   f. 2-3 times a week
   g. 4-6 times a week
   h. Everyday

17. How often in the past 12 months have you had 5 or more drinks on one occasion?
   a. Never
   b. Less than once a month
   c. Once a month
   d. 2-3 times a month
   e. Once a week
   f. More than once a week

18. List below the medications you are taking, the dose, and how often you take the medication.
    Please copy this information from your pill bottle label. If you need more space you may need to use the back of the page.

<table>
<thead>
<tr>
<th>Name of Medication</th>
<th>Dose</th>
<th>How many times a day do you take this medication?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>

5
Version: April 30, 2013
## NUTRITION
In this section we would like to get an idea of your eating habits. Please check the box that best describes your habits in an average week.

<table>
<thead>
<tr>
<th>Topic</th>
<th>In an average week, how often do you:</th>
<th>Usually/Often</th>
<th>Sometimes</th>
<th>Rarely/Never</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Meals</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Skip breakfast?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Eat 4 or more meals from sit-down or take out restaurants?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Grains</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>3. Eat less than 6 servings of whole grain products a day?</td>
<td>Serving = 1 slice of 100% whole grain bread; 1 cup whole grain cereal like Shredded Wheat, Wheaties, Grape Nuts, high fiber cereals, oatmeal, 3-4 whole grain crackers, 1/2 cup brown rice or whole wheat pasta, 1 sm. muffin, 1 1/2 bagel or pita.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fruits &amp; Vegetables</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>4. Eat or drink less than 7 servings of fruits and/or vegetables a day?</td>
<td>Serving = 1/2 cup or 1 med fruit or 4 oz 100% juice, 1/2 cup vegetables, or 1 cup raw leafy vegetables.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Milk &amp; Alternatives</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Eat or drink less than 2-3 servings of milk, yogurt or cheese a day?</td>
<td>Serving = 1 cup milk or 3/4 cup yogurt; 1.5-2 oz. Cheese.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>6. Use 2% (reduced fat) or whole milk instead of skim (non-fat) or 1% (low-fat) milk?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Use regular cheese (American, cheddar, Swiss, Monterey Jack) instead of low fat or part skim cheeses as a snack, on sandwiches, pizza, etc?</td>
<td></td>
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<tr>
<td><strong>Meats &amp; Alternatives</strong></td>
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<tr>
<td>8. Eat beef, pork, or dark meat chicken more than 2 times a week?</td>
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<tr>
<td>9. Eat more than 6 oz. (50-100g) of meat, chicken, turkey or fish per day?</td>
<td>Note: 3 oz of meat or chicken is the size of a deck of cards or one of the following: 1 regular hamburger, 1 chicken breast or leg (thigh &amp; drumstick), or one pork chop, 1/3 cup tofu, 1-2 eggs, 2 tbsp Peanut Butter.</td>
<td></td>
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<tr>
<td>10. Chose higher fat red meats like prime rib, T-bone steak, hamburger, ribs, etc. Instead of lean red meats.</td>
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<tr>
<td>11. Eat the skin on the chicken and turkey or the fat on meat?</td>
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<td></td>
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</tr>
<tr>
<td>Topic</td>
<td>In an average week, how often do you:</td>
<td>Usually/Often</td>
<td>Sometimes</td>
<td>Rarely/Never</td>
</tr>
<tr>
<td>---------------</td>
<td>---------------------------------------</td>
<td>---------------</td>
<td>-----------</td>
<td>--------------</td>
</tr>
<tr>
<td>Meats &amp; Alternatives</td>
<td>12. Use regular processed meats (bologna, salami, corned beef, hotdogs, sausage or bacon) instead of low fat processed meats (roast beef, turkey, lean ham, low-fat cold cuts/hotdogs)?</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Fried Foods</td>
<td>13. Eat fried foods such as fried chicken, fried fish or french fries?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Snacks</td>
<td>14. Eat regular potato chips, nacho chips, corn chips, crackers, regular popcorn, nuts instead of pretzels, low-fat chips or low-fat crackers, air-popped popcorn?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fats and Oils</td>
<td>15. Use regular salad dressing &amp; mayonnaise instead of low-fat or fat-free salad dressing and mayonnaise?</td>
<td></td>
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<tr>
<td></td>
<td>16. Add butter, margarine or oil to bread, potatoes, rice or vegetables on the table?</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>17. Cook with oil, butter, or margarine instead of using non-stick sprays like Pam or cooking without fat?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweets</td>
<td>18. Eat regular sweets like cake, cookies, pastries, donuts, muffins, and chocolate instead of low fat or fat-free sweets?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>19. Eat regular ice cream instead of sherbet, sorbet, low-fat or fat-free ice cream, frozen yogurt, etc.?</td>
<td></td>
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<tr>
<td></td>
<td>20. Eat sweets like cake, cookies, pastries, donuts, muffins, chocolate and candies more than 2 times per day.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Soft drinks</td>
<td>21. Drink 16 oz or more of non-diet soda, fruit drink/punch or Kool-Aid a day?</td>
<td></td>
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<tr>
<td></td>
<td>Serving = 1 can of soda = 12 oz.</td>
<td></td>
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</tr>
<tr>
<td>Sodium</td>
<td>22. Eat high sodium processed foods like canned soup or pasta, frozen packaged meals (TV dinners, etc.) chips?</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>23. Add salt to foods during cooking or at the table?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caffeine</td>
<td>24. Drink more than 3 caffeinated beverages a day?</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Serving = 100 mg caffeine = 1 cup (8oz.) of coffee.</td>
<td></td>
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</tr>
<tr>
<td>Topic</td>
<td>In an average week, how often do you:</td>
<td>Usually/ Often</td>
<td>Sometimes</td>
<td>Rarely/ Never</td>
</tr>
<tr>
<td>-------</td>
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</tr>
<tr>
<td>Alcohol</td>
<td>25. Drink more than 1-2 alcoholic drinks a day? One drink = 12 oz beer, 5 oz wine, one shot of hard liquor or mixed drink with one shot.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Activity</td>
<td>26. Do less than 30 minutes of physical activity 3 days a week or more? (Examples: walking briskly, gardening, golf, jogging, swimming, biking, dancing, etc.)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>27. Watch more than 2 hours of television or videos a day?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

28. Do you usually shop and prepare your own food?  
   a. Yes  
   b. No  

29. Due to time constraints for responsibilities do you ever have trouble being able to shop or cook?  
   a. Yes  
   b. No  

30. Do you follow a special diet, eat or limit certain foods for health or other reasons  
   a. Yes  
   b. No  

31. How able are you to make changes in what, how or how much you eat in order to eat healthier? (Circle the number that best describes how you feel)  
   Very able  
   5  4  3  2  1  
   Not at all able  

32. Are you currently enrolled in any programs involving food or weight management?  
   a. Yes  
   b. No  

If so, describe ________________________________
CHRONOTYPE INFORMATION
In this section, we are interested in your “chronotype”
(i.e. when you go to bed and when you wake up)

I have a regular schedule (this includes being for example, a housewife):
☐ Yes… I work on: 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ days/ per week.
☐ No

(If your answer is “Yes, on 7 days” or “No”, please again think, if your sleep times may differ between regular “Workdays” and “Weekend days”, anyhow and fill out the MCTQ in this in this respect)

Please use a 24-hour time scale (e.g. 23:00 instead of 11pm)

Workdays
I go to bed at _______ o’clock.
(Note that some people stay awake for some time while in bed)
I actually get ready to fall asleep at _______ o’clock
I need _______ minutes to fall asleep
I wake up at _______ o’clock
After _______ minutes, I actually get up.
I use an alarm clock on workdays
☐ Yes
☐ No
If “yes”, I regularly wake up BEFORE the alarm rings
☐ Yes
☐ No

Free Days
I go to bed at _______ o’clock.
(Note that some people stay awake for some time while in bed)
I actually get ready to fall asleep at _______ o’clock
I need _______ minutes to fall asleep
I wake up at _______ o’clock
After _______ minutes, I actually get up.
My wake-up time is due to the use of an alarm clock
☐ Yes
☐ No
There are particular reasons why I CANNOT freely choose my sleep times on free days

☐ Yes
☐ No

If "yes", is it:
☐ Children/pets
☐ Hobbies
☐ Others, for example __________________________

Time Spent Outdoors

On average, I spend the following amount of time outdoors in daylight (without a roof above my head):

In the spring/summer:

On Workdays ________ hours ________ minutes
On Free Days ________ hours ________ minutes

In the fall/winter:

On Workdays ________ hours ________ minutes
On Free Days ________ hours ________ minutes

Work Details

In the last 3 months, I worked as a shift worker.

☐ Yes (please continue at "My work schedules are...")
☐ No

My usual work schedule...

…starts at ________ o’clock
…ends at ________ o’clock

My work schedules are...

☐ very flexible
☐ a little flexible
☐ rather inflexible
☐ very inflexible

I travel to work...

☐ Within an enclosed vehicle (e.g. car, bus)
☐ NOT within an enclosed vehicle (e.g. on foot, by bike)
☐ I work at home
For the commute to work I need _____ hours and _____ minutes
For the commute home I need _____ hours and _____ minutes

Stimulants
Please give approximate/average amounts!

<table>
<thead>
<tr>
<th></th>
<th>per Day</th>
<th>per Week</th>
<th>per Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>I smoke ______ cigarettes</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>I drink ______ glasses of beer…</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>I drink ______ glasses of wine…</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>I drink ______ glasses of liquor…</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>I drink ______ cups of coffee…</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>I drink ______ cans of caffeinated drinks (soda)…</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>I drink ______ cups of black tea…</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>I take sleep medication ______ times…</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

WORK ENVIRONMENT
In this section, we are interested in the characteristics of your employment at KGH or HDH.

1. What is your current position? _______________________
2. In what year did you start working in your current position? _________
3. Is this position permanent, temporary, casual, etc?
   a. Permanent
   b. Temporary
   c. Casual / on call
   d. Other: _________________________
4. Do you currently do shift work or night work?
   □ Yes
   □ No
5. Are you working full-time or part-time?
   a. Full-time
   b. Part-time
6. If working part-time, what is/are the reason(s) for working part-time?
   (Circle all that apply)
   a. Prefer fewer hours
   b. Full-time positions are not available
   c. Could not find full-time work in area of specialization
   d. Flexible work hours
   e. Have another position outside of the hospital
   f. Under-qualified for a full-time position
   g. Full-time positions are too demanding
   h. Do not want to work shift work
   i. Own illness or disability
   j. Caring for own children
   k. Caring for elderly relative
   l. Going to school
   m. Other (please specify): ______________________________________

7. How many paid hours do you usually work per week? __________

8. How many hours of paid overtime do you usually work per week? __________

9. How many hours of unpaid overtime/extra time do you usually work per week? ______

10. Do you usually work?
    a. 8 hour shifts
    b. 12 hour shifts
    c. Various shifts
    d. Some other shift (please describe): ________________________________

11. Do you usually work days, evenings, or nights?
    a. Days
    b. Evenings
    c. Nights
    d. Mixed

12. What level of skill is REQUIRED on your job in terms of years of formal training?
    (Not necessarily the same as your education)
    a. Elementary education only
    b. High school graduate
    c. Post secondary education (certificate/diploma)
    d. University/undergraduate degree
    e. Graduate degree (Masters/PhD, etc)
    f. MD or resident
    g. Other (please specify): ______________________________________
13. Please mark your pre-tax household income for the past year:

- [ ] less than 15,000
- [ ] 15,000 to 19,999
- [ ] 20,000 to 29,999
- [ ] 30,000 to 39,999
- [ ] 40,000 to 49,999
- [ ] 50,000 to 74,999
- [ ] 75,000 to 99,999
- [ ] 100,000 to 150,000
- [ ] > 150,000

**REgarding your current position, please check the box in the most appropriate category for the statements listed in tables 1-8**

**Table 1.**

<table>
<thead>
<tr>
<th></th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
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<tr>
<td>b.</td>
<td></td>
<td></td>
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<tr>
<td>c.</td>
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<tr>
<td>d.</td>
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<tr>
<td>e.</td>
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<tr>
<td>f.</td>
<td></td>
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</tbody>
</table>

13

Version: April 30, 2013
## TABLE 2.

<table>
<thead>
<tr>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. My job allows me to make a lot of decisions on my own.</td>
<td></td>
<td></td>
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<tr>
<td>b. On my job I have very little freedom to decide how I do my work.</td>
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<tr>
<td>c. I have a lot to say about what happens on my job.</td>
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<tr>
<td>d. I have a significant influence over decisions in my work group or unit.</td>
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<tr>
<td>e. My work group or unit makes decisions democratically.</td>
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<tr>
<td>f. I have at least some chance that my ideas will be considered about company policy (e.g., hiring, firing, wage levels, plants closing, new machinery, etc.).</td>
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<tr>
<td>g. My union or employee association is influential in affecting company policy.</td>
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<tr>
<td>h. Have influence over the policies of the union or employee association.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

13. How many people are in your work group or unit?
   a. I work alone
   b. 2-5 people
   c. 6-10 people
   d. 10-20 people
   e. >20 people

14. I supervise people as a part of my job.
   a. No
   b. Yes, 1-4 people
   c. Yes, 5-10 people
   d. Yes, 11-20 people
   e. Yes, more than 20 people

15. I am a member of a union or employee association.
   a. Yes
   b. No
### TABLE 3.

<table>
<thead>
<tr>
<th></th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. My job requires working very fast.</td>
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<tr>
<td>b. My job requires working very hard.</td>
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<tr>
<td>c. I am not asked to do an excessive amount of work.</td>
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<tr>
<td>d. I have enough time to get the job done.</td>
<td></td>
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<tr>
<td>e. I am free from conflicting demands that others make.</td>
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<tr>
<td>f. My job requires long periods of intense concentration on the task.</td>
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<tr>
<td>g. My tasks are often interrupted before they can be completed, requiring attention at a later time.</td>
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<tr>
<td>h. My job is very hectic.</td>
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<td></td>
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<tr>
<td>i. Waiting on work from other people or departments often slows me down on the job.</td>
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</tbody>
</table>

### TABLE 4.

<table>
<thead>
<tr>
<th></th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. My job requires lots of physical effort.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. I am often required to move or lift very heavy loads on my job.</td>
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<tr>
<td>c. My work requires rapid and continuous physical activity.</td>
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<tr>
<td>d. I am often required to work for long periods with my body in physically awkward positions.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. I am required to work for long periods with my head or arms in physically awkward positions.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Strongly Agree</td>
<td>Agree</td>
<td>Disagree</td>
<td>Strongly Disagree</td>
</tr>
<tr>
<td>---</td>
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</tr>
<tr>
<td>a. My job security is good.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>b. My prospects for career development and promotions are good.</td>
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<tr>
<td>c. In five years my skills will still be valuable.</td>
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</tr>
</tbody>
</table>

16. How steady is your work? (check one ONLY)
   a. Regular and steady
   b. Seasonal
   c. Frequent layoffs
   d. Both seasonal and frequent layoffs
   e. Other: ___________________________________

17. During the past year, how often were you in a situation where you faced job loss or layoff?
   a. Never
   b. Faced the possibility once
   c. Faced the possibility more than once
   d. Constantly
   e. Laid off

18. Sometimes people permanently lose jobs they want to keep. How likely is it that during the next couple of years you will lose your present job with your employer?
   a. Not likely at all
   b. Not too likely
   c. Somewhat likely
   d. Very likely

19. In the next 12 months, do you plan to leave your current position?
   a. Yes
   b. No
### TABLE 6.

<table>
<thead>
<tr>
<th></th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td>My supervisor is concerned about the welfare of those under him/her.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b.</td>
<td>My supervisor pays attention to what I am saying.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c.</td>
<td>I am exposed to hostility or conflict from my supervisor.</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>d.</td>
<td>My supervisor is helpful in getting the job done.</td>
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<tr>
<td>e.</td>
<td>My supervisor is successful in getting people to work together.</td>
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<td></td>
</tr>
</tbody>
</table>

### TABLE 7.

<table>
<thead>
<tr>
<th></th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td>People I work with are competent in doing their jobs.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b.</td>
<td>People I work with take a personal interest in me.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c.</td>
<td>I am exposed to hostility or conflict from the people I work with.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d.</td>
<td>People I work with are friendly.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e.</td>
<td>The people I work with encourage each other to work together.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f.</td>
<td>People I work with are helpful in getting the job done.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TABLE 8.

<table>
<thead>
<tr>
<th></th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td>I often have to arrive early or stay late to get my work done.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b.</td>
<td>I often have to work through my breaks to complete my assigned workload.</td>
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<tr>
<td>c.</td>
<td>It often seems like I have too much work for one person to do.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d.</td>
<td>I have too much to do, to do everything well.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

20. If you are planning on leaving, why are you planning to leave? (circle all that apply)
   a. Retirement
   b. Career advancement
   c. Career change
   d. More time with family
   e. Health problems
   f. Physical demands of your position
   g. Too much responsibility
   h. Inability to provide safe, competent care
   i. Burnout
   j. Poor salary
   k. Workload
   l. Management practices
   m. Conflict with management
   n. Lack of respect
   o. Other: ____________________

21. Do you have another paid position outside of your current position?
   a. Yes
   b. No

22. Is this other position full-time or part-time?
   a. Full-time
   b. Part-time

18
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Physical Activity

We are interested in finding out about the time you spend doing different types of physical activity in a typical week. Please answer these questions even if you do not consider yourself to be physically active.

ACTIVITY AT WORK

1. Does your work involve vigorous-intensity activity that causes large increases in breathing or heart rate like [carrying or lifting heavy loads, digging or construction work] for at least 10 minutes continuously?
   - Yes
   - No
   If no, go to Question 4

2. In a typical week, on how many days do you do vigorous-intensity activities as part of your work?
   Number of days ____________

3. How much time do you spend doing vigorous-intensity activities at work on a typical day? (Think of one day you can recall easily. Consider only those activities undertaken continuously for 10 minutes or more.)
   - Hours _______ Minutes _______

4. Does your work involve moderate-intensity activity, that causes small increases in breathing or heart rate such as brisk walking [or carrying light loads] for at least 10 minutes continuously?
   - Yes
   - No
   If no, go to Question 7

5. In a typical week, on how many days do you do moderate-intensity activities as part of your work?
   Number of days ____________

6. How much time do you spend doing moderate-intensity activities at work on a typical day? (Think of one day you can recall easily. Consider only those activities undertaken continuously for 10 minutes or more.)
   - Hours _______ Minutes _______
TRAVEL TO AND FROM PLACES

The next questions exclude the physical activities at work that you have already mentioned. Think about the usual way you travel to and from places. For example, to work, for shopping, to market, to place of worship.

7. Do you walk or use a bicycle (pedal cycle) for at least 10 minutes continuously to get to and from places? (Please circle the appropriate response)
   Yes
   No
   If no, go to Question 10

8. In a typical week, on how many days do you walk or bicycle for at least 10 minutes continuously to get to and from places?
   Number of days ____________

9. How much time do you spend walking or bicycling for travel on a typical day? (Think of one day you can recall easily. Consider the total amount of time walking or bicycling for trips of 10 minutes or more.)
   Hours _______ Minutes _______

RECREATIONAL ACTIVITIES

The next questions exclude the work and transport activities that you have already mentioned. Think about sports, fitness and recreational activities and leisure activities you participate in on a regular basis (not occasionally). It is important to focus on only recreational activities and not to include any activities already mentioned.

10. Do you do any vigorous-intensity sports, fitness or recreational (leisure) activities that cause large increases in breathing or heart rate like running or football for at least 10 minutes continuously?
    Yes
    No
    If no, go to Question 13

11. In a typical week, on how many days do you do vigorous-intensity sports, fitness or recreational (leisure) activities?
    Number of days ____________
12. How much time do you spend doing vigorous-intensity sports, fitness or recreational activities on a typical day? (Think of one day you can recall easily. Consider the total amount of time doing vigorous recreational activities for periods of 10 minutes or more.)

Hours _______ Minutes _______

13. Do you do any moderate-intensity sports, fitness or recreational (leisure) activities that causes a small increase in breathing or heart rate such as brisk walking, cycling, swimming, or volleyball for at least 10 minutes continuously?

Yes
No
If no, go to Question 16

14. In a typical week, on how many days do you do moderate-intensity sports, fitness or recreational (leisure) activities?

Number of days ____________

15. How much time do you spend doing moderate-intensity sports, fitness or recreational (leisure) activities on a typical day? (Think of one day you can recall easily. Consider the total amount of time doing moderate recreational activities for periods of 10 minutes or more.)

Hours _______ Minutes _______

SEDENTARY BEHAVIOUR

The following question is about sitting or reclining at work, at home, getting to and from places, or with friends including time spent sitting at a desk, sitting with friends, travelling in car, bus, train, reading, playing cards or watching television. DO NOT include the time you spend sleeping.

16. How much time do you usually spend sitting or reclining on a typical day? (Consider total time spent at work sitting, in an office, reading, watching television, using a computer, doing hand craft like knitting, resting etc. Do not include time spent sleeping.)

Hours _______ Minutes _______
Overall Health and Quality of Life

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Answer every question by selecting the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is:

   - Excellent
   - Very good
   - Good
   - Fair
   - Poor

2. Compared to one year ago, how would you rate your health in general now?

   - Much better now than one year ago
   - Somewhat better now than one year ago
   - About the same as one year ago
   - Somewhat worse now than one year ago
   - Much worse now than one year ago

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

   - Yes, limited a lot
   - Yes, limited a little
   - No, not limited at all

   a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports

   b. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf

   c. Lifting or carrying groceries

   d. Climbing several flights of stairs
4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

   Yes  No

   a. Cut down on the amount of time you spent on work or other activities

   b. Accomplished less than you would like

   c. Were limited in the kind of work or other activities

   d. Had difficulty performing the work or other activities (for example, it took extra effort)

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

   Yes  No

   a. Cut down on the amount of time you spent on work or other activities

   b. Accomplished less than you would like

   c. Did work or other activities less carefully than usual
6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

<table>
<thead>
<tr>
<th>Not at all</th>
<th>Slightly</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
</table>

7. How much bodily pain have you had during the past 4 weeks?

<table>
<thead>
<tr>
<th>None</th>
<th>Very mild</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Very severe</th>
</tr>
</thead>
</table>

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

<table>
<thead>
<tr>
<th>Not at all</th>
<th>A little bit</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
</table>

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks...

| | All of the time | Most of the time | A good bit of the time | Some of the time | A little of the time | None of the time |
| | | | | | | |
| a Did you feel full of pep? | | | | | | |
| b Have you been a very nervous person? | | | | | | |
| c Have you felt so down in the dumps that nothing could cheer you up? | | | | | | |
| d Have you felt calm and peaceful? | | | | | | |
f  Have you felt downhearted and blue?  ☐ ☐ ☐ ☐ ☐ ☐

g  Did you feel worn out?  ☐ ☐ ☐ ☐ ☐ ☐

h  Have you been a happy person?  ☐ ☐ ☐ ☐ ☐ ☐

i  Did you feel tired?  ☐ ☐ ☐ ☐ ☐ ☐

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

<table>
<thead>
<tr>
<th></th>
<th>All of the time</th>
<th>Most of the time</th>
<th>Some of the time</th>
<th>A little of the time</th>
<th>None of the time</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>☐</td>
<td>☐</td>
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</tbody>
</table>

11. How TRUE or FALSE is each of the following statements for you?

<table>
<thead>
<tr>
<th>Statement</th>
<th>Definitely true</th>
<th>Mostly true</th>
<th>Don’t know</th>
<th>Mostly false</th>
<th>Definitely false</th>
</tr>
</thead>
<tbody>
<tr>
<td>a  I seem to get sick a little easier than other people</td>
<td>☐</td>
<td>☐</td>
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<td>☐</td>
</tr>
<tr>
<td>b  I am as healthy as anybody I know</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>c  I expect my health to get worse</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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<tr>
<td>d  My health is excellent</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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</tbody>
</table>

THANK YOU SO MUCH FOR COMPLETING THIS QUESTIONNAIRE. YOUR FEEDBACK IS VERY IMPORTANT TO US.
### TO WHAT EXTENT IS THE STATEMENT TRUE OF YOU?

1. I rarely exercise.  
2. I rarely have feelings of being trapped or caught in life.  
3. I feel rules were made to be broken.  
4. I take some time not almost every day just to relax.  
5. I laugh easily.  
6. My job provides me many opportunities for challenging and satisfying activities.  
7. When I am on vacation with my family I don’t have as much fun as I think I should.  
8. I get into frequent arguments.  
9. I rarely feel tense and under pressure.  
10. I rarely exercise.  
11. I feel no interest in things.  
12. I would like to be with my family more, but I can never seem to find the time.  
13. I never worry about being a "workaholic".  
14. I believe that if you don’t beat the other guy to the punch, he will beat you.  
15. I never get in for very long.  
16. I am not very good at telling funny stories or jokes.  
17. I get great pleasure from the people I work with.  
18. I have a satisfying sex life.  
19. I have no problems with control of my temper.  
20. I am usually worried about something.  
21. I smoke too much.  
22. I rarely feel lonely.  
23. When I eat, I usually take my time.  
24. I frequently say I am going to spend less time on work, but I don’t seem to be able to.  
25. Most things I do I see as a challenge.  
26. I am not very interested in hobbies or sports.  
27. I seem to be more focused on the future than the present.  
28. My full range of talents are not utilized on my job.  
29. I have a good relationship with my wife/husband (or unmarried partner).  
30. Sometimes I just feel like hitting somebody.  
31. I rarely feel nervous or uptight.  
32. I am in good physical shape.  
33. I sometimes have feelings of worthlessness.  
34. I rarely feel pressed for time.  
35. The more things I achieve in life the less I seem to enjoy them.

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**PAGE ONE**  
**PLEASE CONTINUE ON OTHER SIDE**
TO WHAT EXTENT IS THE STATEMENT TRUE OF YOU?

<table>
<thead>
<tr>
<th>Statement</th>
<th>0</th>
<th>1</th>
<th>2</th>
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<tbody>
<tr>
<td>36. I tend to be impatient.</td>
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<td>37. I sometimes just &quot;tune out&quot; of work and get involved in other things.</td>
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<td>38. Sex is an important part of life for me.</td>
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<td>39. I am frequently frustrated in my work.</td>
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<td>40. Interacting with my family and friends is a great source of enjoyment for me.</td>
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<td>41. I rarely have angry thoughts about people.</td>
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<td>42. When I know I have something unpleasant to do I worry about it for a long time.</td>
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<td>43. I don’t take antacids for heartburn or gas.</td>
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<td>44. I usually have plenty of energy.</td>
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<td>45. I enjoy being under pressure and doing a good job on many projects at the same time.</td>
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<td>46. I really look forward to my vacations.</td>
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<td>47. I make a serious effort to achieve a balance between work and fun.</td>
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<td>48. It is not difficult for me to unwind after work.</td>
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<td>49. I really believe it is lonely at the top.</td>
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<td>50. Doing my job gives me a good feeling about myself.</td>
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<td>51. I have a good balance between family activities and work activities.</td>
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<td>52. I get really annoyed or irritated.</td>
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<td>53. I frequently have the feeling that something bad is going to happen to me.</td>
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<td>54. I believe having good health is more important than anything.</td>
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<td>55. Sometimes I feel hopeless about the future.</td>
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<td>56. When I am driving the car, I almost never rush through traffic.</td>
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<td>57. Every day I must get something tangible accomplished or I don’t feel good about myself.</td>
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<td>58. I feel the most important thing in life is that you achieve something with it.</td>
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<tr>
<td>59. The idea of meditation or relaxation training has not had much appeal for me.</td>
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<tr>
<td>60. I believe you can get a lot of help from others in getting the job done in life.</td>
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<td>61. There are significant parts of my job that are frankly dull and boring.</td>
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<td>62. I don’t interact much with friends or neighbors.</td>
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<td>63. I rarely clear my face during conversation.</td>
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<td>64. I rarely let things get me anxious or tense because I know they always get worked out somehow.</td>
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<td>65. I am very careful about my diet.</td>
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<td>66. I have sometimes thought of ending my life.</td>
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<td>67. When I have an appointment I rarely arrive late or at the last minute.</td>
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<td>68. Once I get started on a project, I don’t like to stop until I am finished.</td>
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<td>69. I believe competition builds character and is good for you.</td>
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<td>70. I have trouble relaxing.</td>
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<td>71. I believe life is a struggle and you don’t get anything for free out of it.</td>
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<td>72. When I wake up in the morning, I really look forward to going to work.</td>
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<td>73. I really enjoy going to parties and meeting people.</td>
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<td>74. If someone expresses a stupid idea, I rarely publicly disagree.</td>
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<td>75. Sometimes I feel tense and anxious for no apparent reason.</td>
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<tr>
<td>76. I take tranquilizers to relax or sleep.</td>
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<tr>
<td>77. I rarely blame myself unduly for things that go wrong.</td>
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</table>

Please indicate what you believe your current level of stress to be by placing an "X" on the line below.

Totally Free of Stress ◣ Extremly Highly Stressed

Also, please assign a number from 0 to 100 where 0 is Totally Free of Stress and 100 is Extremely Highly Stressed in the space provided. ________

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Appendix C: Ethics Approval

Amendment Acknowledgment/Approval Letter

May 07, 2013

Dr. Kyra Pyke
School of Kinesiology & Health Studies
Queen's University

RE: File #600873 PHE-112-11 Stress reactivity and vascular health in patients with chronic pain

Dear Dr. Pyke:

I am writing to acknowledge receipt of the following:

- Request to expand the inclusion criteria to include: 1) men up to the age of 65 years (formerly 55), 2) those with a diagnosis of high blood pressure who are taking blood pressure medication 3) those who have high cholesterol and who are taking cholesterol lowering medication and 4) those who are 2.5 years from diagnosis
- Request to perform a very similar protocol in a group of women who have engaged in overnight shift-work for a period of at least 10 years, and an age-matched non-shift work control group (80 participants total)
  - Shift-work protocol timeline
  - Medical screening form
  - Effort reward balance index – survey related to work stress
  - Derogatis Stress Index
  - Health Status and Work Environment Survey
  - Debrief After the Mental Stress Task
  - Consent form – clean and tracked changes copy

I have reviewed these amendments and hereby give my approval. Receipt of these amendments will be reported to the Health Sciences Research Ethics Board.

Yours sincerely,

Albert Clark, Ph.D.
Chair
Research Ethics Board