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Interplay between Shift Work, Psychological Distress, Sleep Quality, and Cognitive Performance

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Abstract

Shift work schedules are designed to maintain a continuous operation of goods and services. However, engaging in shift work may impact cognitive functioning. This thesis assessed the relationship between shift work and cognitive performance. Using cross-sectional data from the Canadian Longitudinal Study on Aging, multiple linear regression models were used to investigate the association between shift work and cognitive performance, as well as the moderating effects of psychological distress and sleep quality. Differences by sex and retirement status were also investigated. Shift work was significantly associated with poor performance for executive functioning but not for declarative memory. Poorer cognitive performance was found among completely retired and not or partly retired males. No evidence of a moderating effect by psychological distress or sleep quality was found. Our findings highlight important occupational health and safety implications. Future studies using a prospective cohort design is warranted.

Keywords

Shift work, cognition, cognitive performance, psychological distress, sleep quality, Canada

Summary for Lay Audience

Shift work refers to work schedules which take place outside the regular work hours of 7:00 a.m. to 6:00 p.m. Commonly used shift work schedules include work shifts occurring early in the morning, afternoon, evening, or night. A person who works shift work may even alternate between different types of shifts on a weekly or monthly basis. As people with shift work schedules exhibit poor sleep and changes in their body's natural sleep-wake cycle, research has linked the development of many long-term diseases to shift work, including cardiovascular disease, hypertension, diabetes, gastrointestinal conditions, cancer, metabolic syndrome, depression, or anxiety. Given the nature of shift work, negative changes to a person's mental health, may also play a role in the development of disease among shift workers. Research suggests that shift work schedules may impair cognitive function, which are functions in the brain involved in learning, thinking, problem-solving, decision-making and memory. Not much is known about how a person's mental health, specifically psychological distress -a state of emotional suffering- impacts this relationship. The purpose of this thesis was to examine the interrelationships between shift work, psychological distress, sleep quality and cognitive performance using survey data from a sample of Canadian adults aged 45-85 years. To assess cognitive performance, we assessed cognitive domains involved in problem solving (executive functioning) and long-term memory (declarative memory). We found that shift workers performed poorly on cognitive tests for executive functioning but not for declarative memory. Completely retired and not or partly retired male shift workers performed worse than female shift workers. We found that performances on cognitive tests among shift workers were the same regardless of the level of psychological distress or by the quality of sleep.

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List of Abbreviations

BMI = Body mass index

CCA = Complete case analysis

CES-D-10 = Centre for Epidemiologic Studies Depression Scale

CI = Confidence interval

CLSA = Canadian Longitudinal Study on Aging

COPD = Chronic obstructive pulmonary disease

HPA = Hypothalamus-pituitary-adrenal

K10 = Kessler Psychological Distress Scale

MAR = Missing At Random

MAT = Mental Alternation Test

MCAR = Missing Completely At Random

MCI = Mild Cognitive Impairment

MI = Multiple Imputation

MICE = Multiple Imputation by Chained Equations

MMSE = Mini-Mental State Examination

MNAR = Missing Not At Random

PASE = Physical Activity Scale for the Elderly

R = Reference

RAVLT = Rey Auditory Verbal Learning Test

SCREEN II = Seniors in the Community: Risk Evaluation for Eating and Nutrition Version II

SD= Standard deviation

SE= Standard error

VIF= Variance inflation factor

Chapter 1

1 Background and Introduction

This chapter provides a brief background and overview of the thesis, with Section 1.1 providing the overall purpose of the thesis, and Sections 1.1.1, 1.1.2 and 1.1.3 discussing background information on shift work, cognitive impairment, and psychological distress, respectively. The study rationale and thesis objectives are outlined in Section 1.2. An overview of the thesis chapters and the role of the student is provided in Section 1.3.

1.1 Overall Purpose

The purpose of this thesis is to investigate the association between shift work and cognitive performance.

1.1.1 Shift Work

In the Canadian context, shift work may be defined as non-standard work hours scheduled to occur outside the work hours of 7:00 a.m. to 6:00 p.m.[1] As such, different types of shift work schedules exist including shift work occurring early in the morning or afternoon, or regularly in the evening or night, as well as, “rotating shift work”, “split shifts”, “on-call”, or “casual”.[2] The use of the shift system has spread globally as a result of technological advancements and a shift towards a more demanding economy.[3] In particular, both developing and developed countries have been found to use shift work schedules.[3] The shift system is commonly used among certain industries, including the health care, transportation, manufacturing, customer service and protective services industry.[1,2] A number of risk factors and adverse health conditions, which will be described in detail in Chapter 2, have been linked with shift work and highlight an important role of sleep and circadian rhythm.[4,5] Given the nature of shift work schedules, particularly night shift schedules, misalignment of the circadian rhythm as a result of poor sleep has been proposed as a mechanism leading to the development of disease.[4]

1.1.2 Cognitive Impairment

Advancements in technology and health care have led to an increase in global life expectancy.[6] Developed countries, including Canada, are socioeconomically burdened with late-life cognitive impairment and dementia as a result of an aging population.[7–11]

Changes in cognitive function, which refer to mental processes associated with learning, logical thinking, problem-solving, decision-making and memory,[12,13] take place on a continuum[14] and may be classified as normal cognitive aging, cognitive impairment, or dementia.[15] Cognitive impairment is defined as the deterioration of cognitive domains used in daily activities and may range from mild to severe.[11–13] People with cognitive impairment may not satisfy a diagnosis for dementia,[16] however, people with this condition do have an increased risk in developing dementia.[14,17]

Currently, no pharmacological treatments have been developed to prevent or cure this debilitating disease.[9,18] As such, studies have been investigating whether modifiable lifestyle factors may help to mitigate the risk of cognitive impairment.[19] Studies from the literature have identified several risk factors and chronic diseases, some of which have been reported to slow or accelerate the rate of cognitive impairment.[20] Interestingly, similar risk factors and chronic diseases have been linked with people engaging in shift work.[21,22] These risk factors and chronic diseases will be discussed in greater detail in Chapter 2.

1.1.3 Psychological Distress

Given the nature of shift work, shift schedules can have negative implications on an individual's mental health.[23] Mental health problems pose as a significant public health concern and burden to society, especially in Canada.[24–27] Literature investigating relationships between shift work and mental health have assessed psychological distress,[28] which can be defined as a state of emotional suffering, such that a person's daily life is negatively impacted with experiencing depressive, anxiety and somatic symptoms.[29,30] Psychological distress can also be used as a measure of the general mental health status of a population, as well as a measure of symptom severity and disability level among people with mental illnesses.[29,30] A number of hypotheses have been proposed to explain relationships between shift work and psychological distress, including the job-strain model,[31,32] healthy worker effect and the stress-distress model.[29,33,34] These hypotheses are discussed in greater detail in Chapter 2. Psychological distress has also been implicated with cognitive impairment, with studies showing greater rates of cognitive decline among people more susceptible to developing psychological distress than those less vulnerable.[35,36] Hypotheses proposed in explaining this relationship include the job-strain and stress-distress model.[37,38] The personality trait, neuroticism,[16,29,37,39] as well as the hypothalamus–pituitary– adrenal (HPA) axis,[37,40,41] are other mechanisms which may link psychological distress and cognitive impairment. Detailed explanations regarding these mechanisms are provided in Chapter 2.

1.2 Study Rationale and Thesis Objectives

Investigating modifiable risk factors for cognitive impairment is important, given an aging population and no pharmacological treatments to date.[9] Although there are still members of the workforce that work traditional work hours, the demand for a "24/7" economy[42] has led to the widespread use of shift work schedules in several occupations and industries. As shift work and cognitive impairment share common risk factors and chronic diseases, shift work could be a potential modifiable risk factor that may have implications on the development of cognitive impairment. As such, a better understanding on the relationship between shift work and cognitive performance is warranted. Furthermore, although we know that sleep plays an important role in this relationship, we have limited knowledge on the impact of mental health, particularly, psychological distress. Therefore, the objectives of this thesis were:

1. To examine the association between shift work and cognitive performance
2. To explore whether psychological distress moderates the relationship between shift work and cognitive performance
3. To explore whether sleep quality moderates the relationship between shift work and cognitive performance

A detailed description of the thesis objectives is provided in Chapter 2.

1.3 Overview of Thesis Chapters and Role of Student

In Chapter 2, detailed background information regarding shift work, cognitive functioning, and psychological distress, as well as a literature review investigating the association between shift work and cognitive impairment is provided. Chapter 3 outlines the methods used in the thesis. Chapter 4 and 5 respectively provide the main findings of the thesis and the discussion of the results, including the strengths and weaknesses of the study.

The data used in this study was obtained from the Canadian Longitudinal Study on Aging (CLSA). These data were requested by my thesis supervisors Dr. Saverio Stranges and Dr. Kelly Anderson. I collaborated with Dr. Stranges and Dr. Anderson to select our exposure and outcome of interest, as well as develop the objectives of the thesis. Dr. Manuel Montero-Odasso, a member of my thesis committee, provided guidance on which outcome variables would be most appropriate to assess cognitive performance. I proposed a data analysis plan for the thesis, which was further modified by my two supervisors, by providing suggestions on additional confounding variables to adjust for in the analyses, as well as providing guidance on the criteria to recode specific variables. The objectives and data analysis plan were then checked by Dr. Neil Klar, another member of my thesis committee, to ensure statistical methods to assess my thesis objectives were feasible and appropriate. With input from Dr. Stranges and Dr. Anderson, I cleaned the data, recoded the variables and ran the statistical analyses. Interpretation of the findings was conducted in consultation Dr. Stranges and Dr. Anderson. Final revisions of the thesis manuscript involved all committee members.

Chapter 2

2 Literature Review

This chapter provides a review of the literature on the relationship between shift work and cognitive impairment. Background information pertaining to shift work, cognition and psychological distress are provided in Sections 2.1, 2.2 and 2.3, respectively. Section 2.4 reviews the literature on shift work and cognitive impairment. Thesis objectives and a theoretical conceptual framework to guide analyses is provided in Section 2.5.

2.1 Shift Work

Various definitions for shift work exist across the literature, as there is currently no universally agreed upon definition.[28] Broadly, shift work may constitute a work schedule that occurs outside the traditional 9:00 a.m. to 5:00 p.m. work hours[1,2] and may also occur outside regular business days.[2] Shift work schedules are designed to accommodate different work time schedules.[43] As such, shift schedules can be organized in a variety of ways according to the length of the shift and the duration of rest periods within and between shifts.[44]

In Canada, shift work is referred to as non-standard work hours occurring in the hours before 7:00 a.m. or after 6:00 p.m.[1] There are several categories of shift work schedules used in Canada. “Rotating shift work” typically involves work schedules alternating from day shifts to evening or night shifts.[2,3] “Split shift” schedules include work days that are divided into two or more time periods.[3] “On-call” or “casual” work schedules typically have no prearranged schedules available and require individuals to report to work when needed.[4] “Irregular work schedules,” are work schedules which frequently change and have prearranged schedules available at least one week in advance.[5] Other variations of shift work include work schedules occurring early in the morning or afternoon[2,6] or regularly in the evening or night.[2] An important feature of shift work is that the types of shifts assigned to workers are usually not optional but rather as a requirement of the job.[3,7] This differentiates shift work from “overtime” work schedules or “extended hours of work,"[42,48] which typically serve as extra time that some workers may choose to do to complete work-related tasks.[28]

Shift work is designed to uphold a "24/7" economy.[42] As workers alternate assigned shift schedules with other workers, this allows for the continuous and daily operation of production and services.[49,50] As a result of technological advancements and a move towards a more demanding economy,[3] shift work has become more prevalent worldwide.[28,3] In Canada, one in four Canadians are employed in shift work.[51] In 2011, 12% of the Canadian labour force were involved in night shift work specifically.[52] Similarly, workers in the US, UK and Australia are actively engaged in shift work.[53] In China, shift work schedules are primarily used in manufacturing, whereas a widespread use of shift work can be found in almost every industry in South Korea and Jamaica.[54] In Peru, split shift schedules are commonly used in the education sector.[54] Shift work, particularly night shift work, is not less common in Chile and Brazil.[54]

Achieving work-life balance was not perceived as a concern as it was traditionally assumed that people in the labour force worked full-time hours and were usually men, and that domestic duties were placed under the responsibility of women.[55] Changes in employment policies for women and a shift towards a 24-hour economy has resulted in changes in the traditional work and family dynamics between men and women.[53,55] Issues of work-life balance have emerged as a result of these changes.[56] Work-life balance is a subjective state, characterized by a person's ability to balance work, home, and community responsibilities.[2] Government policies and work practices have been put in place to promote work-life balance.[57] For instance, in some Scandinavian countries, control over work schedules among employees is encouraged, including workday start and end times, breaks, days off, and vacation days.[58] However, views on work-life balance appear to differ between Western and Eastern countries.[57] In Western countries, achieving work-life balance is viewed as an issue for both men and women.[57] In Eastern countries, particularly those in Asia where the labour force is predominantly male and societal norms include gender-specific division of labour, work-life balance is perceived only as an issue for women.[57] Studies have found that compressed work weeks and work time control is associated with better work-life balance among shift workers.[59,60]

Specific industries and occupations are highly dependent on shift work. Occupations in the health care, transportation, manufacturing, customer service and protective services sectors commonly use the shift system.[1,2] For instance, physicians and nurses employed in hospitals often work 12-hour rotational shifts to provide continuous patient care.[61–63] Some shifts may be required to take place overnight[64] and others may last for 24-hours, which is often the case for anesthesiologists.[65] In Europe, physicians employed in hospitals are commonly scheduled to work on-call duty, which includes both day and night shifts and is also 24 hours in length.[66–68] Across Canada, resident doctors may be allowed to work shifts of up to 24 to 26 hours in length, with the exception of Quebec, which specifies that residents can only work a maximum of 16 consecutive hours.[69] Although peak traffic periods may vary globally, bus drivers often work split shifts to accommodate increased traffic flow commonly occurring during periods in the morning and in the evening.[46] As pilots are required to travel through different time zones, they are typically subjected to irregular work schedules.[2] To provide 24-hour protection, police officers and firefighters often work night shifts.[70] Nights shifts are also common among occupations in the manufacturing and industrial industry which have machines operating continuously to produce goods.[70]

Shift work, particularly work that occurs at night, is associated with the development of numerous health conditions, including sleep disturbances, cardiovascular diseases, gastrointestinal symptoms, diabetes, and immune system problems.[4] A systematic review by Shariat and colleagues[4] describing associated health problems among shift workers suggests that the increased risk of developing these health conditions may be a product of circadian rhythms disrupted due to abnormal working times. Desynchronization of the circadian rhythm may alter the normal regulation of physiological functions in the body, thereby leading to the development of disease.[4]

2.1.1 Factors Associated with Shift Work

Sociodemographic Factors

Age: Studies from the literature suggest that older people have more difficulty engaging in shift work.[1,71–73] One reason pertains to the desynchronization of the circadian rhythm which naturally occurs as people reach midlife.[1,72,74,75] Another reason may be that older adults have a reduced ability to handle stress.[1,72,74,75] As such, older people may switch to working regular day shifts.[1] The study by Shields[1] found that working shift schedules decreased as age increased. They propose that older people who have remained at the same job for many years may have acquired seniority overtime, and thus may be able to choose more favourable work schedules than younger people.[1]

Marital Status: People who engage in shift work are also more likely to be single.[1,2] However, among those who are married, shift work has been reported to disrupt family relationships, particularly those with one's spouse and children.[1,2,42,76–78] Compared to day workers, people engaged in evening shift work have been found to spend less time with their spouses and children.[2,79] In fact, links between shift work and marital problems have been reported in the literature. Shift work has been found to be associated with poor marital satisfaction and higher levels of conflict.[1,77,78,80] Disruptions in family routine, as well spending less time with one's spouse due to irregular work schedules, has been proposed as a reason for marital strain among shift workers.[76]

Socioeconomic Status: As previously discussed, specific industries and occupations are tied to shift work,[2] meaning that shift work also varies by socioeconomic status. For instance, the manufacturing industry is predominantly comprised of people with lower educational attainment.[81] According to McMenamin,[81] people with higher educational attainment often find employment in jobs which do not use shift work schedules. However, it is the job demands, rather than education, that determine whether shift work schedules are necessary.[81] Shift work schedules are common among people who earn wages and salaries.[81] Some employers offer monetary premiums to promote shift work.[81] Shields[1] found that people working in the health and protective services sector tend to work rotating shift work and come from high-income households, whereas a high proportion of people working evening, night or irregular shifts were from low-income households.[1]

Immigration Status: According to the report on the Canadian Immigrant Labour Market,[82] which assessed trends from 2006 to 2017, immigrants are more likely to be employed in specific industries, including the accommodation and food industry, both of which have a higher likelihood of shift work schedules.[2] In the literature, relationships between migrant status and shift work have been investigated among studies assessing occupational risks and hazards. One European study reported that migrants in the services, manufacturing, construction and agricultural sector with non-manual positions were more likely to be scheduled to work shift work relative to non-migrants.[83] A Canadian study which investigated relationships between immigration status and occupational hazards, considered shift work as an occupational risk factor for work-related injury.[84] After adjusting for potential confounding variables, this study found that factors related to immigration status, including visible minority status, a non-English or French native language, and highest educational attainment outside of Canada, were associated with regularly occurring shift work schedules, but not irregular shifts.[84] However, a systematic review investigating working conditions and occupational health among immigrants in Canada and Europe found that there was insufficient evidence to suggest that immigrants were subjected to poorer working conditions than non-immigrant workers.[85]

Rurality of Residence: Shift work and rural place appear to be linked through the type of occupation and job skill. In 2011, there were more than 6.3 million Canadians residing in rural areas.[86] A review paper by Bollman and Reimer investigating demographic characteristics of rural populations in Canada found that in 2007, of the 3 million rural and small town employed Canadians, 8% were employed in agriculture and 13% worked in manufacturing,[87] with both industries known to use the shift work system.[2] In many rural areas and small towns, the manufacturing industry may be the only source of employment.[87] Furthermore, jobs requiring higher skills have been found to aggregate in urban centers, whereas lower-skilled jobs tend to center around rural areas.[87] A study by Saenz[88] found that compared to urban workers, rural workers were more likely to work non-standard work hours, particularly shifts occurring early in the morning, or during the afternoon or evening.

Social Isolation: Shift work appears to have negative impacts on psychosocial functioning, particularly outside work environments. A review by Cheng and Drake investigating the psychological impact of shift work found that people who engage in shift work were more likely to feel socially isolated.[89–91] They propose that shift workers are at a higher risk of social isolation as shift schedules occur outside regular business hours, such as during nighttime hours.[89] Shift work may also occur outside regular business days.[2] As such, participation in social activities, which frequently take place on the weekends, is lower among shift workers.[89]

Lifestyle and Behavioural Factors

Sleep Habits: As shift work occurs outside the hours of 7:00 a.m. and 6:00 p.m., there is a large focus in the literature on the sleep habits of shift workers. Compared to the general population, sleep problems are more prevalent among shift workers.[5,92] Disruption of the natural circadian rhythm is commonly attributed to the sleep problems observed among shift workers, as work times for shift work typically occur during normal sleeping hours.[56,93] Difficulties in sleep experienced by shift workers may resemble symptoms of jet leg, as physiological functions responsible for maintaining alertness, including increased cortisol levels and body temperature, interfere with sleep.[56] Furthermore, prior studies have estimated that 10% to 30% of shift workers may suffer from a sleep disorder known as, shift work disorder, which results in a misaligned circadian rhythm and symptoms of insomnia.[5,92,94]

Smoking and Alcohol Consumption: Smoking status and alcohol intake have commonly been studied among shift workers. A review by Nea and colleages[5] found a higher prevalence of smoking among those employed in shift work. They also reported that relative to day workers, people employed in shift work are more likely to start smoking and less inclined to quit.[5,95,96] Alleviation of stress and sleepiness and tiredness were some proposed reasons to explain why shift workers were more susceptible to smoking.[96] The literature on alcohol consumption among shift workers is mixed.[97] Some studies identified by a recent systematic review reported positive associations between shift work and heavy alcohol consumption, whereas others did not find any evidence of an association or found an inverse relationship.[97] Similar to smoking, alcohol may be used as a method to appease sleep problems and work-related stress.[5] However, opportunities to consume alcohol in a social context may be reduced, as shift schedules may conflict with social events.[5]

Physical Activity: The associations between shift work and physical activity is unclear, as studies have assessed a mixture of occupational and leisure physical activity.[5] Two cross-sectional studies investigating leisure[98] and non-occupational[99] physical activities between shift workers and non-shift workers did not find significant differences. Higher occupational and lower leisure physical activity was reported by one study assessing nurses and midwives working rotating night shifts, relative to nurses and midwives working day shifts.[100] In contrast, a study assessing railway shift and daytime workers did not find a significant relationship between shift work, and either occupational or leisure physical activity.[101] Many barriers have been identified that prevent shift workers from engaging in physical activity. These include demanding work schedules and consequent fatigue resulting from these types of schedules, difficulty in participating in team sports, and recreational facilities having hours of operation that do not align with shift work schedules.[5] Furthermore, shift workers may expect to feel overly exhausted if exercise were performed early in the morning or at night, which may deter them from engaging in physical activity.[5]

Diet: Given the nature of shift work schedules, those who engage in the shift system tend to exhibit altered meal patterns and consume poor diets.[102] A recent review by Gupta and colleagues,[102] reported that shift workers often snack at night and commonly consume foods high in fat and carbohydrates. Fruit and vegetable consumption was also found to be lower among night shift workers relative to day workers.[102]

Chronic Disease and Other Health-Related Factors

Body Mass Index (BMI): Links between shift work and high BMIs have been identified in the literature. Two longitudinal studies assessing a sample of nurses reported significant increases in BMI after follow-up among those working night shifts,[103] as well as those working rotating shift schedules.[104] A systematic review and meta-analysis by Liu and colleagues[105] found that shift work was associated with a high risk being overweight and obese. They propose that people who work night shifts are at a higher risk than those who work rotating shift schedules.[105] High BMIs among shift workers could occur for a variety of reasons. Glucose metabolism and lipid homeostasis may be impaired as a result of a disturbed circadian rhythm.[106,107] Additionally, hormones that function to regulate appetite may be altered by shorter sleep duration,[107] thereby resulting in associations between shorter sleep duration and higher BMI.[5] Poor dietary behaviours have also been implicated in the association between shift work and elevated BMI.[5]

Menopausal Status: Shift work may impact the age of menopause among women, as previous studies and systematic reviews have identified links between shift work, and menstrual cycle changes.[108–111] Stock and colleagues[108] used data from Nurse's Health Study 2 to assess the risk of early menopause among registered nurses working rotating night shift work from 1991 to 2013. This prospective cohort study found that rotating shift work was associated with an increased risk of early menopause, particularly for those who had engaged in the shift schedule for 10 months or more.[108] The authors propose that shift work and menopause may be linked through disruptions in the circadian rhythm.[108]

Hypertension and Cardiovascular Disease: Prior evidence suggests that people who engage in shift work are at a higher risk of developing hypertension and cardiovascular disease.[112–114] A meta-analysis of observational studies investigating the relationship between shift work status and hypertension found significant associations among rotating shift workers.[112] However, the studies included in this meta-analysis were predominantly focused on male shift workers.[112] A recent Canadian population-based cohort study using data from the Canadian Community Health Survey, showed that the rate of hypertension was higher for both male and female shift workers after a 12-year follow up.[113] Both poor sleep quality and disrupted circadian rhythms are proposed to increase the risk of hypertension among shift workers. [113] A meta-analysis by Torquati and colleagues[114] reported a 17% higher risk of cardiovascular events, including coronary heart diseases, cerebrovascular disease, and peripheral arterial disease, among shift workers relative to non-shift workers. A dose-response relationship between shift work and cardiovascular disease was also observed, such that following the first five years of exposure to shift work, the risk of cardiovascular outcomes increased by 7.1% per five years of additional work in the shift system.[114] Studies propose that exposure to psychosocial stress, engagement in poor health behaviors, and altered metabolism may play a role in the relationship between shift work and cardiovascular disease.[5,114]

Metabolic Syndrome: Metabolic syndrome has been investigated among shift workers. Metabolic syndrome is characterized by the presence of several risk conditions, associated with all-cause mortality, occurring simultaneously within an individual.[4,115,116] These risk conditions include hypertension, central obesity, elevated triglycerides, high fasting glucose, and reduced high-density lipoprotein cholesterol.[4] Two reviews assessing the health impacts of shift work suggest that these adverse health conditions tend to occur together more frequently among shift workers relative to non-shift workers.[4,5,117,118] Shift workers, especially those who work night shifts, are susceptible to metabolic syndrome, particularly hypertension, obesity, and elevated triglyceride levels.[4,117] Poor sleep habits and disrupted circadian rhythms are proposed to increase susceptibility to metabolic syndrome among shift workers.[4,5,118,119] However, the association between shift work and metabolic syndrome remains unclear. A systematic review and meta-analysis by Canuto and colleagues[115] found that positive relationships between shift work and metabolic syndrome were no longer significant when adjusting for the confounding effects of socio-demographic, socioeconomic and behavioural factors.

Gastrointestinal Conditions: Gastrointestinal disorders and symptoms include peptic ulcers, chronic inflammatory diseases, as well as diseases occurring in the digestive system.[120] Literature dating back to the 1950s concurred that peptic ulcers occurred very frequently among shift workers, such that it was classified as the "occupational disease of shift workers".[120,121] A systematic review by Knutsson[120] suggest that there is an association between shift work and gastrointestinal symptoms and disease, including ulcers, irritable bowel syndrome and inflammatory bowel disease. However, the evidence for this relationship is weak as studies identified in this review did not control for confounding variables and were primarily cross-sectional in design.[120]

Diabetes: Links between shift work and diabetes, particularly type 2 diabetes mellitus, have been reported in the literature. Prospective cohort studies suggest that shift work is independently and positively associated with type 2 diabetes mellitus.[5,122–124] However, a systematic review of cohort studies conducted by Knutsson and colleagues[125] only found moderate evidence to support this relationship. Blood sugar regulation is influenced by the circadian rhythm.[5] Studies propose that glucose homeostasis may be disrupted by misaligned circadian rhythms arising from night shift work.[5,126–129]

Cancer: Evidence on the relationship between shift work and cancer is mixed. Most research has focused on breast cancer, with systematic reviews and meta-analyses all reporting links between working shift work and developing breast cancer.[5,130–132] Overall, there is moderate evidence in support of this association, given the many limitations within the studies identified in these reviews.[5,133] Evidence on the association between shift work and other cancers - such as colon, colorectal, and prostate cancer - are inconsistent.[5,133–136] There is also a lack of evidence for a significant relationship between engaging in shift work and the risk of all-site cancer.[5,134,137] Despite the inconclusive findings, night shift work has been listed as a potential carcinogen by the International Agency for Research on Cancer.[138] Studies propose that melatonin, a hormone known to be protective against cancer, is lowered when engaging in shift work at night.[5]

Mental Disorders: Studies that have investigated associations between shift work and mental health conditions have reported poorer mental health among shifts workers, particularly for those with irregular and/or unpredictable shift schedules.[28] Anxiety and depressive disorders are commonly reported among shift workers.[139,140] Shift workers may be more vulnerable to developing psychiatric problems due to disrupted sleep cycles, job strain, demanding work environment and poor work-life balance.[5] However, as Harrington and colleagues[76] pointed out, people self-select themselves into shift work. As such, it is difficult to rule out whether people already have a pre-existing mental health condition prior to entering the shift work system.[76]

Multimorbidity: Studies assessing the association between shift work and multimorbidity are limited.[141,142] Two international studies reported a higher prevalence of multimorbidity among people who engage in shift work compared to those who do not, although this relationship was no longer significant after adjustment for other factors.[141,142] Most research investigating the association between multimorbidity and occupational-related outcomes has focused on work-related aspects, such as work-related productivity, leaves, absences, as well as early retirement and unemployment.[143–145] According to a Canadian study by Smith and colleagues,[145] multimorbidity is associated with a reduction of people in the workforce and poses as a limitation for individuals to meet job demands. Another study found that people with multimorbidity were more likely to switch to partial or full retirement, or seek accommodation as a disabled worker.[143] A systematic review of longitudinal studies also reported positive relationships between multimorbidity and a higher risk of temporary or permanent leaves among workers.[144] This review also found that comorbidity specifically for depression and either cardiovascular disease or diabetes was associated with early retirement and unemployment.[144] As such, assessing associations between multimorbidity and shift work may be difficult to ascertain as people with multimorbidity tend to be those who leave the workforce.

Self-Rated Health Status: Self-rated health refers to a person's perception of their general health status.[146] The level of self-rated health can provide insight about a person's health condition.[147] Findings for the association between shift work and self-rated health are inconsistent. No significant relationships have been reported in some studies,[147,148] whereas others have found that relative to non-shift workers, those working shift schedules perceive themselves to have poorer health.[149,150] Despite the mixed findings, studies assessing work time control and general health status highlight a link between shift work and self-rated health through control over work scheduling.[148,151–153] Particularly, employees who lack control on work-related factors, including choice of shift schedules, have been found to report poorer general health.[148,151–153] Fenwick and Tausig[154] found that although shift work was negatively related to self-rated health, lack of control over work schedules had a stronger effect. They suggest that control over work schedules is beneficial for both shift workers and non-shift workers.[154]

2.2 Cognitive Functioning and Cognitive Domains

Advancements in technology have led to improvements in health care in terms of better facilities, supplies, and access, as well as earlier detection of disease, thereby resulting in a global increase in life expectancy.[6] As such, populations of older adults have been increasing worldwide.[8,9,155] In Canada, it is predicted that by 2030, seniors will constitute 23% of the population, totaling 9.5 million Canadians.[7] For many developed countries with an aging population, such as Canada, late-life cognitive impairment and dementia have generated major social and economic burdens to society, thereby becoming a serious public health problem.[8–11]

Cognitive function describes mental processes associated with learning, logical thinking, problem-solving, decision-making and memory.[12,13] There are several domains involved in cognitive functioning, which can be categorized into domains of sensation, perception, motor skills and construction, attention and concentration, memory, executive functioning, processing speed and verbal abilities.[156] Cognitive changes over a person's lifespan can be conceptualized to take place on a continuum,[14] and in late life can be identified as either normal cognitive aging, cognitive impairment or dementia.[15] Cognitive impairment refers to the deterioration or decline in cognitive domains commonly used in daily activities, including learning, concentrating, decision-making, and memory.[11–13] Some people with cognitive impairment may not meet a diagnosis for dementia, however they do typically experience greater than normal cognitive dysfunction.[16]

Cognitive impairment can range from mild to severe. A diagnosis for Mild Cognitive Impairment (MCI) can be made when one or more cognitive domains are moderately impaired, such that an individual requires more effort to carry out daily activities independently, but in the absence of clinical dementia.[157] People with cognitive impairment or MCI have an increased risk in developing dementia.[14,17] According to the DSM-5, a diagnosis of Major Neurocognitive Disorder, also known as severe cognitive decline or dementia, can be made when cognitive impairment develops into a severe form in which there is significant impairment in one or more cognitive domains, that can sufficiently interfere with independent functioning in everyday life.[157]

Cognitive impairment can be debilitating. A systematic review and meta-analysis examining cognitive impairment in relation to fall-related injuries among older adults found significant associations between impaired cognitive scores and an increased risk of falling.[158] Poor quality of life and increased mortality have also been associated with cognitive impairment among older adults.[159,160] Furthermore, compared to individuals with other health conditions, those with cognitive impairment have over three times as many hospital stays.[11,161] To date, there are currently no pharmacological treatments available to prevent or cure cognitive impairment among older adults.[9,18] Epidemiological studies propose that diet and modifiable lifestyle factors may help minimize the risk of cognitive impairment and dementia.[19]

Changes in cognition may occur naturally as a consequence of aging, and there are some areas of cognition that may be enhanced with age.[21] For example, vocabulary and general knowledge are cognitive skills and abilities which typically remain constant overtime and may even improve across the lifespan.[21] Other domains of cognitive functioning are more vulnerable to brain aging and progressively deteriorate over time, including cognitive domains of memory, executive functioning, processing speed and domains involved in reasoning.[21]

2.2.1 Factors Associated with Cognitive Impairment

Many sociodemographic, behavioural and lifestyle factors and chronic diseases have been identified as risk factors for declines in cognitive functioning.[22] However, some of these factors have been shown to protect individuals from cognitive decline through maintaining and improving brain health, also known as cognitive reserve.[162] The concept of cognitive reserve posits that resilience to brain damage observed in some individuals may be due to the participation in cognitively stimulating activities throughout their life.[162,163] For instance, social support and engagement in social activities is known to stimulate cognitive domains[164,165] and has been shown increase cognitive reserve.[164,166] Another component of cognitive reserve is brain reserve, which proposes that differences in brain structure may contribute to increased resilience to brain damage.[163]

Employment-Related Factors

Employment: Studies suggest that employment may have positive benefits to brain health, which in turn reinforce cognitive reserve, through learning new skills, social interactions at the workplace, forming routines, providing a sense of purpose and generating income.[167] Learning new skills at work, as well as socially interacting with co-workers and customers, requires activation of cognitive functions, thereby enhancing cognitive reserve.[167] Healthy lifestyles may be maintained through routines formed by set work schedules, which may indirectly enhance cognitive reserve.[167] Theoretically, employed individuals with set work schedules must be able to balance specific physiological (e.g. eat, rest, exercise) and social needs (e.g. time spent with friends or family) to function and perform tasks properly at work.[167] This balance is suggested to promote a healthy lifestyle, which in turn would benefit the brain.[167] The income that employment generates, as well as the sense of meaning employment offers can help decrease activation of HPA axis, thereby lowering cortisol secretion and promoting cognitive reserve.[167] Having sufficient income for basic necessities helps to lower financial stress, whereas having extra income provides funds for individuals to engage in enriching activities which enhance cognitive reserve.[167] Meaning and purpose allow people to obtain a subjective perspective in life.[167] As such, they may prioritize the importance of certain matters or occurrences over others, which would lead to a reduction of everyday stress[167] However, this idea does not include work-related stressors which have been observed to have a negative impact on cognition.[167]

Type of Employment: The type of employment has also been shown to have an impact on cognition. Vance and colleagues[167] suggest that cognitive reserve may be enhanced through learning new skills at work, regardless of job type. Older studies have observed a decreased risk of dementia among people working in non-blue collar jobs, as well as those with high occupational attainment.[168–170] This is characterized as occupations involving managerial positions in business or government, as well as professional and/ or technical positions.[168,169] Associations between occupations involving the production of goods, but not services, and incident dementia have also been reported.[168,171] Recent studies have reported that jobs which are intellectually demanding are associated with greater cognitive function later in life.[172–175] Intellectually stimulating jobs may expand neural pathways in the brain or promote flexible use of cognitive functions, thus enhancing cognitive reserve.[172]

Unemployment: There is also evidence of an association between unemployment and cognitive impairment. One prospective cohort study found that people who were employed had a lower risk of cognitive decline relative to those who were unemployed.[168,170] Being unemployed due to training or maternity leave was found to be inversely associated with cognitive impairment.[167,176] However, unemployment due to sickness, including depression and HIV, has been linked with poor cognitive functioning.[167,176] Although these health conditions can directly impact cognition, loss of employment may further exacerbate cognitive impairment over time.[167] Unemployment may be a cause of homelessness,[177] which in turn has been found to be associated with decline in cognitive functioning.[178,179] A recent review by Stone and colleagues,[179] suggest that cognitive impairment may increase the risk of and reinforce homelessness.

Retirement: Evidence on the relationship between retirement and cognitive decline is mixed. Depending on whether a person has retired earlier or later, some studies have reported a negative association,[180–185] whereas others have reported positive[186,187] or no association.[180,188,189] Retirement as a risk factor for cognitive impairment was derived from the "use it or lose it" hypothesis, which posits that engaging in cognitively stimulating activities enhances cognition, whereas mental inactivity can expedite decline in cognitive functioning.[180,190] This hypothesis assumes that people were engaged in mentally demanding jobs before retirement.[180] A study using data from the Whiteall II Cohort study found that verbal memory significantly declined 38% faster 14 years after retirement relative to 14 years before, adjusting for the effects of age.[180] In contrast, one study which used data from the Health and Retirement Study found that slower rates of cognitive decline following retirement were associated with mentally demanding jobs.[174] According to Xue and colleagues,[180] reverse causality is important to consider when assessing the relationship between retirement status and cognitive impairment, as poor cognition may influence the ability to meet job requirements, which in turn may impact the decision to retire.

Sociodemographic Factors

Age: Older age has been consistently identified as the strongest risk factor for cognitive impairment.[157]

Education: The level of education has also been associated with cognitive functioning.[157] It is proposed that through higher cognitive activity, higher levels of education are linked with greater brain volume, thereby leading to increased cognitive reserve.[191] Thus, a high prevalence of cognitive impairment has been commonly found among populations with lower educational attainment.[157]

Marital Status: Cognitive reserve appears to be enhanced among people who are married.[163,192] According to a systematic review and meta-analysis of observational studies, the age-and sex-adjusted risk of developing dementia is 42% and 20% higher respectively, among people who have remained single throughout their lifetime and people who are widowed, respectively, relative to those who are married.[192] Being married may expose individuals to healthier lifestyles, different forms of social engagement, and increased social interaction.[163,192] All of these factors could enhance brain health.[163,192] Stress on cognition from bereavement among widowed people,[53] and unusual personality and cognitive traits among lifelong single people, could explain the increased risk of cognitive decline among these groups.[192]

Socioeconomic Status: Some studies assessing the association between socioeconomic status and cognitive impairment among older adults suggest that low income is a risk factor for cognitive decline,[194–197] whereas other studies did not report a relationship between these factors.[198–200]

Immigration Status: A systematic review investigating the relationship between migrant status and cognitive function among older adults reported mixed findings.[201] Compared to non-immigrants, some studies observed poorer cognitive function among middled-aged and older immigrants,[201–205] whereas, other studies, including one conducted in Canada,[206] did not find a significant association.[201] Lower socioeconomic status, which is common among some immigrant groups, may explain the negative associations.[201] The authors also proposed that language may confound the relationship between migrant status and cognition.[201]

Rural Residence: A recent review investigating the association between urbanicity and cognitive disorders reported lower rates of dementia among older adults living in urban settings relative to rural dwellers.[207] Interestingly, exposure to pollution, particularly air pollution and traffic related pollutants, are greater in urban areas[208] and are associated with an increased risk of cognitive decline.[209,210] Robbins and colleagues[207] suggest that greater access to health care services and higher quality education could explain the differences in cognition between urban and rural settings.[207]

Social Isolation: A systematic review and meta-analysis of longitudinal studies found that social isolation, including low engagement in social activities and small social circles was inversely related to healthy cognitive functioning in late life.[166] As with marriage, participation in social activities and interacting with others may enhance cognitive reserve through the stimulation of cognitive and sensory domains.[211,212] Feelings of social isolation may trigger stress responses which are linked with chronic activation of the HPA axis, thereby promoting cognitive decline.[211,213,214]

Lifestyle and Behavioural Factors

Physical Activity: Engagement in physical activity has been linked with greater resilience to brain damage.[191] The literature suggests that the positive association between physical activity and brain volume results in better cognitive health.[191]

Fruit and Vegetable Consumption: Two recent meta-analyses have reported associations between a reduced risk of cognitive impairment and dementia with increased consumption of fruit and vegetables.[215,216] Oxidative stress has been physiologically implicated in cognitive decline.[216–218] As the brain is susceptible to damage by oxidative stress, prior studies suggest that the high antioxidants found in fruits and vegetables may be related to its protective effect on cognitive functioning.[215,216] Despite these findings, Jiang et al[215] noted that higher intake of fruits and vegetables could be an indicator of healthier lifestyles and dietary patterns overall, such as the Mediterranean Diet,[219,220] which may contribute to healthier cognitive functioning.[215,219,220]

Smoking: Previous studies investigating the effects of smoking on cognition have observed poorer cognitive scores among middle aged current smokers.[221–223] It is proposed that the effects of smoking may act through pathways associated with the cardiovascular system.[223] However, some studies have detected a protective effect of smoking.[224] This protective effect may be due to the stimulating effects of nicotine on dopamine activity[157,224] or be an artefact due to confounding or survival bias.[157,225]

Alcohol Consumption: Chronic intake of alcohol in excessive quantities has been associated with deterioration of memory and executive function.[191] In contrast, a protective effect on cognitive impairment and dementia has been observed with mild to moderate alcohol intake in several population-based studies.[157,226–229]

Chronic Disease and Other Health-Related Factors

Body Mass Index (BMI): BMI status has been associated with cognitive impairment, however conclusions regarding this relationship are mixed. Studies using population-based data have reported significantly poorer scores on neuropsychological assessments among people who were overweight or obese.[230,231] One study proposed that the presence of other health problems known to impact cognitive functioning are common among people who are overweight or obese.[230] On the other hand, it has been proposed that age may interact with BMI status, such that elevated BMI may be associated with decline in cognitive functioning during midlife, but neutral or protective in the late life.[232]

Menopause Status: Findings from a meta-analysis suggest that compared to pre-menopausal women, the transition stages into menopause are associated with a decline in the cognitive domain of memory, particularly delayed verbal memory.[233] A recent review conducted by Pertesi and colleagues[234] suggest that there is strong evidence of an association between menopause and cognition. Changes in estrogen levels during menopause have been proposed as a biological mechanism linking menopause to cognitive changes.[233,234] With regards to hormone therapy, a meta-analysis of prospective cohort studies assessing relationships between estrogen hormone therapy and dementia did not find any significant associations.[235]

Cardiovascular Disease: Cardiovascular disease is a well-established risk factor for both vascular and degenerative dementias such as Alzheimer's Disease.[157] Evidence from a recent systemic review and meta-analysis suggests that coronary heart diseases, such as myocardial infarction and angina are risk factors for cognitive impairment or dementia.[236] Peripheral vascular disease is common among people with coronary heart disease.[237] Associations between peripheral vascular disease and cognitive impairment have been observed in past studies.[238,239]

Hypertension: According to a review paper examining relationships between hypertension and cognitive decline, hypertension is associated with alterations in the structure and function of the brain.[240] This suggests that middle-aged adults with chronic high blood pressure were at a higher risk of developing late life cognitive impairment.[240] In particular, the cognitive domains of executive function and processing speed were particularly susceptible to the effects of hypertension.[240]

Diabetes: Impairments in many cognitive domains have been observed among people with type 1 and type 2 diabetes mellitus.[241–243] MRI scans of people with type 2 diabetes show reduced hippocampal volume.[241,243] Deficits in insulin signaling and metabolism, as well as increased oxidative stress have been proposed as mechanisms to explain the association between diabetes and cognition.[241]

Cancer: Treatment with chemotherapy can induce cognitive impairment among cancer patients.[244,245] A meta-analysis conducted by Hodgson and colleagues[244] found impairments in the cognitive domains of executive function and memory among cancer patients following chemotherapy treatment. A recent review by Pendergrass and colleagues[245] found that cognitive impairment has also been observed among patients with brain tumors and breast cancer prior to chemotherapy treatment. This review also suggested that cognitive functioning may be affected by comorbid conditions, such as fatigue, depression and anxiety, among cancer patients and patients in remission.[245]

Gastrointestinal Disorders: Gastrointestinal disorders may be associated with decline in cognitive functioning through the brain-gut axis theory.[246,247] The theory posits that the gastrointestinal tract and the central nervous system bidirectionally and continuously communicate through neural, immune, hormonal and metabolic signaling.[246,247] As such, disturbances in the gastrointestinal system which may alter the gut microbiota may have detrimental impacts on cognitive functioning.[246,247] Irritable bowel syndrome and inflammatory bowel diseases are gastrointestinal diseases found to be associated with cognitive impairment.[246–249] Associations with cognitive impairment have also been found for ulcers, including peptic, gastric and intestinal ulcers.[246,250] Studies have also reported positive associations between the helicobacter pylori, the bacteria known to cause ulcers, and impairment in cognitive functioning.[246,251,252] Activation of the HPA axis has been proposed as the mechanism linking ulcers to cognitive impairment.[246,250]

Metabolic Syndrome: The metabolic syndrome is a risk factor for cardiovascular disease.[253] As such, studies have linked metabolic syndrome to vascular cognitive impairment.[254] With regards to non-vascular cognitive decline, findings in the literature are unclear. Siervo and colleagues[255] conducted a systematic review and meta-analysis of longitudinal studies and found weak evidence of an association between metabolic syndrome and cognitive changes among young and old people. However, when they analyzed studies which only used the Mini-Mental State Examination (MMSE) to assess cognition, they found a significant association between metabolic syndrome and poor cognition only among people aged 70 and younger.[255] Another systematic review by Assuncao and colleagues[256] investigated this relationship among older adults and also found inconsistent findings. When they assessed individual components of metabolic syndrome, they reported that high blood sugar was commonly associated with poor cognitive function.[256] The authors proposed that the mixed findings may be due to heterogeneity of diagnostic criteria for metabolic syndrome across the studies.[256] Despite the inconsistent findings metabolic syndrome may be linked to decline in cognitive functioning through its associations with health conditions involving inflammation, insulin resistance, oxidative stress, abnormal blood coagulation and altered endothelium.[255]

Mental Disorders: Cognitive impairment is a well-known symptom of major depression.[257] Hugo and Ganguli[157] propose that there is a bi-directional relationship between depression and cognitive decline, that is dependent on the life stage in which the onset of depression occurs. In particular, major depression experienced repeatedly during early adulthood could be a risk factor for late life dementia,[157,258] whereas, depression experienced in the later stages of life could be an early symptom of dementia.[157,259,260] Anxiety has also been linked with cognitive impairment, particularly anxiety occurring during the late-life stage.[157,261,262] Both anxiety and depression have been proposed as early symptoms of cognitive decline.[157,259–261]

Multimorbidity: Prospective cohort studies have found that adults who are multimorbid for chronic conditions at baseline had an increased risk of poor cognitive functioning at follow-up, relative to those without multimorbidity.[263–267] These studies commonly included cardiovascular diseases and cancer in their definition of multimorbidity, among other chronic diseases.[263–265] Aarts and colleagues[263] suggest that the association between multimorbidity and cognitive functioning may be explained by common pathological mechanisms associated with different types of chronic conditions, including inflammatory, immune and mood responses, as well as genetic factors. Other prospective cohort studies assessing adults with dementia show a larger decline in cognitive functioning among people with multiple chronic conditions.[266,267]

Self-Rated Health Status: Prior studies assessing self-rated health and cognition have reported that poor self-rated health was related to declines in cognitive functioning.[268–270] A study by Bendayan et al,[268] which used a nationally representative sample of older adults from the U.S., found that people whose perception of health decreased over time showed an accelerated decrease in memory scores, relative to those who maintained a positive perception of their health. The findings from this study support the idea that self-rated health may be a marker of cognitive decline.[268]

Due to the nature of shift work schedules, shift work has been commonly associated with many of these sociodemographic, lifestyle and behavioral factors, and chronic diseases.[271,272]

2.3 Psychological Distress

Mental health can be impacted by shift work. In particular, the hours of the shift, the number of breaks within and between shifts, as well as the number of successive shifts required to work in a given work week[44] may each influence the mental health of an individual.[23] Mental health problems are another significant public health concern,[28] due to the high prevalence worldwide and the social and economic burden to society.[24] Mental health problems are the leading cause of disability in Canada, which carry a burden of disease that is almost twice as high as all the cancers combined.[25–27] In the literature, research exploring relationships between shift work and mental health are limited.[5,28] A recent systematic review and meta-analysis by Zhao and colleagues[28] examining the association between shift work and mental health using population-based samples found that most studies investigated depression and psychological distress. Psychological distress is a broad term that describes a state of emotional suffering, such that people with psychological distress experience depressive, anxiety, and somatic symptoms which have detrimental impacts on their day-to-day life.[29,30] Assessing the psychological distress of populations and of individuals has several implications. For instance, psychological distress may be used as an indicator of the general mental health status of a population, or it may be used to gauge the severity of symptoms and level of disability among people with mental health disorders.[29,30]

In the general population, psychological distress is pervasive. According to Drapeau and colleagues,[29] the prevalence of psychological distress in the general population is approximately 5% to 27%, with certain subgroups of the population, such as those in the workforce, facing greater psychological distress as a result of stressors in the work environment. In Europe and North America, 15% to 20% of people in the workforce were affected by psychological distress.[29] Findings from the systematic review and meta-analysis by Zhao and colleagues[28] suggest that people engaged in shift work were 32% more likely to experience psychological distress or depression than those who were not. Two prospective cohort studies, identified in the systematic review and meta-analysis,[28] reported significant associations between evening/night shifts and psychological distress.[1,273] In addition, four cross-sectional studies, also identified in the same systematic review and meta-analysis,[28] examined irregular/unpredictable shift work schedules and observed significant relationships with psychological distress.[274–277]

Several hypotheses have been proposed to explain the relationship observed between shift work and psychological distress. One explanation is based on the job-strain model.[31,32] Shift schedules are assigned to workers by employers. Many occupations, particularly those in the health care, industrial, and manufacturing sectors, are commonly associated with physically and mentally demanding work environments. These characteristics of shift work can be found in the job strain model, which is also referred to as the demand-control model.[31,32,] This model posits that job strain occurs in jobs which are highly demanding and offer few opportunities for control and decision-making for workers.[31] A study examining the relationship between work schedules and levels of job-related strain among nurses reported that those engaged in night shift schedules were more likely to experience higher levels of job strain.[278] According to Lopes and colleagues,[31] observational studies of workers employed in high strain jobs found a higher prevalence of psychological distress.[279–283]

Another explanation is the healthy worker effect. People engaged in rotational shift work or who work irregular schedules must alternate between more than one working time arrangement. Workers with these types of shift schedules may have less stability in their work week compared to those who work standard hours daily. The study by Shields[1] investigated the relationship between shift work and changes in psychological distress and found that for both male and female workers employed in evening shift work at baseline, there was an increase in psychological distress two years later at follow-up. This association was no longer significant when participants were followed for an additional two years, which suggests that participants employed in shift work at baseline may have left the shift system or may have developed a strategy to cope with the psychological demands of shift work.[1]

The stress-distress model, which proposes additional characteristics to help define psychological distress,[29] has also been implicated in the relationship between shift work and psychological distress. According to the stress-distress model, when the physical or mental health of a person is threatened due to the presence of a stressful event, and when strategies used to endure or confront the stressor are ineffective and lead to emotional suffering, an individual is in a state of psychological distress.[29,33,34] This model further postulates that when the stressor is removed or when effective tactics are identified to help cope with the stressor, psychological distress is reduced.[29,34] If shift work or aspects of shift work were considered a stressor, then the results from the previous two studies[1,284] are in line with the stress-distress model.

Psychological distress has been linked with cognitive impairment. One potential mechanism is through the personality trait of neuroticism.[16,29] Individuals with this type of personality are more prone to feelings of psychological distress, including feelings of anxiety and depression.[37] Studies have found a significant association between higher neuroticism and psychological distress with mild cognitive impairment.[39,285] Studies which have looked at proneness to psychological distress, have found that people more vulnerable to developing psychological distress had a greater rate of cognitive decline compared to those who were not less vulnerable to developing psychological distress.[35,36]

Links between psychological distress and cognitive impairment have also been observed through the stress-distress model of psychological distress, with studies suggesting that psychological distress stems from external stressors.[37] One study which characterized psychological distress using the stress-distress model, found associations between psychological distress and an increased risk of dementia through the job-strain model of stress.[38]

Pathways involving the HPA system have also been proposed to explain the association between psychological distress and cognitive impairment.[37,40,41] The HPA system is responsible for eliciting neuroendocrine responses to stress[37,40,41] and has been implicated in other mental health conditions such as depression.[29] Hori and colleagues[286] examined the relationship between HPA system reactivity and psychological distress, observed that alterations in the HPA axis reactivity, particularly increased suppression of cortisol, were associated with greater psychological distress. Wilson and colleagues[37] have found that studies examining chronic stress using animal models have observed significant associations between prolonged stress and changes in brain structure, specifically in the limbic-hypothalamic-pituitary-adrenal axis, which leave regions in the brain related to learning and memory susceptible to change.[37,287] They propose that prolonged psychological distress could impair these regions of cognition overtime.[37] Another study suggested that elevated and dysregulated cortisol levels brought about by psychological distress could increase the risk of severe cognitive impairment.[288]

2.4 Search Strategy

Given that shift work and cognitive impairment share common risk factors, a search of the literature was conducted to better understand their relationship. Characteristics of the included studies are provided in section 2.4.1. Sections 2.4.1.1 and 2.4.1.2 discuss the short-term and long-term effects of shift work, respectively. Proposed mechanisms linking shift work and cognitive impairment are outlined in Section 2.4.1.3. Knowledge gaps and limitations are discussed in Section 2.4.1.4.

In consultation with a research librarian, MEDLINE (OVID) and CINAHL electronic databases were searched for studies examining the association between shift work and cognitive impairment. Controlled terms and keywords related to shift work and cognitive impairment were applied. As decline in cognitive functioning often manifests following early adulthood,[289] the age-range was restricted to adults 20 years and older and a filter focusing on human subjects was applied. Identified articles were collated into Zotero Citation Manager and were screened for eligibility. Studies were included if the association between shift work and cognitive impairment was examined, and if shift workers were compared to non-shift workers or regular day workers. No restrictions were imposed on date and language of publication or sample size. Studies without a comparison group were excluded. Case studies, book chapters, editorials, review papers, and randomized trials examining occupational health interventions for workers were excluded. A summary of findings from the included studies is provided in Appendix A.

2.4.1 Shift Work and Cognitive Impairment: Existing Literature

Twenty-five articles investigating the relationship between shift work and cognitive impairment were identified. There were five [22,45,272,290,291] cross-sectional studies and eleven[47,50,61–63,292–297] prospective cohort studies. Five[64,65,298–300] studies had a repeated measures design, two[67,70] had a randomized cross-over design, and two[301,302] were controlled trials with only one using randomization. All studies were conducted in developed countries, with the majority of studies from the United States (n=7), with the remaining studies from Canada (n=3), France (n=2), Brazil (n=2), Austria (n=2), and Sweden (n=2). There were also studies conducted in Croatia (n=1), Norway (n=1), United Kingdom (n=1), Turkey (n=1), Australia (n=1), Netherlands (n=1), and Germany (n=1).

Most studies (n=12) compared night shift workers to day shift workers. Among studies that used population data, shift work was treated either as a binary variable, categorizing workers as having worked in shift work or not,[45,47,297] or as an ordinal variable, grouping workers based on current shift work status[22,291] or years of experience in shift work.[272]

Assessment instruments and outcomes for cognitive functioning varied across studies in this literature review. Specifically, various cognitive domains and subdomains of memory, executive functioning, and psychomotor speed were assessed using objective and subjective measures across studies. To date, there is no gold standard for outcome measurements pertaining to decline in cognitive functioning.[303] However, the cognitive domains of memory and executive functioning have been recommended as outcome measures for assessments of cognitive functioning, as these domains are most applicable for daily activities.[303] As such, the cognitive domains of memory and executive functioning will be assessed for this thesis.

2.4.1.1 Short Term Effects of Shift Work

The majority of studies (n=21) examined the short-term effects of shift work on cognitive functioning. Across these studies, assessments of cognition were conducted shortly before and after work shifts and at multiple times during shifts.

Observational Studies - Prospective Cohort Studies

Nine prospective cohort studies investigated the acute effects of shift work, particularly night shift work, with the longest follow up being 30 consecutive days. One study examined shift workers in the mining industry while the rest (n=8/9) were shift workers in the health care sector. Six[50,62,292,293,295,296] of the nine prospective cohort studies examined psychomotor speed, most of which (n=4/6) did not find statistically significant differences in reaction times between shift workers and those working regular day shifts. Executive functioning was examined in six of the nine prospective cohort studies, of which four[50,294,296,304] found significantly lower cognitive test scores among those in shift work relative to those working day shifts. Among the nine cohort studies, four assessed cognitive domains in memory function, and only two[50,293] observed that shift workers obtained significantly poorer scores in memory tasks compared to day shift workers.

Repeated Measures Studies

Four[64,65,299,300] of the five studies that used a repeated measures design, examined the short-term effects of shift work on cognitive functioning among shift workers in the health care sector. Two[65,300] of the four studies assessed psychomotor speed and found that relative to regular day shifts, psychomotor function significantly decreased after working a night shift. Executive function was assessed by three[64,65,299] of the four studies, all of which found significantly lower cognitive scores following a night shift, as compared to a day shift. Only two[64,65] of the four studies conducted tests for memory. When compared to test scores performed during a day shift, both studies showed that short term memory scores were significantly lower during overnight[64] and 24-hour shift work schedules.[65]

Cross-sectional Studies

Among the five cross-sectional studies, four used population data from the National Population Health Survey,[45] Swedish EpiHealth Cohort study,[22] Shift Your Work study[290] and the VISAT longitudinal study of aging.[291] These studies examined relationships between shift work and short-term impairment in cognitive functioning among shift workers from a variety of occupational sectors. Significant associations were found in three[22,45,291] of the four studies. The study by Wong and colleagues[45] found an association between night shift work and poor subjective cognition through pathways mediated by work stress and sleep quality, while adjusting for age, general health, and gender among currently employed Canadians. The second study by Titova and colleagues[22] found that compared to non-shift workers, current and recent former shift workers performed significantly worse on tests for processing speed and executive function, after adjusting for age, education and sleep duration. Another study by Rouch and colleagues[291] found significantly lower cognitive scores in processing speed among current male shift workers compared to those never exposed to shift work, after adjusting for age and education.

Experimental Studies

The acute effects of shift work on cognitive impairment were assessed in two[67,70] of the five randomized cross-over trials and in the randomized[301] and non-randomized controlled trials.[302] Both randomized cross-over trials[67,70] examined the effects of overnight shifts on cognition among physicians and found that compared to working a regular day schedule, performance on cognitive tests for executive function[67] and memory[70] were significantly worse after working an overnight shift. The controlled trials subjected shift workers and non-shift workers to sleep deprivation conditions. Only one[301] of the controlled trials found a significant effect of shift work on cognition, such that performance on memory tests were significantly worse among shift workers under no sleep conditions relative to permanent day workers also under no sleep conditions. The non-randomized controlled trial by Wehrens and colleagues[302] did not find significant differences in reaction times between shift workers and non-shift workers.

Overall, the majority of studies suggest that shift work, particularly night shift work, is associated with acute cognitive impairment, particularly in the cognitive domains of executive functioning and memory. The prospective cohort and repeated measures studies suggest that shortly following a work shift, shift workers exhibit poor cognitive functioning compared to their non-shift worker counterparts. The cross-sectional studies demonstrate that shift work remains significantly associated with cognitive impairment, even after adjusting for potential confounders. Furthermore, the experimental studies suggest that sleep is an important contributor to the relationship between shift work and cognitive impairment.

2.4.1.2 Long Term Effects of Shift Work

The relationships between shift work and long-term cognitive impairment was examined by six observational studies.[22,47,272,291,297,298] Across these studies, shift work status was assessed once at baseline, and cognitive functioning compared with either among past shift workers, long-term shift workers, or from follow-up data obtained at least one year after baseline.

The majority of studies (n=5/6) examining shift work and chronic impairment in cognitive functioning were observational studies using population-based data. Of these, three[22,47,272] found that performance on cognitive tests among workers who had past or long-term experience in shift work did not differ from non-shift workers. In contrast, data from the VISAT longitudinal study of aging used by Rouch and colleagues,[291] as well Marquie and colleagues[297] both found a significant association between the chronic effects of shift work and cognition. Rouch and colleagues[291] observed people who have past experience working in the shift system exhibited poorer cognitive performance on tests for memory, compared to individuals who have never worked shift work. Marquie and colleagues[297] found that employees who were shift workers at baseline and had left shift work within the last five years had significantly lower cognitive scores.

Although most (n=4/6) of the observational studies did not find evidence to support an association between shift work and long-term cognitive impairment, conclusions cannot be drawn due to the limited number of studies assessing this relationship.

2.4.1.3 Mechanisms Associated with Shift Work and Cognitive Impairment

This section discusses mechanisms commonly proposed by studies identified in this literature review to explain the association between shift work and cognitive impairment.

Findings related to sleep, as well as cortisol and stress, in relation to shift work and cognitive impairment will be discussed in section 2.4.1.3.1 and 2.4.1.3.2, respectively.

2.4.1.3.1 Sleep

Sleep Behaviours

The studies identified in this literature review propose that lack of sleep experienced by shift workers impact cognitive functioning. Experimental studies in this literature review by Osterode and colleagues[70] and Saadat and colleagues[299] assessed the cognitive abilities of healthcare professionals after 24-hour and 17-hour night shifts, respectively. Both studies found that healthcare professionals were sleep deprived and exhibited poor cognitive functioning following the night shift.[70,299] A randomized controlled trial by Mawdsley and colleagues subjected shift workers and permanent day workers to conditions involving either sleep or no sleep and found a significant interaction effect between shift work schedule and sleep. The authors found that when both groups were subjected to the sleep deprivation condition, shift workers performed worse on cognitive assessments for memory relative to day workers, however shift workers performed better than day workers when subjected to the sleep condition.[301] Three prospective cohort studies also found poorer cognitive scores among shift workers who were sleep deprived.[62,292,294]

Studies in this literature review suggest that certain sleep behaviours exhibited by overnight shift workers may have consequences for cognitive impairment. One prospective cohort study by Castro and Almondes[63] found that shift workers with good sleep quality, assessed through self-reported measures, performed better on decision-making tasks. Findings from another cohort study by Rheaume and Mullen,[61] suggest that sleep may alleviate impairment in cognitive abilities. This study found that 12-hour rotating shift workers exhibited less sleep efficiency and total sleep time.[61] However, as they took significantly more naps, 12-hour rotating shift workers did not significantly differ from 8-hour day workers in performance of cognitive assessments.[61]

The Role of Sleep

The cross-sectional studies[22,45,47,297] in this literature review, typically conceptualized sleep as a potential confounder of the relationship between shift work and cognitive impairment. Cross-sectional studies by Marquie and colleagues[297] and Titova and colleagues[22] controlled for sleep and still found significant associations between shift work and cognitive impairment. One cross-sectional study by Wong and colleagues,[45] assessed sleep quality and sleep duration as a mediator of the relationship between shift work and cognitive impairment. The authors found that only sleep quality mediated the relationship, and this was only statistically significant for people employed in night shift work.[45]

Overall, there is strong evidence from the studies identified in the literature review to suggest an important role of sleep on the relationship between shift work and cognitive impairment. For this thesis, we will assess sleep quality as a potential moderator of the relationship between shift work and cognitive impairment, to determine whether differences in the strength or direction of this relationship exist when sleep quality is included as a moderator.

2.4.1.3.2 Cortisol and Stress

Cortisol and stress have also been implicated in the association between shift work and cognitive impairment. Feelings of stress can trigger neuroendocrine responses leading to the secretion of cortisol.[305] Cortisol is also a biomarker of circadian rhythm[306] and elevated levels of cortisol have been observed under conditions of sleep deprivation.[64,126,307] Furthermore, stress has been associated with poor sleep[308] and impairments in memory function.[309,310]

Cortisol

The experimental studies[64,67,70,298] identified in this literature review assessed cortisol levels in relation to shift work and cognitive impairment. Two[64,67] of these studies, which reported lower cognitive performance among shift workers relative to their non-shift worker counterparts, found significantly lower cortisol levels for shift workers at the end of their work shift. The studies propose that low levels of cortisol following a night shift may be product of a disrupted circadian rhythm and HPA axis.[67,311] Alternatively, it may also reflect a circadian rhythm that has adapted to the conditions of shift work.[312]

Stress

From this literature review, observational studies suggest that stress experienced by shift workers may be associated with impairments in cognitive functioning.[22,45,294,297] Two[22,294] studies reported that high levels of stress among shift workers were associated with lower cognitive performance. One[297] study conceptualized stress as a potential confounder in the relationship between shift work and cognitive impairment and controlled for its effects in their analyses. Another study[45] proposed that stress from shift work could have indirect effects on cognitive functioning through poor sleep quality.

The studies assessing stress suggest that physiological mechanisms involving cortisol secretion and the circadian rhythm may be related to shift work and cognitive impairment. These studies also highlight the potential impact of mental health on this relationship. As psychological distress has been linked with stress and secretion of cortisol,[29,286,288] this thesis will assess the moderating effect of psychological distress in the relationship between shift work and cognitive impairment. This will allow us to investigate whether differences in the strength or direction of the relationship between shift work and cognitive impairment exist when psychological distress is included as a moderator.

2.4.1.4 Knowledge Gaps and Limitations in the Literature

Shift work appears to be associated with acute cognitive impairment. However, as studies used both objective and subjective instruments to measure the different cognitive domains, further research on the effects of shift work is warranted.

The literature pertaining to shift work and cognitive impairment is largely focused on workers in the healthcare sector. As the shift system is commonly used by a wide range of occupations, examining shift workers from a wider range of occupations are needed to assess the relationship between shift work and cognitive impairment in a wider context.

Studies assessing the role of stress and cortisol highlight the potential influence of mental health on the relationship between shift work and cognitive impairment. As common mental health outcomes, such as psychological distress, have been identified as an associated risk factor for cognitive impairment,[288] investigating psychological distress may help elucidate the association between shift work and cognitive impairment.

Studies examining sex and gender differences in the relationship between shift work and cognitive impairment are also limited in the literature. As males and females exhibit differences in sleep behaviours, health outcomes, and psychological distress brought about by job stress,[45,313] assessing whether there are sex or gender differences in the relationship between shift work and cognitive impairment would be beneficial.

We identified three[45,61,292] Canadian studies in the literature review that investigated the relationship between shift work and cognitive impairment. All three studies examined acute cognitive impairment, with only one study being a large-scale study. The study by Rheaume and Mullen[61] examined the short-term impact of long work hours and shift work on the cognitive domains of memory and attention among 28 nurses working 12-hour and 8-hour shifts and found no significant differences. As this study only examined female nurses and used a self-reported measure of cognitive outcomes,[61] it may be vulnerable to information bias and lack external validity. Another is that this study combined the effect of shift work and working long hours on cognition.[61] Thus, the findings may not accurately represent the association between shift work and cognitive impairment.

The Canadian study by Legault and colleagues[292] examined the acute effect of sleep deprivation arising from rotating shift work on psychomotor speed and attention among a sample of 19 workers in the mining industry and did not find any significant differences between night shift workers and day shift workers. Although this study used an objective measure to assess cognitive outcomes, the generalizability of this study's findings is limited as the sample only consisted of males in one type of occupational sector.

The last study by Wong and colleagues[45] was a large-scale cross-sectional study which used data from the 2010 National Population Health Survey to examine whether work stress and sleep behaviours mediated the relationship between shift work and short-term subjective cognitive functioning, and whether gender differences existed in this relationship. Using path modelling, this study found evidence to support these relationships, however no statistically significant differences were observed between males and females.[45] Limitations of this study primarily pertain to the use of a self-reported measure for cognition which mainly focused on the domain of memory. Compared to other studies that have also used population data,[22,47,272,291,297] this study did not control for other important confounders such as alcohol use, smoking status, hypertension, physical activity, and education. Thus, the potential confounding factors that will be adjusted for in this thesis will include the majority of the sociodemographic, behavioural, and lifestyle factors, as well as the chronic diseases identified in sections 2.1.1 and 2.2.1. A more detailed description and rationale for the covariates to be controlled for in the statistical analyses will be provided in Chapter 3.

Given the limitations identified in these studies, a knowledge gap still exists regarding the relationship between shift work and cognitive impairment in the Canadian context.

2.5 Thesis Objectives

The aim of this thesis project is to examine the interplay between shift work, psychological distress, sleep quality, and cognitive performance among shift workers compared to non-shift workers in the Canadian Longitudinal Study on Aging (CLSA). The following objectives of this thesis are:

Objective 1: To examine the association between shift work and cognitive performance among shift workers compared to non-shift workers, and to identify whether sex differences exist in this association.

Objective 2: To explore whether psychological distress moderates the relationship between shift work and cognitive performance, adjusting for sociodemographic, lifestyle and behavioural factors, as well as chronic conditions and other health-related factors, and to identify whether there are sex differences in this relationship.

Objective 3: To explore whether sleep quality moderates the relationship between shift work and cognitive performance, adjusting for sociodemographic, lifestyle and behavioural factors, and as well as chronic conditions and other related health factors, and to identify whether there are sex differences in this relationship.

All analyses will be stratified according to retirement status and sex.

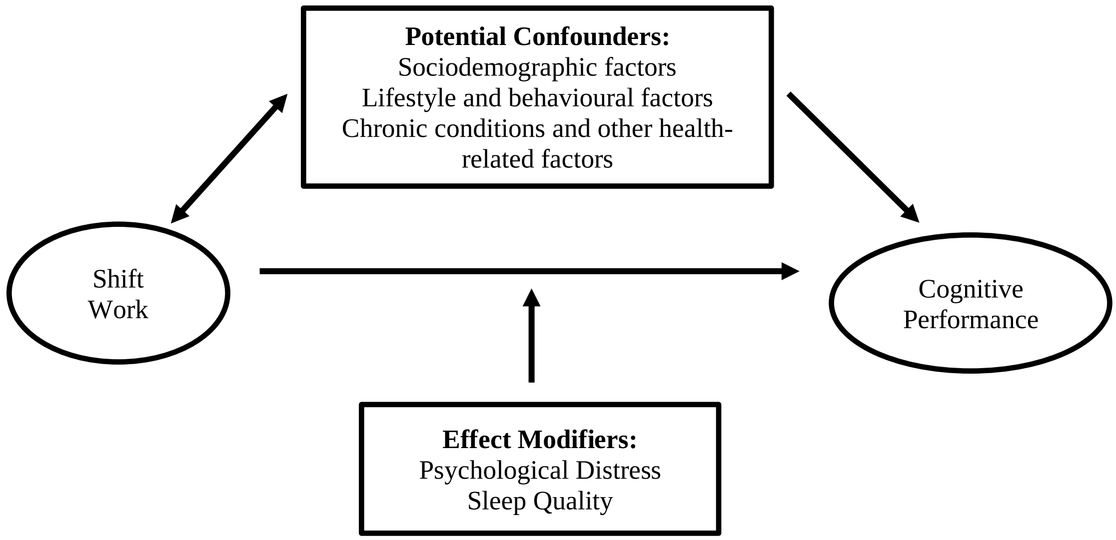

Figure 2.1: Theoretical conceptualization of the association between shift work and cognitive performance

Chapter 3

3 Methods

This chapter describes the data source, as well as the inclusion and exclusion criteria, in Sections 3.1 and 3.2, respectively. Section 3.3 discusses how the data were cleaned prior to conducting the analyses. A description of the variables to be used in the analyses, including the outcome variables, exposure variable, effect modifiers, and covariates are provided in Section 3.4. Methods to handle missing data and the statistical analyses are outlined in Sections 3.5 and 3.6, respectively.

3.1 Data Source

Data from the Canadian Longitudinal Study on Aging (CLSA)[314] were obtained for this thesis project. The CLSA is a national longitudinal study, which collects information from a random stratified sample of 51,338 Canadian men and women aged 45-85 years old at enrollment.[315,316] People residing in the Northwest Territories, Yukon and Nunavut, federal First Nations reserves, and provincial First Nations settlements were excluded from the sample.[316] The CLSA also excluded institutionalized individuals and full-time members of the Canadian Armed Forces.[316] Baseline data from the 51,338 participants were collected between 2010 and 2015.[314,316] Depending on the method of data collection at the start of the study, the CLSA sample was divided into two cohorts; a Tracking cohort and a Comprehensive cohort.[316] The Tracking cohort (N= 21,241) consisted of participants who participated in telephone interviews.[316] Participants who completed in-person home interviews and lived within 25 to 50 km of the data collection sites, located in seven of the provinces, were included in the Comprehensive cohort (N= 30,097).[316]

3.2 Inclusion and Exclusion Criteria

This thesis project is a cross-sectional study using baseline data from the CLSA Comprehensive cohort. Of the 30,097 participants, those who self-reported having conditions known to affect cognitive functioning were excluded from the study. Specifically, respondents were excluded if they were told by a doctor of having memory problems, Alzheimer's Disease, Parkinson's Disease, epilepsy, or multiple sclerosis.[317–]

[320] Participants who reported experiencing a head injury in their lifetime[157,317] or were subjected to chemotherapy treatment within the past month[244] at the time of data collection were excluded. Participants missing data on any of these conditions were also excluded. We also excluded people who had eye, brain, or central nervous system-related cancer, as these types of cancers have been found to directly impair cognitive functioning.[245] People at each level of retirement (completely, partly, or not retired) were included in the study. Only participants considered full-time workers at either their main or only job[321] among the partly and not retired groups, were included in our study. Consequently, we excluded participants considered part-time workers, as well as participants missing data on employment status. We also excluded participants who have never worked and who were currently unemployed at the time the survey was administered.

3.3 Data Cleaning

Baseline data from the Comprehensive cohort was uploaded and cleaned using Stata/SE, version 16.1.[322] This involved converting the baseline data into Stata format (csv to .dta). The baseline data set was merged with an updated version of the data set, released in 2020, containing new sampling weights. The distribution of the variables and potential outliers were assessed. Recoding and relabeling of variables were also conducted.

3.4 Variables

3.4.1 Outcome Variables

Declarative memory

The Rey Auditory Verbal Learning Test (RAVLT), a popular neuropsychological test used to assess learning and retention,[323] was used to measure declarative memory. Different versions of the RAVLT exist.[324] The most common one assesses participants across a total of eight trials.[324] In the first five trials, immediate recall is examined.[324] This involved a list of 15 words read aloud to participants, who are then tasked with recalling the words immediately after each trial.[324] An interference list of words is read out loud at the end of the fifth trial and participants must immediately recall those words.[324] Delayed recall is assessed in the last three trials.[324] In trials six and seven, participants must recall the list of words from the first list, however a delay of 20 minutes occurs at the start of the seventh trial.[324] In the last trial, participants are presented with an oral or written story, which uses all the words from the first list.[324] Participants must correctly identify the words from the first list.[324] Good test-retest reliability has been reported in the RAVLT ($0.51 \leq r \leq 0.86$).[323] The literature has reported that this neuropsychological instrument is sensitive to detecting memory impairment.[323,324]

In the CLSA, only two of the RAVLT trials were administered, one to test immediate recall and the other to test delayed recall. In the first trial, a list of 15 words was read out loud to participants, who were then tasked with immediately recalling the 15 words within 90 seconds.[325] After 30 minutes, the second trial began and participants recalled as many of the 15 words from the first trial within 60 seconds.[325,326] Trained interviewers from the CLSA allocated one point for each correctly recalled word in each of the trials.[325,326] The test scores for these two trials, the immediate recall trial and the delayed recall trial, were used as continuous variables in the current analyses.

Executive Function

Executive function was assessed using the Mental Alternation Test (MAT) and the Victoria version of the Stroop Test, which were both administered by trained CLSA interviewers.[325,326]

The MAT measures mental flexibility and processing speed.[323] Mental flexibility is a subdomain of executive functioning.[323] Scores from this neuropsychological test have been found to correlate well with scores from the Mini-Mental State Examination (MMSE) ($r=0.84$).[327] Billick and colleagues[327] found that the MAT had a 91% and 100% sensitivity and specificity, respectively, for detecting decline in cognitive functioning in older adults, using the MMSE scores as the gold-standard comparison. In the CLSA, participants were asked to complete three sub-tasks, each within 30 seconds.[325,326] First, participants were asked to count from 1 to 20 and then recite the alphabet out loud.[325,326] Participants were then tasked with saying the alphabet in an alternating pattern with numbers (e.g. 1, A, 2, B, 3, C,…).[325,326] Each correct alternation was allocated one point.[325] The MAT test score was used as a continuous variable in the current analyses.

In the CLSA, the Victoria version of the Stroop Test was administered, which assesses inhibition, attention, mental speed and mental control.[323] There are three sub-tasks involved with this neuropsychological test.[323,325] First, participants are presented with coloured dots printed on cards and are tasked with identifying the colour of each dot.[323,325,326] For this thesis, this sub-task will be called "Stroop I". Another set of cards were presented with words printed in different coloured ink and participants must name the ink colours of each word.[323,325,326] This sub-task will be called "Stroop II". The last sub-task, also known as the interference condition,[323,326] involved a set of cards which have coloured words (e.g. blue, green, red, yellow) printed in non-corresponding coloured ink.[323,325,326] Participants were asked to quickly name the colour of the ink (e.g. say "blue" for the word "green" written in blue ink).[323,326] Scores for the Stroop Test were determined based on how fast the task was completed.[323,326] The Victoria version of the Stroop Test has demonstrated good test-retest reliability, with coefficients of r= 0.90, r= 0.83, and r= 0.91 for each of the three sub-tasks, respectively.[323,328] For the current analyses, we only included the interference condition as a measure of executive functioning, as poorer performance on this part of the Stroop Test has been found among people with cognitive decline.[323] The score for the interference condition was used as a continuous variable in the analyses.

3.4.2 Exposure Variable

Shift work

In Canada, shift work is defined as non-standard work hours occurring in the hours before 7:00 a.m. or after 6:00 p.m.[1] Participants who self-reported being partly retired or not retired, were asked to describe their work schedules for work they considered their main job, as well as for a job they worked the longest in. Completely retired participants were also asked about their work schedule for their longest job ever worked, as well as the job they had before retirement. Response options for work schedules included: "daytime schedule or shift", "evening shift", "night shift", "rotating shift, changing periodically from days to evenings or nights”, “seasonal, on-call or casual, no pre-arranged schedules” and “other”.

Following the convention of many studies identified in the literature review, a binary variable for shift work was generated by categorizing “daytime schedule or shift” as “non-shift work” and combining the remaining work schedule responses into one category of “shift work”. Participants were considered shift workers if their main job and longest job fell under any of the responses categorized as shift work. If a participant’s main job was not considered shift work, but their longest job had work schedules that were considered shift work, then they were also classified as shift workers. This was done to better reflect duration of exposure, as those with shift work schedules during their longest job, would have been exposed to shift work for a longer period of time. Using a similar approach as Shields,[1] the variable for shift work was further derived to only include participants who are currently employed and who have worked a duration of at least one year or longer at their main job or last job before retirement, prior to completing the questionnaire. This was done to ensure that participants included in the analyses were workers who have been in the labour force for a substantial period of time.[1]

We also derived a second variable for shift work, where participants were classified as shift workers if their main job (or last job before retirement) and longest job were considered shift work, or if their main job (or last job before retirement) was considered shift work but their longest job was not. Results using this definition of shift work were compared with our first definition of shift work.

3.4.3 Effect Modification Variables

Psychological Distress

Psychological distress was assessed using the 10-item Kessler Psychological Distress Scale (K10),[329] which measures non-specific distress.[329] An overall K10 score was obtained by summing responses to questions related to anxiety and depressive symptoms experienced in the previous month.[330,331] Response values ranged from 1 (“none of the time”) to 5 (“all of the time”), with total scores ranging from 10 to 50, with higher scores indicating greater levels of psychological distress. The K10 scale has demonstrated good psychometric properties in distinguishing between specific mental disorders listed in the DSM-IV and non-specific cases.[332,333] Following the methods outlined by Menec and colleagues,[331] the variable for psychological distress was dichotomized, with scores less than 20 indicating "low distress" and scores greater than or equal to 20 indicating "high distress". We also derived another variable for psychological distress with a wider cut-off score, such that scores less than 15 indicated "low distress" and scores greater than or equal to 15 indicated "high distress". We compared the results of the two variables to determine whether cut-off scores had an impact on our point estimates.

Sleep quality

Sleep quality, also referred to as sleep satisfaction, is a measure of sleep health that has been found to be associated with mortality, metabolic syndrome, diabetes, high blood pressure, coronary heart disease, and depression.[334] CLSA participants were asked to self-report their level of satisfaction regarding their current sleep pattern. For the analyses, a binary variable for sleep quality was derived, such that participants who were "very dissatisfied" or "dissatisfied" with their current sleep pattern were categorized as having "poor sleep quality", whereas those who were "neutral", "satisfied" or "very satisfied" were considered as having "good sleep quality".

Sex

Sex differences in the relationship between shift work and cognitive impairment have not been widely investigated by the studies identified in our literature review. To investigate whether there are sex differences in the relationship between shift work and cognitive performance, we will stratify all analyses to explore effect modification.

Retirement Status

We stratified all analyses by retirement status, given that retirement status has been found to be associated with cognitive functioning.[180–187] As such, we wanted to investigate whether there was effect modification in the relationship between shift work and cognitive performance by retirement status. Retirement status was assessed at baseline by asking participants whether they considered themselves “completely retired”, “partly retired” or “not retired”. The “partly retired” category had a limited number of observations. Following the methods of a past CLSA study by Dogra and colleagues,[335] the “partly retired” group was combined with the “not retired” group, only people who have ever worked and were currently working at the time of baseline data collection were included in this category.

Menopausal Status

One recent prospective cohort study reported that shift work may be associated with accelerating the age at which women experience menopause.[108] Studies have also found associations between menopause and changes in cognition.[234] Menopause has been reported as an important effect modifier in research regarding chronic diseases.[336,337] For this thesis, we derived a variable for menopause status to be used in additional subgroup analyses. We determined whether women were in the stage of menopause using the question “have you gone through menopause, meaning that your menstrual periods stopped for at least one year and did not restart”. We used menopausal status as a categorical variable, classifying women into the following two categories: “pre-menopausal females” and “post-menopausal women”. We included an additional category called “males” for the male participants and excluded participants who reported having a hysterectomy. Participants with missing data on menopausal status were also excluded.

3.4.4 Covariates

3.4.4.1 Sociodemographic Factors

This thesis will control for the confounding effects of age, education, marital status, household income, migrant status, place of residence and social isolation, as these sociodemographic factors have been found to be associated with both shift work and cognitive functioning. Detailed descriptions regarding the relationship between each of these variables with shift work and with cognition is provided in Chapter 2.

Age Group

We adjusted for age in the analyses, as studies suggest that older people have more difficulty engaging in shift work[1,72,73,338] and that age is a risk factor for cognitive decline.[157] Furthermore, literature investigating the relationship between shift work and cognitive impairment commonly adjusted for age. The age of participants was categorized into four groups: "45 - 54 years", "55 - 64 years", "65 - 74 years" and "75 - 85 years". Age group was used as a categorical variable in all analyses.

Level of Education

The relationship between shift work and education level is likely tied to the job demands of the occupation or industry,[81] some of which are associated with using shift work schedules. Education level has been identified as a risk factor for cognitive impairment[157] and has also been commonly adjusted for in past studies. The variable for highest level of education was assessed using the following four categories: "less than secondary school graduation", "secondary school graduation, no postsecondary education", "some post-secondary education", and "post-secondary degree/diploma". Education level was used a categorical variable in all analyses.

Marital Status

Only three studies identified in the literature review controlled for marital status.[62,63,296] As marital status is associated with both shift work and cognitive functioning, we included marital status as a potential confounder in our analyses. Information pertaining to marital status was ascertained from the In-Home Questionnaire, using the question "what is your current marital/partner status?", with the following response options: "single, never married or lived with a partner", "married/ living with a partner in a common-law relationship", "widowed", "divorced", and "separated". Following similar methodology as a past CLSA study by Nicholson and colleagues,[339] the variable for marital status was used as a categorical variable in the analyses, with response options recoded into the following three groups: "Single/never married/ never lived with a partner", "married/common law", "widowed/ divorced/separated".

Household Income

Similar to education, income is likely related to shift work through occupation type or industry. One study found that people from lower-income households tend to report working evening, night, or irregular shifts, whereas rotating shift work was common among people from higher-income households who worked in the health or protective services industry.[1] With regards to cognition, low-income has been identified as a risk factor for cognitive decline.[194–197] For this thesis, we adjusted for household income, which was derived from the survey question asking CLSA participants to self-report an estimate of their total household income before tax deduction in the past year, with the following response options: "Less than $20,000", "20,000 or more, but less than $50,000", "$50,000 or more, but less than $100,000", "$100,000 or more, but less than $150,000" and "$150,000 or more". We used household income as a categorical variable in all analyses.

Migrant Status

The relationship between migrant status and shift work was unclear in the studies identified in our literature review. However, we opted to adjust for migrant status in our analyses, as two studies reported an association between migrant status and shift work.[83,84] Furthermore, there were also a few studies which reported an association between migrant status and poor cognition among older adults.[201–205] Participants were asked "in what country were you born?", and the variable for migrant status was recoded into a binary variable, classifying people born in Canada as "non-migrant" and those not born in Canada as "immigrant".

Place of Residence

We adjusted for place of residence, as one study found that rural residents were more likely to work non-standard hours.[88] Furthermore, an association between place of residence and decline in cognitive functioning has been identified in the literature.[207] Using the Statistic Canada's Postal Code Conversion File[340] the CLSA derived a variable for place of residence, indicating whether an individual resided in an urban or rural area.[341] For the current analyses, we recoded the variable into the following three categories: “rural”, “urban”, “suburban”. Postal codes linked to dissemination areas were categorized into the “urban” category as recommended by the CLSA research team.[342]

Social Isolation

Social isolation has been found to be associated with both shift work[89–91] and cognitive impairment,[166] and one study from the literature review considered living alone as a potential confounder of the relationship between shift work and cognitive impairment.[272] For this thesis, a social isolation index was created using the methods provided by Menec and colleagues.[343] First, five indicators of social isolation were recoded using questions related to a person’s social network and participation in social activities.[343] These indicators were based on information on a person’s living arrangements, as well as their marital and retirement status. The first indicator consisted of CLSA participants being unmarried or not in a common law relationship and living alone.[343] The second indicator classified participants as socially isolated if their most recent time spent time with their friends or neighbours was “within the last six months” or longer, or if they did not have any friends or neighbours.[343] Indicators three and four assessed similar criteria for a person’s relatives/siblings and children, respectively.[343] Indicator five considered a person to be socially isolated if they were completely retired and had little participation in social activities related to sports, education, the church, volunteering, clubs, recreation, as well as spending little or no time with friends, family, or neighbours.[343] The social isolation index was generated by allocating one point to each indicator, thereby resulting in a continuous variable ranging from zero to five.[343] We dichotomized the variable for social isolation used in the current analyses, classifying people with scores of zero to two as “not socially isolated” and scores three to five as “socially isolated”.[343]

3.4.4.2 Lifestyle and Behavioural Factors

The confounding effects of physical activity, smoking status, alcohol consumption, and fruit and vegetable intake will be adjusted for in this thesis, as these lifestyle and behavioural factors have been found to be associated with both shift work and cognitive functioning. Detailed descriptions regarding the relationship between these variables with shift work and with cognition are provided in Chapter 2. The variables for physical activity, smoking status and alcohol consumption were derived using a similar approach as a previous CLSA study.[339]

Physical Activity

Physical activity was included as a potential confounder in our analyses, as the level of physical activity has been linked to both shift work[5] and cognitive impairment.[191] The level of physical activity is also a common covariate adjusted for in the studies identified in the literature review. Physical activity was measured in the Maintaining Contact Questionnaire using the Physical Activity Scale for the Elderly (PASE).[344] The PASE scale assessed self-reported engagement in different types of physical activities within the past week, including: walking outside; light, moderate, and strenuous sports or recreational activities; exercises to increase muscle strength or endurance; light and heavy housework or chores; home repairs, lawn, or yard maintenance; outdoor gardening; work or volunteer-related physical activity; and physical activity related to caring for other people.[344] The frequency and duration of each type of activity was also assessed.[344] The PASE scale has demonstrated good reliability, with a test-retest reliability coefficient of 0.75.[344] Strong validity of the PASE scale has been reported as well, with PASE scores showing correlations with several physiological and health measures.[344]

Taking into account the duration and frequency, each type of physical activity was multiplied by a specific weight and then summed together to create a PASE score, with higher scores reflecting greater levels of physical activity. The derived PASE score was used in the current analyses as a continuous variable. For interpretation purposes, the variable for PASE score was also centered in the current statistical analyses.

Smoking Status

Smoking status is a lifestyle factor that is prevalent among shift workers,[5] and is also a risk factor for cognitive decline.[221–223] Studies identified in the literature review have also commonly controlled for smoking. Participants were asked a series of questions related to smoking history and habits. For the current analyses, the smoking status variable was recoded into a categorical variable with the following three categories: “never smoker”, “former occasional or daily smoker”, “occasional or daily smoker”.

Alcohol Consumption

Alcohol consumption is another lifestyle factor associated with shift work schedules.[5] Depending on the amount consumed, studies have reported both protective and harmful effects of alcohol on cognitive functioning.[157,191,226–229] Alcohol consumption was also commonly adjusted for in past studies investigating the association between shift work and cognitive impairment. Participants were asked questions pertaining to alcohol consumption in the past 12 months. For the current analyses, the variable for alcohol consumption was recoded into a categorical variable with the following four categories: “never drinker”, “former drinker”, “infrequent drinker”, “occasional drinker” and “regular or binge drinker”. The “never drinker” category was recoded using the response “no” to the question “have you ever drank alcohol?”, whereas the rest of the alcohol consumption categories needed to have a response of “yes”. The survey question, “about how often in the past month did you drink alcohol?” was also used to derive the rest of the alcohol consumption groups. Responses of “never” and “less than once a month” were respectively grouped into the “former drinker” and “infrequent drinker” categories, respectively. Participants who answered, “about once a month”, “2-3 times a month,” or “once a week” were categorized as “occasional drinkers”. If participants chose responses of “2-3 times a week”, “4-5 times a week,” or “almost every day (incl. 6 times a week)”, then they were classified as a “regular drinker”. The “binge drinker” category was derived from responses “2-3 times a week”, “4-5 times a week,” or “almost every day (incl. 6 times a week)” to the questions, “about how often during the past 12 months would you say you had five or more drinks at the same sitting or occasion?” and “about how often during the past 12 months would you say you had four or more drinks at the same sitting or occasion”. Due to few observations, the “binge drinker” category was combined with the “regular drinker” category.

Fruit and Vegetable Intake

Fruit and vegetable intake was not adjusted for in any of the studies identified in the literature review. However, fruit and vegetable intake has been found to have a positive association with cognitive reserve.[215,216] As such, we adjusted for this factor, as shift workers have been found to have altered food and vegetable consumption.[102] Daily intake of fruit and vegetables was measured using one item from the abbreviated version of the Seniors in the Community: Risk Evaluation for Eating and Nutrition Version II (SCREEN II) assessment tool.[345] The SCREEN II assessment tool was developed to determine the nutritional risk among community-dwelling seniors.[345] Items assessed in this tool include weight changes, meal patterns, consumption, and preparation of food.[345] The abbreviated SCREEN II instrument demonstrated good test-retest reliability, with an ICC of 0.84.[345] The reliability of the instrument was also good, with an inter-rater reliability of ICC= 0.79 and intra-reliability of ICC= 0.85.[345] Fruit and vegetable intake was used as a categorical variable in the current analyses, with the following seven categories: "Seven or more servings/day", "Six servings/day", "Five servings/day", "Four servings/day", "Three servings/day", "Two servings/day", "Less than two servings/day".

3.4.4.3 Chronic Disease and Other Health-Related Factors

We adjusted for the confounding effects of BMI status, diabetes, hypertension, cardiovascular disease, cancer, gastrointestinal disease, anxiety, or depression, multimorbidity, and self-rated health, as these chronic conditions and other health related factors have been found to be associated with both shift work and cognitive impairment. The variables for BMI status, diabetes, hypertension, cardiovascular disease, and anxiety or depression were recoded using similar methodology as the CLSA study by Nicholson and colleagues.[339] Metabolic syndrome was not controlled for in the current analyses, as we did not have access to hematology or chemistry reports which are needed for defining metabolic syndrome.

BMI Status

We adjusted for BMI in the current analyses, as elevated BMIs has been found to be associated with both shift work[105] and cognitive impairment.[230–232] Studies identified in the literature review also commonly controlled for BMI in the analyses. BMI was extracted from weight and height measurements, which were taken at CLSA data collection sites. For all analyses, the variable for BMI status was recoded into a categorical variable with the following categories: “underweight or normal weight”, “overweight”, and “obese”. Participants with a BMI of less than 18.5 kg/m^2 were considered “underweight”, whereas a BMI greater than or equal to 18.5 kg/m^2 but less than or equal to 24.9 kg/m^2 was categorized as “normal weight”. As the “underweight” category had too few observations for a meaningful analysis, this category was combined with the “normal weight” category. The “overweight” category consisted of BMIs greater than or equal to 25 kg/m^2 but less than or equal to 29.9 kg/m^2. Participants with BMIs greater than or equal to 30 kg/m^2 were considered “obese”.

Diabetes

We controlled for diabetes in the current analyses, as diabetes has been found to be associated with both shift work[5,122–125] and cognitive impairment.[241–243] Participants who self-reported being told by a doctor that they had diabetes, or had borderline diabetes were considered as having diabetes. A binary variable for diabetes was derived and used in all analyses.

Hypertension

Hypertension has been widely studied as a risk condition associated with working shift work,[112,113] as well as a risk factor for cognitive impairment.[240] Furthermore, studies identified from our literature review commonly adjusted for the presence of hypertension. Participants were classified as having hypertension if systolic blood pressure was greater than or equal to 140 mmHg, or the diastolic blood pressure was greater than or equal to 90 mmHg. Those who self-reported currently taking medication for high blood pressure or hypertension and were told by a doctor of having high blood pressure or hypertension were included in the hypertension category. Furthermore, participants who self-reported undergoing non-pharmacological treatments to lower blood pressure were also considered as having hypertension.

Cardiovascular Disease

As cardiovascular disease has been linked with both shift work[114] and cognitive impairment,[157] we also adjusted for this in our current analyses. Participants who self-reported having been told by a doctor of having had a heart attack or myocardial infarction, having angina, or having peripheral vascular disease or poor circulation in limbs were classified as having cardiovascular disease.

Cancer

Although the association between shift work and cancer is unclear, night shift work has been classified as a potential carcinogen.[138] Both cancer and chemotherapy have also been linked with cognitive dysfunctions.[244,245] One study identified in the literature review controlled for cancer in their analyses.[300] As such, the current analyses controlled for the confounding effects of cancer in two ways. First, participants who self-reported having undergone chemotherapy treatment in the past four weeks or had cancer in the eye, brain or central nervous system were excluded from the analyses. We also created a binary variable using responses to the question “has a doctor every told you that you had cancer?”.

Gastrointestinal Disease

Findings from the literature suggest that gastrointestinal diseases, including bowel disorders and ulcers, are associated with both shift work[120] and cognitive impairment.[246–250] CLSA participants were asked to self-report whether they have ever been told by a doctor of having Crohn’s disease, ulcerative colitis, or irritable bowel syndrome, as well as having intestinal or stomach disorders. A binary variable was created, categorizing people as having “gastrointestinal disease” if they responded “yes” to having any of the aforementioned conditions.

Anxiety or Depression

We controlled for the presence of anxiety or depression as these two mental health conditions have been linked with both shift work[139,140] and cognitive decline.[157,259–261] Studies from our literature review also commonly controlled for symptoms of anxiety or depression. Participants included in the anxiety or depression category were those who self-reported either being told by a doctor of having an anxiety disorder or having clinical depression.

Multimorbidity

Having multiple chronic conditions has been found to be associated with decline in cognitive functioning.[263–265] Although studies did not find an association between shift work and multimorbidity, having multiple chronic conditions was found to be associated with early retirement.[144] As such, we opted to adjust for multimorbidity, given that our analyses will include retired people. We used the public health definition of multimorbidity provided by Roberts and colleagues,[346] which included the following chronic conditions: Anxiety or mood disorder, arthritis, asthma, cancer, chronic obstructive pulmonary disease, diabetes, cardiovascular disease, and stroke. Alzheimer's disease was also included in the public health definition,[346] however, we excluded this from our definition as our sample excluded people who had been told by a doctor of having Alzheimer's disease. We also used a cut off score of two chronic diseases for the multimorbidity definition, as most studies investigating the relationship between multimorbidity and cognitive impairment used this cut-off. Variables for diabetes, cardiovascular disease and cancer were recoded as previously described above. For anxiety or mood disorders, we used the same definition described previously. Stroke, asthma, and chronic obstructive pulmonary disease (COPD) were derived from similar questions asking CLSA participants whether they have ever been told by a doctor of having each of the chronic conditions. CLSA participants who self-reported having been told by a doctor of having osteoarthritis in one or both hands, in the knee or in the hip or having rheumatoid arthritis, were considered as having arthritis. Next, a continuous variable was generated by summing the chronic condition variables. A binary variable for multimorbidity was then derived, such that participants having two or more chronic conditions were classified as having "multimorbidity" and having zero to one chronic condition were classified as having "no multimorbidity".

Self-Rated Health

The associations between shift work and self-rated health is most likely linked with work-time control.[148,151–153] There was one study which found an association between shift work and poor self-rated health.[154] Also, poor self-rated health has been found to be associated with decline in cognitive functioning.[268–270] We included self-rated health in our analyses, as the prior study by Wong and Colleagues[45] controlled for this factor. CLSA participants were asked to self-rate their general health, which includes their physical health and mental health, and their well-being - as either "excellent", "very good", "good", "fair", or "poor". The variable for self-rated health used in the current analyses was recoded into a binary variable, classified as having either "excellent or good self-rated health" and "fair or poor self-rated health".

3.5 Missing Data

After applying our inclusion and exclusion criteria, we assessed the amount of missing data in the CLSA dataset, by looking at the total number of observations with missing data, as well as the proportion of missing data for each variable. These results are provided in Table 4.1

Missing data can be classified as (i) missing completely at random (MCAR), which occurs when missing data does not depend on observed or unobserved data; (ii) missing at random (MAR), which occurs when missing data depends on observed data rather than unobserved data; and (iii) missing not at random (MNAR), which occurs when missing data depends on unobserved data.[347] Although it is generally recommended to use imputation methods, such as multiple imputation, to handle missing survey data, specifically for item non-response[348,349] multiple imputation relies on the assumption that data are MAR to generate unbiased estimates.[350] Biased results could be generated using MICE when data are MCAR or MNAR.[350,351] Most missing survey data cannot be assumed to be MCAR as non-response among participants likely depend on personal factors and circumstances.[352] However, determining whether data are MAR or MNAR is not possible using only observed data.[347]

We handled the missing data using multiple imputation (MI), specifically multiple imputation by chained equations (MICE). This is a widely used method for large datasets which have missing data occurring in many variables.[347] MI can also be used to handle missing data for different types of variables (e.g. binary, continuous, categorical, etc),[347] thereby making MICE a reasonable approach to handle missing data for our dataset. As our effect modifiers, psychological distress and sleep quality, are binary variables and both contain missing data, interaction terms for these variables will be passively imputed.[353] We also included auxiliary variables (self-rated mental health, personal income, Center of Epidemiological Studies Short Depression Scale (CES-D-10) score) to improve imputations. To limit the loss of power to be within one percent, we specified 25 copies in the multiple imputation model.[347] Furthermore, we excluded CLSA participants with missing data on the immediate recall trial, delayed recall trial, MAT and interference condition, as we did not generate imputations for these four cognitive outcomes.

3.6 Statistical Analyses

We conducted all analyses using Stata/SE, version 16.1.[322] Diagnostic tests were performed to determine whether the assumptions for a linear regression were satisfied. Given the large sample size, statistical inference could rely to some degree on the Central Limit Theorem for the validity of statistical inferences.[354] We did find evidence that the variance was not constant (i.e. evidence of heteroscedasticity). To ensure validity of estimates, we used linearized standard errors in all our regression models.[355] Sampling weights, particularly, inflation weights for descriptive analyses and analytic weights for regression analyses, were applied to account for the complex sampling design of the CLSA. Multiple imputation was used to account for missing data for our main analysis and we excluded participants missing data on the outcome measures in the multivariable regression analyses. A complete case analysis was used in the sensitivity analysis.

Descriptive Statistics

We summarized descriptive statistics for categorical variables using percentages and frequencies. We generated means and standard deviations for continuous variables. Our descriptive analyses were stratified according to retirement status and sex. We also computed chi-square tests to assess associations between the following: education level and household income; the individual chronic conditions and the multimorbidity variable; gastrointestinal disease and cancer; hypertension and cardiovascular disease.

Objective 1: Statistical Analyses

The first objective was to examine the association between shift work and cognitive performance among shift workers compared to non-shift workers, and to identify whether sex differences exist in this association. We first conducted four separate simple linear regression models, one for each of the outcome measures. Each analysis was stratified by retirement status and sex. Next multivariable linear regression models were fit separately for each of the cognitive tests, adjusting for sociodemographic factors, lifestyle, and behavioural factors and for chronic conditions and other health-related factors. Each multivariable regression model was also stratified by retirement status and sex. Associations were considered statistically significant when the 95% confidence intervals did not include zero.

Objective 2: Statistical Analyses

The second objective was to explore whether psychological distress moderates the relationship between shift work and cognitive performance. We first included the variable for psychological distress as a confounder in four separate multivariable regression models, while adjusting for sociodemographic factors, lifestyle and behavioural factors and chronic diseases and other health-related factors. We then stratified each of the regression models according to retirement status and sex. This was done to determine whether psychological distress was a confounder of the relationship between shift work and psychological distress. Next, we included psychological distress as an interaction term with shift work in four other separate multivariable regression models to investigate effect modification by psychological distress. These models controlled for sociodemographic factors, lifestyle and behavioural factors and chronic conditions and other health-related factors and were stratified by retirement status and sex. The results were considered statistically significant for variables with 95% confidence intervals that excluded regression coefficients of zero.

Objective 3: Statistical Analyses

The third objective was to investigate the moderating effect of sleep quality on the association between shift work and cognitive performance. As such, we used the same approach as objective 2, but used the sleep quality variable in place of psychological distress.

Subgroup Analyses

We performed subgroup analyses for objectives 1, 2 and 3 to investigate differences in the association between shift work and cognitive performance by menopausal status.

Sensitivity Analysis

To assess the robustness of our findings, we conducted a sensitivity analysis comparing results for objectives 1, 2 and 3, which classified participants whose longest job was shift work as shift workers, to another definition of shift work that classified people whose main job, but not longest job was shift work, as shift workers. A second sensitivity analysis was performed comparing results for objective 2, which used a cut-off of score of 20 to results using a cut-off score of 15 for psychological distress. A third sensitivity analysis using both the second definition for shift work and the second psychological distress measure was also conducted to assess the robustness of our findings for objective 2. Furthermore, we performed another sensitivity analysis comparing results for objectives 1, 2 and 3 from our complete case analysis to our imputed dataset. This was conducted to investigate the impact of multiple imputation on the magnitude and direction of point estimates.

Chapter 4

4 Results

This chapter provides an outline of the inclusion and exclusion of CLSA participants in Section 4.1 and discusses the missingness of data in Section 4.2. Sections 4.3, through 4.5, present the sample characteristics, associations between categorical variables, and assessments for multicollinearity, respectively. Results for objectives 1, 2, and 3 are shown, respectively in Sections 4.6, 4.7 and 4.8. The subgroup analyses, and sensitivity analyses are presented in Sections 4.9 and 4.10, respectively.

4.1 Sample

Of the 30,097 CLSA participants from the Comprehensive cohort, only 13,238 participants met our inclusion criteria of being a full-time worker at either their main job (or last job before retirement) or longest job and having reported no conditions known to affect cognitive functioning, as described in Chapter 3. We excluded participants with missing data on cognitive outcome measures from our multivariable analyses. Thus, after imputation, our multivariable analyses included 12,152 participants in total. An overview of the sample of CLSA participants selected into this study, as well as the reasons for exclusion, is provided in Figure 4.1.

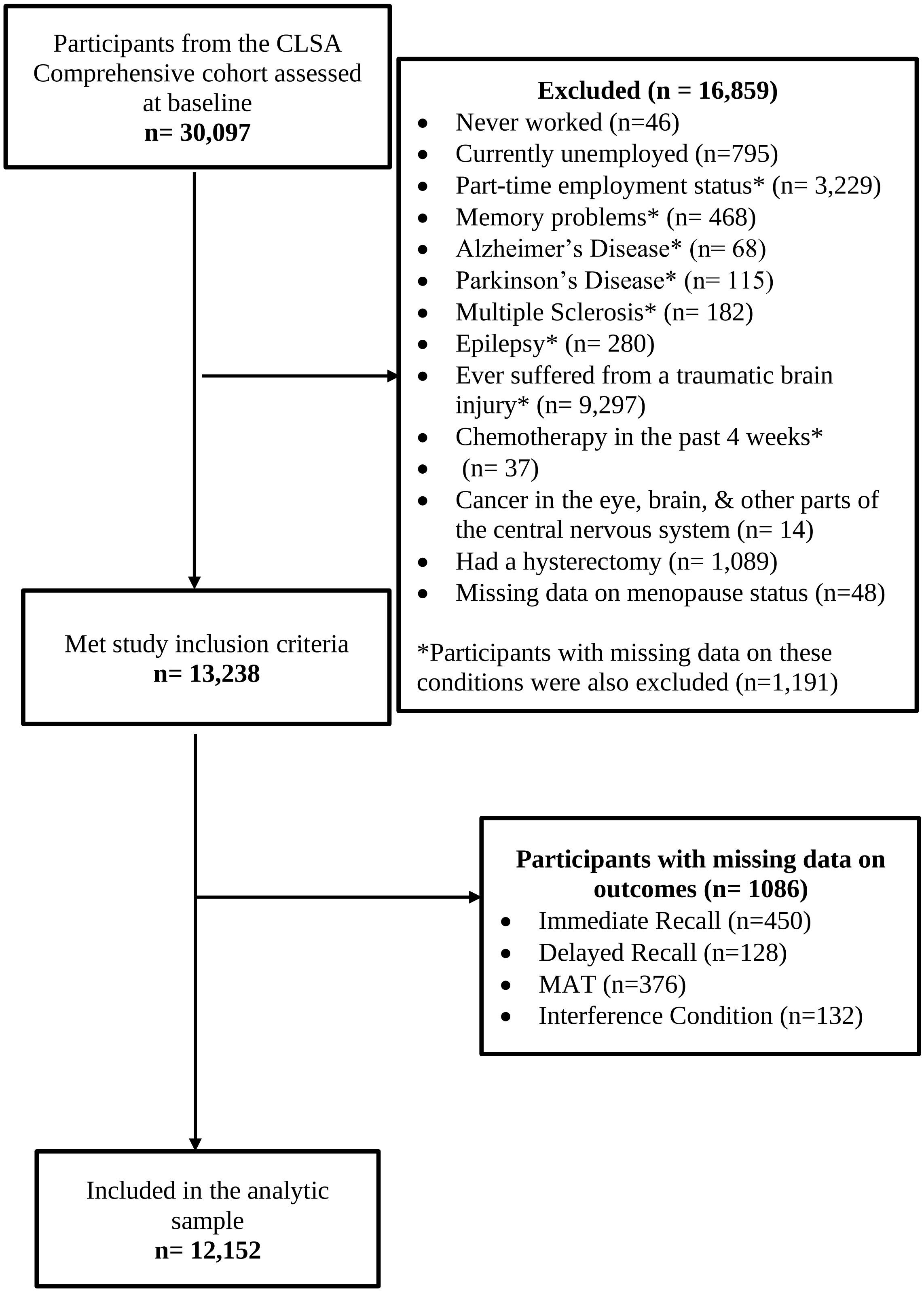

Figure 4.1: Flow chart outlining inclusion and exclusion of CLSA participants

4.2 Extent of Missingness

A description of the missing data is provided in Table 4.1. Of the 13,238 participants included in the study, 25.1% (n=3,326) had missing data on at least one of the variables of interest. Variables with a proportion of missingness greater than 5.0% greater were variables for migrant status (n=742), household income (n =740) and psychological distress (n=672). Variables for age group, place of residence, social isolation, multimorbidity, sex, retirement status and menopausal status did not have any missing values.

Given the high case-wise missingness, we performed a sensitivity analysis comparing our multiple imputed data set to a complete case analysis. Results for our sensitivity analysis are described in Section 4.9.

Table 4.1: Description of missing data (N= 13,238)

	n (% missing)
Total number of participants with missing data	3326 (25.1)
Total number of missing values for variables	
Exposure Variable	
Shift work	5 (0.0)
Outcome variables	
Immediate Recall Trial	450 (3.4)
Delayed Recall Trial	446 (3.4)
MAT	658 (5.0)
Interference Condition	151 (1.1)
Effect Modifiers	
Psychological Distress	672 (5.1)
Sleep Quality	7 (0.05)
Sex	0 (0.0)
Retirement Status	0 (0.0)
Menopausal Status	0 (0.0)
Covariates	
Age group	0 (0.0)
Education	19 (0.1)
Marital Status	3 (0.0)
Household Income	740 (5.6)
Migrant Status	742 (5.6)
Place of Residence	0 (0.0)
Social Isolation	0 (0.0)
Smoking Status	73 (0.6)
Alcohol Consumption	6 (0.1)
Fruit and Vegetable Intake	648 (4.9)
Physical Activity (PASE Scale)	639 (4.8)
BMI Status	176 (1.3)
Self-rated Health	11 (0.1)
Gastrointestinal Disease	46 (0.4)
Anxiety or Depression	25 (0.2)
Diabetes	22 (0.2)
Cancer	9 (0.1)
Cardiovascular Disease	69 (0.5)
Hypertension	72 (0.5)
Multimorbidity	0 (0.0)

4.3 Sample Characteristics

4.3.1 Sociodemographic Characteristics of Included and Excluded Participants

Table 4.2 presents sociodemographic characteristics of both included and excluded participants. Compared to those who were included, most participants who were excluded from this study were female and slightly younger in age. Similar to included participants, the majority of those excluded received a post-secondary education, had a household income between $50,000 and $99,999, were married or in a common law relationship, were non-immigrants and lived in urban residences.

Table 4.2: Weighted descriptive analysis of sociodemographic characteristics comparing included and excluded participants (N=30,097)

Characteristic	Included (N= 13,238)	Excluded (N= 16,859)
	%	%
Sex		
Male	56.0	45.0
Age (years)		
Mean (Standard Deviation)	59.6 (10.0)	59.4 (10.0)
45 – 54 years	41.6	42.3
55 – 64 years	29.8	29.8
65 – 74 years	17.5	16.9
75 – 85 years	11.1	11.1
Education		
Less than secondary	4.0	5.4
Secondary	8.9	9.0
Some post-secondary	6.0	7.2
Post-secondary	81.0	78.2
Missing	0.1	0.2
Household Income		
Less than $20,000	2.3	6.0
$20,000 - $49,999	15.7	19.1
$50,000 - $99,999	32.2	30.9
$100,000 - $149,999	22.5	19.8
Greater than $150,000	22.6	17.9
Missing	4.7	6.3
Marital Status		
Single, never married, or never lived with a partner	7.6	8.9
Married or common law	78.0	74.3
Widowed, divorced, or separated	14.5	16.7
Missing	0.0	0.0
Migrant Status		
Non-Immigrant	80.8	82.8
Immigrant	12.6	11.5
Missing	6.7	5.7
Place of Residence		
Rural	8.3	8.6
Urban	87.5	87.1
Suburban	4.2	4.3

4.3.2 Characteristics of Included Participants

The sample characteristics of the CLSA participants who met the study criteria are displayed through Tables 4.3-4.6 and are stratified by retirement status and sex.

Employment-Related Factors

The variables for work schedule and shift work displayed in Table 4.3 are based on a person's main job (or last job before retirement) and longest job and is described in detail in Chapter 3. In each stratified group, the most common work schedule for all participants was daytime schedules or shifts (completely retired and male: 83.5%; completely retired and female: 87.0%; not or partly retired and male: 85.0%; not or partly retired and female: 85.4%). In terms of shift work, there was only a small proportion of shift workers across all groups, which is consistent with the Canadian studies identified in the literature review. However, across all groups, completely retired males had the largest proportion of prior shift work (completely retired and male: 16.0%; completely retired and female: 11.7%; not or partly retired and male: 15.0%; not or partly retired and female: 14.5%).

Sociodemographic Characteristics

The average age of completely retired male participants was 68.5 years (SD: 8.1) and the majority of them were between the ages of 65 to 74 years old (36.2%). Completely retired female participants had a mean age of 68.1 years (SD: 8.1) and most of them were also between 65 to 74 years old (38.6%). Among not or partly retired participants, the average age of males and females was 55.1 years (SD: 7.1) and 53.9 years (SD: 6.1), respectively. The majority of participants who were not or partly retired were under the age of 55 (males: 60.8%; females: 64.0%).

In all four groups, the majority of participants had attained post-secondary education (70.7% to 84.3%). Compared to the other groups, there was a larger proportion of females who were completely retired who had less than secondary school education (8.3%). Household incomes between $50,000 and $99,999 were most common for participants who were completely retired and male, completely retired and female, and not or partly retired and female (30.9% to 41.8%). The majority of male participants who were not or partly retired had higher household incomes, which were greater than $150,000 (33.8%). Most participants in both retirement groups were married or in a common law relationship and lived in urban residences (Table 4.3). A small proportion of participants were immigrants (11.0% to 15.3%) and considered socially isolated (5.6% to 38.5%).

Lifestyle and Behavioural Factors

Across the four groups, most participants were former smokers and regular or binge drinkers (Table 4.4). The majority of participants who were overweight were completely retired and male (45.8%), completely retired and female (37.5%), and not or partly retired and male (46.0%). Most female participants who were not or partly retired were underweight or were normal weight (41.7%). Across the four groups, male participants who were not or partly retired were the most physically active, with an average PASE score of 177.9 (SD: 82.6). With regards to fruit and vegetable intake, two servings of fruit and vegetables per day was the most common for all male participants, whereas five servings per day was the most common for female participants (Table 4.4).

Chronic Diseases and Other Health-Related Factors

The majority of male and female participants in both retirement groups self-rated their health as good or excellent (Table 4.5). There was only a small proportion of participants who self-reported having cancer, hypertension, cardiovascular disease, diabetes, anxiety or depression, or gastrointestinal disease (Table 4.5). Most participants in all the stratified groups reported having 0 to 1 chronic disease (65.0% to 86.3%), good sleep quality (71.7% to 81.9%), and low psychological distress (84.8% to 88.2%). For female participants, the majority were in post-menopause (completely retired: 96.3%; not or partly retired: 57.0%).

Table 4.3: Weighted descriptive analysis of employment-related factors, stratified by retirement status and sex (N=13,238)

Characteristic	All (N= 13,238)	Completely Retired		Not or Partly Retired	
		Males (n= 3,351)	Females (n= 2,802)	Males (n= 4,071)	Females (n= 3,014)
	%	%	%	%	%
Work Schedule					
Daytime schedule or shift	85.2	83.5	87.0	85.0	85.4
Evening shift	1.3	0.7	1.2	1.4	1.7
Night shift	0.7	0.5	1.2	0.6	0.6
Rotating shift	7.8	9.4	6.9	7.4	7.7
Seasonal, on-call or casual, no pre-arranged schedules	1.1	1.0	0.9	1.2	1.0
Other	4.0	5.0	2.7	4.4	3.6
Missing	0.0	0.0	0.2	0.0	-
Shift Work Status					
No shift work	85.2	83.5	87.0	85.0	85.4
Shift work	14.8	16.5	12.9	15.0	14.6
Missing	0.0	0.0	0.2	0.0	-

Note: Participants who are not retired includes only those who were currently employed at the time of the survey.

Table 4.4: Weighted descriptive analysis of sociodemographic characteristics, stratified by retirement status and sex (N=13,238)

Characteristic	All (N= 13,238)	Completely Retired		Not or Partly Retired	
		Males (n= 3,351)	Females (n= 2,802)	Males (n= 4,071)	Females (n= 3,014)
	%	%	%	%	%
Age (years)					
Mean (Standard Deviation)	59.6 (10.0)	69.5 (8.1)	68.1 (8.2)	55.1 (7.1)	53.9 (6.1)
45 -54 years	41.6	3.3	4.7	60.8	64.0
55 -64 years	29.8	28.8	31.2	29.3	30.2
65 - 74 years	17.5	36.2	38.6	7.8	5.1
75 – 85 years	11.1	31.7	25.5	2.2	0.7
Education					
Less than secondary	4.0	7.7	8.3	1.8	1.9
Secondary	8.9	9.3	13.8	7.1	7.9
Some post-secondary	6.0	6.9	7.2	5.2	5.8
Post-secondary	81.0	75.9	70.7	85.8	84.3
Missing	0.1	0.2	0.1	0.1	0.1
Household Income					
Less than $20,000	2.3	3.8	5.3	0.9	1.3
$20,000 - $49,999	15.7	25.0	31.2	7.3	11.4
$50,000 - $99,999	32.2	41.8	36.8	26.5	30.9
$100,000 - $149,999	22.5	15.8	11.4	28.7	25.5
Greater than $150,000	22.6	8.3	6.7	33.8	26.7
Missing	4.7	5.4	8.5	2.8	4.2

Table 4.4 (Continued)

Characteristic	All (N= 13,238)	Completely Retired		Not or Partly Retired	
		Male (n= 3,351)	Female (n= 2,802)	Male (n= 4,071)	Female (n= 3,014)
	%	%	%	%	%
Marital Status					
Single, never married, or never lived with a partner	7.6	5.0	7.8	7.2	9.7
Married or common law	78.0	81.7	63.0	85.9	73.8
Widowed, divorced, or separated	14.5	13.3	29.2	6.9	16.5
Missing	0.0	-	0.0	-	0.1
Migrant Status					
Non-Immigrant	80.8	79.0	82.5	79.5	82.8
Immigrant	12.6	15.3	12.4	12.4	11.0
Missing	6.7	5.7	5.1	8.1	6.2
Place of Residence					
Rural	8.3	7.5	9.1	8.2	8.5
Urban	87.5	87.8	86.1	87.8	87.7
Suburban	4.2	4.8	4.8	3.9	3.9
Socially Isolated					
No	82.3	61.5	62.8	92.6	94.4
Yes	17.7	38.5	37.2	7.4	5.6
Missing	0.0	0.0	-	-	-

Table 4.5: Weighted descriptive analysis of behavioural and lifestyle factors, stratified by retirement status and sex (N=13,238)

Characteristic	All (N= 13,238)	Completely Retired		Not or Partly Retired	
		Male (n= 3,351)	Female (n= 2,802)	Male (n= 4,071)	Female (n= 3,014)
	%	%	%	%	%
Smoking Status					
Never smoker	33.7	25.3	33.0	35.5	37.3
Former smoker	57.9	67.6	59.4	56.2	52.7
Occasional or daily smoker	7.9	6.2	7.0	7.9	9.7
Missing	0.5	0.9	0.6	0.4	0.4
Alcohol Consumption					
Never drinker	2.2	1.5	3.0	1.9	2.7
Former drinker	9.1	10.6	11.5	7.8	8.3
Infrequent drinker	10.1	8.3	14.8	7.2	12.1
Occasional drinker	26.4	22.3	27.0	25.8	29.8
Regular or binge drinker	52.1	57.2	43.7	57.1	47.0
Missing	0.1	0.1	-	0.0	0.1
BMI (kg/m^2)					
Underweight or normal weight	31.3	26.2	33.7	25.2	41.7
Overweight	40.8	45.8	37.5	46.0	32.2
Obese	26.7	26.4	27.7	27.5	24.9
Missing	1.3	1.6	1.2	1.3	1.2

Table 4.5 (Continued)

Characteristic	All (N= 13,238)	Completely Retired		Not or Partly Retired	
		Male (n= 3,351)	Female (n= 2,802)	Male (n= 4,071)	Female (n= 3,014)
	%	%	%	%	%
Past Week Physical Activity (PASE scale; 0 - 693)					
Mean (Standard Deviation)	154.0 (77.2)	128.2 (56.5)	115.6 (53.5)	177.9 (82.6)	162.0 (79.7)
Missing	639	177	131	187	144
Fruit and Vegetable Intake (Servings/ day)					
Seven or more	11.5	7.4	14.2	9.5	15.4
Six	11.1	7.4	15.1	8.3	15.2
Five	17.4	14.2	22.7	13.5	21.5
Four	17.5	15.5	18.0	17.2	19.1
Three	15.9	18.5	13.4	17.5	13.4
Two	13.9	18.6	8.7	18.2	7.9
Less than two	8.3	13.2	3.5	11.6	3.4
Missing	4.4	5.2	4.4	4.2	4.2

Table 4.6: Weighted descriptive analysis of chronic diseases and other-heath related factors, stratified by retirement status and sex (N=13,238)

Characteristic	All (N= 13,238)	Completely Retired		Not or Partly Retired	
		Males (n= 3,351)	Females (n= 2,802)	Males (n= 4,071)	Females (n= 3,014)
	%	%	%	%	%
Self-rated Health					
Excellent or Good Self-Rated Health	94.0	91.0	93.4	94.3	96.0
Fair or Poor Self-Rated Health	5.9	8.9	6.5	5.6	4.0
Missing	0.1	0.1	0.1	0.0	0.0
Cancer					
No	88.6	79.0	83.9	93.1	91.7
Yes	11.3	20.9	16.0	6.9	8.3
Missing	0.0	0.1	0.1	-	0.0
Hypertension					
No	85.2	81.1	80.9	84.9	91.1
Yes	14.2	18.4	18.7	14.1	8.6
Missing	0.6	0.5	0.4	1.0	0.3
Cardiovascular Disease					
No	90.7	81.1	87.8	93.5	95.1
Yes	8.8	18.3	11.6	6.1	4.3
Missing	0.5	0.7	0.5	0.3	0.6

[a:] Gastrointestinal disease includes ulcers or bowel disease.

[b:] Multimorbidity is defined as $\geq$ 2 of the following conditions: anxiety or depression, cancer, cardiovascular disease, asthma, COPD, diabetes, arthritis, stroke.

Table 4.6 (Continued)

Characteristic	All (N= 13,238)	Completely Retired		Not or Partly Retired	
		Males (n= 3,351)	Females (n= 2,802)	Males (n= 4,071)	Females (n= 3,014)
	%	%	%	%	%
Diabetes					
No	85.9	77.4	84.4	87.7	90.1
Yes	14.0	22.4	15.5	12.2	9.7
Missing	0.1	0.2	0.1	0.1	0.2
Anxiety or Depression					
No	83.7	87.0	78.9	77.7	78.6
Yes	16.2	12.8	20.9	22.1	21.3
Missing	0.1	0.2	0.2	0.2	0.2
Gastrointestinal Disease[a]					
No	87.7	86.7	83.2	90.0	87.8
Yes	12.0	13.0	16.5	9.6	11.9
Missing	0.3	0.4	0.3	0.4	0.3
Multimorbidity[b]					
0 -1 Chronic Disease	77.8	68.7	65.0	86.3	80.2
$\geq$ 2 Chronic Diseases	22.2	31.3	35.0	13.7	19.8
Sleep Quality					
Good Sleep Quality	76.4	81.9	74.8	77.7	71.7
Poor Sleep Quality	23.6	18.0	25.1	22.3	28.3
Missing	0.1	0.1	0.1	0.0	-

[a:] Gastrointestinal disease includes ulcers or bowel disease.

[b:] Multimorbidity is defined as $\geq$ 2 of the following conditions: anxiety or depression, cancer, cardiovascular disease, asthma, COPD, diabetes, arthritis, stroke.

Table 4.6 (Continued)

Characteristic	All (N= 13,238)	Completely Retired		Not or Partly Retired	
		Males (n= 3,351)	Females (n= 2,802)	Males (n= 4,071)	Females (n= 3,014)
	%	%	%	%	%
Psychological Distress					
Low Distress	86.7	88.2	84.8	87.9	85.4
High Distress	8.8	7.1	10.5	7.8	10.4
Missing	4.4	4.7	4.7	4.3	4.3
Menopausal Status					
Males	56.0	100.0	-	100.0	-
Pre-menopause	12.1	-	3.7	-	43.9
Post-menopause	31.9	-	96.3	-	57.0

[a:] Gastrointestinal disease includes ulcers or bowel disease.

[b:] Multimorbidity is defined as $\geq$ 2 of the following conditions: anxiety or depression, cancer, cardiovascular disease, asthma, COPD, diabetes, arthritis, stroke.

4.4 Associations between Categorical Variables

Weighted chi-square tests were performed for associations between categorical variables and are presented in Tables 1 - 4 in Appendix B. Missing observations were excluded from the chi-square analyses.

The chi-square test shows significant associations between education level and household income (X^2= 956.6, $p < 0.001$), thereby suggesting that the categorical variables are not independent of each other. No significant associations were found between the variables for hypertension and cardiovascular disease (Table 2), as well as cancer and gastrointestinal disease (Table 3).

In terms of the individual chronic diseases and multimorbidity, the chi-square tests show significant associations between multimorbidity and hypertension (X^2= 25.2, $p<0.001$), cancer (X^2= 925.3, $p<0.001$), cardiovascular disease (X^2= 1213.6, $p<0.001$), diabetes (X^2= 1570.0, $p<0.001$), anxiety or depression (X^2= 1413.2, $p<0.001$) and gastrointestinal disease (X^2= 115.2, $p<0.001$). These results suggest that the individual chronic conditions are associated with multimorbidity.

As significant associations were found among the categorical variables, we performed a test of multicollinearity for all the independent variables, and the outputs are described in Section 4.5

4.5 Assessing the Impact of Multicollinearity

We ran weighted multivariable linear regression models for objectives 1, 2 and 3 for all four cognitive outcomes to test for multicollinearity. For objectives 2 and 3, we ran regression models including the interaction term between shift work and psychological distress (objective 2), as well as the interaction term between shift work and sleep quality (objective 3). Missing observations were excluded from all the analyses. The results are shown in Tables 1 to 3 in Appendix C.

The VIFs for objectives 1, 2 and 3 for each of the four outcomes were similar. Specifically, the VIF was 1.2, 1.2, 1.1 and 1.4 when the outcome was the immediate recall trial, delayed recall trial, the MAT, and the interference condition, respectively. As the VIFs were below 10, this suggests low collinearity among the variables in the regression models. Therefore, it is not necessary to remove any of the variables from the models. However, as the chi-square tests from Section 4.5 show that the individual chronic conditions are associated with multimorbidity, we will include hypertension and gastrointestinal disease into our definition of multimorbidity and only control for multimorbidity in our multivariable analyses.

4.6 Objective 1

In Table 4.7, weighted descriptive analysis of cognition scores stratified by retirement status and sex are presented. Table 4.8 shows the unadjusted and adjusted association between shift work and performance on the cognitive tests for declarative memory and executive functioning. Full models including all covariates are presented in Table 1 and 2 in Appendix D. Results of the stratified analysis are presented in Table 4.9.

Female participants who were not or partly retired showed the highest scores for the immediate recall trial (Mean= 6.7, SD: 1.8), delayed recall trial (Mean= 5.2, SD: 2.1), and the interference condition (Mean= 14.0, SD: 3.2), compared to participants in the other groups. Not or partly retired males showed the highest score for the MAT, with an average score of 29.6 (SD: 8.9).

4.6.1 Declarative Memory

Immediate Recall Trial

The unadjusted model shows that average performance on the immediate recall trial was 0.20 points lower among people who engage in shift work (95% CI: -0.30 to -0.09), compared to those who do not engage in shift work. After controlling for sociodemographic characteristics, behavioural and lifestyle factors and chronic diseases and other health-related factors, the estimated decrease in average cognitive score for the immediate recall trial was 0.04 points lower among shift workers (95% CI: -0.14 to 0.06) relative to non-shift workers, an association that did not remain statistically significant. This finding suggests that the unadjusted association between shift work and performance on the immediate recall trial can be entirely explained by sociodemographic characteristics, behavioural and lifestyle factors and chronic diseases and other health-related factors.

Delayed Recall Trial

In the unadjusted model, average performance on the delayed recall trial was 0.20 points lower among shift workers (95% CI: -0.32 to -0.08), compared to non-shift workers. This association was attenuated and did not retain statistical significance after adjusting for sociodemographic characteristics, behavioural and lifestyle factors, and chronic diseases other health-related factors. Specifically, average score for the delayed recall trial is 0.05 points lower among those who engage in shift work (ß: 0.05; 95% CI: -0.16, to 0.06) relative to those that do not, holding all variables constant. These results suggest that the sociodemographic characteristics, behavioural and lifestyle factors and chronic diseases and other health-related factors can entirely explain the unadjusted association between shift work and performance on the delayed recall trial.

Stratified Analyses

The estimated effect of shift work was attenuated in all stratified analyses for the immediate and delayed recall trial when controlling for confounders in the analyses. The stratified analyses revealed that completely retired females performed the worst on the immediate recall trial, whereas not or partly retired males had the poorest performance on the delayed recall trial. These associations were not statistically significant.

4.6.2 Executive Functioning

MAT

The unadjusted model shows that average score for the MAT was 1.59 points lower among shift workers (95% CI: -2.08 to -1.10) compared to non-shift workers. In the fully adjusted model, the estimated decrease in average MAT score was 0.89 points lower among those with shift work schedules (95% CI: -1.36 to -0.42) relative to those with non-shift work schedules, holding all covariates constant. The addition of the covariates into the model attenuated the magnitude of the effect of shift work on average MAT score, but the association remained statistically significant. This finding suggests that the sociodemographic characteristics, behavioural and lifestyle factors and chronic diseases and other health-related factors partly explain the unadjusted association between shift work and performance on the MAT.

Interference Condition

The unadjusted analysis suggests that average time to complete the interference condition test was 0.78 seconds longer among those who engage in shift work (95% CI: 0.54 to 1.03), relative to those that do not. When adjusting for the confounding effects of sociodemographic characteristics, behavioural and lifestyle factors and chronic diseases and other health-related factors, the effect of shift work on the performance for the interference condition was attenuated and remained statistically significant. In particular, average completion time for the interference condition was 0.42 seconds longer among shift workers (95% CI: 0.21 to 0.63) compared to non-shift workers, holding all factors constant. These findings suggest that the unadjusted association between shift work and performance on the interference condition is partly explained by the sociodemographic characteristics, behavioural and lifestyle factors and chronic diseases and other health-related factors.

Stratified Analyses

For both the MAT and the interference condition, the point estimate for shift work in all stratified analyses was reduced when confounders were adjusted for in the regression models. Stratifying by sex and retirement status revealed that performance for executive functioning was the worst among completely retired males, followed by not or partly retired males. This association was significant for the MAT (completely retired males: ß= -1.31, 95% CI: -2.18 to -0.44; not or partly retired males: ß= -1.12, 95% CI: -1.94 to -0.27) and the interference condition (completely retired males: ß= 0.83, 95% CI: 0.29 to 1.37; not or partly retired males: ß= 0.47, 95% CI: 0.13 to 0.81). We did not observe any significant findings for females in any of the stratified analyses.

Table 4.7: Weighted descriptive analysis of cognition scores, stratified by retirement status and sex (N=13,238)

Characteristic	All (N= 13,238)	Completely Retired		Not or Partly Retired	
		Males (n= 3,351)	Females (n= 2,802)	Males (n= 4,071)	Females (n= 3,014)
	n	n	n	n	n
Immediate Recall Score (0 – 14)					
Mean (Standard Deviation)	6.0 (1.9)	5.0 (1.8)	6.0 (1.9)	6.0 (1.8)	6.7 (1.8)
Missing	450	141	95	122	92
Delayed Recall Score (0 – 14)					
Mean (Standard Deviation)	4.3 (2.2)	3.1 (1.9)	4.2 (2.1)	4.2 (2.0)	5.2 (2.1)
Missing	446	164	96	100	86
MAT Score (0 - 51)					
Mean (Standard Deviation)	27.7 (8.9)	25.8 (8.9)	24.9 (8.6)	29.6 (8.9)	28.1 (8.2)
Missing	658	211	147	183	117
Interference Condition Score (1-132 seconds)					
Mean (Standard Deviation)	15.5 (4.6)	18.1 (5.3)	17.1 (5.4)	14.6 (3.8)	14.0 (3.2)
Missing	151	62	22	47	20

Table 4.8: Unadjusted and adjusted association between shift work and performance on cognitive tests for declarative memory and executive functioning among CLSA participants

	Unadjusted Model			**Adjusted Model**		
	ß	**SE**	**95% CI**	**ß**	**SE**	**95% CI**
Immediate Recall Trial						
No Shift Work	R			R		
Shift Work	**-0.20**	**0.05**	**-0.30, -0.09**	-0.04	0.05	-0.14, 0.06
Delayed Recall Trial						
No Shift Work	R			R		
Shift Work	**-0.20**	**0.06**	**-0.32, -0.08**	-0.05	0.06	-0.16, 0.06
MAT						
No Shift Work	R			R		
Shift Work	**-1.59**	**0.25**	**-2.08, -1.10**	**-0.89**	**0.24**	**-1.36, -0.42**
Interference Condition						
No Shift Work	R			R		
Shift Work	**0.78**	**0.12**	**0.54, 1.03**	**0.42**	**0.11**	**0.21, 0.63**

Abbreviations: CI: confidence interval; R: reference; SE: standard error.
Significant results are bolded.
Note: Adjusted models were adjusted for sociodemographic factors, behavioural and lifestyle factors, and chronic diseases and other health-related factors.

Table 4.9: Multiple linear regression models for shift work and performance on cognitive tests, stratified by sex and retirement status

	Males		Females	
	Completely Retired (n=2984)	**Not or Partly Retired (n=3775)**	**Completely Retired (n=2576)**	**Not or Partly Retired (n=2817)**
Immediate Recall Trial				
Model 1 ß (95% CI)	**-0.20 (-0.37, -0.03)**	**-0.23 (-0.40, -0.06)**	-0.18 (-0.41, 0.05)	-0.08 (-0.29, 0.13)
Model 2 ß (95% CI)	-0.05 (-0.21, 0.11)	-0.07 (-0.24, 0.10)	-0.08 (-0.29, 0.13)	0.03 (-0.17, 0.25)
Delayed Recall Trial				
Model 1 ß (95% CI)	-0.13 (-0.32, 0.06)	**-0.25 (-0.44, -0.06)**	-0.15 (-0.41, 0.10)	-0.11 (-0.37, 0.15)
Model 2 ß (95% CI)	0.01 (-0.16, 0.19)	-0.11 (-0.30, 0.07)	-0.08 (-0.32, 0.15)	-0.02 (-0.27, 0.24)
MAT				
Model 1 ß (95% CI)	**-1.95 (-2.88, -1.02)**	**-2.17 (-3.01, -1.34)**	**-1.85 (-3.10, -0.59)**	-0.56 (-1.47, 0.35)
Model 2 ß (95% CI)	**-1.31 (-2.18, -0.44)**	**-1.12 (-1.94, -0.27)**	-1.07 (-2.21, 0.06)	-0.11 (-1.00, 0.77)
Interference Condition				
Model 1 ß (95% CI)	**1.27 (0.65, 1.89)**	**0.91 (0.56, 1.26)**	**0.72 (0.10, 1.34)**	0.27 (-0.11, 0.65)
Model 2 ß (95% CI)	**0.83 (0.29, 1.37)**	**0.47 (0.13, 0.81)**	0.31 (-0.24, 0.87)	0.08 (-0.27, 0.44)

Abbreviations: CI: confidence interval; SE: standard error.
Significant results are bolded.
Model 1: Unadjusted association between shift work and performance on cognitive tests.
Model 2: Adjusted association between shift work and performance on cognitive tests.

4.7 Objective 2

We assessed both the moderating and confounding effects of psychological distress on the relationship between shift work and performance on cognitive tests for declarative memory and executive functioning. Table 4.10 shows the relationship between shift work and performance on the cognitive tests with the inclusion of psychological distress as a confounder. Results for the interaction effect between psychological distress and shift work are shown in Table 4.11.

4.7.1 Declarative Memory

Immediate Recall Trial

The interaction term between psychological distress and shift work was not statistically significant (ß: 0.34; 95% CI: -0.06 to 0.73), thereby suggesting that the effect of shift work on performance for the immediate recall trial was not modified by psychological distress. When psychological distress was included as a confounder in the adjusted model, the effect estimate remained the same.

Delayed Recall Trial

We did not find evidence of effect modification by psychological distress on the relationship between shift work and performance on the delayed recall trial, as the product term between psychological distress and shift work was not statistically significant (ß: -0.20; 95% CI: -0.24 to 0.64). Inclusion of psychological distress as a confounder into the adjusted model also did not change the effect estimate for shift work.

4.7.2 Executive Functioning

MAT

The interaction effect between shift work and psychological distress was not statistically significant (ß: -0.31; 95% CI: -1.98 to 1.36), suggesting that the relationship between shift work and performance on the MAT was not moderated by psychological distress. Furthermore, controlling for psychological distress into the adjusted model did not change the estimated effect of shift work. This result indicates that psychological distress was not a confounder of the relationship between shift work and performance on the MAT.

Interference Condition

When psychological distress was included as an interaction term with shift work, the interaction effect was not statistically significant (ß: 0.32; 95% CI: -0.66 to 1.30). This finding suggests that the relationship between shift work and performance on the interference condition was not modified by psychological distress. Adjusting for the confounding effects of psychological distress in the adjusted model did not change the association between shift work and performance on the interference condition. This indicates that psychological distress does not confound this relationship.

Table 4.10: **Multiple linear regression models for shift work and performance on cognitive tests, adjusting for psychological distress and other potential confounders**

	Adjusted Model			Fully Adjusted Model		
	ß	**SE**	**95% CI**	**ß**	**SE**	**95% CI**
Immediate Recall Trial						
No Shift Work	R			R		
Shift Work	-0.04	0.05	-0.14, 0.06	-0.04	0.05	-0.14, 0.06
Delayed Recall Trial						
No Shift Work	R			R		
Shift Work	-0.05	0.06	-0.16, 0.06	-0.05	0.06	-0.17, 0.06
MAT						
No Shift Work	R			R		
Shift Work	**-0.89**	**0.24**	**-1.36, -0.42**	**-0.89**	**0.24**	**-1.36, -0.42**
Interference Condition						
No Shift Work	R			R		
Shift Work	**0.42**	**0.11**	**0.21, 0.63**	**0.43**	**0.11**	**0.22, 0.64**

Abbreviations: CI: confidence interval; R: reference; SE: standard error.
Significant results are bolded.
Adjusted models adjusted for sociodemographic factors, behavioural and lifestyle factors, and chronic diseases and other health-related factors.
Fully adjusted models adjusted for psychological distress and other confounders.

Table 4.11: **Interaction effect between psychological distress and shift work**

	ß	**SE**	**95% CI**
Immediate Recall Trial			
Shift Work x High Distress	0.34	0.20	-0.06, 0.73
Delayed Recall Trial			
Shift Work x High Distress	-0.20	0.22	-0.24, 0.64
MAT			
Shift Work x High Distress	-0.31	0.85	-1.98, 1.36
Interference Condition			
Shift Work x High Distress	0.32	0.50	-0.66, 1.30

Abbreviations: CI: confidence interval; SE: standard error.
Significant results are bolded.

4.8 Objective 3

We assessed both the moderating and confounding effects of sleep quality on the relationship between shift work and performance on cognitive tests for declarative and executive functioning. Table 4.12 shows the association between shift work and performance on the cognitive tests, while controlling for the confounding effects of sleep quality. Results for the interaction effect between sleep quality and shift work are shown in Table 4.13.

4.8.1 Declarative Memory

Immediate Recall Trial

The interaction effect between sleep quality and shift work was not statistically significant (ß: 0.20; 95% CI: -0.02 to 0.42). This suggests that the effect of shift work on performance for the immediate recall trial does not vary by sleep quality. When we assessed the confounding effect of sleep quality on this relationship, the inclusion of sleep quality into the adjusted model did not change the association between shift work and performance on the immediate recall trial. This result indicates that sleep quality is not a confounder of this relationship.

Delayed Recall Trial

When we included an interaction term between sleep quality and shift work into the adjusted model, the product term was not statistically significant (ß: 0.09; 95% CI: -0.16 to 0.35), thereby suggesting that sleep quality does not modify the relationship between shift work and performance on the delayed recall trial. Upon controlling for the confounding effects of sleep quality in the adjusted model, the estimated decrease in performance on the delayed recall trial among shift workers remained the same. As such, the findings indicate sleep quality does not confound the relationship between shift work and performance on the delayed recall trial.

4.8.2 Executive Functioning

MAT

The association between shift work and performance on the MAT was not found to vary by sleep quality as there was no evidence of an interaction effect between shift work and sleep quality (ß: 0.94; 95% CI: -0.15 to 2.03). The estimate for the effect of shift work on MAT performance when adjusting for the confounding effects of sleep quality were similar to the estimate of shift work in the adjusted model. This finding suggests that sleep quality does not confound the relationship between shift work and performance on the MAT.

Interference Condition

The analyses for effect modification show that the product term between sleep quality and shift work was not statistically significant (ß: -0.25; 95% CI: -0.75 to 0.25). This suggests that the effect of shift work on performance for the interference condition does not vary by sleep quality. Compared to the adjusted model, the estimated effect of shift work was similar when sleep quality was included into the model. This result indicates that sleep quality does not confound the relationship between shift work and performance on the interference condition.

Table 4.12: Multiple linear regression models for shift work and performance on cognitive tests adjusting for sleep quality and other potential confounders

	Adjusted Model			Fully Adjusted Model		
	ß	**SE**	**95% CI**	**ß**	**SE**	**95% CI**
Immediate Recall Trial						
No Shift Work	R			R		
Shift Work	-0.04	0.05	-0.14, 0.06	-0.04	0.05	-0.14, 0.06
Delayed Recall Trial						
No Shift Work	R			R		
Shift Work	-0.05	0.06	-0.16, 0.06	-0.05	0.06	-0.16, 0.06
MAT						
No Shift Work	R			R		
Shift Work	**-0.89**	**0.24**	**-1.36, -0.42**	**-0.89**	**0.24**	**-1.36, -0.42**
Interference Condition						
No Shift Work	R			R		
Shift Work	**0.42**	**0.11**	**0.21, 0.63**	**0.43**	**0.11**	**0.22, 0.64**

Abbreviations: CI: confidence interval; R: reference; SE: standard error.
Significant results are bolded.
Adjusted models adjusted for sociodemographic factors, behavioural and lifestyle factors, and chronic diseases and other health-related factors.
Fully adjusted models adjusted for sleep quality and other confounders.

Table 4.13: Interaction effect between sleep quality and shift work

	ß	**SE**	**95% CI**
Immediate Recall Trial			
Shift Work x Poor Sleep Quality	0.20	0.11	-0.02, 0.42
Delayed Recall Trial			
Shift Work x Poor Sleep Quality	0.09	0.13	-0.16, 0.35
MAT			
Shift Work x Poor Sleep Quality	0.94	0.56	-0.15, 2.03
Interference Condition			
Shift Work x Poor Sleep Quality	-0.25	0.26	-0.75, 0.25

Abbreviations: CI: confidence interval; SE: standard error.
Significant results are bolded.

4.9 Subgroup Analyses by Menopausal Status

Results of the subgroup analyses are presented in Table 4.14. For all the cognitive outcomes, the subgroup analysis by menopause status showed similar findings to the main analyses.

Table 4.14: Multiple linear regression models for shift work and performance on cognitive tests, by menopausal status

	Males (n=6759)	**Pre-Menopause (n=1052)**	**Post-Menopause (n=4341)**
Immediate Recall Trial			
Model 1 ß (95% CI)	**-0.23 (-0.37, -0.10)**	-0.18 (-0.50, 0.15)	-0.09 (-0.27, 0.10)
Model 2 ß (95% CI)	-0.07 (-0.19, 0.06)	-0.06 (-0.38, 0.26)	0.03 (-0.13, 0.20)
Delayed Recall Trial			
Model 1 ß (95% CI)	**-0.23 (-0.37, -0.08)**	**-0.19 (-0.61, 0.23)**	**-0.10 (-0.30, 0.10)**
Model 2 ß (95% CI)	-0.07 (-0.20, 0.07)	-0.11 (-0.52, 0.30)	-0.00 (-0.19, 0.18)
MAT			
Model 1 ß (95% CI)	**-2.16 (-2.81, -1.51)**	-0.84 (-2.20, 0.52)	**-1.14 (-2.03, -0.25)**
Model 2 ß (95% CI)	**-1.12 (-1.74, -0.49)**	-0.34 (-1.67, 0.98)	-0.58 (-1.41, 0.26)
Interference Condition			
Model 1 ß (95% CI)	**1.08 (0.75, 1.41)**	0.44 (-0.13, 1.00)	**0.45 (0.02, 0.87)**
Model 2 ß (95% CI)	**0.59 (0.30, 0.89)**	0.31 (-0.22, 0.84)	0.11 (-0.25, 0.47)

Abbreviations: CI: confidence interval; SE: standard error.
Note: Significant results are bolded.
Model 1: Unadjusted association between shift work and performance on cognitive tests.
Model 2: Adjusted association between shift work and performance on cognitive tests.

4.10 Sensitivity Analyses

4.10.1 Sensitivity Analysis for Second Shift Work Definition

The second shift work definition classified participants as shift workers if their main job (or last job before retirement) but not their longest job had a shift work schedule, or if their main job (or last job before retirement) and longest job had a shift work schedule. For objectives 1, 2 and 3, results from the sensitivity analysis which used the second definition for shift work showed that the estimated effect of shift work was similar for performances on the immediate recall trial and the delayed recall trial. For objective 1, although the magnitude of the effect of shift work was larger and smaller, respectively for performances on the MAT (unadjusted: ß= -1.59, 95% CI: -2.08 to -1.10; adjusted: ß= -1.13, 95% CI: -1.62 to -0.65) and the interference condition (unadjusted: ß= 0.72, 95% CI: 0.48 to 0.96; adjusted: ß= 0.35, 95% CI: 0.14 to 0.56), the overall conclusions were consistent with the main analysis.

In contrast to the main analysis, the sensitivity analysis revealed a significant interaction effect between poor sleep quality and shift work for performances on the MAT (ß= 1.46; 95% CI: 0.33 to 2.59) and the interference condition (ß= -0.57; 95% CI: -1.01 to -0.12). All other results for objectives 2 and 3 were consistent with the main analyses.

4.10.2 Sensitivity Analysis for Psychological Distress Measure

We performed a sensitivity analysis comparing the main results from objective 2, which used a cut-off score of 20 for psychological distress, to results which used a cut-off score of 15. For all four cognitive outcomes, the estimated effect of shift work was similar and consistent to the main analyses. Furthermore, the results of the sensitivity analysis did not find any significant interaction or confounding effects by psychological distress in any of the four outcomes, which is consistent with the main analyses.

4.10.3 Sensitivity Analysis for Second Shift Work Definition and Psychological Distress Measure

We conducted another sensitivity analysis, using both the second definition for shift work and the psychological distress measure with a cut-off score of 15. The estimated effect of shift work was similar to the main analyses for the immediate and delayed recall trials, whereas the estimates for shift work was larger and smaller, respectively for performances on the MAT (ß= -1.12; 95% CI: -1.61 to -0.64) and the interference condition (adjusted: ß= 0.35; 95% CI: 0.14 to 0.54). Overall, the results for all four outcomes were consistent with the main analysis, such that no evidence of interaction effect was found and controlling for psychological distress did not change the effect of shift work.

4.10.4 Sensitivity Analysis for Complete Case Analysis

Results of the sensitivity analysis for objectives 1, 2 and 3 are shown in Tables 1 - 4 in Appendix D. For all the objectives, results of the sensitivity analysis which had participants with complete data were consistent with the main analysis.

Chapter 5

5 Discussion

In this last chapter, Section 5.1 discusses and interprets the key findings of our study in the context of existing literature. The strengths and limitations of our study are outlined in Sections 5.2 and 5.3, respectively. The implications and future directions are discussed in Section 5.4 and the overall conclusion in Section 5.5.

5.1 Summary of Key Findings

5.1.1 Objective 1

Studies investigating the relationship between shift work and cognitive functioning have used a mix of objective and subjective measures of cognition and have commonly measured psychomotor speed. We sought to examine the association between shift work and cognitive performance using objective measures for memory and executive functioning, cognitive domains which are known to affect daily activities.[303] Our results suggest that shift workers showed poorer cognitive scores on tests for declarative memory and executive functioning compared to non-shift workers. After adjusting for potential confounding factors, this relationship was only significant for performances on tests for executive functioning, namely the MAT and the interference condition. Our results align with prior studies which have shown poor performance on tests for executive functioning among shift workers relative to non-shift workers.[22,64,294,356] In contrast to previous studies,[45,50,64,291,297,301] our results did not find a significant association between shift work and poor performance on declarative memory, after controlling for potential confounders. Given that cognitive processes are regulated by the endogenous circadian clock,[45,357] misaligned circadian rhythm is a common mechanism used to explain the relationship between shift work and cognitive performance. In particular, as shift work schedules take place outside regular daytime working hours, working against the natural sleep-wake cycle may disrupt the circadian rhythm, resulting in impaired cognition.[45,357] However, research suggests that shift work may not impact all cognitive domains equally.[89,358,359] For example, findings from a randomized cross-over trial, which simulated shift work conditions to assess the effects of circadian misalignment on cognitive functioning found a steady performance on declarative memory during conditions of circadian rhythm alignment and misalignment, thereby suggesting that declarative memory performance may not be largely altered by circadian misalignment as opposed to other cognitive domains such as processing speed and sustained attention.[358]

We also investigated whether there were differences by sex and retirement status in this relationship. No significant findings were found for any of the stratified groups for declarative memory performance. For executive functioning performance, we found that completely retired males who engaged in shift work showed significantly poorer performance than not or partly retired males engaging in shift work, whereas no significant findings were observed for females in any of the stratified analyses. These findings suggest that the effects of shift work on cognition may be persistent as they are not reversed among those in retirement. Given that females report more sleep problems than men,[76] evidence from the literature suggest that female shift workers are more vulnerable to the adverse consequences of shift work.[360] In our sample, more females reported poorer sleep quality than males. Interestingly, we found poorer cognitive performance among male shift workers. This finding may be due to females in our sample having higher cognitive scores in general. Male shift workers who were completely retired, as well as those not or partly retired showed poorer cognitive performance for executive functioning. This is consistent with Marquie and colleagues,[297] who found lower cognitive scores in employed shift workers and retired shift workers who have left the shift system within the past five years. However, in contrast to Marquie and colleagues,[297] we were unable to ascertain information pertaining to the length of time since leaving shift work among our retired sample.

Overall, differences by sex and retirement in this relationship have not been widely studied. Most studies have looked at gender differences rather than sex differences, with one study showing poorer cognitive performance among male shift workers[291] and another study showing no differences in cognitive functioning between male and female shift workers.[45] The study by Bokenberger and colleagues[47] assessed changes in cognitive functioning among shift workers before and after the age of retirement and did not find evidence of an association. As such, the findings of this thesis can help expand the current literature regarding differences in sex and retirement status on shift work and decline in cognitive functioning.

5.1.2 Objective 2

For this thesis, we explored whether the level of psychological distress moderated the relationship between shift work and cognitive performance. Results from our main analysis did not find any significant moderating or confounding effects by psychological distress on the relationship between shift work and cognitive performance. These findings suggest that the effect of shift work on cognitive functioning was the same regardless of the level of psychological distress. Engaging in shift work may elicit stress and lead to psychological distress.[29–31] Consequently, results from a meta-analysis found that shift workers were more likely to experience psychological distress than non-shift workers.[28] People who are more susceptible to psychological distress may experience greater rates of cognitive decline compared to those less prone.[35,36] Furthermore, psychological distress may be present in people with MCI and increase the risk of dementia progression.[361] To the best of our knowledge, no other study has examined potential effect modification by psychological distress on the relationship between shift work and cognitive performance. Future studies are warranted to further explore this relationship and confirm this finding.

5.1.3 Objective 3

Night shifts and rotating shift schedules have been found to be associated with sleep loss,[362] which negatively impacts the quality of sleep.[76,363] Sleep disturbances can interact with work environmental conditions, such as shift work, to cause human errors, work accidents and injuries.[364] Prospective cohort studies have reported lower cognitive scores among people with poor sleep quality.[365–367] We wanted to investigate whether the relationship between shift work and cognitive performance varied by sleep quality. Our main analysis did not find evidence for any moderating or confounding effects by sleep quality on the relationship between shift work and cognitive performance. Interestingly, results from our sensitivity analysis, which used a different definition for shift work, showed significant moderating effects by sleep quality on the relationship between shift work and performance on both tests for executive functioning. Both definitions for shift work classified participants as shift workers if both their main job (or last job before retirement) and longest job had a shift work schedule. Our finding may be explained by the second definition focusing more on current or former-recent shift workers, as those whose main job (or last job before retirement) had a shift work schedule, but not their longest job, were also classified as shift workers. Sleep quality as a moderator is consistent with experimental studies which have found that sleep behaviours, including sleep quality can impact cognitive performance among shift workers.[63,70,299,301] For example, results from the study by Mawdsley and colleagues[301] found a significant interaction effect between sleep quality and shift work on cognitive performance. Castro and Almondes[63] observed that among physicians working a 12-hour work schedule, those who had good sleep quality performed better on cognitive tests.

5.1.4 Differences by Menopausal Status

We performed subgroup analyses by menopausal status to further elucidate the relationship between shift work and cognitive performance. Although our subgroup analyses were consistent with the main analyses, we did not find any significant results for pre-menopausal and post-menopausal women on this relationship. A systematic review and meta-analysis found that those in menopausal transition (perimenopause), as well as those in the post-menopausal stage, show lower performance on cognitive tests for memory compared to women in the pre-menopausal stage.[233] It is likely that some female participants included in the pre-menopause group for our analyses were in menopausal transition. However, we had limited information to distinguish between those in the pre-menopausal stage and perimenopausal stage. Future studies could explore differences by menopausal status on the relationship between shift work and cognitive performance by taking into account the different stages of menopause to further clarify this relationship.

5.2 Strengths

There are several strengths to our study. First, we assessed two domains of cognition known to affect day-to-day activities,[303] using multiple objective neuropsychological measures. Using more than one neuropsychological test to assess each domain allowed us to assess a wider range of skills known to be affected by executive functioning and declarative memory.[328] Although we did not control for the individual chronic conditions in the analyses, we did control for multimorbidity using a public health definition that is appropriate for a community-wide sample, which captured more chronic conditions, in addition to those associated with shift work and cognitive decline. Participants included in the Comprehensive cohort are generally of higher socioeconomic status.[316] However, adding sampling weights to our analyses allowed us to make our findings more generalizable to the Canadian population. Our measure of shift work was derived by taking into account the work schedules of a participant's main and longest job. If the participant was retired, their longest job and job before retirement were used. This composite measure of shift work allowed us to better reflect the duration of exposure to shift work schedules. We also derived an alternative measure of shift work and a second measure for psychological distress. By performing sensitivity analyses we were able to assess the robustness of our findings. Furthermore, by exploring differences in sex and retirement status, as well as menopause status, our study is able to broaden the literature on shift work and cognitive performance.

5.3 Limitations

Our study also had several limitations. We were unable to adjust for the confounding effects of metabolic syndrome, as we did not have access to lab reports from the CLSA. As such, residual confounding by metabolic syndrome may be present in our findings. We also did not examine the occupation type of our study participants, which may impact the external validity of our results. Occupation type was measured using an open-response survey question and was recorded verbatim. To our knowledge, no efficient methods have been identified to categorize these data, and given the large sample size, manual methods may be unfeasible and subject to error. We used a binary measure of shift work, commonly used by previous studies, that grouped the various types of shift work schedules into one category of shift work. Due to a limited number of observations, we were unable to separate the effects of the different types of shift work schedules on cognition. Bokenberger and colleagues[47] suggest that accounting for differences in shift work schedules may not be important. However, results from a prospective cohort study which assessed the relationship between the type of shift work and risk of cognitive decline found that permanent night shift work, but not other types of shift work, were associated with an increased risk of dementia.[368] Another limitation is that our definition of shift work combined a participant's main (or last job before retirement) and longest job. Discordance in work schedule between these jobs may have resulted in misclassification of our shift work variable, which may underestimate the effect of shift work in this study.[297] As our measure of sleep quality was self-reported, the results of our study may be subject to differential misclassification. In particular, participants may underestimate or overestimate their sleep quality, which may lead to estimates being closer or further away from the null. Our study had a cross-sectional design, which precluded us from inferring temporality and directionality on the relationship between shift work and decline in cognitive functioning, with the possibility of reverse causation. Furthermore, our measure of menopause status was limited to only two groups (pre-menopause and post-menopause), thereby resulting in an inability to account for the other stages of menopause.

Due to the lack of follow-up studies conducted for the CLSA, we did not have data to compare non-respondents to respondents and as such, we were limited in our ability to assess the mechanism of missingness for the data. As such, our results may be biased if the data is MNAR. Some authors have proposed that the MAR assumption may be reasonable if a large number of predictor variables are included in the analysis,[347,352] whereas others have suggested that multiple imputation may be still be performed when data are MNAR.[347,369] Results of our sensitivity analyses comparing our multiply imputed data set to a complete data set excluding missing observations demonstrates the robustness of our findings as our main results were consistent in both data sets.

5.4 Implications and Future Directions

As the demand for a 24/7 economy continues, the results of this study may have important occupational health and safety implications that can be used to inform employers, workplace policy health and safety committees, as well as potential and current employees. The finding that engaging in shift work is negatively associated with executive functioning performance supports the potential detrimental effect of shift work on cognitive functioning. Our findings, and the findings of other studies, can help employers and health and safety policy committees to better design shift work schedules that are less disruptive to the circadian rhythm.[76] Although our main analysis did not find significant moderating effects by psychological distress or sleep quality, employers and health and policy safety committees should still create workplace environments that will help people cope with shift schedules.[76] This includes promoting strategies to help employees cope with stress, as well as developing workplace interventions aimed at promoting healthy sleep habits and mental wellbeing. The finding that completely retired males who engaged in shift work, as well as not or partly retired males engaging in shift work showed lower cognitive scores for executive functioning than females in either groups, can help inform potential and current employees about potential risks involved in working in the shift system and consider the impact it may have on daily activities which rely on sound cognitive functioning.[297]

Future studies using a prospective cohort design are needed to help assess the causal effect of shift work on cognitive functioning. Future research should continue to look for differences in sex and retirement status on this relationship, as well as the potential impact of psychological distress. Differences by menopause status including all stages of menopause and the type of shift work schedule should be explored to further elucidate the relationship between shift work and cognitive performance. Finally, occupation type should be considered to ensure generalizability of findings.

5.5 Conclusion

The use of shift work schedules will continue to sustain the continuous operation of goods and services. Our study found evidence of an association between shift work and cognitive performance, particularly in the domain of executive functioning, but not for declarative memory. Males showed the poorest performance on executive functioning tests, with the worst performance from completely retired males who engaged in shift work followed by not or partly retired males. We did not find evidence of a moderating effect by psychological distress or sleep quality on this relationship. Findings of this study contribute to the literature on shift work and cognitive performance, especially in the Canadian context. Future research using a prospective cohort design is warranted.

References

1. Shields M. Shift work and health. *Health Rep*. 2002;13(4):11-33.

2. Williams C. Work-life balance of shift workers. *Perspectives*. 2008;9(8):5-16.

3. Almondes K, Araujo J. The impact of different shift work schedules on the levels of anxiety and stress in workers in a petrochemicals company. *Estudos De Psicologia (campinas)*. 2009;26. doi:10.1590/S0103-166X2009000100002

4. Shariat A, Bahri Mohd Tamrin Sh, Daneshjoo A, Sadeghi H. The Adverse Health Effects of Shift Work in Relation to Risk of Illness/Disease: A Review. *Acta Medica Bulgarica*. 2015;42(1):63-72. doi:10.1515/amb-2015-0009

5. Nea FM, Kearney J, Livingstone MBE, Pourshahidi LK, Corish CA. Dietary and lifestyle habits and the associated health risks in shift workers. *Nutr Res Rev*. 2015;28(2):143-166. doi:10.1017/S095442241500013X

6. Oeppen J, Vaupel JW. Broken Limits to Life Expectancy. *Science*. 2002;296(5570):1029. doi:10.1126/science.1069675

7. Government of Canada. Government of Canada- Actions for Seniors Report. Government of Canada. Published 2014. Accessed June 17, 2020. https://www.canada.ca/en/employment-social-development/programs/seniors-action-report.html

8. Wu C-R, Chen P-Y, Hsieh S-H, et al. Sleep Mediates the Relationship Between Depression and Cognitive Impairment in Older Men. *Am J Mens Health*. 2019;13(1):155798831982576. doi:10.1177/1557988319825765

9. Naqvi R, Liberman D, Rosenberg J, Alston J, Straus S. Preventing cognitive decline in healthy older adults. *CMAJ*. 2013;185(10):881-885. doi:10.1503/cmaj.121448

10. WHO, Alzheimer’s Disease International, eds. *Dementia: A Public Health Priority*. World Health Organization; 2012.

11. Centers For Disease Control and Prevention. Cognitive Impairment: A Call for Action, Now! Accessed May 25, 2020. https://www.cdc.gov/aging/pdf/cognitive_impairment/cogimp_poilicy_final.pdf

12. Kiely KM. Cognitive Function. In: Michalos AC, ed. *Encyclopedia of Quality of Life and Well-Being Research*. Springer Netherlands; 2014:974-978. doi:10.1007/978-94-007-0753-5_426

13. Morley JE, Morris JC, Berg-Weger M, et al. Brain Health: The Importance of Recognizing Cognitive Impairment: An IAGG Consensus Conference. *J Am Med Dir Assoc*. 2015;16(9):731-739. doi:10.1016/j.jamda.2015.06.017

14. Hsiung G-Y, Donald A, Grand J, et al. Outcomes of cognitively impaired not demented at 2 years in the Canadian Cohort Study of Cognitive Impairment and Related Dementias. *Dement Geriatr Cogn Disord*. 2006;22(5-6):413-420. doi:doi:10.1159/000095751

15. Fillit H, Butler R, O'Connell A, et al. Achieving and maintaining cognitive vitality with aging. *Mayo Clin Proc*. 2002;77(7):681-696. doi:doi:10.4065/77.7.681

16. Hughes T, Ganguli M. Modifiable Midlife Risk Factors for Late-Life Cognitive Impairment and Dementia. *CPSR*. 2009;5(2):73-92. doi:10.2174/157340009788167347

17. Petersen RC, Doody R, Kurz A, et al. Current Concepts in Mild Cognitive Impairment. *Arch Neurol*. 2001;58(12):1985-1992. doi:10.1001/archneur.58.12.1985

18. Olivera-Pueyo J, Pelegrin-Valero C. Dietary supplements for cognitive impairment. *Actas Esp Psiquiatr*. 2017;45(Suppl. 1):37-47.

19. Andrade C, Radhakrishnan R. The prevention and treatment of cognitive decline and dementia: An overview of recent research on experimental treatments. *Indian J Psychiatry*. 2009;51(1):12-25. doi:10.4103/0019-5545.44900

20. Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *Lancet*. 2020;396(10248):413-446. doi:10.1016/S0140-6736(20)30367-6

21. Harada CN, Natelson Love MC, Triebel KL. Normal Cognitive Aging. *Clin Geriatr Med*. 2013;29(4):737-752. doi:10.1016/j.cger.2013.07.002

22. Titova OE, Lindberg E, Elmstahl S, Lind L, Schioth HB, Benedict C. Association between shift work history and performance on the trail making test in middle-aged and elderly humans: the EpiHealth study. *Neurobiol Aging*. 2016;45(nx5, 8100437):23-29. doi:10.1016/j.neurobiolaging.2016.05.007

23. Dall'Ora C, Ball J, Recio-Saucedo A, Griffiths P. Characteristics of shift work and their impact on employee performance and wellbeing: A literature review. *Int J Nurs Stud*. 2016;57:12-27. doi:10.1016/j.ijnurstu.2016.01.007

24. Whiteford HA, Degenhardt L, Rehm J, et al. Global Burden of Disease Attributable to Mental and Substance Use Disorders: Findings From the Global Burden of Disease Study 2010. *Lancet*. 2013;382(9904):1575-1586. doi:doi:10.1016/S0140-6736(13)61611-6

25. Lim K, Jacobs P, Ohinmaa A, Schopflocher, D, Dewa C. A new population-based measure of the burden of mental illness in Canada. *Chronic Dis Can*. 2008;28:92-98.

26. Chesney E, Goodwin GM, Fazel S. Risks of All-Cause and Suicide Mortality in Mental Disorders: A Meta-Review. *World Psychiatry*. 2014;13(2):153-160. doi:doi: 10.1002/wps.20128.

27. Mental Illness and Addiction: Facts and Statistics. The Center of Addition and Mental Health (CAMH). Accessed May 30, 2020. https://www.camh.ca/en/driving-change/the-crisis-is-real/mental-health-statistics

28. Zhao Y, Richardson A, Poyser C, Butterworth P, Strazdins L, Leach LS. Shift work and mental health: a systematic review and meta-analysis. *Int Arch Occup Environ Health*. 2019;92(6):763-793. doi:10.1007/s00420-019-01434-3

29. Drapeau A, Marchand A, Beaulieu-Prévost D. Epidemiology of Psychological Distress. In: *Mental Illnesses-Understanding, Prediction and Control*. L'Abate L (Ed.). InTech; 2012.

30. Davison KM, Lung Y, Lin S (Lamson), Tong H, Kobayashi KM, Fuller-Thomson E. Psychological distress in older adults linked to immigrant status, dietary intake, and physical health conditions in the Canadian Longitudinal Study on Aging (CLSA). *J Affect Disord*. 2020;265:526-537. doi:10.1016/j.jad.2020.01.024

31. Lopes CS, Araya R, Werneck GL, Chor D, Faerstein E. Job strain and other work conditions: relationships with psychological distress among civil servants in Rio de Janeiro, Brazil. *Soc Psychiat Epidemiol*. 2010;45(3):345-354. doi:10.1007/s00127-009-0066-9

32. Karasek RA. Job Demands, Job Decision Latitude, and Mental Strain: Implications for Job Redesign. *Adm Sci Q*. 1979;24(2):285-308. doi:10.2307/2392498

33. Horwitz AV. Distinguishing distress from disorder as psychological outcomes of stressful social arrangements. *Health*. 2007;11(3):273-289.

34. Ridner S. Psychological distress: concept analysis. *J Adv Nurs*. 2004;45(5):536-545. doi:doi:10.1046/j.1365-2648.2003.02938.x

35. Wilson RS, Bennett DA, Mendes de Leon CF, Bienias JL, Morris MC, Evans DA. Distress proneness and cognitive decline in a population of older persons. *Psychoneuroendocrinology*. 2005;30(1):11-17. doi:10.1016/j.psyneuen.2004.04.005

36. Wilson RS, Evans DA, Bienias JL, Bennett DA. Proneness to psychological distress is associated with risk of Alzheimer's disease. *Neurology*. 2003;61(11):1479-1485. doi:10.1212/01.wnl.0000096167.56734.59

37. Wilson R, Bennett D. How Does Psychosocial Behavior Contribute to Cognitive Health in Old Age? *Brain Sci*. 2017;7(12):56. doi:10.3390/brainsci7060056

38. Andel R, Crowe M, Hahn E, et al. Work-related Stress May Increase the Risk of Vascular Dementia. *J Am Geriatr Soc*. 2012;60(1):60-67. doi:doi:10.1111/j.1532-5415.2011.03777.x

39. Crowe M, Andel R, Pedersen NL, Fratiglioni L, Gatz M. Personality and risk of cognitive impairment 25 years later. *Psychol Aging*. 2006;21(3):573-580. doi:10.1037/0882-7974.21.3.573

40. Sutin AR, Stephan Y, Terracciano A. Psychological Distress, Self-Beliefs, and Risk of Cognitive Impairment and Dementia. *JAD*. 2018;65(3):1041-1050. doi:10.3233/JAD-180119

41. Oyola MG, Handa RJ. Hypothalamic–pituitary–adrenal and hypothalamic–pituitary–gonadal axes: sex differences in regulation of stress responsivity. *Stress*. 2017;20(5):476-494. doi:10.1080/10253890.2017.1369523

42. Presser HB. *Working in a 24/7 Economy: Challenges for American Families.* Russell Sage Foundation; 2003:xiii, 267.

43. Knutsson A. Methodological Aspects of Shift-Work Research. *Chronobiol Int*. 2004;21(6):1037-1047. doi:10.1081/CBI-200038525

44. Folkard S, Robertson KA, Spencer MB. A Fatigue/Risk Index to assess work schedules. *Somnologie*. 2007;11(3):177-185. doi:10.1007/s11818-007-0308-6

45. Wong IS, Smith PM, Ibrahim S, Mustard CA, Gignac MAM. Mediating pathways and gender differences between shift work and subjective cognitive function. *Occup Environ Med*. 2016;73(11):753-760. doi:10.1136/oemed-2016-103774

46. Anund A, Fors C, Ihlström J, Kecklund G. An on-road study of sleepiness in split shifts among city bus drivers. *Accid Anal Prev*. 2018;114:71-76. doi:10.1016/j.aap.2017.05.005

47. Bokenberger K, Strom P, Dahl Aslan AK, Akerstedt T, Pedersen NL. Shift work and cognitive aging: a longitudinal study. *Scand J Work Environ Health*. 2017;43(5):485-493. doi:10.5271/sjweh.3638

48. Fenwick R, Tausig M. The health and family- Social consequences of shift work and schedule control: 1977 and 1997. *Fighting for Time: Shifting Boundaries of Work and Social Life*. Published online January 1, 2006:77-110.

49. Pati AK, Chandrawanshi A, Reinberg A. Shift work: consequence and management. *Current Science*. 2002;81:32-47.

50. Ozdemir PG, Selvi Y, Ozkol H, et al. The influence of shift work on cognitive functions and oxidative stress. *Psychiatry Res*. 2013;210(3):1219-1225. doi:10.1016/j.psychres.2013.09.022

51. Workers Health & Safety Centre. Shift Work: disrupting worker health and lives. *Hazard Resource Lines*. Published online May 30, 2020. https://www.whsc.on.ca/Files/Resources/Hazard-Resource-Lines/RL_Shift-Work_V3_web.aspx

52. Rydz E, Hall A, Peters C. Prevalence and Recent Trends in Exposure to Night Shiftwork in Canada. *Ann Work Expo Health*. 2020;64(3):270-281. doi:10.1093/annweh/wxaa001

53. Strazdins L, Korda RJ, Lim LL-Y, Broom DH, D'Souza RM. Around-the-clock: parent work schedules and children's well-being in a 24-h economy. *Soc Sci Med*. 2004;59(7):1517-1527. doi:10.1016/j.socscimed.2004.01.022

54. Messenger JC, Lee S, McCann D. *Working Time Around the World*. 0 ed. Routledge; 2007. doi:10.4324/9780203945216

55. Crompton R, Lyonette C. Work-Life 'Balance' in Europe. *Acta Sociologica*. 2006;49(4):379-393. doi:10.1177/0001699306071680

56. Bambra CL, Whitehead MM, Sowden AJ, Akers J, Petticrew MP. Shifting Schedules. *Am J Prev Med*. 2008;34(5):427-434.e30. doi:10.1016/j.amepre.2007.12.023

57. Chandra V. Work–life balance: eastern and western perspectives. *Hum Resour Manag J*. 2012;23(5):1040-1056. doi:10.1080/09585192.2012.651339

58. Beckers DG, Kompier MA, Kecklund G, Härmä M. Worktime control: theoretical conceptualization, current empirical knowledge, and research agenda. *Scand J Work Environ Health*. 2012;38(4):291-297. doi:10.5271/sjweh.3308

59. Bambra C, Whitehead M, Sowden A, Akers J, Petticrew M. "A hard day's night?" The effects of Compressed Working Week interventions on the health and work-life balance of shift workers: a systematic review. *J Epidemiol Community Health*. 2008;62(9):764-777. doi:10.1136/jech.2007.067249

60. Moen P, Kelly E, Huang Q. Work, family and life-course fit. *J Vocat Behav*. 2008;73(3):414-425. doi:10.1016/j.jvb.2008.08.002

61. Rheaume A, Mullen J. The impact of long work hours and shift work on cognitive errors in nurses. *J Nurs Manag*. 2018;26(1):26-32. doi:10.1111/jonm.12513

62. Geiger-Brown J, Rogers VE, Trinkoff AM, Kane RL, Bausell RB, Scharf SM. Sleep, sleepiness, fatigue, and performance of 12-hour-shift nurses. *Chronobiol Int*. 2012;29(2):211-219. doi:10.3109/07420528.2011.645752

63. Castro E de AS, de Almondes KM. Sleep pattern and decision-making in physicians from mobile emergency care service with 12-h work schedules. *Int J Neurosci*. 2018;128(6):530-539. doi:10.1080/00207454.2017.1400970

64. Machi MS, Staum M, Callaway CW, et al. The relationship between shift work, sleep, and cognition in career emergency physicians. *Acad Emerg Med*. 2012;19(1):85-91. doi:10.1111/j.1553-2712.2011.01254.x

65. Karanovic N, Carev M, Kardum G, et al. The impact of a single 24 h working day on cognitive and psychomotor performance in staff anaesthesiologists. *Eur J Anaesthesiol*. 2009;26(10):825-832. doi:10.1097/EJA.0b013e32832bb6e4

66. Smith-Coggins R, Rosekind M, Hurd S, Buccino K. Relationship of day versus night sleep to physician performance and mood. *Ann Emerg Med*. 1994;24(5):928-934. doi:doi:10.1016/s0196-0644(94)70209-8

67. Ernst F, Rauchenzauner M, Zoller H, et al. Effects of 24 h working on-call on psychoneuroendocrine and oculomotor function: a randomized cross-over trial. *Psychoneuroendocrinology*. 2014;47(7612148, qgc):221-231. doi:10.1016/j.psyneuen.2014.05.019

68. Akerstedt T. Altered sleep/wake patterns and mental performance. *Physiol Behav*. 2007;90(2-3):209-218. doi:10.1016/j.physbeh.2006.09.007

69. Pattani R, Wu PE, Dhalla IA. Resident duty hours in Canada: past, present and future. *CMAJ*. 2014;186(10):761-765. doi:10.1503/cmaj.131053

70. Osterode W, Schranz S, Jordakieva G. Effects of night shift on the cognitive load of physicians and urinary steroid hormone profiles - a randomized crossover trial. *Chronobiol Int*. 2018;35(7):946-958. doi:10.1080/07420528.2018.1443942

71. Brugère D, Barrit J, Butat C, Cosset M, Volkoff S. Shiftwork, Age, and Health: An Epidemiologic Investigation. *Int J Occup Environ Health*. 1997;3(Supplement 2):S15-S19.

72. Costa G. The problem: shiftwork. *Chronobiol Int*. 1997;14(2):89-98. doi:10.3109/07420529709001147

73. Härmä M. Ageing, physical fitness and shiftwork tolerance. *Appl Ergon*. 1996;27(1):25-29. doi:10.1016/0003-6870(95)00046-1

74. Glazner LK. Shiftwork: its effect on workers. *AAOHN J*. 1991;39(9):416-421.

75. Härmä M. Individual differences in tolerance to shiftwork: a review. *Ergonomics*. 1993;36(1-3):101-109. doi:10.1080/00140139308967860

76. Harrington JM. Health effects of shift work and extended hours of work. *Occup Environ Med*. 2001;58(1):68-72. doi:10.1136/oem.58.1.68

77. Colligan MJ, Rosa RR. Shiftwork effects on social and family life. *Occup Med*. 1990;5(2):315-322.

78. Tai S-Y, Lin P-C, Chen Y-M, et al. Effects of Marital Status and Shift Work on Family Function among Registered Nurses. *Ind Health*. 2014;52(4):296-303. doi:10.2486/indhealth.2014-0009

79. Golla AM, Vernon V. *Late for Dinner Again: Do Work Schedules and Home Schedules Clash?*; 2006. http://www.sfi.dk/graphics/SFI/Pdf/IATUR2006/golla%20- %20paper.pdf

80. Presser HB. Job, family, and gender: determinants of nonstandard work schedules among employed Americans in 1991. *Demography*. 1995;32(4):577-598.

81. McMenamin TM. A time to work: recent trends in shift work and flexible schedules. *Mon Labor Rev*. Published online 2007:13.

82. Government of Canada SC. *The Canadian Immigrant Labour Market: Recent Trends from 2006 to 2017.*; 2018. Accessed December 21, 2020. https://www150.statcan.gc.ca/n1/pub/71-606-x/71-606-x2018001-eng.htm

83. Ronda Pérez E, Benavides FG, Levecque K, Love JG, Felt E, Van Rossem R. Differences in working conditions and employment arrangements among migrant and non-migrant workers in Europe. *Ethn Health*. 2012;17(6):563-577. doi:10.1080/13557858.2012.730606

84. Smith PM, Mustard CA. The unequal distribution of occupational health and safety risks among immigrants to Canada compared to Canadian-born labour market participants: 1993–2005. *Safety Science*. 2010;48(10):1296-1303. doi:10.1016/j.ssci.2010.03.020

85. Sterud T, Tynes T, Mehlum IS, et al. A systematic review of working conditions and occupational health among immigrants in Europe and Canada. *BMC Public Health*. 2018;18. doi:10.1186/s12889-018-5703-3

86. Martel L, Chagnon J. *Canada's Rural Population since 1851 Population and Dwelling Counts, 2011 Census*. Statistics Canada; 1851:5. Accessed December 26, 2020. https://www12.statcan.gc.ca/census-recensement/2011/as-sa/98-310-x/98-310-x2011003_2-eng.pdf

87. Bollman RD, Reimer W. Demographics, employment, income, and networks: differential characteristics of rural populations. *J Agromedicine*. 2009;14(2):132-141. doi:10.1080/10599240902845120

88. Saenz R. Rural workers more likely to work nontraditional shifts. *The Carsey School of Public Policy at the Scholars' Repository*. Published online June 24, 2009. doi:https://dx.doi.org/10.34051/p/2020.74

89. Cheng P, Drake CL. Psychological Impact of Shift Work. *Curr Sleep Med Rep*. 2018;4(2):104-109.

90. Jensen HI, Larsen JW, Thomsen TD. The impact of shift work on intensive care nurses' lives outside work: A cross-sectional study. *J Clin Nurs*. 2018;27(3-4):e703-e709. doi:10.1111/jocn.14197

91. Hawthorne G. Perceived social isolation in a community sample: its prevalence and correlates with aspects of peoples' lives. *Soc Psychiatry Psychiatr Epidemiol*. 2008;43(2):140-150. doi:10.1007/s00127-007-0279-8

92. Gumenyuk V, Roth T, Drake C. Circadian phase, sleepiness, and light exposure assessment in night workers with and without shift work disorder. *Chronobiol Int*. 2012;29:928-936.

93. Ng-A-Tham JE, Thierry H. An experimental change of the speed of rotation of the morning and evening shift. *Ergonomics*. 1993;36(1-3):51-57. doi:10.1080/00140139308967854

94. Dagan Y. Circadian rhythm sleep disorders. *Sleep Med Rev*. 2002;6:45-54.

95. van Amelsvoort LGPM, Jansen NWH, Kant Ij. Smoking among Shift Workers: More Than a Confounding Factor. *Chronobiol Int*. 2006;23(6):1105-1113. doi:10.1080/07420520601089539

96. Bae M-J, Song Y-M, Shin J-Y, Choi B-Y, Keum J-H, Lee E-A. The Association Between Shift Work and Health Behavior: Findings from the Korean National Health and Nutrition Examination Survey. *Korean J Fam Med*. 2017;38(2):86. doi:10.4082/kjfm.2017.38.2.86

97. Richter K, Peter L, Rodenbeck A, Weess HG, Riedel-Heller SG, Hillemacher T. Shiftwork and Alcohol Consumption: A Systematic Review of the Literature. *Eur Addict Res*. Published online May 26, 2020:1-7. doi:10.1159/000507573

98. Hulsegge G, Gupta N, Holtermann A, Jørgensen MB, Proper KI, van der Beek AJ. Shift workers have similar leisure-time physical activity levels as day workers but are more sedentary at work. *Scand J Work Environ Healt*. 2017;43(2):127-135. doi:10.5271/sjweh.3614

99. Loef B, Hulsegge G, Wendel-Vos GCW, et al. Non-occupational physical activity levels of shift workers compared with non-shift workers. *Occup Environ Med*. 2017;74(5):328-335. doi:10.1136/oemed-2016-103878

100. Peplonska B, Bukowska A, Sobala W. Rotating night shift work and physical activity of nurses and midwives in the cross-sectional study in Łódź, Poland. *Chronobiol Int*. 2014;31(10):1152-1159. doi:10.3109/07420528.2014.957296

101. Barbadoro P, Santarelli L, Croce N, et al. Rotating shift-work as an independent risk factor for overweight Italian workers: a cross-sectional study. *PLoS ONE*. 2013;8(5):e63289. doi:10.1371/journal.pone.0063289

102. Gupta CC, Coates AM, Dorrian J, Banks S. The factors influencing the eating behaviour of shiftworkers: what, when, where and why. *Ind Health*. 2019;57(4):419-453. doi:10.2486/indhealth.2018-0147

103. Buchvold HV, Pallesen S, Waage S, Bjorvatn B. Shift work schedule and night work load: Effects on body mass index - a four-year longitudinal study. *Scand J Work Environ Health*. 2018;44(3):251-257. doi:10.5271/sjweh.3702

104. Zhao I, Bogossian F, Turner C. Does maintaining or changing shift types affect BMI? A longitudinal study. *J Occup Environ Med*. 2012;54(5):525-531. doi:10.1097/JOM.0b013e31824e1073

105. Liu Q, Shi J, Duan P, et al. Is shift work associated with a higher risk of overweight or obesity? A systematic review of observational studies with meta-analysis. *Int J Epidemiol*. 2018;47(6):1956-1971. doi:10.1093/ije/dyy079

106. Buchvold HV, Pallesen S, Øyane NMF, Bjorvatn B. Associations between night work and BMI, alcohol, smoking, caffeine and exercise - a cross-sectional study. *BMC Public Health*. 2015;15(1):1112. doi:10.1186/s12889-015-2470-2

107. Kim TW, Jeong J-H, Hong S-C. The Impact of Sleep and Circadian Disturbance on Hormones and Metabolism. Horowitz M, ed. *Int J Endocrinol*. 2015;2015:591729. doi:10.1155/2015/591729

108. Stock D, Knight JA, Raboud J, et al. Rotating night shift work and menopausal age. *Hum Reprod*. 2019;34(3):539-548. doi:10.1093/humrep/dey390

109. Chung F-F, Yao C-CC, Wan G-H. The associations between menstrual function and life style/working conditions among nurses in Taiwan. *J Occup Health*. 2005;47(2):149-156. doi:10.1539/joh.47.149

110. Su S-B, Lu C-W, Kao Y-Y, Guo H-R. Effects of 12-hour rotating shifts on menstrual cycles of photoelectronic workers in Taiwan. *Chronobiol Int*. 2008;25(2):237-248. doi:10.1080/07420520802106884

111. Lawson CC, Whelan EA, Lividoti Hibert EN, Spiegelman D, Schernhammer ES, Rich-Edwards JW. Rotating shift work and menstrual cycle characteristics. *Epidemiology*. 2011;22(3):305-312. doi:10.1097/EDE.0b013e3182130016

112. Manohar S, Thongprayoon C, Cheungpasitporn W, Mao MA, Herrmann SM. Associations of rotational shift work and night shift status with hypertension: a systematic review and meta-analysis. *J Hypertens*. 2017;35(10):1929-1937. doi:10.1097/HJH.0000000000001442

113. Rahim A, McIsaac MA, Aronson KJ, Smith PM, Tranmer JE. The associations of shift work, sleep quality and incident of hypertension in Ontario adults: a population-based study. *Can J Cardiol*. Published online September 12, 2020. doi:10.1016/j.cjca.2020.09.003

114. Torquati L, Mielke GI, Brown WJ, Kolbe-Alexander T. Shift work and the risk of cardiovascular disease. A systematic review and meta-analysis including dose-response relationship. *Scand J Work Environ Health*. 2018;44(3):229-238. doi:10.5271/sjweh.3700

115. Canuto R, Garcez AS, Olinto MTA. Metabolic syndrome and shift work: a systematic review. *Sleep Med Rev*. 2013;17(6):425-431. doi:10.1016/j.smrv.2012.10.004

116. Wu SH, Hui WS, Liu Z, Ho SC. Metabolic syndrome and all-cause mortality: a meta-analysis of prospective cohort studies. *Eur J Epidemiol*. 2010;25(6):375-384. doi:10.1007/s10654-010-9459-z

117. Chen J-D, Lin Y-C, Hsiao S-T. Obesity and high blood pressure of 12-hour night shift female clean-room workers. *Chronobiol Int*. 2010;27(2):334-344. doi:10.3109/07420520903502242

118. Karlsson B, Knutsson A, Lindahl B. Is there an association between shift work and having a metabolic syndrome? Results from a population based study of 27,485 people. *Occup Environ Med*. 2001;58(11):747-752. doi:10.1136/oem.58.11.747

119. Burgueño A, Gemma C, Gianotti TF, Sookoian S, Pirola CJ. Increased levels of resistin in rotating shift workers: a potential mediator of cardiovascular risk associated with circadian misalignment. *Atherosclerosis*. 2010;210(2):625-629. doi:10.1016/j.atherosclerosis.2009.12.032

120. Knutsson A, Bøggild H. Gastrointestinal disorders among shift workers. *Scand J Work Environ Health*. 2010;36(2):85-95. doi:10.5271/sjweh.2897

121. Thiis-Evensen E. Shift work and health. *Ind Med Surg*. 1958;27(10):493-497.

122. Morikawa Y, Nakagawa H, Miura K, et al. Shift work and the risk of diabetes mellitus among Japanese male factory workers. *Scand J Work Environ Health*. 2005;31(3):179-183. doi:10.5271/sjweh.867

123. Suwazono Y, Sakata K, Okubo Y, et al. Long-term longitudinal study on the relationship between alternating shift work and the onset of diabetes mellitus in male Japanese workers. *J Occup Environ Med*. 2006;48(5):455-461. doi:10.1097/01.jom.0000214355.69182.fa

124. Pan A, Schernhammer ES, Sun Q, Hu FB. Rotating night shift work and risk of type 2 diabetes: two prospective cohort studies in women. *PLoS Med*. 2011;8(12):e1001141. doi:10.1371/journal.pmed.1001141

125. Knutsson A, Kempe A. Shift work and diabetes--a systematic review. *Chronobiol Int*. 2014;31(10):1146-1151. doi:10.3109/07420528.2014.957308

126. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. *Lancet*. 1999;354(9188):1435-1439. doi:10.1016/S0140-6736(99)01376-8

127. Scheer FAJL, Hilton MF, Mantzoros CS, Shea SA. Adverse metabolic and cardiovascular consequences of circadian misalignment. *PNAS*. 2009;106(11):4453-4458. doi:10.1073/pnas.0808180106

128. Buxton OM, Cain SW, O’Connor SP, et al. Adverse metabolic consequences in humans of prolonged sleep restriction combined with circadian disruption. *Sci Transl Med*. 2012;4(129):129ra43. doi:10.1126/scitranslmed.3003200

129. Buxton OM, Pavlova M, Reid EW, Wang W, Simonson DC, Adler GK. Sleep restriction for 1 week reduces insulin sensitivity in healthy men. *Diabetes*. 2010;59(9):2126-2133. doi:10.2337/db09-0699

130. Megdal SP, Kroenke CH, Laden F, Pukkala E, Schernhammer ES. Night work and breast cancer risk: a systematic review and meta-analysis. *Eur J Cancer*. 2005;41(13):2023-2032. doi:10.1016/j.ejca.2005.05.010

131. Kamdar BB, Tergas AI, Mateen FJ, Bhayani NH, Oh J. Night-shift work and risk of breast cancer: a systematic review and meta-analysis. *Breast Cancer Res Treat*. 2013;138(1):291-301. doi:10.1007/s10549-013-2433-1

132. Wang F, Yeung KL, Chan WC, et al. A meta-analysis on dose-response relationship between night shift work and the risk of breast cancer. *Ann Oncol*. 2013;24(11):2724-2732. doi:10.1093/annonc/mdt283

133. Salamanca-Fernández E, Rodríguez-Barranco M, Guevara M, Ardanaz E, Olry de Labry Lima A, Sánchez MJ. Night-shift work and breast and prostate cancer risk: updating the evidence from epidemiological studies. *An Sist Sanit Navar*. 2018;41(2):211-226. doi:10.23938/ASSN.0307

134. Kolstad HA. Nightshift work and risk of breast cancer and other cancers--a critical review of the epidemiologic evidence. *Scand J Work Environ Health*. 2008;34(1):5-22. doi:10.5271/sjweh.1194

135. Schernhammer ES, Laden F, Speizer FE, et al. Night-shift work and risk of colorectal cancer in the nurses’ health study. *J Natl Cancer Inst*. 2003;95(11):825-828. doi:10.1093/jnci/95.11.825

136. Sigurdardottir LG, Valdimarsdottir UA, Fall K, et al. Circadian disruption, sleep loss, and prostate cancer risk: a systematic review of epidemiologic studies. *Cancer Epidemiol Biomarkers Prev*. 2012;21(7):1002-1011. doi:10.1158/1055-9965.EPI-12-0116

137. Schwartzbaum J, Ahlbom A, Feychting M. Cohort study of cancer risk among male and female shift workers. *Scand J Work Environ Health*. 2007;33(5):336-343. doi:10.5271/sjweh.1150

138. Zhang Y, Papantoniou K. Night shift work and its carcinogenicity. *Lancet Oncol*. 2019;20(10):e550. doi:10.1016/S1470-2045(19)30578-9

139. Scott A, Monk T, Brink L. Shiftwork as a Risk Factor for Depression: A Pilot Study. *Int J Occup Environ Health*. 1997;3(Supplement 2):S2-S9.

140. Selvi Y, Özdemir PG, Özdemir O, Aydın A, Beşiroğlu L. Influence of night shift work on psychologic state and quality of life in health workers. *Dusunen Adam*. Published online December 30, 2010:238-243. doi:10.5350/DAJPN2010230403t

141. Souza ACD de, Barbosa IR, Souza DLB de. Prevalence of multimorbidity and associated factors in the Brazilian working population. *Rev Bras Med Trab*. 2020;18(03):302-311. doi:10.47626/1679-4435-2020-568

142. Seo S. Multimorbidity Development in Working People. *Int J Environ Res Public Health*. 2019;16(23). doi:10.3390/ijerph16234749

143. van Zon SKR, Reijneveld SA, Galaurchi A, Mendes de Leon CF, Almansa J, Bültmann U. Multimorbidity and the Transition Out of Full-Time Paid Employment: A Longitudinal Analysis of the Health and Retirement Study. *J Gerontol B Psychol Sci Soc Sci*. 2020;75(3):705-715. doi:10.1093/geronb/gbz061

144. Cabral GG, Dantas de Souza AC, Barbosa IR, Jerez-Roig J, Souza DLB. Multimorbidity and Its Impact on Workers: A Review of Longitudinal Studies. *Saf Health Work*. 2019;10(4):393-399. doi:10.1016/j.shaw.2019.08.004

145. Smith P, Chen C, Mustard C, Bielecky A, Beaton D, Ibrahim S. Examining the relationship between chronic conditions, multi-morbidity and labour market participation in Canada: 2000–2005. *Ageing Soc*. 2014;34(10):1730-1748. doi:10.1017/S0144686X13000457

146. Jylhä M. What is self-rated health and why does it predict mortality? Towards a unified conceptual model. *Soc Sci Med*. 2009;69(3):307-316. doi:10.1016/j.socscimed.2009.05.013

147. Song J-T, Lee G, Kwon J, Park J-W, Choi H, Lim S. The Association between Long Working Hours and Self-Rated Health. *Ann of Occup and Environ Med*. 2014;26(1):2. doi:10.1186/2052-4374-26-2

148. Ihlström J, Kecklund G, Anund A. Split-shift work in relation to stress, health and psychosocial work factors among bus drivers. *Work*. 2017;56(4):531-538. doi:10.3233/WOR-172520

149. Kwon K, Park JB, Lee K-J, Cho Y-S. Association between employment status and self-rated health: Korean working conditions survey. *Ann Occup Environ Med*. 2016;28(1). doi:10.1186/s40557-016-0126-z

150. Cheng S-Y, Lin P-C, Chang Y-K, Lin Y-K, Lee P-H, Chen S-R. Sleep quality mediates the relationship between work-family conflicts and the self-perceived health status among hospital nurses. *J Nurs Manag*. 2019;27(2):381-387. doi:10.1111/jonm.12694

151. Ala-Mursula L, Vahtera J, Kivimäki M, Kevin MV, Pentti J. Employee control over working times: associations with subjective health and sickness absences. *J Epidemiol Community Health*. 2002;56(4):272-278. doi:10.1136/jech.56.4.272

152. Nijp HH, Beckers DG, Guerts SA, Tucker P, Kompier MA. Systematic review on the association between employee worktime control and work–non-work balance, health and well-being, and job-related outcomes. *Scand J Work Environ Health*. 2012;38(4):299-313. doi:10.5271/sjweh.3307

153. Salo P, Ala-Mursula L, Rod NH, et al. Work time control and sleep disturbances: prospective cohort study of Finnish public sector employees. *Sleep*. 2014;37(7):1217-1225. doi:10.5665/sleep.3842

154. Fenwick R, Tausig M. Scheduling Stress Family and Health Outcomes of Shift Work and Schedule Control. *Am Behav Sci*. 2001;44:1179-1198. doi:10.1177/00027640121956719

155. Bhatti GK, Reddy AP, Reddy PH, Bhatti JS. Lifestyle Modifications and Nutritional Interventions in Aging-Associated Cognitive Decline and Alzheimer’s Disease. *Front Aging Neurosci*. 2020;11:369. doi:10.3389/fnagi.2019.00369

156. Harvey P. Domains of cognition and their assessment. *Dialogues Clin Neurosci*. 2019;21(3):227-237. doi:10.31887/DCNS.2019.21.3/pharvey

157. Hugo J, Ganguli M. Dementia and Cognitive Impairment. *Clin Geriatr Med*. 2014;30(3):421-442. doi:10.1016/j.cger.2014.04.001

158. Muir SW, Gopaul K, Montero Odasso MM. The role of cognitive impairment in fall risk among older adults: a systematic review and meta-analysis. *Age Ageing*. 2012;41(3):299-308. doi:10.1093/ageing/afs012

159. Tilvis RS, Kahonen-Vare MH, Jolkkonen J, Valvanne J, Pitkala KH, Strandberg TE. Predictors of Cognitive Decline and Mortality of Aged People Over a 10-Year Period. *J Gerontol A Biol Sci Med Sci*. 2004;59(3):M268-M274. doi:10.1093/gerona/59.3.M268

160. Mariani E, Monastero R, Mecocci P. Mild cognitive impairment: A systematic review. *J Alzheimers Dis*. 2007;12(1):23-35.

161. Alzheimer's Association. *Characteristics, Costs and Health Service Use for Medicare Beneficiaries with a Dementia Diagnosis: Report 1: Medicare Current Beneficiary Survey*.

162. Perquin M, Diederich N, Pastore J, et al. Prevalence of Dementia and Cognitive Complaints in the Context of High Cognitive Reserve: A Population-Based Study. Bayer A, ed. *PLoS ONE*. 2015;10(9):e0138818. doi:10.1371/journal.pone.0138818

163. Stern Y. Cognitive reserve in ageing and Alzheimer's disease. *Lancet Neurol*. 2012;11(11):1006-1012. doi:10.1016/S1474-4422(12)70191-6

164. Kuiper JS, Zuidersma M, Zuidema SU, et al. Social relationships and cognitive decline: a systematic review and meta-analysis of longitudinal cohort studies. *Int J Epidemiol*. 2016;45(4):38.

165. Brown CL, Robitaille A, Zelinski EM, Dixon RA, Hofer SM, Piccinin AM. Cognitive activity mediates the association between social activity and cognitive performance: A longitudinal study. *Psychol Aging*. 2016;31(8):831-846. doi:10.1037/pag0000134

166. Evans IEM, Martyr A, Collins R, Brayne C, Clare L. Social Isolation and Cognitive Function in Later Life: A Systematic Review and Meta-Analysis. *J Alzheimers Dis*. 2019;70(s1):S119-S144. doi:10.3233/JAD-180501

167. Vance DE, Bail J, Enah C, Palmer J, Hoenig A. The impact of employment on cognition and cognitive reserve: implications across diseases and aging. *NRR*. 2016;Volume 6:61-71. doi:10.2147/NRR.S115625

168. Scarmeas N, Stern Y. Cognitive reserve: Implications for diagnosis and prevention of Alzheimer's disease. *Curr Neurol Neurosci Rep*. 2004;4(5):374-380. doi:10.1007/s11910-004-0084-7

169. Stern Y, Gurland B, Tatemichi TK, Tang MX, Wilder D, Mayeux R. Influence of education and occupation on the incidence of Alzheimer's disease. *JAMA*. 1994;271(13):1004-1010.

170. Zhang X, Li C, Zhang M. Psychosocial risk factors of Alzheimer's disease. *Zhonghua Yi Xue Za Zhi*. 1999;79(5):335-338.

171. Qiu C, Karp A, von Strauss E, Winblad B, Fratiglioni L, Bellander T. Lifetime principal occupation and risk of Alzheimer's disease in the Kungsholmen project. *Am J Ind Med*. 2003;43(2):204-211. doi:10.1002/ajim.10159

172. Potter GG, Helms MJ, Plassman BL. Associations of job demands and intelligence with cognitive performance among men in late life. *Neurology*. 2008;70(Issue 19, Part 2):1803-1808. doi:10.1212/01.wnl.0000295506.58497.7e

173. Pool LR, Weuve J, Wilson RS, Bültmann U, Evans DA, Mendes de Leon CF. Occupational cognitive requirements and late-life cognitive aging. *Neurology*. 2016;86(15):1386-1392. doi:10.1212/WNL.0000000000002569

174. Fisher GG, Stachowski A, Infurna FJ, Faul JD, Grosch J, Tetrick LE. Mental work demands, retirement, and longitudinal trajectories of cognitive functioning. *J Occup Health Psychol*. 2014;19(2):231-242. doi:10.1037/a0035724

175. Vemuri P, Lesnick TG, Przybelski SA, et al. Association of Lifetime Intellectual Enrichment With Cognitive Decline in the Older Population. *JAMA Neurol*. 2014;71(8):1017. doi:10.1001/jamaneurol.2014.963

176. Leist AK, Glymour MM, Mackenbach JP, van Lenthe FJ, Avendano M. Time away from work predicts later cognitive function: differences by activity during leave. *Ann Epidemiol*. 2013;23(8):455-462. doi:10.1016/j.annepidem.2013.05.014

177. Burke C, Johnson EE, Bourgault C, Borgia M, O'Toole TP. Losing work: regional unemployment and its effect on homeless demographic characteristics, needs, and health care. *J Health Care Poor Underserved*. 2013;24(3):1391-1402. doi:10.1353/hpu.2013.0150

178. Spence S, Stevens R, Parks R. Cognitive dysfunction in homeless adults: a systematic review. *J R Soc Med*. 2004;97(8):375-379. doi:10.1258/jrsm.97.8.375

179. Stone B, Dowling S, Cameron A. Cognitive impairment and homelessness: A scoping review. *Health Soc Care Community*. 2019;27(4). doi:10.1111/hsc.12682

180. Xue B, Cadar D, Fleischmann M, et al. Effect of retirement on cognitive function: the Whitehall II cohort study. *Eur J Epidemiol*. 2018;33(10):989-1001. doi:10.1007/s10654-017-0347-7

181. Behncke S. Does retirement trigger ill health? *Health Econ*. 2012;21(3):282-300. doi:10.1002/hec.1712

182. Bonsang E, Adam S, Perelman S. Does retirement affect cognitive functioning? *J Health Econ*. 2012;31(3):490-501. doi:10.1016/j.jhealeco.2012.03.005

183. Rohwedder S, Willis RJ. Mental Retirement. *J Econ Perspect*. 2010;24(1):119-138. doi:10.1257/jep.24.1.119

184. Clouston SAP, Denier N. Mental retirement and health selection: Analyses from the U.S. Health and Retirement Study. *Soc Sci Med*. 2017;178:78-86. doi:10.1016/j.socscimed.2017.01.019

185. Kajitani S, Sakata K, Mckenzie C. Occupation, retirement and cognitive functioning. *Ageing & Society*. 2017;37(8):1568-1596. doi:10.1017/S0144686X16000465

186. Grotz C, Meillon C, Amieva H, et al. Why Is Later Age at Retirement Beneficial for Cognition? Results from a French Population-based Study. *J Nutr Health Aging*. 2016;20(5):514-519. doi:10.1007/s12603-015-0599-4

187. Lupton MK, Stahl D, Archer N, et al. Education, occupation and retirement age effects on the age of onset of Alzheimer's disease. *Int J Geriatr Psychiatry*. 2010;25(1):30-36. doi:10.1002/gps.2294

188. Coe NB, von Gaudecker H-M, Lindeboom M, Maurer J. The effect of retirement on cognitive functioning. *Health Econ*. 2012;21(8):913-927. doi:10.1002/hec.1771

189. Coe NB, Zamarro G. Retirement effects on health in Europe. *J Health Econ*. 2011;30(1):77-86. doi:10.1016/j.jhealeco.2010.11.002

190. Hultsch DF, Hertzog C, Small BJ, Dixon RA. Use it or lose it: engaged lifestyle as a buffer of cognitive decline in aging? *Psychol Aging*. 1999;14(2):245-263. doi:10.1037//0882-7974.14.2.245

191. Kivipelto M, Mangialasche F, Ngandu T. Lifestyle interventions to prevent cognitive impairment, dementia and Alzheimer disease. *Nat Rev Neurol*. 2018;14(11):653-666. doi:10.1038/s41582-018-0070-3

192. Sommerlad A, Ruegger J, Singh-Manoux A, Lewis G, Livingston G. Marriage and risk of dementia: systematic review and meta-analysis of observational studies. *J Neurol Neurosurg Psychiatry*. 2018;89(3):231-238. doi:10.1136/jnnp-2017-316274

193. Johansson L, Guo X, Hällström T, et al. Common psychosocial stressors in middle-aged women related to longstanding distress and increased risk of Alzheimer's disease: a 38-year longitudinal population study. *BMJ Open*. 2013;3(9):e003142. doi:10.1136/bmjopen-2013-003142

194. Lee Y, Back JH, Kim J, Byeon H. Multiple Socioeconomic Risks and Cognitive Impairment in Older Adults. *Dement Geriatr Cogn Disord*. 2010;29(6):523-529. doi:10.1159/000315507

195. Qin H, Zhao X, Zhu B, Hu C. Demographic Factors and Cognitive Function Assessments Associated with Mild Cognitive Impairment Progression for the Elderly. *Biomed Res Int*. 2020;2020:1-9. doi:10.1155/2020/3054373

196. Evans DA, Hebert LE, Beckett LA, et al. Education and other measures of socioeconomic status and risk of incident Alzheimer disease in a defined population of older persons. *Arch Neurol*. 1997;54(11):1399-1405. doi:10.1001/archneur.1997.00550230066019

197. Lang IA, Llewellyn DJ, Langa KM, Wallace RB, Huppert FA, Melzer D. Neighborhood deprivation, individual socioeconomic status, and cognitive function in older people: analyses from the English Longitudinal Study of Ageing. *J Am Geriatr Soc*. 2008;56(2):191-198. doi:10.1111/j.1532-5415.2007.01557.x

198. Jang S-N, Choi Y-J, Kim D-H. Association of socioeconomic status with successful ageing: differences in the components of successful ageing. *J Biosoc Sci*. 2009;41(2):207-219. doi:10.1017/S0021932008003052

199. Lee S, Kawachi I, Berkman LF, Grodstein F. Education, other socioeconomic indicators, and cognitive function. *Am J Epidemiol*. 2003;157(8):712-720. doi:10.1093/aje/kwg042

200. Fei M, Qu YC, Wang T, Yin J, Bai JX, Ding QH. Prevalence and distribution of cognitive impairment no dementia (CIND) among the aged population and the analysis of socio-demographic characteristics: the community-based cross-sectional study. *Alzheimer Dis Assoc Disord*. 2009;23(2):130-138. doi:10.1097/WAD.0b013e318190a59d

201. Xu H, Zhang Y, Wu B. Association between migration and cognitive status among middle-aged and older adults: a systematic review. *BMC Geriatr*. 2017;17(1):184. doi:10.1186/s12877-017-0585-2

202. Segers K, Benoit F, Colson C, Kovac V, Nury D, Vanderaspoilden V. Pioneers in migration, pioneering in dementia: first generation immigrants in a European metropolitan memory clinic. *Acta Neurol Belg*. 2013;113(4):435-440. doi:10.1007/s13760-013-0245-z

203. Touradj P, Manly JJ, Jacobs DM, Stern Y. Neuropsychological test performance: a study of non-Hispanic White elderly. *J Clin Exp Neuropsychol*. 2001;23(5):643-649. doi:10.1076/jcen.23.5.643.1246

204. Nielsen TR, Vogel A, Waldemar G. Comparison of performance on three neuropsychological tests in healthy Turkish immigrants and Danish elderly. *Int Psychogeriatr*. 2012;24(9):1515-1521. doi:10.1017/S1041610212000440

205. Stouten LH, Veling W, van der Helm M, Laan W, van der Gaag M. Cognitive deficits and ethnicity: a cohort study of early psychosis patients in The Netherlands. *Soc Psychiatry Psychiatr Epidemiol*. 2013;48(1):37-47. doi:10.1007/s00127-012-0521-x

206. Chertkow H, Whitehead V, Phillips N, Wolfson C, Atherton J, Bergman H. Multilingualism (but not always bilingualism) delays the onset of Alzheimer disease: evidence from a bilingual community. *Alzheimer Dis Assoc Disord*. 2010;24(2):118-125. doi:10.1097/WAD.0b013e3181ca1221

207. Robbins RN, Scott T, Joska JA, Gouse H. Impact of Urbanization on Cognitive Disorders. *Curr Opin Psychiatry*. 2019;32(3):210-217. doi:10.1097/YCO.0000000000000490

208. Vlahov D, Freudenberg N, Proietti F, et al. Urban as a Determinant of Health. *J Urban Health*. 2007;84(1):16-26. doi:10.1007/s11524-007-9169-3

209. Power MC, Adar SD, Yanosky JD, Weuve J. Exposure to air pollution as a potential contributor to cognitive function, cognitive decline, brain imaging, and dementia: A systematic review of epidemiologic research. *Neurotoxicology*. 2016;56:235-253. doi:10.1016/j.neuro.2016.06.004

210. Clifford A, Lang L, Chen R, Anstey KJ, Seaton A. Exposure to air pollution and cognitive functioning across the life course--A systematic literature review. *Environ Res*. 2016;147:383-398. doi:10.1016/j.envres.2016.01.018

211. Lara E, Martín-María N, De la Torre-Luque A, et al. Does loneliness contribute to mild cognitive impairment and dementia? A systematic review and meta-analysis of longitudinal studies. *Ageing Res Rev*. 2019;52:7-16. doi:10.1016/j.arr.2019.03.002

212. Berkman LF. Which influences cognitive function: living alone or being alone? *Lancet*. 2000;355(9212):1291-1292. doi:10.1016/S0140-6736(00)02107-3

213. Cacioppo JT, Cacioppo S, Capitanio JP, Cole SW. The Neuroendocrinology of Social Isolation. *Annu Rev Psychol*. 2015;66(1):733-767. doi:10.1146/annurev-psych-010814-015240

214. Cacioppo JT, Hawkley LC, Thisted RA. Perceived social isolation makes me sad: 5-year cross-lagged analyses of loneliness and depressive symptomatology in the Chicago Health, Aging, and Social Relations Study. *Psychol Aging*. 2010;25(2):453-463. doi:10.1037/a0017216

215. Jiang X, Huang J, Song D, Deng R, Wei J, Zhang Z. Increased Consumption of Fruit and Vegetables Is Related to a Reduced Risk of Cognitive Impairment and Dementia: Meta-Analysis. *Front Aging Neurosci*. 2017;9. doi:10.3389/fnagi.2017.00018

216. Mottaghi T, Amirabdollahian F, Haghighatdoost F. Fruit and vegetable intake and cognitive impairment: a systematic review and meta-analysis of observational studies. *Eur J Clin Nutr*. 2018;72(10):1336-1344. doi:10.1038/s41430-017-0005-x

217. Lovell MA, Markesbery WR. Oxidative damage in mild cognitive impairment and early Alzheimer’s disease. *J Neurosci Res*. 2007;85(14):3036-3040. doi:10.1002/jnr.21346

218. Praticò D, Clark CM, Liun F, Rokach J, Lee VY-M, Trojanowski JQ. Increase of brain oxidative stress in mild cognitive impairment: a possible predictor of Alzheimer disease. *Arch Neurol*. 2002;59(6):972-976. doi:10.1001/archneur.59.6.972

219. Petersson SD, Philippou E. Mediterranean Diet, Cognitive Function, and Dementia: A Systematic Review of the Evidence. *Adv Nutr*. 2016;7(5):889-904. doi:10.3945/an.116.012138

220. Lourida I, Soni M, Thompson-Coon J, et al. Mediterranean diet, cognitive function, and dementia: a systematic review. *Epidemiology*. 2013;24(4):479-489. doi:10.1097/EDE.0b013e3182944410

221. Kalmijn S. Cigarette Smoking and Alcohol Consumption in Relation to Cognitive Performance in Middle Age. *Am J Epidemiol*. 2002;156(10):936-944. doi:10.1093/aje/kwf135

222. Richards M, Jarvis MJ, Thompson N, Wadsworth MEJ. Cigarette Smoking and Cognitive Decline in Midlife: Evidence From a Prospective Birth Cohort Study. *Am J Public Health*. 2003;93(6):994-998. doi:10.2105/AJPH.93.6.994

223. Sabia S, Elbaz A, Dugravot A, et al. Impact of Smoking on Cognitive Decline in Early Old Age: The Whitehall II Cohort Study. *Arch Gen Psychiatry*. 2012;69(6). doi:10.1001/archgenpsychiatry.2011.2016

224. Campos MW, Serebrisky D, Castaldelli-Maia JM. Smoking and Cognition. *Curr Drug Abuse Rev*. 2016;9(2):76-79. doi:10.2174/1874473709666160803101633

225. Chang C-CH, Zhao Y, Lee C-W, Ganguli M. Smoking, death, and Alzheimer's disease: A case of competing risks. *Alzheimer Dis Assoc Disord*. 2012;26(4):300-306. doi:10.1097/WAD.0b013e3182420b6e

226. Anttila T, Helkala E-L, Viitanen M, et al. Alcohol drinking in middle age and subsequent risk of mild cognitive impairment and dementia in old age: a prospective population based study. *BMJ*. 2004;329(7465):539. doi:10.1136/bmj.38181.418958.BE

227. Mukamal KJ, Kuller LH, Fitzpatrick AL, Longstreth WT, Mittleman MA, Siscovick DS. Prospective study of alcohol consumption and risk of dementia in older adults. *JAMA*. 2003;289(11):1405-1413. doi:10.1001/jama.289.11.1405

228. Ruitenberg A, van Swieten JC, Witteman JCM, et al. Alcohol consumption and risk of dementia: the Rotterdam Study. *Lancet*. 2002;359(9303):281-286. doi:10.1016/S0140-6736(02)07493-7

229. Ganguli M, Vander Bilt J, Saxton JA, Shen C, Dodge HH. Alcohol consumption and cognitive function in late life: a longitudinal community study. *Neurology*. 2005;65(8):1210-1217. doi:10.1212/01.wnl.0000180520.35181.24

230. Gunstad J, Paul RH, Cohen RA, Tate DF, Spitznagel MB, Gordon E. Elevated body mass index is associated with executive dysfunction in otherwise healthy adults. *Comp Psychiatry*. 2007;48(1):57-61. doi:10.1016/j.comppsych.2006.05.001

231. Benito-León J, Mitchell AJ, Hernández-Gallego J, Bermejo-Pareja F. Obesity and impaired cognitive functioning in the elderly: a population-based cross-sectional study (NEDICES). *Eur J Neurol*. 2013;20(6):899-e77. doi:10.1111/ene.12083

232. Bischof GN, Park DC. Obesity and Aging: Consequences for Cognition, Brain Structure, and Brain Function. *Psychosom Med*. 2015;77(6):697-709. doi:10.1097/PSY.0000000000000212

233. Weber MT, Maki PM, McDermott MP. Cognition and mood in perimenopause: a systematic review and meta-analysis. *J Steroid Biochem Mol Biol*. 2014;142:90-98. doi:10.1016/j.jsbmb.2013.06.001

234. Pertesi S, Coughlan G, Puthusseryppady V, Morris E, Hornberger M. Menopause, cognition and dementia - A review. *Post Reprod Health*. 2019;25(4):200-206. doi:10.1177/2053369119883485

235. O'Brien J, Jackson JW, Grodstein F, Blacker D, Weuve J. Postmenopausal Hormone Therapy Is Not Associated With Risk of All-Cause Dementia and Alzheimer's Disease. *Epidemiol Rev*. 2014;36(1):83-103. doi:10.1093/epirev/mxt008

236. Deckers K, Schievink SHJ, Rodriquez MMF, et al. Coronary heart disease and risk for cognitive impairment or dementia: Systematic review and meta-analysis. Ginsberg SD, ed. *PLoS ONE*. 2017;12(9):e0184244. doi:10.1371/journal.pone.0184244

237. Shah AM, Banerjee T, Mukherjee D. Koronare, periphere und zerebrovaskuläre Krankheit: ein komplexes Beziehungsmuster. *Herz*. 2008;33(7):475-480. doi:10.1007/s00059-008-3152-y

238. Rao Rahul, Jackson Steven, Howard Robert. Neuropsychological Impairment in Stroke, Carotid Stenosis, and Peripheral Vascular Disease. *Stroke*. 1999;30(10):2167-2173. doi:10.1161/01.STR.30.10.2167

239. Phillips Natalie A., Mate-Kole C. Charles. Cognitive Deficits in Peripheral Vascular Disease. *Stroke*. 1997;28(4):777-784. doi:10.1161/01.STR.28.4.777

240. Walker KA, Power MC, Gottesman RF. Defining the Relationship Between Hypertension, Cognitive Decline, and Dementia: a Review. *Curr Hypertens Rep*. 2017;19(3):24. doi:10.1007/s11906-017-0724-3

241. Zilliox LA, Chadrasekaran K, Kwan JY, Russell JW. Diabetes and Cognitive Impairment. *Curr Diab Rep*. 2016;16(9):87. doi:10.1007/s11892-016-0775-x

242. Biessels GJ, Staekenborg S, Brunner E, Brayne C, Scheltens P. Risk of dementia in diabetes mellitus: a systematic review. *Lancet Neurol*. 2006;5(1):64-74. doi:10.1016/S1474-4422(05)70284-2

243. Chen Y, Liu Z, Zhang J, et al. Altered brain activation patterns under different working memory loads in patients with type 2 diabetes. *Diabetes Care*. 2014;37(12):3157-3163. doi:10.2337/dc14-1683

244. Hodgson KD, Hutchinson AD, Wilson CJ, Nettelbeck T. A meta-analysis of the effects of chemotherapy on cognition in patients with cancer. *Cancer Treat Rev*. 2013;39(3):297-304. doi:10.1016/j.ctrv.2012.11.001

245. Pendergrass JC, Targum SD, Harrison JE. Cognitive Impairment Associated with Cancer: A Brief Review. *Innov Clin Neurosci*. 2018;15(1-2):36-44.

246. Kowalski K, Mulak A. Brain-Gut-Microbiota Axis in Alzheimer's Disease. *J Neurogastroenterol Motil*. 2019;25(1):48-60. doi:10.5056/jnm18087

247. Lam NC-Y, Yeung H-Y, Li W-K, et al. Cognitive impairment in Irritable Bowel Syndrome (IBS): A systematic review. *Brain Res*. 2019;1719:274-284. doi:10.1016/j.brainres.2019.05.036

248. Clarke G, Kennedy PJ, Groeger JA, et al. Impaired cognitive function in Crohn's disease: Relationship to disease activity. *BBI-Health*. 2020;5:100093. doi:10.1016/j.bbih.2020.100093

249. Fan W, Zhang S, Hu J, et al. Aberrant Brain Function in Active-Stage Ulcerative Colitis Patients: A Resting-State Functional MRI Study. *Front Hum Neurosci*. 2019;13:107. doi:10.3389/fnhum.2019.00107

250. Hsu C-C, Hsu Y-C, Chang K-H, et al. Association of Dementia and Peptic Ulcer Disease: A Nationwide Population-Based Study. *Am J Alzheimers Dis Other Demen*. 2016;31(5):389-394. doi:10.1177/1533317515617546

251. Han M-L, Chen J-H, Tsai M-K, et al. Association between Helicobacter pylori infection and cognitive impairment in the elderly. *J Formos Med Assoc*. 2018;117(11):994-1002. doi:10.1016/j.jfma.2017.11.005

252. Cárdenas VM, Boller F, Román GC. Helicobacter pylori, Vascular Risk Factors and Cognition in U.S. Older Adults. *Brain Sci*. 2019;9(12). doi:10.3390/brainsci9120370

253. Alshehri AM. Metabolic syndrome and cardiovascular risk. *J Family Community Med*. 2010;17(2):73-78. doi:10.4103/1319-1683.71987

254. Craft S. The role of metabolic disorders in Alzheimer disease and vascular dementia: two roads converged. *Arch Neurol*. 2009;66(3):300-305. doi:10.1001/archneurol.2009.27

255. Siervo M, Harrison SL, Jagger C, Robinson L, Stephan BCM. Metabolic syndrome and longitudinal changes in cognitive function: a systematic review and meta-analysis. *J Alzheimers Dis*. 2014;41(1):151-161. doi:10.3233/JAD-132279

256. Assuncao N, Sudo FK, Drummond C, de Felice FG, Mattos P. Metabolic Syndrome and cognitive decline in the elderly: A systematic review. *PLoS ONE*. 2018;13(3):e0194990. doi:10.1371/journal.pone.0194990

257. Culpepper L, Lam RW, McIntyre RS. Cognitive Impairment in Patients With Depression: Awareness, Assessment, and Management. *J Clin Psychiatry*. 2017;78(9):1383-1394. doi:10.4088/JCP.tk16043ah5c

258. Dotson VM, Beydoun MA, Zonderman AB. Recurrent depressive symptoms and the incidence of dementia and mild cognitive impairment. *Neurology*. 2010;75(1):27-34. doi:10.1212/WNL.0b013e3181e62124

259. Panza F, Frisardi V, Capurso C, et al. Late-life depression, mild cognitive impairment, and dementia: possible continuum? *Am J Geriatr Psychiatry*. 2010;18(2):98-116. doi:10.1097/JGP.0b013e3181b0fa13

260. Butters MA, Young JB, Lopez O, et al. Pathways linking late-life depression to persistent cognitive impairment and dementia. *Dialogues Clin Neurosci*. 2008;10(3):345-357.

261. Gulpers B, Ramakers I, Hamel R, Köhler S, Oude Voshaar R, Verhey F. Anxiety as a Predictor for Cognitive Decline and Dementia: A Systematic Review and Meta-Analysis. *Am J Geriatr Psychiatry*. 2016;24(10):823-842. doi:10.1016/j.jagp.2016.05.015

262. Beaudreau SA, O'Hara R. Late-life anxiety and cognitive impairment: a review. *Am J Geriatr Psychiatry*. 2008;16(10):790-803. doi:10.1097/JGP.0b013e31817945c3

263. Aarts S, van den Akker M, Tan FES, Verhey FRJ, Metsemakers JFM, van Boxtel MPJ. Influence of multimorbidity on cognition in a normal aging population: a 12-year follow-up in the Maastricht Aging Study. *Int J Geriatr Psychiatry*. 2011;26(10):1046-1053. doi:10.1002/gps.2642

264. Wei MY, Levine DA, Zahodne LB, Kabeto MU, Langa KM. Multimorbidity and Cognitive Decline Over 14 Years in Older Americans. *J Gerontol A Biol Sci Med Sci*. 2020;75(6):1206-1213. doi:10.1093/gerona/glz147

265. Vassilaki M, Aakre JA, Cha RH, et al. Multimorbidity and Risk of Mild Cognitive Impairment. *J Am Geriatr Soc*. 2015;63(9):1783-1790. doi:10.1111/jgs.13612

266. Bäckman L, Jones S, Small BJ, Agüero-Torres H, Fratiglioni L. Rate of cognitive decline in preclinical Alzheimer's disease: the role of comorbidity. *J Gerontol B Psychol Sci Soc Sci*. 2003;58(4):P228-236. doi:10.1093/geronb/58.4.p228

267. Solomon A, Dobranici L, Kåreholt I, Tudose C, Lăzărescu M. Comorbidity and the rate of cognitive decline in patients with Alzheimer dementia. *Int J Geriatr Psychiatry*. 2011;26(12):1244-1251. doi:10.1002/gps.2670

268. Bendayan R, Piccinin AM, Hofer SM, Muniz G. Are Changes in Self-Rated Health Associated With Memory Decline in Older Adults? *J Aging Health*. 2017;29(8):1410-1423. doi:10.1177/0898264316661830

269. Carmelli D, Swan GE, LaRue A, Eslinger PJ. Correlates of change in cognitive function in survivors from the Western Collaborative Group Study. *Neuroepidemiology*. 1997;16(6):285-295. doi:10.1159/000109699

270. Sargent-Cox K, Cherbuin N, Sachdev P, Anstey KJ. Subjective health and memory predictors of mild cognitive disorders and cognitive decline in ageing: the Personality and Total Health (PATH) through Life Study. *Dement Geriatr Cogn Disord*. 2011;31(1):45-52. doi:10.1159/000322373

271. Wang X, Armstrong M, Cairins B, Key T, Travis R. Shift work and chronic disease: the epidemiological evidence. *Occup Med (Lond)*. 2011;61(2):78-89. doi:doi:10.1093/occmed/kqr001

272. Devore EE, Grodstein F, Schernhammer ES. Shift work and cognition in the Nurses' Health Study. *Am J Epidemiol*. 2013;178(8):1296-1300. doi:10.1093/aje/kwt214

273. Bara A-C, Arber S. Working shifts and mental health – findings from the British Household Panel Survey (1995-2005). *Scand J Work Environ Health*. 2009;35(5):361-367.

274. Marchand A, Demers A, Durand P, Simard M. The moderating effect of alcohol intake on the relationship between work strains and psychological distress. *J Stud Alcohol*. 2003;64(3):419-427. doi:10.15288/jsa.2003.64.419

275. Marchand A, Demers A, Durand P, Simard M. Occupational variations in drinking and psychological distress: a multilevel analysis. *Work*. 2003;21(2):153-163.

276. Marchand A, Demers A, Durand P. Does work really cause distress? The contribution of occupational structure and work organization to the experience of psychological distress. *Soc Sci Med*. 2005;61(1):1-14. doi:10.1016/j.socscimed.2004.11.037

277. Marchand A, Beauregard N, Blanc M-E. Work and non-work stressors, psychological distress and obesity: evidence from a 14-year study on Canadian workers. *BMJ Open*. 2015;5(3):e006285. doi:10.1136/bmjopen-2014-006285

278. Buja A, Zampieron A, Mastrangelo G, et al. Strain and health implications of nurses' shift work. *Int J Occup Med Environ Health*. 2013;26(4):511-521. doi:doi:10.2478/s13382-013-0122-2

279. Ferrie JE, Head J, Shipley MJ, Vahtera J, Marmot MG, Kivimaki M. Injustice at Work and Incidence of Psychiatric Morbidity: The Whitehall II Study. *Occup Environ Med*. 2006;63(7):443-450. doi:doi:10.1136/oem.2005.022269

280. Paterniti S, Niedhammer I, Lang T, Consoli S. Psychosocial Factors at Work, Personality Traits and Depressive Symptoms. Longitudinal Results From the GAZEL Study. *Br J Psychiatry*. 2002;181:111-117.

281. Stansfeld SA, Fuhrer R, Head J, Ferrie J, Shipley M. Work and psychiatric disorder in the Whitehall II Study. *J Psychosom Res*. 1997;43(1):73-81.

282. Stansfeld SA, Fuhrer R, Shipley MJ, Marmot MG. Work characteristics predict psychiatric disorder: prospective results from the Whitehall II Study. *Occup Environ Med*. 1999;56(5):302-307. doi:10.1136/oem.56.5.302

283. Virtanen M, Vahtera J, Pentti J, Honkonen T, Elovainio M, Kivimäki M. Job Strain and Psychologic Distress Influence on Sickness Absence Among Finnish Employees. *Am J Prev Med*. 2007;33(3):182-187. doi:doi:10.1016/j.amepre.2007.05.003

284. De Raeve L, Jansen NW, Kant I. Health effects of transitions in work schedule, workhours and overtime in a prospective cohort study. *Scand J Work Environ Health*. 2007;33(2):105-113. doi:10.5271/sjweh.1113

285. Wilson R, Schneider J, Boyle P, Arnold S, Tang Y, Bennett D. Chronic distress and incidence of mild cognitive impairment. *Neurology*. 2007;68(24):2085-2092. doi:doi:10.1212/01.wnl.0000264930.97061.82

286. Hori H, Ozeki Y, Teraishi T, et al. Relationships between psychological distress, coping styles, and HPA axis reactivity in healthy adults. *J Psychiatr Res*. 2010;44(14):865-873. doi:10.1016/j.jpsychires.2010.02.007

287. McEwen B. Allostasis and Allostatic Load Implications for Neuropsychopharmacology. *Neuropsychopharmacology*. 2000;22(2):108-124. doi:10.1016/S0893-133X(99)00129-3

288. Ennis GE, An Y, Resnick SM, Ferrucci L, O'Brien RJ, Moffat SD. Long-term Cortisol Measures Predict Alzheimer Disease Risk. *Neurology*. 2017;88(4):371-378. doi:doi: 10.1212/WNL.0000000000003537

289. Colcombe SJ, Erickson KI, Raz N, et al. Aerobic Fitness Reduces Brain Tissue Loss in Aging Humans. *J Gerontol A Biol Sci Med Sci*. 2003;58(2):M176-M180. doi:10.1093/gerona/58.2.M176

290. Nigatu YT, van de Ven HA, van der Klink JJL, Brouwer S, Reijneveld SA, Bultmann U. Overweight, obesity and work functioning: the role of working-time arrangements. *Appl Ergon*. 2016;52(cyz, 0261412):128-134. doi:10.1016/j.apergo.2015.07.016

291. Rouch I, Wild P, Ansiau D, Marquie J-C. Shiftwork experience, age and cognitive performance. *Ergonomics*. 2005;48(10):1282-1293.

292. Legault G, Clement A, Kenny GP, Hardcastle S, Keller N. Cognitive consequences of sleep deprivation, shiftwork, and heat exposure for underground miners. *Appl Ergon*. 2017;58(cyz, 0261412):144-150. doi:10.1016/j.apergo.2016.06.007

293. Molzof HE, Prapanjaroensin A, Patel VH, Mokashi MV, Gamble KL, Patrician PA. Misaligned core body temperature rhythms impact cognitive performance of hospital shift work nurses. *Neurobiol Learn Mem*. 2019;160(9508166):151-159. doi:10.1016/j.nlm.2019.01.002

294. Williams GW, Shankar B, Klier EM, et al. Sensorimotor and executive function slowing in anesthesiology residents after overnight shifts. *J Clin Anesth*. 2017;40(an9, 8812166):110-116. doi:10.1016/j.jclinane.2017.04.002

295. Ruggiero JS, Redeker NS, Fiedler N, Avi-Itzhak T, Fischetti N. Sleep and psychomotor vigilance in female shiftworkers. *Biol Res Nurs*. 2012;14(3):225-235. doi:10.1177/1099800411408413

296. de Oliveira B, De Martino MMF. [Analysis of cognitive function and sleep of nursing staff on different shift work]. *Rev Gaucha Enferm*. 2013;34(1):30-36.

297. Marquie J-C, Tucker P, Folkard S, Gentil C, Ansiau D. Chronic effects of shift work on cognition: findings from the VISAT longitudinal study. *Occup Environ Med*. 2015;72(4):258-264. doi:10.1136/oemed-2013-101993

298. Harris A, Waage S, Ursin H, Hansen AM, Bjorvatn B, Eriksen HR. Cortisol, reaction time test and health among offshore shift workers. *Psychoneuroendocrinology*. 2010;35(9):1339-1347. doi:10.1016/j.psyneuen.2010.03.006

299. Saadat H, Bissonnette B, Tumin D, et al. Effects of partial sleep deprivation on reaction time in anesthesiologists. *Paediatr Anaesth*. 2017;27(4):358-362. doi:10.1111/pan.13035

300. Behrens T, Burek K, Pallapies D, et al. Decreased psychomotor vigilance of female shift workers after working night shifts. *PLoS ONE*. 2019;14(7):e0219087. doi:10.1371/journal.pone.0219087

301. Mawdsley M, Grasby K, Talk A. The effect of sleep on item recognition and source memory recollection among shift-workers and permanent day-workers. *J Sleep Res*. 2014;23(5):538-544. doi:10.1111/jsr.12149

302. Wehrens SMT, Hampton SM, Kerkhofs M, Skene DJ. Mood, alertness, and performance in response to sleep deprivation and recovery sleep in experienced shiftworkers versus non-shiftworkers. *Chronobiol Int*. 2012;29(5):537-548. doi:10.3109/07420528.2012.675258

303. Ngandu T, Lehtisalo J, Solomon A, et al. A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial. *Lancet*. 2015;385(9984):2255-2263. doi:10.1016/S0140-6736(15)60461-5

304. Molzof HE, Wirth MD, Burch JB, et al. The impact of meal timing on cardiometabolic syndrome indicators in shift workers. *Chronobiol Int*. 2017;34(3):337-348. doi:10.1080/07420528.2016.1259242

305. Tsigos C, Kyrou I, Kassi E, Chrousos GP. Stress: Endocrine Physiology and Pathophysiology. In: Feingold KR, Anawalt B, Boyce A, et al., eds. *Endotext*. MDText.com, Inc.; 2000. Accessed May 17, 2021. http://www.ncbi.nlm.nih.gov/books/NBK278995/

306. Born J, Fehm HL. The neuroendocrine recovery function of sleep. *Noise Health*. 2:25-38.

307. Leproult R, Copinschi G, Buxton O, Van Cauter E. Sleep loss results in an elevation of cortisol levels the next evening. *Sleep*. 1997;20(10):865-870.

308. Akerstedt T, Knutsson A, Westerholm P, Theorell T, Alfredsson L, Kecklund G. Sleep disturbances, work stress and work hours: a cross-sectional study. *J Psychomo Res*. 2002;53:741-748.

309. Qin S, Hermans E, van Marle H, Luo J, Fernández G. Acute psychological stress reduces working memory-related activity in the dorsolateral prefrontal cortex. *Biol Psychiatry*. 2009;66:25-32.

310. Schellekens J, Sijtsma G, Vegter E, Meijman T. Immediate and delayed after-effects of long lasting mentally demanding work. *Biol Psycho*. 2000;53:37-56.

311. Motohashi Y. Alteration of circadian rhythm in shift- working ambulance personnel. Monitoring of salivary cortisol rhythm. *Ergonomics*. 1992;35:1331-1340. doi:doi:10.1080/ 00140139208967396

312. Smith A, Morris P, Rowell K, Clarke S, Jones T, Channer K. Junior doctors and the full shift rota– Psychological and hormonal changes: A comparative cross-sectional study. *Clin Med*. 2006;6:174-177. doi:doi:10.7861/ clinmedicine.6-2-174

313. Vermeulen M, Mustard C. Gender differences in job strain, social support at work, and psychological distress. *J Occup Health Psychol*. 2005;5.

314. About the CLSA Research Platform | Canadian Longitudinal Study on Aging. Accessed December 5, 2020. https://www.clsa-elcv.ca/about-us/about-clsa-research-platform

315. Raina PS, Wolfson C, Kirkland SA, et al. The Canadian Longitudinal Study on Aging (CLSA). *Can J Aging*. 2009;28(3):221-229. doi:10.1017/S0714980809990055

316. Raina P, Wolfson C, Kirkland S, et al. Cohort Profile: The Canadian Longitudinal Study on Aging (CLSA). *Int J Epidemiol*. 2019;48(6):1752-1753j. doi:10.1093/ije/dyz173

317. Bedard M, Steffener J, Taler V. Long-term cognitive impairment following single mild traumatic brain injury with loss of consciousness: Findings from the Canadian Longitudinal Study on Aging. *J Clin Exp Neuropsychol*. 2020;42(4):344-351. doi:10.1080/13803395.2020.1714552

318. Aarsland D, Creese B, Politis M, et al. Cognitive decline in Parkinson disease. *Nat Rev Neurol*. 2017;13(4):217-231. doi:10.1038/nrneurol.2017.27

319. Holmes GL. Cognitive impairment in epilepsy: the role of network abnormalities. *Epileptic Discod*. 2015;17(2):101-116. doi:10.1684/epd.2015.0739

320. Guimarães J, Sá MJ. Cognitive Dysfunction in Multiple Sclerosis. *Front Neur*. 2012;3. doi:10.3389/fneur.2012.00074

321. Statistics Canada. Classification of Full-time and Part-Time Work Hours - 1 - Full-time (work hours). Published July 20, 2011. Accessed January 4, 2021. https://www23.statcan.gc.ca/imdb/p3VD.pl?Function=getVD&TVD=114437&CVD=114437&CLV=0&MLV=1&D=1

322. StataCorp. *Stata Statistical Software: Release 16*. StataCorp LLc

323. Tuokko H, Griffith LE, Simard M, Taler V. Cognitive measures in the Canadian Longitudinal Study on Aging. *Clin Neuropsychol*. 2017;31(1):233-250. doi:10.1080/13854046.2016.1254279

324. Strauss E, Sherman EMS, Spreen O. Rey Auditory Verbal Learning Test (RAVLT). In: *A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary, Third Edition*. 3rd ed. Oxford University Press; 2006:776-810.

325. Canadian Longitudinal Study on Aging. CLSA Tracking and Comprehensive Cognitive Measures (Baseline) Portal Dataset Overview. Published online 2019. Accessed January 2, 2021. https://www.clsa-elcv.ca/doc/3457

326. Cross NE, Carrier J, Postuma RB, et al. Association between insomnia disorder and cognitive function in middle-aged and older adults: a cross-sectional analysis of the Canadian Longitudinal Study on Aging. *Sleep*. 2019;42(8):zsz114. doi:10.1093/sleep/zsz114

327. Billick SB, Siedenburg E, Burgert W, Bruni-Solhkhah SM. Validation of the mental alternation test with the mini-mental state examination in geriatric psychiatric inpatients and normal controls. *Compr Psychiatry*. 2001;42(3):202-205. doi:10.1053/comp.2001.23146

328. Strauss E, Sherman EMS, Spreen O. Stroop Test. In: *A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary, Third Edition*. 3rd ed. Oxford University Press; 2006:477-499.

329. Kessler RC, Barker PR, Colpe LJ, et al. Screening for serious mental illness in the general population. *Arch Gen Psychiatry*. 2003;60(2):184-189. doi:10.1001/archpsyc.60.2.184

330. Andrews G, Slade T. Interpreting scores on the Kessler Psychological Distress Scale (K10). *Aust N Z J Public Health*. 2001;25(6):494-497. doi:10.1111/j.1467-842x.2001.tb00310.x

331. Menec VH, Newall NE, Mackenzie CS, Shooshtari S, Nowicki S. Examining social isolation and loneliness in combination in relation to social support and psychological distress using Canadian Longitudinal Study of Aging (CLSA) data. Reppermund S, ed. *PLoS ONE*. 2020;15(3):e0230673. doi:10.1371/journal.pone.0230673

332. Kessler RC, Andrews G, Colpe LJ, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychol Med*. 2002;32(6):959-976. doi:10.1017/s0033291702006074

333. Andersen LS, Grimsrud A, Myer L, Williams DR, Stein DJ, Seedat S. The psychometric properties of the K10 and K6 scales in screening for mood and anxiety disorders in the South African Stress and Health study. *Int J Methods Psychiatr Res*. 2011;20(4):215-223. doi:10.1002/mpr.351

334. Buysse DJ. Sleep health: can we define it? Does it matter? *Sleep*. 2014;37(1):9-17. doi:10.5665/sleep.3298

335. Dogra S, Good J, Buman MP, Gardiner PA, Stickland MK, Copeland JL. Movement behaviours are associated with lung function in middle-aged and older adults: a cross-sectional analysis of the Canadian longitudinal study on aging. *BMC Public Health*. 2018;18(1):818. doi:10.1186/s12889-018-5739-4

336. Stranges S, Dorn JM, Cappuccio FP, et al. A population-based study of reduced sleep duration and hypertension: the strongest association may be in premenopausal women. *J Hypertens*. 2010;28(5):896-902. doi:10.1097/HJH.0b013e328335d076

337. Sowers MR, La Pietra MT. Menopause: its epidemiology and potential association with chronic diseases. *Epidemiol Rev*. 1995;17(2):287-302. doi:10.1093/oxfordjournals.epirev.a036194

338. Brugère null, Barrit null, Butat null, Cosset null, Volkoff null. _oldShiftwork, Age, and Health: An Epidemiologic Investigation. *Int J Occup Environ Health*. 1997;3(Supplement 2):S15-S19.

339. Nicholson K, Rodrigues R, Anderson KK, Wilk P, Guaiana G, Stranges S. Sleep behaviours and multimorbidity occurrence in middle-aged and older adults: findings from the Canadian Longitudinal Study on Aging (CLSA). *Sleep Med*. 2020;75:156-162. doi:10.1016/j.sleep.2020.07.002

340. Statistics Canada. Postal Code OM Conversion File. Published December 13, 2017. Accessed December 28, 2020. https://www150.statcan.gc.ca/n1/en/catalogue/92-154-X

341. Canadian Longitudinal Study on Aging. Data Support Document Urban / Rural Classification. Published online 2018. Accessed December 28, 2020. https://www.clsa-elcv.ca/sites/default/files/documents/urbanrural_dsd_01_03_2018_final.pdf

342. Canadian Longitudinal Study on Aging. Urban/Rural Classification. Published online 2018. Accessed March 4, 2021. https://www.clsa-elcv.ca/sites/default/files/documents/urbanrural_dsd_01_03_2018_final.pdf

343. Menec VH, Newall NE, Mackenzie CS, Shooshtari S, Nowicki S. Examining individual and geographic factors associated with social isolation and loneliness using Canadian Longitudinal Study on Aging (CLSA) data. Latham-Mintus K, ed. *PLoS ONE*. 2019;14(2):e0211143. doi:10.1371/journal.pone.0211143

344. Washburn RA, Smith KW, Jette AM, Janney CA. The Physical Activity Scale for the Elderly (PASE): development and evaluation. *J Clin Epidemiol*. 1993;46(2):153-162. doi:10.1016/0895-4356(93)90053-4

345. Keller HH, Goy R, Kane S-L. Validity and reliability of SCREEN II (Seniors in the community: risk evaluation for eating and nutrition, Version II). *Eur J Clin Nutr*. 2005;59(10):1149-1157. doi:10.1038/sj.ejcn.1602225

346. Roberts KC, Rao DP, Bennett TL, Loukine L, Jayaraman GC. Prevalence and patterns of chronic disease multimorbidity and associated determinants in Canada. *Health Promot Chronic Dis Prev Can*. 2015;35(6):87-94. doi:10.24095/hpcdp.35.6.01

347. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med*. 2011;30(4):377-399. doi:10.1002/sim.4067

348. Carpenter JR, Kenward MG. *Multiple Imputation and Its Application*. 1st ed. John Wiley & Sons; 2013.

349. Kalton G, Kasprzyk D. The Treatment of Missing Survey Data. *Surv Methodol*. 1986;12(1986001):1-16.

350. Hughes RA, Heron J, Sterne JAC, Tilling K. Accounting for missing data in statistical analyses: multiple imputation is not always the answer. *Int J Epidemiol*. 2019;48(4):1294-1304. doi:10.1093/ije/dyz032

351. Azur MJ, Stuart EA, Frangakis C, Leaf PJ. Multiple imputation by chained equations: what is it and how does it work? *Int J Methods Psychiatr Res*. 2011;20(1):40-49. doi:10.1002/mpr.329

352. Wilson MD, Lueck K. Working with Missing Data: Imputation of Nonresponse Items in Categorical Survey Data with a Non-Monotone Missing Pattern. *J Appl Math*. 2014;2014:1-9. doi:10.1155/2014/368791

353. Buuren S van. *Flexible Imputation of Missing Data*. 2nd ed. CRC Press; 2018. https://doi.org/10.1201/9780429492259

354. Lumley T, Diehr P, Emerson S, Chen L. The Importance of the Normality Assumption in Large Public Health Data Sets. *Annu Rev Public Health*. 2002;23(1):151-169. doi:10.1146/annurev.publhealth.23.100901.140546

355. Vittinghoff E, Glidden DV, Shiboski SC, McCulloch CE. *Regression Methods in Biostatistics: Linear, Logistic, Survival, and Repeated Measures Models*. 2nd ed. Springer-Verlag; 2012. doi:10.1007/978-1-4614-1353-0

356. Elhami Athar M, Atef-Vahid M-K, Ashouri A. The Influence of Shift Work on the Quality of Sleep and Executive Functions. *J Circadian Rhythms*. 2020;18(1):4. doi:10.5334/jcr.194

357. Wright KP, Lowry CA, LeBourgeois MK. Circadian and wakefulness-sleep modulation of cognition in humans. *Front Mol Neurosci*. 2012;5(50). doi:10.3389/fnmol.2012.00050

358. Chellappa SL, Morris CJ, Scheer FAJL. Daily circadian misalignment impairs human cognitive performance task-dependently. *Sci rep*. 2018;8(1):3041. doi:10.1038/s41598-018-20707-4

359. Chellappa SL, Morris CJ, Scheer FAJL. Effects of circadian misalignment on cognition in chronic shift workers. *Sci Rep*. 2019;9. doi:10.1038/s41598-018-36762-w

360. Hajali V, Andersen ML, Negah SS, Sheibani V. Sex differences in sleep and sleep loss-induced cognitive deficits: The influence of gonadal hormones. *Horm Behav*. 2019;108:50-61. doi:10.1016/j.yhbeh.2018.12.013

361. Simard M, Hudon C, van Reekum R. Psychological distress and risk for dementia. *Curr Psychiatry Rep*. 2009;11(1):41-47. doi:10.1007/s11920-009-0007-z

362. Åkerstedt T, Wright KP. Sleep Loss and Fatigue in Shift Work and Shift Work Disorder. *Sleep Med Clin*. 2009;4(2):257-271. doi:10.1016/j.jsmc.2009.03.001

363. Kazemi R., Haidarimoghadam R., Motamedzadeh M., Golmohamadi R., Soltanian A., Zoghipaydar M.R. Effects of shift work on cognitive performance, sleep quality, and sleepiness among petrochemical control room operators. *J Circadian Rhythms*. 2016;14(1):1-8. doi:10.5334/jcr.134

364. Costa G. Shift Work and Health: Current Problems and Preventive Actions. *Saf Health Work*. 2010;1(2):112-123. doi:10.5491/SHAW.2010.1.2.112

365. Spira AP, Chen-Edinboro LP, Wu MN, Yaffe K. Impact of sleep on the risk of cognitive decline and dementia. *Curr Opin Psychiatry*. 2014;27(6):478-483. doi:10.1097/YCO.0000000000000106

366. Virta JJ, Heikkilä K, Perola M, et al. Midlife sleep characteristics associated with late life cognitive function. *Sleep*. 2013;36(10):1533-1541, 1541A. doi:10.5665/sleep.3052

367. Blackwell T, Yaffe K, Laffan A, et al. Associations of objectively and subjectively measured sleep quality with subsequent cognitive decline in older community-dwelling men: the MrOS sleep study. *Sleep*. 2014;37(4):655-663. doi:10.5665/sleep.3562

368. Jørgensen JT, Hansen J, Westendorp RGJ, et al. Shift work and incidence of dementia: A Danish Nurse Cohort study. *Alzheimers Dement*. 2020;16(9):1268-1279. doi:10.1002/alz.12126

369. Bartlett JW, Seaman SR, White IR, Carpenter JR. Multiple imputation of covariates by fully conditional specification: Accommodating the substantive model. *Stat Methods Med Res*. 2015;24(4):462-487. doi:10.1177/0962280214521348

Appendices

Appendix A: Summary of Included Studies Examining the Association Between Shift Work and Cognitive Impairment (n=25)

Study	Country	Study Design	N	%M	Occupation	Shift Type (n)	Work Schedule	Cognitive Assessment Tool(s)	Relationship between Shift Work and Cognition
Rouch et al. (2005)[e]	France	Cross-sectional study	3237	51	Various	Current SW (586) Former SW (588)	NR	Memory test (adapted from Rey Verbal Learning Test), Digit-Symbol Substitution subtest of WAIS, Selective attention test (derived from the Sternberg Test)	Compared to never exposed SW, current male SW showed significantly lower cognitive scores for immediate free recall and speed tests but not for delayed retrieval tests.
						Never SW (2063)			
Karanovic et al. (2009)[b]	Croatia	Prospective repeated measures design	11	55	Staff anesth-esiologists	24-H shift (11)	NR	Complex Reactionmeter Drenovac Series	Compared to an ordinary workday, tests for psychomotor and cognitive functioning were significantly impaired during the 24-H shift
						Ordinary day (11)			
Harris et al. (2010)[d]	Norway	Prospective repeated measures design	19	68	Offshore oil rig industry	Fixed shift: Day and Night (19)	1st week Day shift: 7am – 7pm	10 min simple serial reaction time test	There were no significant differences in reaction time when changing from day work to night work on the swing shift, relative to the fixed shift
							2nd week Night shift: 7pm – 7am		
						Swing shift: Day and Night (19)	Night shift ends at 4am or 6am and day shift begins 8-H later at 12pm or 2pm		
						Day (15)	7am – 7pm		

Abbreviations: H: hour; M: male; NR: not reported; PVT: psychomotor vigilance test; SW: shift work or shift workers WAIS: Wechsler Adult Intelligence Scale; % M: proportion of males

[a]Cognition assessed before and after work shift; [b]Cognition assessed during work shift; [c]Cognition assessed after work shift; [d]Cognition assessed at follow-up; [e]Time of cognition assessment not specified

Appendix A (continued)

Study	Country	Study Design	N	%M	Occupation	Shift Type (n)	Work Schedule	Cognitive Assessment Tool(s)	Relationship between Shift Work and Cognition
Geiger-Brown et al. (2012)[a]	USA	Prospective cohort study	80	0	Registered nurses	12-H day (39) 12-H night (41)	NR	5-min PVT	There were no significant differences in mean reaction time between day and night shifts
Machi et al. (2012)[a]	USA	Prospective repeated measures design	13	69	Emergency physicians	Day (13) Overnight (13)	NR	Paced Auditory Serial Addition Test, The University of Southern California Repeatable Episodic Memory Test, Trail Making Test, Stroop Color-Word Test	Short-term memory scores significantly decreased after both day and overnight shifts. Scores for executive functioning significantly decreased after an overnight shift while no significant difference was observed after the day shift
Ruggiero et al. (2012)[a]	USA	Prospective cohort study	16	0	Staff registered nurses	Day (10) Night (6)	7am – 7:30pm or 6am – 6:30pm 7pm–7:30am	10-min PVT	There were no significant differences in PVT test results comparing night shift to day shift
Wehrens et al. (2012)[c]	UK	Non-randomized controlled trial	25	100	Various	SW (11) Non-SW (14)	NR	10-min PVT	There were no significant differences in PVT parameters between SW and non-SW

Abbreviations: H: hour; M: male; NR: not reported; PVT: psychomotor vigilance test; SW: shift work or shift workers WAIS: Wechsler Adult Intelligence Scale; % M: proportion of males

[a]Cognition assessed before and after work shift; [b]Cognition assessed during work shift; [c]Cognition assessed after work shift; [d]Cognition assessed at follow-up; [e]Time of cognition assessment not specified

Appendix A (continued)

Study	Country	Study Design	N	%M	Occupation	Shift Type (n)	Work Schedule	Cognitive Assessment Tool(s)	Relationship between Shift Work and Cognition
Devore et al. (2013)[d]	USA	Cross-sectional study	16190	0	Nurses	1-9 years SW (7685) 10-19 years SW (1341) $\geq$ 20 years SH (1028)	NR	Telephone Interview of Cognitive Status	Compared to no history of SW, there were no significantly consistent associations between history of SW and cognitive impairment in later life
						No SW history (6136)			
De Oliveria and De Martino. (2012)[a]	Brazil	Prospective cohort study	109	NR	Nursing staff	Night (41)	7pm – 7am	Digit Span Subtest, Digit Symbol Subtest (WAIS III)	Compared to night SW, day SW performed significantly better on tests of attention. No significant differences were observed between the two groups for tests of short-term memory
						Day (68)	7am – 7pm		
Ozdemir et al. (2013)[a]	Turkey	Prospective cohort study	90	49	Health care industry	Rotating SW (45)	8am- 4pm (3 weeks), 4pm – 8am (3 weeks)	Wechsler Memory Scale-Revised, Auditory Verbal Learning Test, Stroop Color-Word Interference Test-TBAG	Night SW preformed significantly worse compared to daytime SW on all cognitive tests
						Day (45)	8am- 4pm		
Ernst et al. (2014)[a]	Austria	Randomized crossover trial	30	70	Physicians	On-call duty (12)	24 H (including routine workday)	The D2 Test of Attention	Compared to routine day workers, cognitive performance was significantly decreased after on-call duty SW
						Routine day (12)	8am – 4:30pm		

Abbreviations: H: hour; M: male; NR: not reported; PVT: psychomotor vigilance test; SW: shift work or shift workers WAIS: Wechsler Adult Intelligence Scale; % M: proportion of males

[a]Cognition assessed before and after work shift; [b]Cognition assessed during work shift; [c]Cognition assessed after work shift; [d]Cognition assessed at follow-up; [e]Time of cognition assessment not specified

Appendix A (continued)

Study	Country	Study Design	N	%M	Occupation	Shift Type (n)	Work Schedule	Cognitive Assessment Tool(s)	Relationship between Shift Work and Cognition
Mawdsley et al. (2014)[c]	Australia	Randomized controlled trial	40	48	Health care industry	SW (20)	Any shift ending between 12 – 8am	Paper and pencil source memory test	There was a significant association between work schedule and word recognition
						Permanent day (20)	Any other shift		
Marquie et al. (2015)[d]	France	Prospective cohort study	3119	51	Various	Current or past rotating SW (1484)	NR	Memory test (adapted from Rey Verbal Learning Test), Digit-Symbol Substitution subtest of WAIS, Selective attention test (derived from the Sternberg Test)	There was a significant association with exposure to SW on chronic cognitive impairment
						No SW experience (1635)			
Nigatu et al. (2016)[e]	Nether-lands	Cross-sectional study	622	NR	Industrial process and chemical sector	Rotating SW (384)	NR	Mental demands (subscale of Work Role Functioning Questionnaire-Dutch version)	There were no significant differences in the mental demands subscale between the work shifts
						On-call (171)	NR		
						Day (67)	9am – 5pm		
Saadat et al. (2016)[b]	USA	Prospective Repeated measures design	21	71	Anesth-esiologists	17-H on-call night (21)	3pm – 7am	Simple Cognitive Tests	Compared to regular day shifts, cognitive skills were significantly altered after on-call shifts
						Regular day (21)	NR		

Abbreviations: H: hour; M: male; NR: not reported; PVT: psychomotor vigilance test; SW: shift work or shift workers WAIS: Wechsler Adult Intelligence Scale; % M: proportion of males

[a]Cognition assessed before and after work shift; [b]Cognition assessed during work shift; [c]Cognition assessed after work shift; [d]Cognition assessed at follow-up; [e]Time of cognition assessment not specified

Appendix A (continued)

Study	Country	Study Design	N	%M	Occupation	Shift Type (n)	Work Schedule	Cognitive Assessment Tool(s)	Relationship between Shift Work and Cognition
Titova et al. (2016)[e]	Sweden	Cross-sectional study	7143	40	Various	Past SW (1531) Recent former SW (358) Current SW (643)	NR	Trail Making Test	Compared to non-SW, current and recent former SW performed significantly worse on cognitive tests. Scores did not significantly differ between past and non-SW
						Non-SW (4611)			
Wong et al. (2016)[e]	Canada	Cross-sectional study	4255	46	Various	Regular night/ graveyard (223) Rotating (441) Other (404)	NR	Self-reported cognitive function from the Health Utility Index	Night shifts and cognitive impairment were indirectly associated through work stress and sleep quality
						Day (3184)			
Bokenberger et al. (2017)[d]	Sweden	Prospective cohort study	595	50	Various	SW history (106)	NR	Battery of cognitive tests used in the Swedish Adoption Twin Study of Aging	Compared to no SW history, there was no significant association between SW history and cognitive impairment in later life
						No SW history (489)			

Abbreviations: H: hour; M: male; NR: not reported; PVT: psychomotor vigilance test; SW: shift work or shift workers WAIS: Wechsler Adult Intelligence Scale; % M: proportion of males

[a]Cognition assessed before and after work shift; [b]Cognition assessed during work shift; [c]Cognition assessed after work shift; [d]Cognition assessed at follow-up; [e]Time of cognition assessment not specified

Appendix A (continued)

Study	Country	Study Design	N	%M	Occupation	Shift Type (n)	Work Schedule	Cognitive Assessment Tool(s)	Relationship between Shift Work and Cognition
Legault et al. (2017)[b]	Canada	Prospective cohort study	19	100	Miners	Rotating day and night (14)	Day shift: start at 5:30 - 7:30 am end at 4 - 6pm	3-min PVT	There were no significant differences in reaction time over the course of a day shift, however there were significant changes in reaction time during a night shift
							Night shift: start at 5:30 7:30pm end at 4 - 6am		
						Rotating day and afternoon (5)	Day shift: start at 5:30-7:30 am end at 4-6pm		
							Afternoon shift: start at 5:30 – 6:30 pm end at 2 – 3am		
Williams et al. (2017)[a]	USA	Prospective cohort study	57	59	Anesth-esiologist residents	Overnight on-call (28)	5pm – 7am	AntiPoint Task	Compared to daytime SW, overnight on-call workers showed significantly increased reaction time across their shift
						Day (29)	7am – 5pm		
Castro and De Almondes. (2018)[a]	Brazil	Prospective cohort study	26	65	Emergency physicians	Rotating (20)	NR	Iowa Gambling Task	There were no significant differences in the decision-making task between the two shifts
						Day (6)			

Abbreviations: H: hour; M: male; NR: not reported; PVT: psychomotor vigilance test; SW: shift work or shift workers WAIS: Wechsler Adult Intelligence Scale; % M: proportion of males

[a]Cognition assessed before and after work shift; [b]Cognition assessed during work shift; [c]Cognition assessed after work shift; [d]Cognition assessed at follow-up; [e]Time of cognition assessment not specified

Appendix A (continued)

Study	Country	Study Design	N	%M	Occupation	Shift Type (n)	Work Schedule	Cognitive Assessment Tool(s)	Relationship between Shift Work and Cognition
Osterode et al. (2018)[a]	Austria	Randomized crossover trial	34	77	Physicians	Day-night (34)	8am – 4pm	Visual Recognition Test (by Kessler, Pietrzyk and Schuhfried)	Compared to day shifts, after a night shift, physicians exhibited significantly more mistakes in the visual recognition test
						Regular day (34)	8am – 8am the next day		
Rheaume and Mullen. (2018)[c]	Canada	Prospective cohort study	28	NR	Nurses	12-H rotating (14)	NR	Workplace Cognitive Failure Scale	There were no significant differences in cognitive errors between the two shifts
						8-H day (14)			
Behrens et al. (2019)[c]	Germany	Prospective repeated measures design	71	0	Nurses	Night (71)	9pm – 6am	3-min PVT	Compared to day shifts, there was a significant association between nurses working night shifts and decreased psychomotor vigilance
						Day (71)	6am – 2pm		
Molzof et al. (2019)[c]	USA	Prospective cohort study	30	0	Nurses	Night (15)	7pm – 7am	Two Digit Addition Test, 10-min PVT	Compared to day shift nurses, night shift nurses exhibited significantly slower cognitive proficiency at the end of the shift. There were no significant differences in reaction time between the two shifts
						Day (15)	7am – 7pm		

Abbreviations: H: hour; M: male; NR: not reported; PVT: psychomotor vigilance test; SW: shift work or shift workers WAIS: Wechsler Adult Intelligence Scale; % M: proportion of males

[a]Cognition assessed before and after work shift; [b]Cognition assessed during work shift; [c]Cognition assessed after work shift; [d]Cognition assessed at follow-up; [e]Time of cognition assessment not specified

Appendix B: Associations between Categorical Variables

Table 1: Association between Education Level and Household Income

Household Income	Level of Education				
	Less than Secondary Education (%)	Secondary Education (%)	Some Post-Secondary Education (%)	Post-Secondary Education (%)	Chi-Square Test (X^2)
Less than $20,000	0.5	0.3	0.2	1.2	956.6**
$20,000 – $49,999	1.8	2.4	1.3	9.9	
$50,000 - $99,999	0.1	3.4	2.2	27.1	
$100,000 - $149,99	0.2	1.7	1.2	21.0	
Greater than $150,000	0.1	0.7	0.	22.7	

* p <0.05, **p <0.001

Table 2: Association between Cardiovascular Disease and Hypertension

Hypertension	Cardiovascular Disease		
	No (%)	Yes (%)	Chi-Square Test (X^2)
No	79.2	7.3	1.3
Yes	12.3	1.3	

* p <0.05, **p <0.001

Table 3: Association between Cancer and Gastrointestinal Disease

Gastrointestinal Disease	Cancer		
	No (%)	Yes (%)	Chi-Square Test (X^2)
No	78.6	9.7	2.9
Yes	10.2	1.5	

* p <0.05, **p <0.001

Table 4: Associations between Individual Chronic Conditions and Multimorbidity

	Multimorbidity		
	0 to 1 Chronic Condition (%)	**Two or More Chronic Conditions (%)**	**Chi-Square Test (X^2)**
Hypertension			
No	68.2	18.3	25.2**
Yes	9.8	3.7	
Cancer			
No	73.3	15.5	925.3**
Yes	4.7	6.5	
Cardiovascular Disease			
No	75.4	16.1	1213.6**
Yes	2.6	5.9	
Diabetes			
No	73.1	13.3	1570.0**
Yes	5.0	8.6	
Anxiety or Depression			
No	70.9	12.5	1413.2**
Yes	7.1	9.5	
Gastrointestinal Disease			
No	70.3	18.0	115. 2**
Yes	7.7	4.0	

* p <0.05, **p <0.001

Appendix C: Results of Multicollinearity Assessments

Table 1: Results of Multicollinearity Assessment for Objective 1

	Variance Inflation Factor (VIF)	Tolerance
Model 1	1.2	0.8
Model 2	1.2	0.8
Model 3	1.1	0.9
Model 4	1.4	0.7

Model 1: Association between shift work and performance on the immediate recall
Model 2: Association between shift work and performance on the delayed recall
Model 3: Association between shift work and performance on the MAT
Model 4: Association between shift work and performance on the interference condition

Table 2: Results of Multicollinearity Assessment for Objective 2

	Variance Inflation Factor (VIF)	Tolerance
Model 1	1.2	0.8
Model 2	1.2	0.8
Model 3	1.1	0.9
Model 4	1.4	0.7

Model 1: Moderating effect of psychological distress on the association between shift work and performance on the immediate recall
Model 2: Moderating effect of psychological distress on the association between shift work and performance on the delayed recall
Model 3: Moderating effect of psychological distress on the association between shift work and performance on the MAT
Model 4: Moderating effect of psychological distress on the association between shift work and performance on the interference condition

Table 3: Results of Multicollinearity Assessment for Objective 3

	Variance Inflation Factor (VIF)	Tolerance
Model 1	1.19	0.838
Model 2	1.20	0.836
Model 3	1.13	0.885
Model 4	1.36	0.887

Model 1: Moderating effect of sleep quality on the association between shift work and performance on the immediate recall
Model 2: Moderating effect of sleep quality on the association between shift work and performance on the delayed recall
Model 3: Moderating effect of sleep quality on the association between shift work and performance on the MAT
Model 4: Moderating effect of sleep quality on the association between shift work and performance on the interference condition

Appendix D: Sensitivity Analysis Comparing Results of Multiple Imputation to Complete Case Analysis

Table 1. Unadjusted and adjusted association between shift work and performance on cognitive tests for declarative memory

	Immediate Recall Trial				**Delayed Recall Trial**			
	MI (N =12,152)		**CCA (N=9,912)**		**MI (N =12,152)**		**CCA (N=9,912)**	
	ß (SE)	**95% CI**	**ß (SE)**	**95% CI**	**ß (SE)**	**95% CI**	**ß (SE)**	**95% CI**
Unadjusted Association								
Intercept	**6.07 (0.02)**	**6.03, 6.12**	**6.13 (0.02)**	**6.08, 6.17**	**4.31 (0.02)**	**4.26, 4.36**	**4.39 (0.03)**	**4.34, 4.44**
No Shift work	R		R		R		R	
Shift work	**-0.20 (0.05)**	**-0.30, -0.09**	**-0.18 (0.06)**	**-0.29, -0.06**	**-0.20 (0.06)**	**-0.32, -0.08**	**-0.24 (0.07)**	**-0.37, -0.11**
Adjusted Association								
Intercept	**5.48 (0.21)**	**5.07, 5.89**	**5.81 (0.25)**	**5.32, 6.30**	**4.12 (0.23)**	**3.66, 4.58**	**4.45 (0.28)**	**3.90, 5.01**
No Shift work	R		R		R		R	
Shift work	-0.04 (0.05)	-0.14, 0.06	-0.02 (0.05)	-0.13, 0.09	-0.05 (0.06)	-0.16, 0.06	-0.08 (0.06)	-0.21, 0.04
Age (years)								
45 -54 years	R		R		R		R	
55 -64 years	**-0.23 (0.05)**	**-0.32, -0.14**	**-0.23 (0.05)**	**-0.33, -0.13**	**-0.43 (0.05)**	**-0.54, -0.33**	**-0.45 (0.06)**	**-0.56, -0.33**
65 - 74 years	**-0.61 (0.06)**	**-0.72, -0.49**	**-0.60 (0.07)**	**-0.73, -0.47**	**-0.92 (0.07)**	**-1.05, -0.79**	**-0.95 (0.07)**	**-1.10, -0.81**
75 – 85 years	**-1.44 (0.07)**	**-1.58, -1.30**	**-1.44 (0.08)**	**-1.59, -1.29**	**-1.74 (0.08)**	**-1.88, -1.58**	**-1.74 (0.09)**	**-1.91, -1.57**
Sex								
Female	R		R		R		R	
Male	**-0.76 (0.04)**	**-0.84, -0.68**	**-0.74 (0.04)**	**-0.83, -0.66**	**-0.96 (0.05)**	**-1.06, -0.87**	**-0.98 (0.05)**	**-1.08, -0.88**

Abbreviations: CCA: complete case analysis; CI: confidence interval; MI: multiple imputation; R: reference; SE: standard error. Significant results are bolded.

Table 1. (continued)

	Immediate Recall Trial				Delayed Recall Trial			
	MI (N =12,152)		CCA (N=9,912)		MI (N =12,152)		CCA (N=9,912)	
	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI
Retirement Status								
Completely	R		R		R		R	
Not or Partly	0.03 (0.05)	-0.06, 0.13	0.04 (0.05)	-0.06, 0.14	0.07 (0.06)	-0.04, 0.18	0.08 (0.06)	-0.04, 0.20
Education								
Less than secondary	R		R		R		R	
Secondary	**0.42 (0.09)**	**0.23, 0.60**	**0.42 (0.10)**	**0.22, 0.63**	**0.31 (0.11)**	**0.10, 0.52**	**0.36 (0.12)**	**0.13, 0.59**
Some post-secondary	**0.70 (0.10)**	**0.50, 0.90**	**0.72 (0.11)**	**0.50, 0.95**	**0.65 (0.12)**	**0.42, 0.88**	**0.71 (0.13)**	**0.46, 0.95**
Post-secondary	**0.78 (0.08)**	**0.62, 0.94**	**0.79 (0.09)**	**0.62, 0.98**	**0.69 (0.09)**	**0.51, 0.87**	**0.75 (0.10)**	**0.55, 0.94**
Household Income								
Less than $20,000	R		R		R		R	
$20,000 - $49,999	**0.24 (0.10)**	**0.03, 0.44**	**0.13 (0.11)**	**-0.09, 0.36**	0.21 (0.11)	-0.01, 0.43	0.14 (0.12)	-0.10, 0.38
$50,000 - $99,999	**0.54 (0.10)**	**0.34, 0.75**	**0.44 (0.12)**	**0.21, 0.67**	**0.42 (0.11)**	**0.21, 0.64**	**0.31 (0.12)**	**0.06, 0.55**
$100,000 - $149,999	**0.65 (0.11)**	**0.43, 0.87**	**0.52 (0.12)**	**0.28, 0.77**	**0.51 (0.12)**	**0.26, 0.75**	**0.34 (0.13)**	**0.08, 0.60**
Greater than $150,000	**0.82 (0.12)**	**0.59, 1.05**	**0.69 (0.13)**	**0.44, 0.94**	**0.59 (0.13)**	**0.34, 0.84**	**0.42 (0.14)**	**0.15, 0.70**

Abbreviations: CCA: complete case analysis; CI: confidence interval; MI: multiple imputation; R: reference; SE: standard error. Significant results are bolded.

Table 1. (continued)

	Immediate Recall Trial				Delayed Recall Trial			
	MI (N =12,152)		CCA (N=9,912)		MI (N =12,152)		CCA (N=9,912)	
	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI
Marital Status								
Single, never married, or never lived with a partner	R		R		R		R	
Married or common law	0.04 (0.07)	-0.09, 0.17	0.02 (0.08)	-0.13, 0.17	0.01 (0.08)	-0.14, 0.17	-0.03 (0.09)	-0.20, 0.13
Widowed, divorced, or separated	0.07 (0.07)	-0.08, 0.22	0.06 (0.08)	-0.11, 0.22	-0.01 (0.08)	-0.17, 0.16	-0.02 (0.09)	-0.20, 0.16
Migrant Status								
Non-immigrant	R		R		R		R	
Immigrant	0.02 (0.06)	-0.09, 0.13	0.07 (0.06)	-0.06, 0.19	-0.03 (0.07)	-0.16, 0.10	0.06 (0.07)	-0.08,0.20
Place of Residence								
Rural	R		R		R		R	
Urban	0.05 (0.06)	-0.08, 0.17	0.06 (0.07)	-0.08, 0.19	0.10 (0.08)	-0.05, 0.26	0.11 (0.08)	-0.05, 0.27
Suburban	0.03 (0.10)	-0.17, 0.23	-0.01 (0.11)	-0.23, 0.21	0.08 (0.12)	-0.17, 0.32	0.04 (0.13)	-0.22, 0.30
Socially Isolated								
No	R		R		R		R	
Yes	-0.05 (0.05)	-0.14, 0.04	-0.04 (0.05)	-0.15, 0.06	-0.08 (0.05)	-0.18, 0.03	-0.04 (0.06)	-0.15, 0.08

Abbreviations: CCA: complete case analysis; CI: confidence interval; MI: multiple imputation; R: reference; SE: standard error. Significant results are bolded.

Table 1. (continued)

	Immediate Recall Trial				Delayed Recall Trial			
	MI (N =12,152)		CCA (N=9,912)		MI (N =12,152)		CCA (N=9,912)	
	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI
Smoking Status								
Never smoker	R		R		R		R	
Former smoker	**-0.18 (0.04)**	**-0.26, -0.10**	**-0.19 (0.04)**	**-0.28, -0.11**	**-0.14 (0.05)**	**-0.24, -0.05**	**-0.15 (0.05)**	**-0.25, -0.04**
Occasional or daily smoker	**-0.30 (0.07)**	**-0.44, -0.15**	**-0.28 (0.08)**	**-0.44, -0.12**	-0.10 (0.08)	-0.26, 0.06	-0.05 (0.09)	-0.22, 0.13
Alcohol Consumption								
Never drinker	R		R		R		R	
Former drinker	0.10 (0.14)	-0.18, 0.37	-0.06 (0.18)	-0.41, 0.31	-0.07 (0.16)	-0.39, 0.25	-0.29 (0.22)	-0.71, 0.14
Infrequent drinker	0.06 (0.14)	-0.22, 0.33	-0.15 (0.18)	-0.51, 0.21	0.04 (0.16)	-0.27, 0.36	-0.17 (0.21)	-0.59, 0.24
Occasional drinker	0.16 (0.13)	-0.10, 0.42	-0.00 (0.18)	-0.34, 0.35	0.17 (0.15)	-0.13, 0.47	-0.01 (0.21)	-0.42, 0.40
Regular or binge drinker	0.22 (0.13)	-0.03, 0.48	0.05 (0.18)	-0.29, 0.40	0.24 (0.15)	-0.06, 0.54	0.08 (0.21)	-0.33, 0.48
BMI								
Underweight or normal weight	R		R		R		R	
Overweight	-0.01 (0.04)	-0.10, 0.08	-0.03 (0.05)	-0.13, 0.06	0.00 (0.05)	-0.10, 0.11	0.00 (0.06)	-0.11, 0.11
Obese	-0.02 (0.05)	-0.12, 0.07	-0.05 (0.05)	-0.15, 0.06	-0.11 (0.06)	-0.23, 0.00	-0.08 (0.06)	-0.20, 0.04
Past Week Physical Activity	0.00 (0.00)	0.00, 0.00	0.00 (0.00)	0.00, 0.00	0.00 (0.00)	0.00, 0.00	0.00 (0.00)	0.00, 0.00

Abbreviations: CCA: complete case analysis; CI: confidence interval; MI: multiple imputation; R: reference; SE: standard error. Significant results are bolded.

Table 1. (continued)

	Immediate Recall Trial				Delayed Recall Trial			
	MI (N =12,152)		CCA (N=9,912)		MI (N =12,152)		CCA (N=9,912)	
	ß (SE)	**95% CI**	**ß (SE)**	**95% CI**	**ß (SE)**	**95% CI**	**ß (SE)**	**95% CI**
Fruit and Vegetable Intake								
Seven or more	R		R		R		R	
Six	-0.04 (0.08)	-0.19, 0.11	-0.07 (0.09)	-0.24, 0.09	0.04 (0.09)	-0.14, 0.21	0.03 (0.10)	-0.16, 0.22
Five	0.00 (0.07)	-0.14, 0.15	-0.02 (0.08)	-0.17, 0.13	0.05 (0.08)	-0.12, 0.21	0.06 (0.09)	-0.12, 0.23
Four	-0.08 (0.07)	-0.22, 0.07	-0.13 (0.08)	-0.28, 0.03	-0.07 (0.08)	-0.23, 0.09	-0.09 (0.09)	-0.26, 0.08
Three	**-0.19 (0.07)**	**-0.33, -0.05**	**-0.22 (0.08)**	**-0.38, -0.07**	-0.17 (0.08)	-0.33, 0.00	-0.15 (0.09)	-0.32, 0.03
Two	**-0.31 (0.08)**	**-0.46, -0.16**	**-0.32 (0.08)**	**-0.49, -0.16**	**-0.27 (0.09)**	**-0.44, -0.10**	**-0.27 (0.09)**	**-0.45, -0.08**
Less than two	**-0.27 (0.09)**	**-0.43, -0.10**	**-0.33 (0.09)**	**-0.51, -0.15**	**-0.27 (0.10)**	**-0.46, -0.08**	**-0.26 (0.10)**	**-0.47, -0.06**
Self-rated Health								
Excellent or Good	R		R		R		R	
Fair or Poor	0.00 (0.08)	-0.16, 0.15	-0.05 (0.09)	-0.23, 0.13	-0.01 (0.09)	-0.18, 0.17	-0.11 (0.10)	-0.31, 0.08
Multimorbidity								
0 -1 Chronic Disease	R		R		R		R	
$\geq$ 2 Chronic Diseases	0.01 (0.03)	-0.07, 0.09	0.02 (0.04)	-0.07, 0.11	0.01 (0.05)	-0.08, 0.10	0.01 (0.05)	-0.09, 0.11

Abbreviations: CCA: complete case analysis; CI: confidence interval; MI: multiple imputation; R: reference; SE: standard error. Significant results are bolded.

Table 2. Unadjusted and adjusted association between shift work and performance on cognitive tests for executive functioning

	MAT				**Interference Condition**			
	MI (N =12,152)		**CCA (N=9,912)**		**MI (N =12,152)**		**CCA (N=9,912)**	
	ß (SE)	**95% CI**	**ß (SE)**	**95% CI**	**ß (SE)**	**95% CI**	**ß (SE)**	**95% CI**
Unadjusted Association								
Intercept	**27.95 (0.10)**	**27.76, 28.14**	**28.41 (0.10)**	**28.21, 28.62**	**15.22 (0.04)**	**15.13, 15.30**	**14.96 (0.04)**	**14.88, 15.05**
No Shift work	R		R		R		R	
Shift work	**-1.59 (0.25)**	**-2.08, -1.10**	**-1.76 (0.28)**	**-2.30, -1.21**	**0.78 (0.12)**	**0.54, 1.03**	**0.75 (0.12)**	**0.51, 0.99**
Adjusted Association								
Intercept	**20.17 (1.04)**	**18.13, 22.21**	**22.04 (1.19)**	**19.71, 24.36**	**18.26 (0.54)**	**17.19, 19.33**	**17.00 (0.52)**	**15.98, 18.02**
No Shift work	R		R		R		R	
Shift work	**-0.89 (0.24)**	**-1.36, -0.42**	**-1.10 (0.26)**	**-1.62, -0.59**	**0.43 (0.11)**	**0.22, 0.64**	**0.45 (0.10)**	**0.24, 0.65**
Age (years)								
45 -54 years	R		R		R		R	
55 -64 years	**-1.05 (0.23)**	**-1.50, -0.61**	**-1.08 (0.24)**	**-1.55, -0.60**	**1.07 (0.09)**	**0.89, 1.24**	**1.12 (0.09)**	**0.95, 1.29**
65 - 74 years	**-2.26 (0.29)**	**-2.83, -1.70**	**-2.51 (0.31)**	**-3.12, -1.90**	**2.69 (0.13)**	**2.44, 2.94**	**2.80 (0.13)**	**2.55, 3.05**
75 – 85 years	**-5.04 (0.34)**	**-5.70, -4.37**	**-5.05 (0.38)**	**-5.79, -4.31**	**5.03 (0.17)**	**4.71, 5.37**	**5.03 (0.17)**	**4.70, 5.38**
Sex								
Female	R		R		R		R	R
Male	**1.58 (0.19)**	**1.21, 1.94**	**1.70 (0.21)**	**1.30, 2.11**	**0.59 (0.08)**	**0.43, 0.74**	**0.44 (0.08)**	**0.28, 0.59**

Abbreviations: CCA: complete case analysis; CI: confidence interval; MI: multiple imputation; R: reference; SE: standard error. Significant results are bolded.

Table 2. (continued)

	MAT				Interference Condition			
	MI (N =12,152)		CCA (N=9,912)		MI (N =12,152)		CCA (N=9,912)	
	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI
Retirement Status								
Completely	R		R		R		R	
Not or Partly	0.30 (0.23)	-0.15, 0.75	0.45 (0.25)	-0.04, 0.94	**-0.37 (0.10)**	**-0.57, -0.17**	**-0.47 (0.11)**	**-0.69, -0.26**
Education								
Less than secondary	R		R		R		R	
Secondary	**3.07 (0.53)**	**2.04, 4.09**	**3.32 (0.59)**	**2.16, 4.47**	**-1.39 (0.29)**	**-1.95, -0.82**	**-1.31 (0.28)**	**-1.86, -0.76**
Some post-secondary	**3.30 (0.55)**	**2.22, 4.38**	**3.50 (0.61)**	**2.30, 4.70**	**-2.07 (0.29)**	**-2.64, -1.50**	**-1.99 (0.28)**	**-2.54, -1.44**
Post-secondary	**3.91 (0.46)**	**3.00, 4.82**	**4.20 (0.52)**	**3.19, 5.22**	**-1.90 (0.27)**	**-2.42, -1.38**	**-1.78 (0.26)**	**-2.27, -1.28**
Household Income								
Less than $20,000	R		R		R		R	
$20,000 - $49,999	**1.54 (0.56)**	**0.45, 2.63**	0.56 (0.61)	-0.63, 1.76	**-0.89 (0.34)**	**-1.56, -0.22**	-0.40 (0.32)	-1.02, 0.22
$50,000 - $99,999	**3.04 (0.56)**	**1.95, 4.14**	**1.90 (0.60)**	**0.72, 3.08**	**-1.67 (0.34)**	**-2.34, -1.01**	**-1.11 (0.31)**	**-1.73, -0.50**
$100,000 - $149,999	**3.90 (0.60)**	**2.73, 5.08**	**2.53 (0.64)**	**1.28, 3.79**	**-2.07 (0.35)**	**-2.75, -1.39**	**-1.33 (0.32)**	**-1.96, -0.70**
Greater than $150,000	**4.65 (0.62)**	**3.44, 5.85**	**3.18 (0.66)**	**1.90, 4.47**	**-2.40 (0.35)**	**-3.09, -1.71**	**-1.64 (0.33)**	**-2.29, -1.01**

Abbreviations: CCA: complete case analysis; CI: confidence interval; MI: multiple imputation; R: reference; SE: standard error. Significant results are bolded.

Table 2. (continued)

	MAT				Interference Condition			
	MI (N =12,152)		CCA (N=9,912)		MI (N =12,152)		CCA (N=9,912)	
	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI
Marital Status								
Single, never married, or never lived with a partner	R		R		R		R	
Married or common law	0.11 (0.35)	-0.58, 0.79	0.51 (0.38)	-0.24, 1.26	0.06 (0.17)	-0.28, 0.39	-0.10 (0.18)	-0.46, 0.25
Widowed, divorced, or separated	0.71 (0.36)	-0.00, 1.42	**1.12 (0.40)**	**0.33, 1.91**	-0.01 (0.18)	-0.36, 0.34	-0.16 (0.19)	-0.54, 0.22
Migrant Status								
Non-immigrant	R		R		R		R	
Immigrant	**-1.00 (0.27)**	**-1.54, -0.48**	**-0.93 (0.28)**	**-1.49, -0.38**	**0.40 (0.12)**	**0.15, 0.63**	**0.36 (0.11)**	**0.14, 0.59**
Place of Residence								
Rural	R		R		R		R	
Urban	0.71 (0.32)	**0.09, 1.34**	**0.85 (0.35)**	**0.17, 1.54**	**-0.31 (0.12)**	**-0.54, -0.08**	**-0.42 (0.12)**	**-0.66, -0.18**
Suburban	0.02 (0.52)	-0.42, 1.63	0.49 (0.55)	-0.59, 1.57	-0.04 (0.20)	-0.43, 0.34	-0.04 (0.21)	-0.46, 0.37
Socially Isolated								
No	R		R		R		R	
Yes	-0.36 (0.23)	-0.82, 0.09	-0.28 (0.25)	-0.76, 0.21	0.04 (0.11)	-0.17, 0.25	-0.09 (0.11)	-0.30, 0.12

Abbreviations: CCA: complete case analysis; CI: confidence interval; MI: multiple imputation; R: reference; SE: standard error.
Significant results are bolded.

Table 2. (continued)

	MAT				Interference Condition			
	MI (N =12,152)		CCA (N=9,912)		MI (N =12,152)		CCA (N=9,912)	
	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI
Smoking Status								
Never smoker	R		R		R		R	
Former smoker	**-0.48 (0.19)**	**-0.85, -0.11**	-0.42 (0.21)	-0.83, 0.01	0.13 (0.08)	-0.02, 0.28	0.16 (0.08)	-0.01, 0.31
Occasional or daily smoker	**-1.17 (0.36)**	**-1.88, -0.46**	**-1.18 (0.39)**	**-1.96, -0.41**	0.80 (0.20)	0.41, 1.18	**0.68 (0.15)**	**0.39, 0.97**
Alcohol Consumption								
Never drinker	R		R		R		R	
Former drinker	1.06 (0.70)	-0.32, 2.44	-0.03 (0.84)	-1.67, 1.61	-0.61 (0.33)	-1.25, 0.03	-0.09 (0.31)	-0.70, 0.52
Infrequent drinker	0.64 (0.69)	-0.71, 2.00	-0.45 (0.82)	-2.05, 1.15	**-0.85 (0.32)**	**-1.48, -0.22**	-0.13 (0.30)	-0.73, 0.47
Occasional drinker	1.06 (0.66)	-0.25, 2.36	-0.12 (0.79)	-1.68, 1.43	**-0.95 (0.31)**	**-1.55, -0.34**	-0.23 (0.29)	-0.80, 0.34
Regular or binge drinker	1.68 (0.66)	0.38, 2.97	0.32 (0.79)	-1.22, 1.86	**-1.14 (0.31)**	**-1.74, -0.54**	-0.32 (0.29)	-0.89, 0.24
BMI								
Underweight or normal weight	R		R		R		R	
Overweight	**-0.44 (0.21)**	**-0.85, -0.03**	-0.44 (0.23)	-0.89, 0.00	**0.19 (0.08)**	**0.03, 0.36**	**0.21 (0.08)**	**0.05, 0.37**
Obese	-0.25 (0.23)	-0.70, 0.20	-0.37 (0.25)	-0.86, 0.12	**0.31 (0.10)**	**0.11, 0.51**	**0.32 (0.10)**	**0.13, 0.52**

Abbreviations: CCA: complete case analysis; CI: confidence interval; MI: multiple imputation; R: reference; SE: standard error. Significant results are bolded.

Table 2. (continued)

	MAT				Interference Condition			
	MI (N =12,152)		CCA (N=9,912)		MI (N =12,152)		CCA (N=9,912)	
	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI	ß (SE)	95% CI
Past Week Physical Activity	0.00 (0.00)	0.00, 0.00	0.00 (0.00)	0.00, 0.00	0.00 (0.00)	0.00, 0.00	0.00 (0.00)	0.00, 0.00
Fruit and Vegetable Intake								
Seven or more	R		R		R		R	
Six	0.30 (0.34)	-0.38, 0.97	0.37 (0.37)	-0.34, 1.09	-0.17 (0.14)	-0.45, 0.11	-0.20 (0.14)	-0.48, 0.08
Five	0.11 (0.31)	-0.50, 0.73	0.12 (0.34)	-0.54, 0.79	-0.09 (0.13)	-0.35, 0.17	-0.15 (0.14)	-0.42, 0.12
Four	-0.08 (0.31)	-0.69, 0.52	-0.14 (0.33)	-0.79, 0.51	0.01 (0.13)	-0.25, 0.27	-0.01 (0.13)	-0.27, 0.25
Three	**-0.79 (0.33)**	**-1.43, -0.15**	**-0.88 (0.35)**	**-1.56, -0.19**	-0.01 (0.13)	-0.27, 0.25	-0.01 (0.14)	-0.27, 0.26
Two	**-1.28 (0.35)**	**-1.96, -0.60**	**-1.19 (0.37)**	**-1.91, -0.46**	0.14 (0.14)	-0.14, 0.42	0.15 (0.15)	-0.14, 0.43
Less than two	**-1.23 (0.41)**	**-2.04, -0.43**	**-1.18 (0.45)**	**-2.06, -0.31**	0.25 (0.17)	-0.09, 0.59	0.14 (0.17)	-0.19, 0.47
Self-rated Health								
Excellent or Good	R		R		R		R	
Fair or Poor	-0.80 (0.40)	-1.57, 0.02	-0.77 (0.44)	-1.64, 0.10	**0.50 (0.17)**	**0.16, 0.84**	**0.44 (0.17)**	**0.11, 0.77**
Multimorbidity								
0 -1 Chronic Disease	R		R		R		R	
≥ 2 Chronic Diseases	0.06 (0.19)	-0.30, 0.43	-0.02 (0.21)	-0.42, 0.37	-0.15 (0.09)	-0.02, 0.32	**0.17 (0.08)**	**0.01, 0.33**

Abbreviations: CCA: complete case analysis; CI: confidence interval; MI: multiple imputation; R: reference; SE: standard error. Significant results are bolded.

Table 3. Multiple linear regressions models for shift work and performance on cognitive tests, with the inclusion of psychological distress and sleep quality

	MI (N =12,152)		CCA (N=9,912)	
	ß (SE)	**95% CI**	**ß (SE)**	**95% CI**
Immediate Recall Trial				
Model 1	-0.04 (0.05)	-0.14, 0.06	-0.02 (0.05)	-0.13, 0.09
Model 2	-0.04 (0.05)	-0.14, 0.06	-0.02 (0.05)	-0.13, 0.09
Delayed Recall Trial				
Model 1	-0.05 (0.06)	-0.17, 0.06	-0.08 (0.06)	-0.21, 0.04
Model 2	-0.05 (0.06)	-0.16, 0.06	-0.08 (0.06)	-0.21, 0.04
MAT				
Model 1	**-0.89 (0.24)**	**-1.36, -0.42**	**-1.10 (0.26)**	**-1.62, -0.59**
Model 2	**-0.89 (0.24)**	**-1.36, -0.42**	**-1.10 (0.26)**	**-1.62, -0.59**
Interference Condition				
Model 1	**0.43 (0.11)**	**0.22, 0.64**	**0.44 (0.10)**	**0.23, 0.65**
Model 2	**0.42 (0.11)**	**0.22, 0.63**	**0.44 (0.10)**	**0.24, 0.65**

Abbreviations: CCA: complete case analysis; CI: confidence interval; MI: multiple imputation; SE: standard error.
Significant results are bolded.
Model 1: Association between shift work and performance on cognitive tests, controlling for psychological distress and other potential confounders
Model 2: Association between shift work and performance on cognitive tests, controlling for sleep quality and other potential confounders

Table 4. Interaction effects between psychological distress and shift work and sleep quality and shift work

	MI (N =12,152)		CCA (N=9,912)	
	ß (SE)	**95% CI**	**ß (SE)**	**95% CI**
Immediate Recall Trial				
Shift Work x High Distress	-0.34 (0.20)	-0.06, 0.73	0.42 (0.23)	-0.02, 0.86
Shift Work x Poor Sleep Quality	0.20 (0.11)	-0.02, 0.42	0.18 (0.12)	-0.06, 0.41
Delayed Recall Trial				
Shift Work x High Distress	-0.20 (0.22)	-0.24, 0.64	0.33 (0.25)	-0.16, 0.83
Shift Work x Poor Sleep Quality	0.09 (0.13)	-0.16, 0.35	0.09 (0.14)	-0.19, 0.37
MAT				
Shift Work x High Distress	-0.31 (0.85)	-1.98, 1.36	-0.53 (0.97)	-2.43, 1.37
Shift Work x Poor Sleep Quality	0.94 (0.56)	-0.15, 2.03	0.68 (0.60)	-0.58, 1.86
Interference Condition				
Shift Work x High Distress	0.32 (0.50)	-0.66, 1.30	0.03 (0.40)	-0.75, 0.80
Shift Work x Poor Sleep Quality	-0.25 (0.26)	-0.75, 0.25	-0.25 (0.23)	-0.71, 0.20

Abbreviations: CCA: complete case analysis; CI: confidence interval; MI: multiple imputation; SE: standard error.
Significant results are bolded.

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