ASSOCIATION BETWEEN SLEEP DISORDERS AND VISION PROBLEMS AMONG FIRST NATIONS PEOPLE

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ABSTRACT

Background: Sleep disorders have an adverse effect on the quantity and quality of sleep, leading to reduced alertness and impaired ability to function normally. Recent studies show sleep disorders can cause vision-threatening conditions. Most research has not considered Indigenous people living in on-reserve communities. Thus, current knowledge regarding sleep disorders and vision problems among Indigenous people is limited.

Purpose: This study aimed to estimate the current prevalence of vision problems and examined the association between sleep disorders and vision problems among First Nations living on-reserve communities in Saskatchewan. Additionally, potential mediators in this relationship were explored.

Methods: This cross-sectional study used baseline data from "Assess, Redress, Re-assess: Addressing Disparities in Sleep Health among First Nations People," an ongoing cohort study. A survey was conducted in 2018-2019 with approximately 588 individuals in two First Nation communities. In the present study, the outcome variable was vision problems. Primary predictors were sleep apnea, insomnia, sleep deprivation, Epworth sleepiness score (ESS), and STOP-BANG. Multivariable logistic regression analysis and generalized structural equation modelling were employed.

Results: The prevalence of vision problems was 18.71%. Sleep apnea, clinical insomnia, and ESS were significantly associated with vision problems after adjusting for other variables. The odds of having vision problems were 2.93 times (95% CI: 1.19 – 7.19) higher among those who self-reported physician-diagnosed sleep apnea and 2.21 times (95% CI: 1.12 – 4.37) higher among participants with clinical insomnia. Similarly, with each unit increase in ESS, the likelihood of developing vision problems increased by 1.11 (95% CI: 0.97- 1.28). Mediation analysis revealed that depression accounted for approximately 32% of the association between sleep disorders and vision problems.

Conclusion: These findings indicate a higher prevalence of vision problems and a positive association between sleep disorders and vision problems among First Nations people. Longitudinal studies are needed to determine the nature of this association.

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DEDICATION

I would like to dedicate this research work to my beloved husband, ***Haseeb Shafqat****. Your unwavering love, support, and encouragement have been the pillars of my success throughout this journey. Thank you for being my constant companion and standing by me through thick and thin.*

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ABBREVIATION

CDC	Centers for Disease Control and Prevention
EDS	Excessive Daytime Sleepiness
CHMS	Canadian Health Measures Survey
WHO	World Health Organization
AHI	Apnea Hypopnea Index
ESS	Epworth Sleepiness Score
COPD	Chronic Obstructive Pulmonary Disease
AMD	Age-related Macular Degeneration
NHIS	National Health Interview Survey
PSQI	Pittsburgh Sleep Quality Index
NTG	Normal Tension Glaucoma
OSA	Obstructive Sleep Apnea
UNDP	United Nations Development Program
HDI	Human Development Index
CIHR	Canadian Institutes of Health Research
BMI	Body Mass Index
PTSD	Post-Traumatic Stress Disorder
CI	Confidence Interval
GSEM	Generalized Structural Equation Modeling
STATA	Statistical software for data science
OR	Odds Ratio
$\widehat{\boldsymbol{\beta}}$	Sample Estimate
$\boldsymbol{SE}\ (\widehat{\boldsymbol{\beta}})$	Standard Error of Coefficient
RIT	Ratio of Indirect effect to total effect
RID	Ratio of the indirect effect to the direct effect
OSDI	Ocular Surface Disease Index
ISI	Insomnia Severity Index
OCT	Optical Coherence Tomography
CSCR	Central Serous Chorioretinopathy

CHAPTER 1: INTRODUCTION AND RATIONALE

1.1 Introduction

Several eye disorders and eye diseases can cause vision problems; the most common causes are refractive errors, diabetic retinopathy, cataract, glaucoma, dry eyes, age-related macular degeneration (AMD) and retinal detachment [1,2]. Most of these vision problems are avoidable with proper management if detected earlier, thus can reduce individual and societal burdens significantly [3]. Growing age is a significant risk factor in developing vision problems; however, socio-economic status is integral in determining eye health and accessing healthcare [4]. Moreover, vision problems can impede education attainment, which may reduce the likelihood of getting jobs and considerably reduce the quality of life [5,6]. The predisposed population of Canada, Indigenous people, having low socio-economic status, are at higher risk of developing chronic health conditions, including vision problems, compared to the rest of the Canadian population [7].

1.2 Global Perspective of Vision Problems

According to Global Burden of Diseases, vision problems affect 330 million people globally, causing visual impairment and blindness, with 295.3 million with moderate to severe visual impairment and 43.3 million blind [2]. However, World Health Organization (WHO) reported in 2019 that about 2.2 billion people have a vision impairment worldwide, among whom half cases could have been prevented [8].

According to National Aboriginal and Torres Strait Islander Health 2018–19 Survey, estimated vision problems for Indigenous Australians, ranged from 10% to 93%; these rates varied depending upon the age group of Indigenous participants [9]. Most national surveys on visual loss do not sub-categorize their estimates based on Indigeneity, including the United States of America, Canada, and New Zealand, even though these estimates are expected to be higher for specific ethnic groups [10]. Recently a study reported the prevalence of vision impairment and blindness among American Indigenous Peoples varied from 11.1% to 28.5% depending upon the geographical factor [11].

1.3 Canadian Perspective of Vision Problems

The Canadian Survey on Disability reported that 1.5 million Canadians (5.4%) were visually handicapped in 2017 [12] compared to 1.4% of 40-79 years old Canadians as estimated

in the 2018-2019 Canadian Health Measures Survey (CHMS) [13]. Nonetheless, the prevalence of vision loss and visual impairment among Indigenous people in Canada is unknown [10].

1.4 Vision Care Access to Canadian Indigenous People

Indigenous people living in on-reserve communities often receive a lower rate of healthcare services and fewer doctor visits, including access to eye care which increases their risk of developing chronic eye diseases and disorders since childhood [14]. Diabetic retinopathy, an ocular complication of diabetes, is one of the common causes of vision loss in Canada [15]. According to a recent report, First Nations people with diabetes in Ontario had sub-optimal eye care examination rates compared to others, regardless of living in on-reserve communities or off-reserve [16].

Eye health services were reported to be substandard than the recommended guidelines among Nunavik Inuit in Northern Canada [17]. Although, several health conditions impact the eye health, including diabetes, high blood pressure, depression, and thyroid diseases [18–20]; the eye care programs and interventions for Indigenous people in Canada are focused on diabetic retinopathy eye care compared to other eye diseases and disorders [21]. Recently, researchers also found an association between vision-threatening eye diseases and sleep disorders [22,23]. Moreover, growing rates of sleep disorders among First Nations people is another public health concern in Canada [24,25].

1.5 Sleep Disorders: A Pressing Public Health Issue

Sleep disorders such as insomnia, sleep deprivation, sleep apnea, and narcolepsy affect sleep timings, duration, and quality and thus impair individuals' ability to function normally during the daytime [26]. Among all sleep disorders, obstructive sleep apnea (OSA) is recognized as a serious public health issue characterized by repeated episodes of complete cessation of breathing for more than 10 seconds during sleep [27]. Insomnia is a common sleep disorder that causes difficulty falling/staying asleep at night [28], whereas daytime sleepiness can cause an excessive desire to sleep and cause trouble staying alert during the day [29]. The Centers for Disease Control and Prevention (CDC) recommended amount of sleep for adults is 7 or more hours in a 24-hour period [30].

1.6 Global Perspective of Sleep Disorders

Epidemiological studies from the United States, United Kingdom, Ethiopia, Taiwan, China, and Canada and countries across Africa and Asia revealed that the prevalence of several sleep problems and insomnia varies from 15% - 43% [31–37]. A recent publication estimated that around 1 billion people were affected with OSA globally, with the highest number of cases in China, followed by the United States [38]. According to this study, 425 million adults aged between 30 to 69 years reported moderate to severe OSA. Likewise, excessive daytime sleepiness (EDS) varied from 4% to 28% in the general population; and contributed to 15- 30% of all sleep problems [29,39,40].

1.7 Canadian Perspective of Sleep Disorders

The CHMS 2014-2015 survey reported that about 26% of Canadian adults sleep less than seven hours, and about half reported trouble sleeping/ going to sleep/falling asleep [41]. Additionally, as per CHMS 2016-2017, 6.4% of the Canadian population have received a diagnosis of sleep apnea [42]. In addition, based on the STOP-BANG questionnaire, tool to assess the risk of developing OSA, approximately 15% of participants were at higher risk, and about the same percentage were at moderate risk of developing sleep apnea [42,43]. However, a major limitation of the CHMS survey was the exclusion of people living in on-reserve communities from the sampling frame.

1.8 Sleep Disorders among Indigenous People

Studies conducted in Northern British Columbia and the United States revealed a higher prevalence of poor sleep quality among Indigenous North Americans (American Indians) [44,45] compared to non-Indigenous residents. Structural determinants such as governing processes, and economic and social policies can impact Indigenous people's health; however, the mechanism of these determinants affecting health is not well articulated in the literature [7]. Compared to the non-Indigenous population, Indigenous people in Canada are more likely to live under suboptimal conditions such as poor housing conditions, overcrowding, and lack of privacy; hence, they are at higher risk of developing chronic conditions than the rest of Canadians, given the history of colonization, residential school, and racism [46,47]. Therefore, a multi-lens approach is crucial to examine Indigenous health.

Recent studies have explored the prevalence of insomnia, sleep duration, and sleep quality among First Nations people in rural Saskatchewan [25,48]. Another study in Canada determined the predictors of sleep apnea in the general population [49]; however, the prevalence and risk factors of sleep apnea and other sleep disorders among First Nations people in Canada are yet to be established. Moreover, it is essential to identify the co-existing chronic conditions among First Nations suffering from sleep disorders in Canada.

1.9 Sleep Disorders and Vision Problems

Recent research revealed that the risk of vision-threatening ocular diseases was greater among obstructed sleep apnea patients [22,50]. Several studies showed a relationship between dry eyes, reduced sleep duration, and poor sleep quality [23,51–53]. In these publications, some researchers used dry eyes to predict poor sleep quality, whereas others positioned sleep as the predictor. Reduced sleep duration or poor sleep quality can cause eye dryness which can harvest eye infections [23,54]. However, the exact mechanism that links sleep apnea and ocular diseases is poorly understood.

The studies described the mechanical and vascular effects of the ocular manifestations, including floppy eyelid syndrome, central serous retinopathy, non-arteritic anterior ischemic optic neuropathy, retinal vein occlusion, and glaucoma of OSA [55,56]. These studies underscored increased communication and co-management between sleep specialists and ophthalmologists to prevent ocular complications in patients with sleep disorders; on the other hand, recognizing the signs and symptoms of undiagnosed sleep disorders, especially sleep apnea, in patients with ocular manifestations.

1.10 Rationale of the Study

Given Indigenous people's colonization and residential history, First Nations people are at higher risk of sleep disorders than non-Indigenous people [57–59], but whether this pattern holds for vision problems is not currently known. Also, the understanding of the relationship between sleep disorders and vision problems among Indigenous populations is limited. First Nations communities in remote areas suffer from social and financial burdens from chronic conditions like sleep disorders and ocular diseases [11,38]. Most ocular diseases that cause visual impairment are preventable if detected early, and vision loss is avoidable in certain conditions [2]. Lack of awareness, inadequate resources, and delayed diagnosis of sleep disorders for several

reasons, including travel long distances to the nearest cities to access tertiary healthcare make on-reserve Indigenous communities vulnerable. Hence, targeted health intervention and demand-focused research are solicited.

In many cases of sleep disorders, proper management requires timely diagnosis and treatment as required, which further prevents associated conditions [60,61]. To the best of my knowledge, the current prevalence of vision problems among First Nations in Canada is unknown. In addition, no research was found during an extensive literature search that examined the association between sleep disorders and vision problems among First Nations people in Canada. Therefore, more research is warranted to identify the prevalence of both, vision problems and sleep disorders, and the association between them in First Nations people living in on-reserve communities.

1.11 Research Purpose

To the best of my knowledge, no study examined the relationship between sleep disorders and vision problems in the context of Indigenous people in Canada. The results from the current study can serve as a reference point and set pathways for future research in the domain of sleep disorders and vision problems. The current study will estimate the prevalence of vision problems among two First Nations communities in rural Saskatchewan. In addition, this study will examine the association between sleep-health-related predictors and vision problems accounting for individual (lifestyle factors, personal smoking status, body-mass index) and contextual factors (socio-economic status, household smoking) among First Nation people in rural Saskatchewan.

The current study findings can be used to compare the prevalence of vision problems between First Nations communities and non-Indigenous people in Canada. Moreover, these results can help in planning/conducting longitudinal studies to establish the directional/causal relationship between sleep disorders and vision problems.

1.12 Specific Objectives

The primary objectives of this study were:

1. To estimate the 2018-2019 prevalence of vision problems among First Nations people living in two rural reserve communities in Saskatchewan.
2. To determine the association between sleep disorders and vision problems in First Nations people living in two rural reserve communities in Saskatchewan.

3. To investigate the potential mediators in the relationship between sleep disorders and vision problems in First Nations people living in two rural reserve communities in Saskatchewan.

1.13 Thesis Layout

This dissertation is comprised of six chapters. Chapter one, "Introduction," presented an overview of the study's purpose and rationale; furthermore, provided the research questions and objectives. Chapter two, "Literature Review," delivered a comprehensive discussion of vision problems as well as sleep disorders. It included the prevalence, and risk factors of vision problems, economic burden due to visual disability; moreover, explained the different types of sleep disorder, associated factors, long term consequences of sleep disorders and the previous research on the relationship between sleep disorders and vision problems. In addition, this chapter discussed the potential mediators in the relationship between sleep disorders and vision problems and the current knowledge on these issues in the context of Indigenous people in Canada. Chapter three, "Methods and Materials," explained the general methodology and statistical analysis used in the study. Chapter four, "Results," displayed the descriptive findings, estimated the prevalence of vision problems, analyzed the association between sleep disorders and vision problems among First Nations living on-reserve in rural Saskatchewan, Canada, and explored the potential mediator. Chapter five, "Discussion," focused on the associated risk factors of vision problems and investigated potential mediators among First Nations populations in Saskatchewan, Canada. This chapter also discussed the strengths and limitations of the study. Finally, chapter six, "Conclusion," addressed the specific objectives of the thesis and provided recommendations for further research.

CHAPTER 2: LITERATURE REVIEW

2.1 Identification of Literature

The literature review will initially focus on vision problems, including visual impairment, causes, epidemiology, and the economic burden associated with visual disability. Then, the literature on sleep disorders will be reviewed, including the types of sleep disorders, measurement tools, and associated risk factors. Later, I discuss the literature on sleep disorders and vision problems and potential mediators linking sleep disorders and vision problems. Finally, Indigeneity in relation to sleep and vision problems will be incorporated into the review.

Researchers used different terminologies for vision problems in their studies, including visual impairment, vision loss, and visual disability. While referring to previous research, I used the same terminology as in the original article. However, the current study used the term "vision problems" for outcome variables. In the following sections, visual problems will be defined, the epidemiology of vision problems will be briefly described, followed by a review of the literature examining the association between sleep disorders and vision problems.

2.2 Vision Problems

Vision problems are inevitable with aging. The most common vision problems that impair or cause loss of vision with growing age are refractive errors, cataracts, glaucoma, dry eyes, AMD and optic disc and retinal disorders, which are daunting ocular health concerns [62]. However, unaddressed refractive errors, including presbyopia, though easily preventable/corrected, are the most common vision problems found among all age groups globally [2].

A study published in 2010 reported that 57% of adults had some form of vision problem in Canada [63]. Among these most common problems were cataracts, glaucoma, and diabetic retinopathy. Furthermore, older age, female sex, and low socio-economic status were significant determinants of vision problems. Likewise, a cohort study in Canada reported that the prevalence of visual impairment was 5.7%, with refractive errors being the most common cause [64]. Furthermore, risk factors were old age, lower income, smoking, diabetes, and memory problems. However, these studies excluded people living on a First Nations reserve.

2.2.1 Visual Disability and Economic Burden

Visual disability can limit everyday activities, drastically reducing the quality of life. It also increases the social care cost and economic burden. A study published in 2020 reported that the annual costs of blindness and visual impairment in Germany were € 49.6 billion, and informal support from families accounted for 80% of this cost [65]. Another study stated that the estimated annual cost of visual problems by Prevent Blindness America (PBA) in 2013 was $139 billion, of which $65.1 billion directly contributed to medical expenses [66]. Similarly, in 2012 the estimated global burden of visual impairment was $3 trillion in 2010, and $2.3 trillion of this amount was direct health costs [3].

2.2.2 Visual Impairment: Prevalence and Risk Factors

Recent literature estimated the prevalence of visual impairment and blindness using data from various national surveys in the United States [67]. They reported blindness varied between 0.1% to 5.6% among individuals younger than 65 years and 0.6% to 16.6% for 65 years and older. Similarly, the estimates ranged for visual impairment from 1.6% and 24.8% for younger than 65 years individuals and between 2.2% and 26.6% for 65 years old and above. Another study published in 2005 reported older age, Hispanic race, poor or fair health (self-reported) and low accessibility to social support were some of the risk factors for visual impairment that affected 45 years and older American adults [68]. Similarly, a three-year prospective cohort study in seven provinces (data collection sites were: Victoria, Vancouver, Surrey, Calgary, Winnipeg, Hamilton, Ottawa, Montreal, Sherbrooke, Halifax, and St. John's) revealed that 3.9% of Canadian adults developed visual impairment over the period of three years, and uncorrected refractive errors were the primary cause [69]. They further demonstrated the variability in incidence among provinces from 1.42% to 7.33%. The risk factors were old age, black race, smoking, location (province) and low household income. However, this study excluded individuals living in on-reserve communities. Furthermore, no study estimated the incidence or prevalence of visual impairment in rural Saskatchewan.

A study in Finland used the nationwide health examination survey data to evaluate the average incidence of eye diseases between 2000-2011 [5]. They reported visual impairment among the population aged 30 and above for glaucoma, cataract, retinal degeneration, and impaired distance visual acuity were 22, 109, 35 and 10 /year/10,000 individuals, respectively [5]. Furthermore, these conditions were more common among women and increased with age.

A recent CDC study using the 2016 National Health Interview Survey (NHIS) data reported an association between social determinants of health and self-reported visual difficulty [70]. The study found that lower education level, food insecurity, inaccessibility to doctors, non-heterosexual male, and financial problems paying bills were some of the social determinants associated with visual difficulty. Another study from North India reported literacy, income status, locality, and delayed diagnosis as predictors of visual impairment among advanced and end-stage glaucoma patients [71].

Recently researchers developed an interest in finding the link between sleep disorders and vision problems [72,73].

2.3 Types of Sleep Disorders

Sleep disorders are prevalent among the general population—there are about 80 different forms of sleep disorders; however, they often remain undiagnosed [74]. The most common are sleep apnea, insomnia, narcolepsy, restless leg syndrome, and rapid eye movement (REM) sleep behaviour disorder [61]. Unrecognized sleep problems can be present in all age groups, varies between sex/gender, ethnicity, and socio-economic class, and, if left untreated, may become a chronic ailment [75–77]. However, sleep apnea is more common among males than females, evident by research and clinical settings [78]. However, insomnia and associated symptoms were found to be more common among females as compared to males [79].

The current study is interested in sleep apnea, insomnia, sleep deprivation (duration of sleep), and excessive daytime sleepiness (EDS). Sleep apnea is the cessation of breathing during sleep for 10 or more seconds [80]. STOP-BANG is a widely used screening tool for OSA; however, an apnea-hypopnea index is a gold standard to assess the severity of sleep apnea. Insomnia is defined as having trouble falling and/or staying asleep [43,81]. Sleep deprivation is known as not getting a sufficient amount of sleep i.e. less than 7 hours of sleep [82]. EDS is defined as difficulty staying awake or an increased desire to sleep during the day; Epworth Sleepiness Score (ESS) estimates if a person is experiencing excessive or abnormal daytime sleepiness [83].

From a health perspective, sleep is crucial to revitalizing all the body's organs. Persistent sleep disturbances cause individuals to wake up tired and struggle to concentrate, negatively impacting overall health and work productivity [82]. Quantity and quality of sleep are essential to assess physical and mental well-being.

2.3.1 Measurement of Sleep Disorders

Researchers developed reliable tools to assess sleep quality, such as the apnea-hypopnea index (AHI), ESS, STOP-BANG, and Pittsburgh quality sleep index; among these, AHI is considered a gold standard. Apnea is the cessation of breathing for 10 seconds or more, and hypopnea is the reduction in the airflow by 50% or below [84]. AHI is the average number of events, including apnea and hypopnea, per hour of the sleep study [84].

Several studies used the apnea-hypopnea index (AHI), the number of respiratory events per hour, to measure the severity of sleep apnea [85–87]. Likewise, the literature used the ESS to assess the subjective daytime sleepiness or excessive sleepiness that required medical attention [88–90]. CHMS also uses the STOP-BANG tool to determine the population proportion at risk of developing OSA [43]. However, AHI is measured by clinical variables, and ESS is a self-administered tool. Moreover, many devices such as Actiwatch are available that record the wake/sleep patterns of the patients, and data is used to assess if the patient is at risk of any sleep disorder [91,92].

2.3.2 Sleep Problems: Consequences/Associated Factors

Sleep disorders significantly predict depression, chronic health conditions, bodily pain, and memory problems [93]. Long-term health consequences of untreated/undiagnosed sleep apnea include cardiovascular disease, metabolic disorders, injuries, depression, cognitive impairment, and vision-threatening ocular conditions [50,94–97].

Evidence suggests that sleep apnea can put the patient at high risk of stroke and heart attack, increasing mortality and morbidity, and is often associated with comorbidities such as type 2 diabetes, metabolic syndrome, and daytime sleepiness [98,99]. A recent study assessed the relationship between sleep disorders and health-related quality of life using the short-form health survey (SF-12) [100]. The results revealed that sleep disorders such as insomnia, sleep apnea, and daytime sleepiness score very low for SF-12 components, physical component summaries (PCS) and mental component summaries (MCS). This study further demonstrated that the effect of insomnia was more marked on MCS, and the severity of apnea was highly significant with PCS [100].

Another study conducted in the primary health unit of a Brazilian hospital revealed an association between sleep disorders and chronic health conditions such as osteoporosis, arthritis, lower back pain, obesity, and depression in patients 50 years and older [101]. Insomnia, sleep

deprivation, snoring, and poor sleep quality are associated with poor health outcomes, such as depression, hypertension, obesity, fatigue, coronary heart disease, and diabetes mellitus [28,102–122]. Likewise, studies showed that sleep apnea is linked with diabetes, high BMI, stroke, arrhythmia, chronic obstructive pulmonary disease (COPD), retinal changes, and other respiratory health-related problems [88,123,124].

In the early stages of sleep disorders, the stress or anxiety of not performing well during the day can cause mental health problems [125]. Research has identified relationships between sleep disturbances and mental health problems such as depression, anxiety, social functioning, and mental distress in the general population [126,127]. This relationship between sleep disorders and mental health problems is bidirectional [128]. A study indicated the bilateral nature of sleep disorders and mental health problems and estimated that chronic insomnia affected 40% of schizophrenia spectrum disorders compared to the general population (6%) [129].

2.4 Sleep Disorders and Vision Problems

A paper was published using the data from National Center for Health Statistics (NCHS), and the CDC on the association between sleep duration and visual impairment [130]. The authors reported a relationship between visual impairment and both short sleep duration (<6 hours) and long sleep duration (>8 hours). Likewise, a cross-sectional survey of young and middle-aged Japanese office employees assessed the relationship between poor sleep quality and dry eye and reported a significant association between these two variables [131]. Moreover, the authors in this study used the Japanese version of the Pittsburgh Sleep Quality Index (PSQI) (global score) to examine the sleep quality and the Japanese dry eye diagnosis criteria to examine the dry eyes.

A population-based study in Korea revealed a u-shaped association between visual impairment and self-reported sleep duration. The research stated that both short sleep duration (5 hours or less) and long sleep duration (9 hours or more) were significantly associated with visual impairment [132]. Another cross-sectional study from South-East Asia investigated the relationship between primary glaucoma on sleep quality and daytime sleepiness using the Pittsburg Sleep Quality Index (PSQI) and ESS, respectively [133]. They found a significant relationship between primary angle-closure glaucoma and poor sleep quality compared to controls; however, the ESS was insignificant.

A cross-sectional study in South Africa used the national sample of older adults to examine the association between visual impairment/ low vision with sleep duration and quality

[134]. The results demonstrated that visual impairment (self-reported) was associated with both short and poor sleep quality; however, low vision was associated with long sleep hours and poor quality in the unadjusted model. Another study conducted among the white population explored a higher-than-expected prevalence of normal tension glaucoma (NTG) among patients with OSA and suggested OSA as an important risk factor for NTG [135]. Furthermore, a thesis reported the effects of OSA on the optic nerve. This thesis used night polysomnography testing to show that OSA patients exhibited more significant optic nerve swelling after sleep than the control group [136].

Researchers conducted a meta-analysis and systematic review to explore the association between glaucoma and OSA [137]. After extensively reviewing previous cross-sectional, case-control, and cohort studies on the topic, this study concluded that OSA is linked with an increased prevalence of glaucoma. However, the study did not consider potential confounders [137]. Another study reviewed the literature on PubMed and explored that OSA is most associated with several eye diseases such as glaucoma, optics neuropathy, papilledema, and floppy eyelid syndrome among sleep disorders [138].

A recent study investigated the relationship of dry eye with other systematic comorbidities [139]. The researchers included dry eye subtypes, quality of life, and health utility (Human Utility Index mark 3). The interesting finding of this study was that patients with dry eyes and depression, and insomnia exhibited significantly worse ocular parameters as compared to those who did not have dry eyes. Their results revealed that friction-related diseases such as conjunctivochalasis (excess folds of conjunctival skin) or lid wiper epitheliopathy (disrupted epithelium surface of lid wiper) were common among dry eyes patients with depression and insomnia [139].

Another study examined the association between sleep complaints and visual impairment among adult Americans [140]. The investigators explored several sleep-related problems, including difficulty falling asleep, difficulty maintaining sleep, early morning awakening, daytime sleep, and sleep medicine among older adults. According to their findings, a significant association was present that shows an association between sleep-wake problems and ocular diseases. In addition, researchers analyzed variance (ANOVA) to investigate further and concluded that the index rate of sleep disturbances was higher among individuals with visual impairment compared to their counter-group [140].

2.5 Potential Mechanisms (Mediators) Linking Sleep and Vision Problems

Researchers around the globe are working to establish the predictors that cause irreversible vision loss. Chronic health conditions like diabetes and hypertension can damage retinal blood vessels, which cause irreversible retinal changes [18,141]. Other conditions, such as high blood pressure and coronary heart diseases, may lead to glaucoma, which causes progressive optic nerve damage and remains undetected until the late stages [142,143]. Moreover, ocular problems, such as AMD and dry eyes, are impacted by lifestyle factors such as smoking, poor diet, excessive digital device exposure, and inactivity [144–147]. These findings indicate that ocular conditions are prone to other chronic health conditions. Recent clinical research provided a possible relationship between sleep disorders and retinal changes [72,89,124,148,149]. Moreover, a recent study revealed that higher perceived stress predicted more significant self-reported vision difficulties or sensory impairment in later life after adjusting for risk factors. Additionally, the effect of stress remained constant with increased age [150].

Diabetes is associated with various ocular complications, such as diabetic retinopathy, diabetic macular edema, papillopathy, cataracts, and glaucoma, which can cause permanent vision loss [151]. A recent study showed that the prevalence of visual impairment among type-2 diabetic patients was 37.58% northeast Ethiopia [152]. In addition, the study stated that some of the risk factors were physical inactivity, insulin treatment, duration of diabetes above five years, and poor glycemic control. According to a report, the prevalence of diabetic retinopathy was 35%; among them, 12% were at high risk of vision loss [153]. Ocular complications associated with diabetes are linked to the age of diabetes rather than the age of patients, rapidly becoming the most significant cause of morbidity globally [154]. Vision loss due to diabetes can be prevented or delayed, providing early detection and timely management of these chronic health conditions [141].

Perceived life stress can be another potential mediator in the relationship between sleep disorders and vision problems. A study emphasized considering stress as a mediator in sleep deprivation studies rather than adjusting for confounder [155]. Many studies evaluated the role of psychological distress (particularly stress) as a mediator in the relationship between predictor(s) and health outcome(s) [156,157]. These studies found that stress significantly impacts health outcome.

A recent study used WHO data on global Ageing and adult health to explore the relationship between far vision impairment and perceived stress among older adults [158]. Data from six low- and middle-income countries, revealed that increased perceived stress levels among older adults were significantly associated with visual impairment. The researchers concluded that perceived stress might aggravate certain eye conditions. However, this study did not provide the directionality of this association and recommended exploring it in future research.

Depression is another potential mediator and should be considered in sleep disorders studies. The studies suggest of the bilateral relationship between sleep problems and depression [128,159]. Insomnia is a common symptom of depression; conversely, patients with sleep problems are more likely to present psychological issues such as depression, anxiety, and bipolar disorder. The study highlighted the importance of considering sleep health before, during, and after treating depression to prevent recurring depressive symptoms [159].

On the other hand, depression is comorbid/ correlated with ocular diseases as well. A study suggested that glaucoma is associated with sleep disorders, circadian misalignment, and depression [160]. Their finding showed a positive correlation between progressive glaucoma and the prevalence of depression and sleep disturbance. Their results showed that severe visual field defects were highly associated with depression and sleep disturbance. Likewise, another study investigated depression and Insomnia among individuals with dry and healthy eyes [161]. The findings exhibited a significant association among these comorbidities. They showed that depressive symptoms and insomnia severity were higher among patients with dry eye diseases compared to the healthy control group.

The following section discusses Indigenous people's health in Canada. Researchers used different terminologies such as Indigenous people, Status Indian, Native people, First Nation, and Aboriginal people while addressing Indigenous people. I used the same terminology as the original article throughout this thesis. My thesis was focused on First Nations people; however, I used Indigenous people for collective terminology.

2.6 Indigenous People in Canada

Indigenous is the collective term used to refer to the original/first inhabitants or their decedents in Canada, which includes First Nations, Inuit, and Métis peoples. First Nations are people registered under Indian Act and refer to those living in a reserve-based community, a band, or a larger tribal grouping. However, Inuit are specific groups of people generally living in

the far north. Métis are used for people resulting from unions between Aboriginal and European people in Canada [162].

About 4.9% of the Canadian population is comprised of Indigenous people, 1.67 million, according to the 2016 census [163]. Furthermore, the First Nations population constituted 58.4%, the Métis were 35%, and the Inuit population was about 3.9% of the total Indigenous population. Moreover, according to the 2016 census, about 16.3% of Saskatchewan's population is comprised of First Nations [163].

The United Nations Development Program (UNDP) 2016 report ranked Canada 12th worldwide, with a very high human development index (HDI) based on life expectancy at birth, education, and income per capita [164]. However, after modifying the 2018 HDI methodology per the Canadian context for Indigenous peoples, Canada ranked 52nd internationally [164]. Indigenous people in Canada exhibit low socio-economic status and poor health outcomes [165]. Furthermore, colonization is a substantial determinant of health for Indigenous peoples, impacting their health through systematic inequality [57,166].

According to 2015 Canadian statistics, on-reserve First Nations were seven times more likely to live in crowded houses than non-Indigenous people, profoundly affecting their health [46]. Qualitative research explored policy-driven systemic inequities, which caused significant barriers to accessing diagnostic and treatment services; furthermore, delayed management of OSA for status Indians compared to other Canadians [167].

A systematic review and meta-analysis of epidemiological research revealed that Aboriginal people are at higher risk of developing breathing problems such as asthma and COPD than non-Aboriginal [168]. This study included Native Americans, Canadian Aboriginals, Australian Aboriginals, and New Zealand Maori. Another Canadian study showed that chronic conditions as risk factors for osteoporotic fractures make Aboriginal people more prone than non-Aboriginal [59]. Research reported all-cause mortality rate (10 years) was 29.3% among 40 years above Indigenous Australians living in remote communities of Central Australia [169]. This figure was twice the rate of the Australian population. Furthermore, mortality was significantly associated with visual acuity after adjustment for age, sex, diabetes, and hypertension [169].

Recently Knowledge, Attitude, and Practice (KAP) survey was conducted to assess the diabetic retinopathy awareness and eye care behaviour of Indigenous women identified as First Nations and Métis in Saskatoon, Canada [170]. The results suggested that participants had

limited knowledge of diabetic eye care and attitude scores even less than knowledge scores; however, practice scores were reported higher than knowledge and attitude. The study suggested developing strategies to promote prevention and timely management of diabetes and its complications by educating Indigenous people and encouraging positive behaviour towards eye care management [170].

Recent studies conducted in two First Nations communities of Saskatchewan estimated that the prevalence of insomnia was 32.6% based on the symptoms of nighttime insomnia [25], and the prevalence of sleep deprivation (<7 h of sleep) was 25.4% [24,48]. Furthermore, the seasonal effects on sleep were also estimated; results revealed that 68.6% of the participants had changes in sleep patterns across seasons, and about 26.0% had significantly marked shifts in sleep patterns across seasons. The significant associated factors were money left over by the end of the month and damage caused by dampness in the house [171]. Health inequities exist between Indigenous and non-Indigenous peoples in Canada.

A recent study reported that socio-economic inequalities in health among Indigenous Canadians living off-reserve increased over time, particularly among First Nations and Metis [172]. These health inequalities can affect their sleep and general health and are linked to many chronic health conditions. Related to the ocular problems, a study that estimated the prevalence of diabetic retinopathy revealed that Indigenous people had more significant changes in diabetic retinopathy compared to non-Indigenous people in Canada, indicating ethnicity plays a role in advancing diabetic retinopathy [173]. However, to our knowledge, no research has explored the association between sleep disorders and vision problems among Indigenous people in Canada. Furthermore, fewer studies subdivided the data into Indigenous and non-Indigenous people in Canada.

Based on the literature, sleep disorder, including sleep apnea, clinical insomnia, daytime sleepiness, and sleep deprivation might be related to vision problems among First Nations people; therefore, this important relationship was examined in the current study.

CHAPTER 3: METHODS AND MATERIALS

In the methods and materials chapter, I will discuss the study design, sample size, and study population, followed by a discussion of questionnaire development and data collection procedures. Later, I describe the conceptual framework employed to conduct the current research, the variables considered, and the ethics approval. Finally, I discuss the statistical analysis plan and the statistical tests used to achieve study objectives.

3.1 Study Design

The "Assess, Redress, Re-assess: Addressing Disparities in Sleep Health among First Nations People" is the ongoing Canadian Institutes of Health Research (CIHR) funded cohort study in partnership with two Cree First Nation communities in Saskatchewan [174,175]. Apart from the vast array of sleep health-related data, the study is also collecting information on various socio-demographic, lifestyle, clinical, and environmental factors. This study collected baseline data between 2018–2019.

3.2 Study Population

The study population consists of two First Nations communities. The sampling frame consisted of adults 18 years and older for this study. In 2018-2019, the data was collected on approximately 588 individuals from both communities. This sample size was sufficient to test the hypothesis and accomplish the study objectives with adequate statistical power.

3.3 Questionnaire

The questionnaire was developed in consultation with both Cree communities to ensure their socio-economic and environmental determinants and cultural appropriateness. Moreover, the communities reviewed and edited the final questionnaire before submission of the original bio-medical research application for ethics approval. Apart from the sleep variables, the survey questionnaire collected baseline data on social, environmental, and individual factors deemed essential to sleep health.

3.4 Data Collection

The investigators hired research assistants from both communities. The research assistants were trained to invite community members and spread the ongoing survey news, ensuring all eligible individuals could participate in the study.

Different recruitment methods employed to approach study participants were:

i) Research assistants (RAs) went door-to-door and invited community residents to participate in the baseline survey. RAs distributed pamphlets describing the purpose of the study.

ii) Pamphlets were distributed during community events such as “Treaty Days” as well.

iii) At the same time, community residents were invited to participate in the survey via social media campaigns.

iv) Eligible participants were invited to the Community Health Centre/ Youth Centre, to complete interviewer-administered surveys and clinical assessments.

3.5 Conceptual Framework

A theoretical framework (figure 3.1), based on the population health framework of Health Canada, was designed to understand the conceptual mechanism involved in the effect of exposure variables (sleep disorders) in developing outcome variables (vision problems) [176]. This theoretical framework guided the study on determinants of health influencing factors at individual, socio-economic, and environmental levels. Contextual factors affect all the members living in the same context, such as socio-economic, environmental, and cultural factors. However, covariates may vary from person to person and impact the individuals' aspects.

After adjusting for contextual factors and covariates, I evaluated the direct path through Individual factors (predictors) leading to a health outcome. An indirect path was evaluated by adjusted Individual (predictor) factors leading to health outcomes through a mediator in its path.

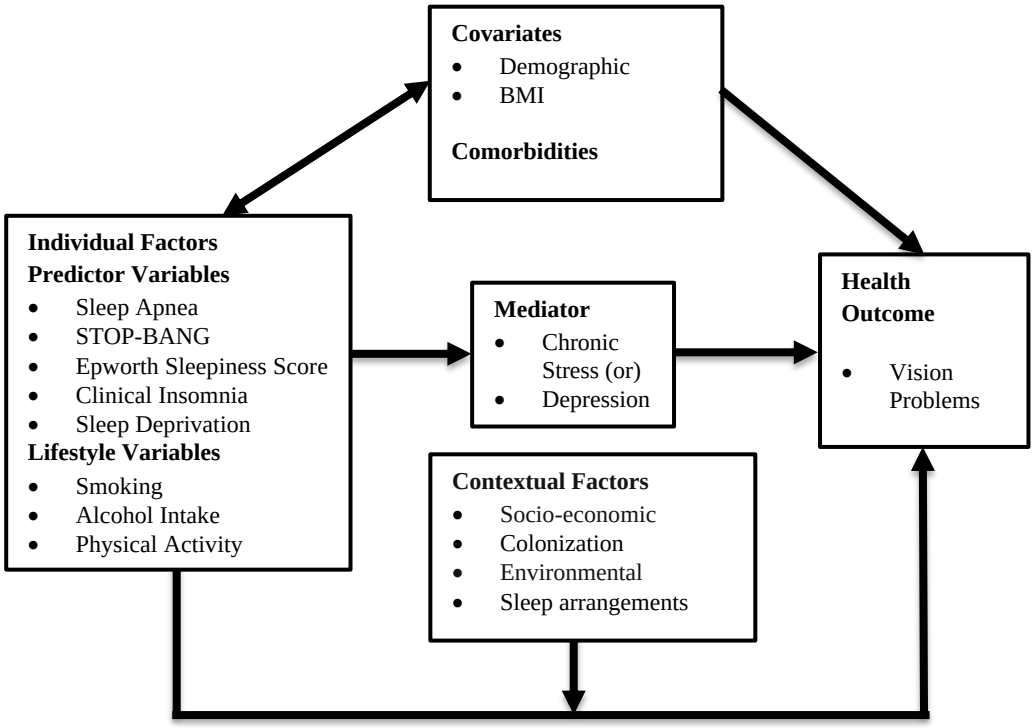

Figure 3.1 A proposed conceptual framework of the association between sleep disorders and vision problems, based on Population Health Framework of Health Canada

3.6 Study Variables

3.6.1 Outcome Variable

Vision Problems

The outcome variable 'Vision Problems' was self-reported, based on the survey question: "Has a doctor or nurse practitioner ever said you had severe eyesight problems?" Options were "Yes," "No," "Don't know."

I dichotomized all medical history (chronic health conditions) variables as Yes/No by combining the "No" and "Don't know" into a single category. Since if the patient has ever been diagnosed for a chronic health condition and taking medication/treatment, they should be certain in their answer regarding the diagnosis.

3.6.2 Independent Variables

3.6.2.1 Individual Factors

Primary Predictor Variables

I considered all sleep disorders as predictor variables; therefore, included were sleep apnea, insomnia, sleep deprivation, ESS, and STOP-BANG as the primary predictors of interest.

Sleep Apnea

Sleep apnea was self-reported based on the survey question: “Has a doctor or nurse practitioner ever said you had sleep apnea?” Options were “Yes,” “No,” “Don’t know.”

I dichotomized all medical history (chronic health conditions) variables, including sleep apnea, as Yes/No by combining the “No” and “Don’t know” into a single category.

STOP-BANG

STOP-BANG tool is used to assess the risk of developing OSA [43]. The questions in the tool evaluate the presence of “Snoring” (S), “Tiredness” (T), “Obstruction” (O) during sleep, high blood “Pressure” (P), “Body” mass index (B), “Age” of the patient (A), “Neck” (N) circumference, and “Gender” (G) (male).

The STOP-BANG was categorized as low risk (0-2), moderate risk (3-4), and high risk (5-8) based on the score [177].

Excessive Daytime Sleepiness

The ESS questions were administered to estimate EDS and score was calculated. ESS consists of eight questions [178]:

Over the past month, how likely are you to doze off or fall asleep in the following situation(s), in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you haven't done some of these things recently, try to work out how they would have affected you.

1. Sitting and reading
2. Watching television
3. Sitting inactive in a public place (e.g. theater or meeting)
4. As a passenger in a car for an hour without a break
5. Lying down to rest in the afternoon when circumstances permit
6. Sitting down and talking to someone
7. Sitting quietly after lunch (with no alcohol)
8. In a car, while stopped in traffic.

Scale to choose the most appropriate number for each situation:

0 = would never doze

1 = slight chance of dozing

2 = moderate chance of dozing

3 = high chance of dozing

Based on the score (0 to 24) participants were categorized as “normal” (0-10) or “abnormal” (11-24) [179].

Clinical Insomnia

Clinical insomnia was assessed using Insomnia Severity Index (ISI) by administrating seven Likert scale questions:

i) “Difficulty falling asleep”

ii) “Difficulty staying asleep”

iii) “Problems waking up too early”

iv) “How satisfied/dissatisfied are you with your current sleep pattern?”

v) “How noticeable to others do you think your sleep problem is in terms of impairing the quality of your life?”

vi) “How worried/distressed are you about your current sleep problem?”

vii) “To what extent do you consider your sleep problem to interfere with your daily functioning (e.g. daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, etc.) currently?”

The scale ranges; none, mild, moderate, severe, and very severe. Based on the guidelines for scoring/interpreting [180], it is categorized as:

0-7 = No Clinically Significant Insomnia

8-14 = Subthreshold Insomnia

15-21 = Clinical Insomnia-Moderate Severity

22-28 = Clinical Insomnia- Severe

However, current study categorized clinical insomnia as “absent” or “present” by merging ‘No Clinically Significant Insomnia’ and ‘Subthreshold Insomnia’ as “absent”; and ‘Clinical Insomnia-Moderate Severity’ and ‘Clinical Insomnia- Severe’ as “present”.

Sleep Deprivation

Sleep deprivation was based on the duration of sleep. The number of sleeping hours were measured and based on the cut-off point of seven hours of sleep as recommended by CDC [30,48].

Lifestyle Variables

The lifestyle factors considered were related to smoking, alcohol use, caffeine use, physical activity, and screen time.

Smoking Status

The smoking status was based on the survey question: "Have you ever smoked cigarettes? "No" means less than 20 packs in a lifetime or less than one cigarette per day for a year." In addition, survey questions collected information regarding frequency and change in smoking exposure. I categorized the smoking status as current "current smoker", "ex-smoker", and "non-smoker".

Ceremonial Use of Tobacco

I considered the ceremonial use of tobacco based on the question: "Do you smoke tobacco for ceremonial purpose?" and responses were "Yes" or "No."

Alcohol Consumption

The status of alcohol consumption was considered from a blank question in the survey:

i) "In a typical week during the past year, how many days per week do you have an alcoholic drink?"

And if participants responded "yes", additional questions were asked:

ii) "On days when you drink alcohol, how many standard drinks of alcohol do you think you would have? (No. of Drinks per day)"

iii) "Do you drink alcohol within two hours of going to bed?"

The data was classified as "non-drinker", "once per week", and "more than once per week".

Caffeine Consumption

Information collected on caffeinated beverages was based on survey questions: "How many cups of caffeinated beverages do you drink per day on average?" Answers were based on an ordinal scale and categorized as "none", "one cup per day", "two to five cups per day" and "more than five cups per day".

Another related question was: “Do you drink caffeinated beverages within two hours going to bed?” response was collected as “Yes” or “No.”

Physical Activity

The next lifestyle variable was based on information regarding physical activity. Participants were asked if they perform any type of physical activity; and if they chose “Yes” several other questions regarding physical activity were asked, such as number of days per week and level of exercises. The level of physical activity was based on the question:

i) “How long do you usually exercise?” (each time) and categorized as “never”, “less than 30 minutes” and “more than 30 minutes”.

In addition, the survey collected information on physical activity in the past year based on the question:

ii) “In a typical week during the past year, how many days per week do you usually exercise (including walking, biking etc.)? No. of days (i.e. none, 1, 2, 3, ….,7).”

Screentime

Similarly, screen time was considered based on the questions:

i) “How many hours per day spend on screen time (a phone, or other mobile devices or computer including playing computer or video games and using the internet (social media etc.), or Web)?”

ii) “In a typical week in the past 3 months, how much time did you usually spend watching television or videos?”

The data was categorized as “none”, “1-3 hours”, “4-6 hours”, “7 and more hours”.

iii) “How many minutes/hours before bedtime you stop screen time?” categorized as “<15 minutes”, “15 to less than 30 minutes”, “30 minutes to less than 1 hour”, “1 to less than 2 hours”, and “2 hours or more”. The data was categorized as “screentime less than two hours” and “screentime two hours or more”

3.6.2.2 Covariates

Demographic Variables

The demographic variables included were:

i) Age was classified into “18–39 years”, “40–49 years”, “50–59 years”, and “60 years and above”

ii) Sex was categorized as “Male” and “Female”

iii) Weight self-reported in Lbs/Kg

iv) Height self-reported in cm/inches

v) Neck circumference (self-reported in cm/inches), used for STOP-BANG variable.

vi) Body mass index (BMI) was derived from self-reported “height” and “weight”, and classified into “Neither overweight or obsese” (BMI < 25 kg/m2), “Overweight” (BMI 25–30 kg/m2) and “Obese” (BMI >30 kg/m2)

Comorbidities

I considered a number of chronic conditions based on the literature. These were “hypertension”, “diabetes”, “stroke”, “COPD/ emphysema”, “coronary heart diseases”, “asthma”, “chronic pain”, “pneumonia”, “chronic bronchitis”, “hypothyroidism”, “sinus problem”, “kidney problems”, “chronic stress”, “restless leg”, “post-traumatic stress disorder” (PTSD), “depression” and “anxiety”.

Since the systematic health conditions shares common risk factors, I created a composite ‘multimorbidity variable’ by combining hypertension, diabetes, stroke, COPD/ emphysema, coronary heart diseases, asthma, chronic pain, pneumonia, chronic bronchitis, hypothyroidism, sinus problem, and kidney problems; and categorized as “No or one morbidity” and “Two or more morbidities.”

The medical history was collected based on the question: “Has a doctor or nurse practitioner ever said you had?” with several conditions written in the table with options “Yes,” “No,” and “Don’t know.”

As mentioned above, I dichotomized all medical history (chronic health conditions) variables as Yes/No by combining the “No” and “Don’t know” into a single category.

3.6.2.3 Contextual Factors

Socio-economic Factors

The socio-economic variables included were:

i) Educational level and responses were “Grade 8 or less”, “Did not complete high school” “Completed high school”, “Some University”, “Completed University”, “Completed technical school”.

I categorized the responses as “Less than Secondary School” and “Secondary or University completed”

ii) Employment status was collected as “Employed full time”, “Employed part-time”, “Self-employed”, ”Social assistance”, “Unemployment insurance”, “Unemployed, Retired”, “Homemaker”, and “Other”

I categorized the responses as “Unemployed” and “Other (people had some source of income)”

iii) Shift worker based on responses “Yes” and “No”

iv) Money left over at the end of the month was classified as “Some money”, “Just enough money”, and “Not enough money”

Socio-cultural

Colonization history was based on the attendance of Residential School and responses were “Yes” and “No”. In addition, history of attending Residential School by Parents/Grandparents was also collected and responses were “Yes” and “No”.

Environmental Factors

Information on environmental factors was based on housing conditions. I considered the following variables:

i) Damage caused by dampness based on the question “Does your house have any damage caused by dampness (wet spots on walls, floors)?” and responses were “Yes” and “No”

ii) Moldy or musty smell was asked as: “Does your house (including basement) often have a moldy or musty smell?” and responses were “Yes” and “No”

iii) Signs of mold was based on question: “Are there signs of mold in any living areas in your house?” and responses were “Yes” and “No”

iv) Live smoking in the house was based on question “Do people regularly smoke in your house?” and responses were “Yes” and “No”

Sleep Arrangements

I considered the effect of variables related to sleep arrangements in the statistical analysis. The variables included were:

i) Sleeping place in the house based on the question: “Where did you sleep in the house?” and responses categorized as “Bedroom”, “Livingroom”, “Basement”, and “Other”

ii) Piece of furniture used to sleep on was based on the survey question: "What did you sleep on in the house?" and responses categorized as "Bed", "Couch/Sofa", "Floor", and "Other"

iii) Information regarding area/place sharing with others was collected from the question: "Who else shared that sleeping arrangements?" and categorized as "Alone", "Child", "Spouse", and "Other"

iv) Disturbance due to pets was based on questions: "Does a dog or a cat sleep on your bed/couch? or in the room?" and "Does your pet disturb your sleep?" responses were answered as "Yes" and "No."

3.6.2.4 Mediator

I planned to explore chronic stress and depression as potential mediators based on the previous studies. However, a large percentage of data was missing for chronic stress; thus I was unable to assess it as a mediator in the analysis. Nevertheless, the literature showed a correlation between depression and ocular diseases [160,181]. Hence, I considered depression as a mediator in the relationship between sleep disorders and vision problems.

3.7 Ethical Approval

The current study used the secondary data of the "Assess, Redress, Re-assess: Addressing Disparities in Sleep Health among First Nations People" project (ethics approval ref: Bio 18-110). This study was approved by the Biomedical Research Ethics Board (ref: Bio 2895).

3.8 Statistical Analysis

3.8.1 Descriptive Statistics

The socio-demographic variables were displayed using frequencies for categorical variables and mean ± standard error for continuous variables. The prevalence of vision problems was estimated among First Nations people.

Multicollinearity among independent variables was assessed by using Spearman correlation statistical test [182]. Non-collinear variables were considered for statistical model building.

3.8.2 Multivariable Logistics Regression

I used the standard model-building technique, as explained by Hosmer and Lemshow to build a parsimonious predictive model [183]. This technique mainly consists of two steps, as explained below:

Step 1. Univariable Logistic Regression

Firstly, I performed univariable analysis by fitting a number of simple logistic regression models by taking each single independent variable at a time. This step identified variables for multivariable model. Variables with $p < 0.25$ became candidate variables for multivariable analysis.

Step 2. Multivariable Logistic Regression

Based on the variables selected in Step I, The multivariable logistic regression of main effects was obtained based on the variables selected in Step I. All variables with $p<0.05$ and of clinical/biological/scientific importance were retained in the main effects model. Next, the potentially important two-way interaction terms (the product term of two variables of interest) were assessed for statistical significance. The interactions significant at $p<0.10$ were kept in the model. The strength of associations were presented in terms of odds ratios with 95% confidence intervals (95% CIs).

3.8.3 Generalized Structural Equation Modeling for Mediation

Mediation analysis was conducted by utilizing a generalized structural equation modeling (gsem) with nonlinear combinations of parameter estimates approach. We achieved the results by computing the mediation method described by Andrew F. Hayes [184].

According to this technique, various confounders threaten the causal relationship under investigation. Hence, it is crucial to control for this spurious relationship for the validity of the results. I statistically controlled the covariates by including them in the model and interpreted direct, indirect, and total effects obtained from the results. The indirect and direct effects of sleep disorders on vision problems are graphically shown in Figure 3.2 [184].

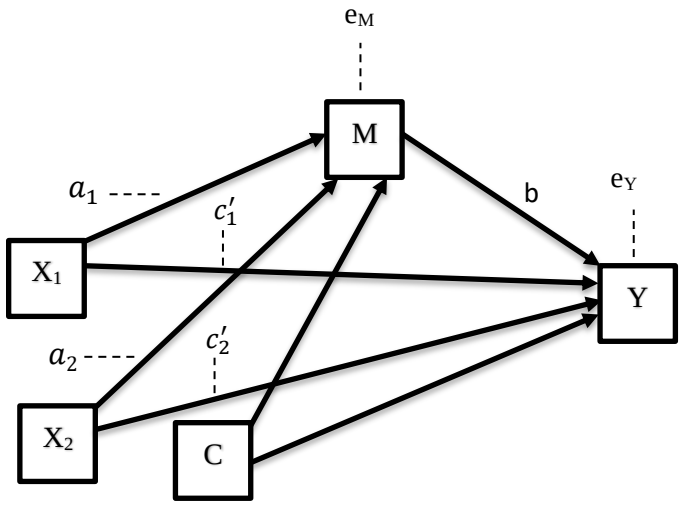

Figure 3.2: A statistical diagram of a simple mediation model: relationship among sleep disorders, depression, vision problems, and covariates, figure adopted from book [184]

M = Mediator = Depression

Y = Outcome variable = Vision problems

X_1 = Predictor variable = Sleep Apnea

X_2 = Predictor variable = Clinical Insomnia

C_i = Potential confounding variable constant

a_1 = Statistically significant effect of X_1 on M

a_2 = Statistically significant effect of X_2 on M

b = Statistically significant effect of M on Y

$a * b = a_1 * b + a_2 * b$ = Indirect effect or mediated effect

$c' = c'_1 + c'_2$ = Direct effect

I considered all three primary predictors, sleep apnea, clinical insomnia, and ESS, for mediation analysis and started from the model finalized for the multivariable model. However, ESS smoking in the house and restless leg were not significant. Therefore, I did not keep them for the final analysis based on the principal of parsimony. I presented the results in terms of percent mediated. Moreover, the direct, indirect, and total effects were calculated and presented graphically.

3.8.4 Software

The study used the SPSS version 28 and Statistical software for data science (STATA) version 17 software for data management, statistical analysis, and graphical illustrations.

CHAPTER 4: RESULTS

This chapter will initially present the prevalence of vision problems among First Nations people in rural Saskatchewan to achieve objective 1. Then, I display the descriptive statistics of various variables in percentages. To achieve objective 2, I then interpret the univariable and multivariable analyses results. Finally, I describe the mediation model results in section 4.3 to achieve objective 3 of my thesis.

4.1 Prevalence and Descriptive Statistics

The prevalence of vision problems among First Nations people in two rural Saskatchewan communities was 18.71% (110/588). Table 4.1a illustrates the distribution of various individual and contextual factors, and important covariates, briefly described below.

4.1.1 Individual Factors

Table 4.1(a) illustrates the outcome variable and sleep health-related variables. Considering sleep-related variables, 6.12% reported sleep apnea, 18.54% exhibited clinical insomnia, and about one-quarter (24.49%) presented sleep deprivation. Moreover, the STOP-BANG score showed that 42.69% are at moderate to high risk of sleep apnea, and EDS score was abnormal in 17.69% of the study participants. Furthermore, the mean score for EDS was 6.8 (S.E =0.18).

4.1.2 Demographic and Socio-economic Characteristics

The various demographic and socio-economic factors are displayed in Table 4.1(a). The largest group that participated in the survey was 18-39 years of age (54.5%) of the total sample size. More than half of the study population were females (55.78%). Among all participants, 61.56% attained secondary education or some university degree; however, 37.41% had less than secondary education. About 25.34% reported unemployment, rest of the participants (71.94%) had some source of income through full- or part-time employment, self-employment, social assistance, unemployment insurance, and retirement; furthermore, 9.86% of participants reported shift work. Around 34% of participants said they attended residential school. Regarding financial strain, more than half study population (57.31%) stated they did not have enough money by the end of the month.

Table 4.1(a) Percentage Distribution of Participants' Vision Problems, Sleep Disorders, Individual Demographic and Socio-Economic Characteristics

Variable	Frequency n (%)	Missing value n (%)
Outcome		
Vision Problems		1.7
Yes	18.71	
No	79.59	
Predictors		
Sleep Apnea		2.2
Yes	6.12	
No	91.67	
Clinical Insomnia		3.6
Yes	18.54	
No	77.89	
STOP-BANG		10.5
Intermediate to High Risk (3-8)	42.69	
Low Risk (0-2)	46.77	
Excessive Daytime Sleepiness		2.6
Abnormal	17.69	
Normal	79.76	
Sleep Deprivation		3.6
Yes	24.49	
No	71.94	
PSQI		6.1
Poor Sleep	61.05	
Good Sleep	32.82	
Medical aids to Sleep		1.9
Yes	11.90	
No	86.22	
Age group		0.0
18-39	54.25	
40-49	16.16	
50-59	17.18	
60 and above	12.41	
Sex		0.0
Male	44.22	
Female	55.78	
Education		1.0
Less than Secondary School	37.41	
Secondary or University completed	61.56	
Employment		2.7
Unemployed	25.34	
Other (some source of income)	71.94	
Shift Work		0.0
Yes	9.86	

No	90.14	
Residential School		0.0
Yes	34.0	
No	66.0	
Money left at month end		1.4
Some Money	20.41	
Just enough money	20.92	
Not enough money	57.31	
Continuous variable	**Mean (S.E)**	**Missing (%)**
Epworth sleepiness score	6.8 (0.18)	2.6

4.1.3 Environmental Factors, Sleeping Arrangements, Lifestyle Factors and Covariates

Table 4.1(b) displayed the environment, lifestyle, and sleep arrangements. About 43% of participants reported someone in the house smoking regularly. Similarly, more than half of the population (55.4%) reported house damage caused by dampness, either wet floor or walls; and about half of the study population reported a moldy smell in their house. Likewise, almost the same number of individuals (50.8%) said they had signs of mold in any living area in their house.

Various sleeping arrangements were reported such as bedroom (57%), living room (9%), basement (8.2%), and other places (2.2%). About 88.6% reported they sleep on the bed. Moving to the next factor, i.e., sharing sleep arrangements with others, only 35.20% of participants said they sleep alone. Regarding sleep disturbances, 8.16% reported that their pets disturbed their sleep during the night. Considering the crowding index, only 27.21% population was living with one or fewer persons per bedroom.

Considering lifestyle factors such as smoking, most individuals reported currently smoking (70.92%). Furthermore, one-third population reported smoking tobacco for ceremonial purposes (33.67%). Likewise, 26.70% study population reported they consumed alcohol more than once a week, and about 21% of participants reported consuming alcohol once a week. When asked about caffeinated beverages, including coffee, tea, and other carbonated drinks, the most reported consumption of 2-5 cups per day with frequencies of 46.43%.

Considering physical activity (including walking, biking etc.), about half of the study population reported exercising at least three times a week. However, regarding intensity, only 35.54% said they worked out for 30 minutes or more (each time). The calculated BMI showed that about one-quarter population was neither overweight nor obese. Nonetheless, 43.20% of participants were obese. Screentime before bed was another lifestyle factor considered, and about half of the population reported using it for two or more hours before bed.

Table 4.2 (b) Percentage Distribution of Participants' Environmental Factors, Sleeping Arrangements, Lifestyle Factors and Covariates

Variable	Frequency n (%)	Missing value n (%)
Environmental factors		
Smoking in house		1.4
Yes	42.86	
No	55.78	
Damage by dampness		1.0
Yes	55.44	
No	43.54	
Moldy Smell		0.9
Yes	49.32	
No	49.83	
Signs of mold		1.2
Yes	50.85	
No	47.96	
Sleep Arrangements		
Sleep in house		**23.1**
Bedroom	57.48	
Livingroom	9.01	
Basement	8.16	
Other	2.21	
Furniture use to sleep-on		1.0
Bed	88.61	
Couch/Sofa	5.78	
Floor	2.89	
Other	1.70	
Sharing bed		1.9
Alone	35.20	
Spouse/partner	31.29	
Child	19.73	
Other	11.90	
Pet Disturb Sleep		**23.8**
Yes	8.16	
No	68.03	
Crowding Index		2.2
More than 1 person/ bedroom	70.58	
1 or less person/ bedroom	27.21	
Lifestyle Factors		
Cigarette Smoking		1.2
Current Smoker	70.92	
Ex. Smoker	11.90	
Never Smoker	15.99	
Tobacco (Recreational) Smoking		4.6
Yes	33.67	

No	61.73	
Alcohol Consumption		**30.3**
Non-drinker	21.94	
Once per week	21.09	
More than once per week	26.70	
Physical Activity (At least three days per week)		7.8
Yes	50.68	
No	41.50	
Exercise Duration		2.7
Never	18.54	
Less than 30 mins	43.20	
30 minutes or more	35.54	
Caffeinated drink (cups per day)		1.9
None	11.56	
One	16.84	
Two- Five	46.43	
More than five	23.30	
Screentime (2 hours or more)		**24.1**
Yes	50.00	
No	25.85	
Body Mass Index (BMI)		6.6
Obese	43.20	
Overweight	26.53	
Normal	23.64	
Depression		2.0
Yes	28.74	
No	69.22	
Anxiety		2.7
Yes	29.76	
No	67.52	
Post-traumatic stress disorder (PTSD)		1.9
Yes	10.20	
No	87.93	
Restless Leg		1.7
Yes	33.33	
No	64.97	
Chronic Stress		**23.5**
Yes	16.50	
No	60.03	
Multimorbidity		5.4
None or one Morbidity	62.24	
Two or more Morbidities	32.31	

Table 4.1(b) also displays the comorbidities. The most reported morbidity was restless leg (33.33%), followed by anxiety (29.76%), and depression (28.74%). PTSD was reported by

10.20%, and chronic stress by 16.50% of study participants. Multimorbidity, i.e., two or more morbidities, was reported by 32.31% of study participants.

4.2 Cross-Tabulation and Univariable Analysis

Table 4.2(a) displays the cross-tabulation and unadjusted relationship between vision problems with primary predictors, various contextual factors, individual factors, and covariates. Results revealed that the presence of vision problems was higher among those with sleep apnea (50.0%) than those without sleep apnea (16.5%). Similarly, among those who reported clinical insomnia, 30.6% of participants had vision problems; however, among those who did not diagnose with clinical insomnia, 15.7% of individuals reported vision problems. Likewise, individuals with an intermediate to high risk of developing sleep apnea (using the STOP-BANG tool) were more likely to report vision problems (21.95%) than a low risk of developing sleep apnea (17.3%). The next predictor variable, ESS, 26.0% reported vision problems among mild ESS, followed by moderate to severe and normal ESS, reported 20.7% and 17.6% vision problems, respectively. Lastly, vision problems among sleep-deprived individuals were 17.6%, whereas, with no sleep deprivation, it was reported by 19.4%.

Among all predictor variables, sleep apnea, clinical insomnia, STOP-BANG, and ESS were significant in univariable analysis. However, sleep deprivation was not significant in univariable analysis.

Regarding other explanatory variables, vision problems were predominant among individuals aged 60 years and older, 42.0%, followed by age group 50-59 years (23.2%). Moreover, it was higher among women (21.8%) compared to males (15.4%). Likewise, the risk of having vision problems increased by 25.6% with less than secondary education, 21.5% with unemployment, and 22.4% with attending residential school. Similarly, live smoking in the house (24.8%), damage by dampness (21.6%), and signs of mold (20.1%) all contributed to the risk of developing vision problems. Nevertheless, the crowd index displayed that one or fewer persons/bedrooms increased the risk of vision problems (22.6%). Being overweight also increases the risk of having vision problems (23.7%).

Table 3.4(a) Univariable Analysis: Crude Association of Vision Problem (Yes vs No) with Primary Predictor and Other Potential Risk Factors (Contextual factors and Covariates) presented in terms of unadjusted odds ratio (OR_{unadj}) estimates and 95% confidence intervals (CI)

Variable	Vision Problems Yes/Total (%)	OR_{unadj} (95% CI)	p-value
Sleep Apnea			
No	89/538 (16.5)	1	
Yes	18/36 (50.0)	5.05 (2.53-10.08)	<0.001
Clinical Insomnia			
No	71/453 (15.7)	1	
Yes	33/108 (30.6)	2.37 (1.46- 3.83)	<0.001
STOP-BANG			
Low risk	47/272 (17.3)	1	
Intermediate to high risk	54/246 (21.9)	1.35 (0.87- 2.08)	0.181
ESS			
Normal	82/465 (17.6)	1	
Mild	19/73 (26.0)	1.64 (0.93- 2.92)	0.090
Moderate to severe	6/29 (20.7)	1.22 (0.48- 3.09)	0.677
ESS (cont.)	-	1.05 (1.00- 1.10)	0.041
Sleep deprivation			
No	81/417 (19.4)	1	
Yes	25/142 (17.6)	0.89 (0.54- 1.45)	**0.633**
Age			
18-39 years	40/315 (12.7)	1	
40-49 years	18/95 (18.9)	1.61 (0.87- 2.96)	0.128
50-59 years	23/99 (23.2)	2.08 (1.17- 3.69)	0.012
60 years and above	29/69 (42.0)	4.98 (2.79- 8.92)	<0.001
Sex			
Male	39/253 (15.4)	1	
Female	71/325 (21.8)	1.53 (1.00-2.36)	0.052
Education			
Lower than Secondary School	55/215 (25.6)	1	
Secondary school or university	54/357 (15.1)	0.52 (0.34 – 0.79)	0.002
Employment			
Unemployed	31/144 (21.5)	1	
Other (Some source of income	75/419 (17.9)	0.79 (0.50- 1.27)	**0.337**
Residential school			
No	66/382 (17.3)	1	
Yes	44/196 (22.4)	1.39 (0.90 – 2.13)	0.135
Smoking in house			
No	48/325 (14.8)	1	
Yes	61/246 (24.8)	1.90 (1.25 – 2.90)	0.003
Damage by dampness			
No	40/253 (15.8)	1	
Yes	69/320 (21.6)	1.46 (0.95 – 2.25)	0.083

Moldy Smell			
No	51/286 (17.8)	1	
Yes	58/288 (20.1)	1.16 (0.77 – 1.76)	**0.481**
Signs of mold			
No	46/276 (16.7)	1	
Yes	62/296 (20.9)	1.32 (0.87 – 2.02)	0.191
Sharing bed			
Alone	47/205 (22.9)	1	
Spouse/partner	28/183 (15.3)	0.61 (0.37 – 1.02)	0.059
Child	18/116 (15.5)	0.62 (0.34 – 1.12)	0.115
Other	16/68 (23.5)	1.03 (0.54 – 1.98)	0.919
Crowding Index			
One or less person/ bedroom	36/159 (22.6)	1	
More than 1 person/ bedroom	73/407 (17.9)	0.75 (0.48 – 1.17)	0.203

Table 4.2(b) demonstrates lifestyle factors and covariates. Lifestyle factors such as cigarette smoking, tobacco smoking, physical activity, and caffeinated drink intake were not significantly associated with vision problems. Likewise, moldy smell did not show a significant association with vision problems.

Since multiple chronic diseases were associated with a vision problem, a multimorbidity variable was created using comorbidities which were strongly associated with vision problems. Individuals with two or more morbidities reported 31.6% of vision problems compared to no or one morbidity with vision problems at 11.8%. With other comorbidities such as depression, PTSD, and restless leg syndrome, the reported vision problems were 29.2%, 44.8% and 30.9%, respectively. Results showed that these variables were highly associated with vision problems in univariable analysis.

I did not consider sleep in house, pet disturb sleep, alcohol consumption, screentime, chronic stress, AHI for analysis since more than 20% data was missing for these variables.

Table 5.6(b) Univariable Analysis: Crude Association of Vision Problem (Yes vs No) with Potential Risk Factors (Lifestyle factors and Comorbidities) presented in terms of unadjusted odds ratio (OR_{unadj}) estimates and 95% confidence intervals (CI)

Variable	Vision Problems Yes/Total (%)	OR_{unadj} (95% CI)	p-value
Cigarette Smoking			
Never	15/92 (16.3)	1	
Current	81/412 (19.7)	1.26 (0.69 – 2.30)	**0.459**
Ex.	12/68 (17.6)	1.10 (0.48 – 2.53)	**0.823**
Tobacco (Recreational) Smoking			
No	65/362 (18.0)	1	
Yes	37/193 (19.2)	1.08 (0.69 – 1.69)	**0.725**
Physical Activity			
At least three days per week			
No	47/240 (19.6)	1	
Yes	56/295 (19.0)	0.96 (0.63 – 1.48)	**0.861**
Exercise Duration			
Never	20/108 (18.5)	1	
Less than 30 mins	54/249 (21.7)	1.22 (0.69 – 2.16)	**0.498**
30 minutes or more	30/208 (14.4)	0.74 (0.40 – 1.38)	**0.345**
Caffeinated drink (cups per day)			
No	12/67 (17.9)	1	
One	17/99 (17.2)	0.95 (0.42 – 2.14)	**0.902**
Two- Five	47/269 (17.5)	0.97 (0.48 – 1.95)	**0.933**
More than five	31/135 (23.0)	1.37 (0.65 – 2.87)	**0.410**
Body Mass Index (BMI)			
Nor overweight or obese	30/137 (21.9)	1	
Obese	40/250 (16.0)	0.68 (0.40 – 1.15)	0.151
Overweight	36/152 (23.7)	1.11 (0.64 – 1.92)	0.718
Multimorbidity			
No or one Morbidity	43/365 (11.8)	1	
Two or more morbidities	60/190 (31.6)	3.46 (2.22 – 5.37)	<0.001
Depression			
No	58/407 (14.3)	1	
Yes	49/168 (29.2)	2.48 (1.62 – 3.82)	<0.001
PTSD			
No	82/516 (15.9)	1	
Yes	26/58 (44.8)	4.30 (2.43 – 7.59)	<0.001
Restless Leg			
No	49/381 (12.9)	1	
Yes	60/194 (30.9)	3.03 (1.98 – 4.65)	<0.001

4.3 Multivariable Analysis

I employed a model building technique to conduct variable selection that constructed the parsimonious model, as described below.

Using univariable analysis, I selected variables with p <0.25 for multivariable analysis; furthermore, I kept employment status in the multivariable analysis because of its significance from the literature. Various variables remained significant after adjusting for other variables; however, I excluded damage by dampness, signs of molds, moldy smell, sharing sleep arrangements, crowding index, cigarette smoking, tobacco smoking, physical activity, exercise duration, caffeine consumption, and depression from the multivariable model based on p-value <0.05. Similarly, among primary predictors, STOP-BANG was not significant in the multivariable model, thus, excluded from the final model. EDS was also non-significant in the final model therefore, I included it as a continuous variable, which was significant.

I tested various possible interactions; sleep apnea and clinical insomnia; sleep apnea and residential school; sleep apnea and age; sleep apnea and multimorbidity; sleep apnea and sex; sleep apnea and restless leg; clinical insomnia and multimorbidity; clinical insomnia and PTSD; clinical insomnia and sex; clinical insomnia and restless leg; multimorbidity and residential school; BMI and residential school; PTSD and residential school; income and BMI; multimorbidity and ESS; multimorbidity and sex; age and multimorbidity; BMI and multimorbidity; and BMI and ESS. However, interaction terms with p<0.10 were kept in the final model.

Table 4.3 demonstrates the findings of the logistics multivariable model after adjusting for various contextual variables and covariates. According to the study finding, sleep apnea, clinical insomnia, and ESS were significant predictors of vision problems. The likelihood of having vision problems was 2.93 times (95% CI: 1.19 – 7.19) more among individuals with sleep apnea than those with no sleep apnea. Similarly, the odds of having vision problems with clinical insomnia were 2.21 times (95% CI: 1.12 – 4.37) higher compared to without clinical insomnia. With each unit increase in ESS, the likelihood of developing vision problems increased by 1.11 (95% CI: 0.97- 1.28).

The participants' age showed a dose-response relationship; with increasing age, there was a higher risk of developing vision problems. The odds of having vision problems among the age group 60 years or more and 50-59 years were 5.84 (95% CI: 2.43 – 14.06) and 2.87 (95% CI: 1.32 – 6.21), respectively, compared to participants with age 18-39 years. In addition, being female increased the odds of having vision problems 1.35 times (95% CI: 0.63 – 2.90) more compared to males. However, secondary school or university education and having some source

of employment decreased the likelihood of developing vision problems by 0.46 (95% CI: 0.26 - 0.80) and 0.43 times (95% CI: 0.23 – 0.80), respectively, compared to education lower than secondary school and unemployment status.

The odds of developing vision problems increased by 1.81 times with live smoking in the house compared to no smoking in the house (95% CI: 1.03 – 3.17). Whereas, having PTSD and restless legs increased the odds of developing vision problems by 3.53 times (95% CI: 1.62 – 7.68) and 1.88 times (95% CI: 1.05 – 3.38), respectively, compared to not having PTSD and restless leg.

Table 7.3 Multivariable Logistic Analysis: Estimates Adjusted Odds Ratio and 95% CI of Vision Problems Among First Nation Adults with Associated Risk Factors

Variable	Odds Ratio	95% Confidence Interval	p-value
Sleep Apnea			
No	1		
Yes	2.93	1.19 – 7.19	0.019
Clinical Insomnia			
No	1		
Yes	2.21	1.12 – 4.37	0.023
ESS	1.11	0.97- 1.28	0.117
Age			
18-39 years	1		
40-49 years	1.68	0.72 – 3.93	0.228
50-59 years	2.87	1.32 – 6.21	0.008
60 years and above	5.84	2.43 – 14.06	<0.001
Sex			
Male	1		
Female	1.35	0.63 – 2.90	0.436
Education			
Lower than Secondary School	1		
Secondary school or university	0.46	0.26 - 0.80	0.006
Employment			
Unemployed	1		
Other (Some source of income	0.43	0.23 – 0.80	0.008
Residential school			
No	1		
Yes	2.32	0.76 – 7.12	0.140
Smoking in house			
No	1		
Yes	1.81	1.03 – 3.17	0.038

Body Mass Index (BMI)	6		
Nor overweight or obese	1		
Obese	2.43	0.51 – 11.53	0.264
Overweight	6.96	1.40 – 34.54	0.018
Multimorbidity			
No or one Morbidity	1		
Two or more morbidities	0.58	0.22 – 1.56	0.281
PTSD			
No	1		
Yes	3.52	1.62 – 7.68	0.002
Restless Leg			
No	1		
Yes	1.88	1.05 – 3.38	0.035
BMI*Residential School			
Obese *Yes	0.32	0.08 – 1.30	0.110
Overweight*Yes	0.18	0.04 - 0.82	0.027
BMI*ESS			
Obese *ESS	0.91	0.77 – 1.08	0.292
Overweight*ESS	0.84	0.70 – 1.01	0.058
Multimorbidity*Sex			
Two or more morbidities*Female	3.13	1.00 – 9.80	0.050

Significant interactions emerged between BMI and residential school, BMI and ESS, and multimorbidity and sex. As shown in Figure 4.1, the probability of vision problems was lower among individuals who were either obese or overweight and attended residential school than among individuals neither overweight nor obese and did not attend residential school.

Likewise, in figure 4.2, the logit lines were not parallel and overlapped between obese, overweight, and those neither overweight nor obese. An increase in Epworth sleepiness indicates a significant interaction between the BMI of the individuals and ESS. In other words, the probability of developing vision problems among different BMI groups changes as the ESS increases.

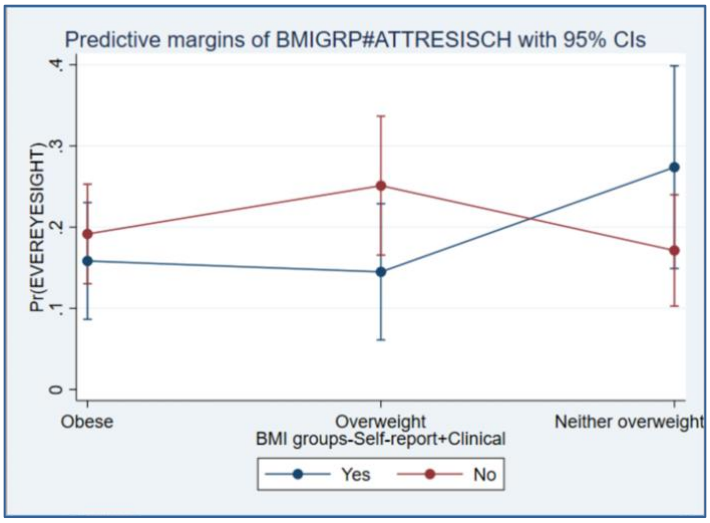

Figure 4.3: Predictive log odds margins for significant interaction between BMI and Attending Residential School

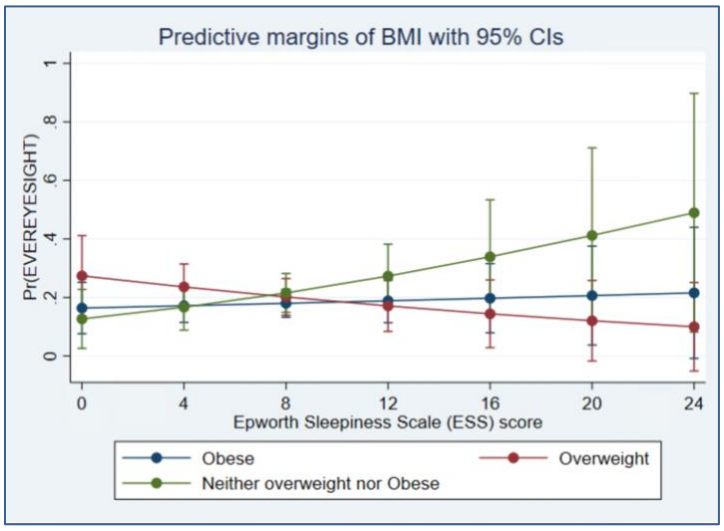

Figure 4.4: Predictive log odds margins for significant interaction between BMI and ESS

As demonstrated by Figure 4.3, the likelihood of developing vision problems between men and women widens with two or more multimorbidity. The probability of vision problems was greater among women than men with two or more chronic conditions.

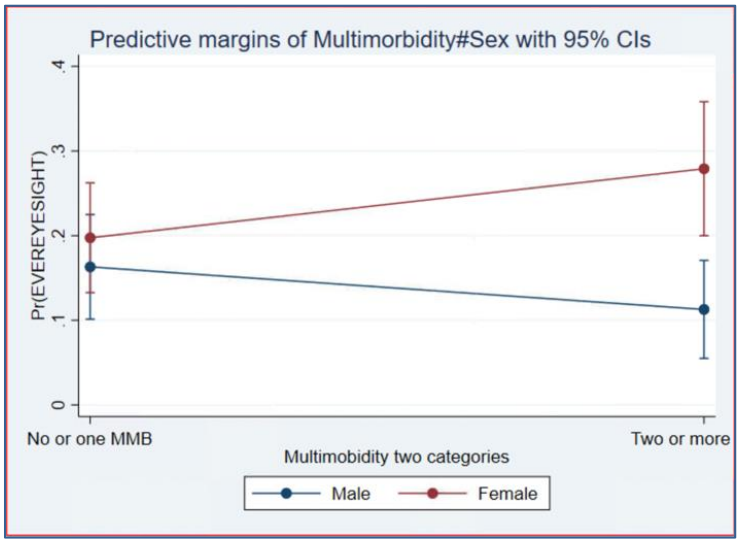

Figure 4.5: Predictive log odds margins for significant interaction between Sex and Multimorbidity

4.4 Mediation Analysis

To achieve object 2 of my study, I employed gsem to conduct mediation analysis. Results were displayed in Tables 4.4(a) and 4.4(b).

Direct and indirect paths can explain the relationship between sleep disorders and vision problems as shown in Figures 5 and 6. The direct path is when sleep disorders go to vision problems; however, in the indirect path, sleep disorder goes through some mediator in the pathway. I tested various potential mediators, including STOP-BANG and Depression, in order to find the causal path in the relationship between sleep disorders and vision problems. Although a potential mediator, as per the literature, I could not test perceived stress as a mediator since a considerable data was missing. Nevertheless, only depression was significant in this relationship meaning sleep disorders cause depression, and depression causes vision problems.

Tables 4.4(a) demonstrate the results from gsem with nonlinear combinations of parameter estimates to determine direct and indirect paths. The p-value <0.10 was considered significant. The p-value obtained from nonlinear combinations of parameter estimates showed significant results.

All three primary predictors, sleep apnea, clinical insomnia, and ESS, were tested simultaneously for mediation analysis. ESS was not significant, thus, did not select for the final analysis; likewise, an interaction term between ESS and BMI was also removed from the model. Furthermore, other variables that were not significant in the final model were "smoking in the house" and "restless leg" and did not select for mediation analysis to make our model more parsimonious.

Table 8.9(a) Mediation Analysis: Coefficient (Std. Err.) and Adjusted Odds Ratio in the Relationship among Sleep Disorders, Depression and Vision Problems

		Y (Vision Problem)				M (Depression)		
Variable		$\widehat{\boldsymbol{\beta}}$	$(\boldsymbol{SE}\ (\widehat{\boldsymbol{\beta}}))$	**p-value**		$\widehat{\boldsymbol{\beta}}$	$(\boldsymbol{SE}\ (\widehat{\boldsymbol{\beta}}))$	**p-value**
Sleep Apnea								
No		-				-		
Yes	$\boldsymbol{c_1'}$	0.92	(0.44)	0.035	$\boldsymbol{a_1}$	0.61	(0.43)	0.157
Clinical Insomnia								
No		-				-		
Yes	$\boldsymbol{c_2'}$	0.91	(0.33)	0.006	$\boldsymbol{a_2}$	0.60	(0.28)	0.033
Depression								
No		-				-	-	-
Yes	$\boldsymbol{b}$	0.71	(0.30)	0.019		-	-	-

Age						
18-39 years	-			-		
40-49 years	-0.55	(0.42)	0.192	-0.31	(0.35)	0.386
50-59 years	1.18	(0.39)	0.002	-0.51	(0.35)	0.148
60 years and above	1.90	(0.45)	<0.001	-1.27	(0.45)	0.005
Sex						
Male	-			-		
Female	0.18	(0.38)	0.634	0.36	(0.30)	0.231
Education						
Lower than Secondary School	-			-		
Secondary school or university	-0.79	(0.28)	0.005	-0.15	(0.24)	0.527
Employment						
Unemployed	-			-		
Other (Some source of income	-0.86	(0.31)	0.006	-0.17	(0.26)	0.531
Residential school						
No	-			-		
Yes	0.60	(0.55)	0.276	-0.36	(0.48)	0.454
PTSD						
No	-			-		
Yes	1.07	(0.40)	0.006	2.00	(0.38)	<0.001
Body Mass Index						
Nor overweight or obese	-			-		
Obese	0.16	(0.42)	0.691	-0.68	(0.32)	0.031
Overweight	0.65	(0.43)	0.136	-0.77	(0.37)	0.035
Multimorbidity						
No or one Morbidity	-			-		
Two or more morbidities	-0.46	(0.49)	0.354	1.61	(0.39)	<0.001
BMI*Residential School						
Obese *Yes	-1.02	(0.70)	0.147	0.35	(0.59)	0.550
Overweight*Yes	-1.53	(0.74)	0.039	0.03	(0.68)	0.959
Multimorbidity*Sex						
Two or more morbidities*Female	1.18	(0.57)	0.039	-0.81	(0.47)	0.084

Sleep apnea and clinical insomnia were added together after adjusting for other covariates in the mediation model. Table 4.4(b) and Figure 4.4 displayed the direct and indirect effects obtained from gsem and nonlinear combinations of parameter estimates; the direct effect (c') was 1.83, and the indirect effect was 0.861.

Table 10.11(b): Illustrations of GSEM and Bootstrap Mediation Methods: Effect of Sleep Disorders (X) on Vision Problems (Y) as Mediated Through Depression (M)

Direct effect **Sleep Disorders → Vision Problems**	$\widehat{\boldsymbol{\beta}}(\boldsymbol{SE}\ (\widehat{\boldsymbol{\beta}}))$	**95 % CI**	**p-value**
Sleep Apnea→ Vision Problems (c_1')	0.92 (0.44)	0.07 – 1.78	0.035
Clinical Insomnia→ Vision Problems (c_2')	0.91 (0.33)	0.26 – 1.56	0.006
$c' = c_1' + c_2'$	1.83		
Indirect effect **Sleep Disorders → Depression → Vision Problems**	$\widehat{\boldsymbol{\beta}}(\boldsymbol{SE}\ (\widehat{\boldsymbol{\beta}}))$	**95 % CI**	**p-value**
Sleep Apnea→ Depression (a_1)	0.61 (0.43)	-0.24 – 1.46	0.157
Clinical Insomnia→ Depression (a_2)	0.60 (0.28)	0.05 – 1.15	0.033
Depression → Vision Problems (b)	0.71 (0.30)	0.11 – 1.30	0.019
$a * b = a_1 * b + a_2 * b$	0.861 (0.51)	-0.15 – 1.87	0.094
With Bootstrap $a * b = a_1 * b + a_2 * b$	0.861 (0.67)	-0.45 – 2.17	0.197
Total Effect = $C = c' + (\mathbf{a} * \mathbf{b})$	2.691		

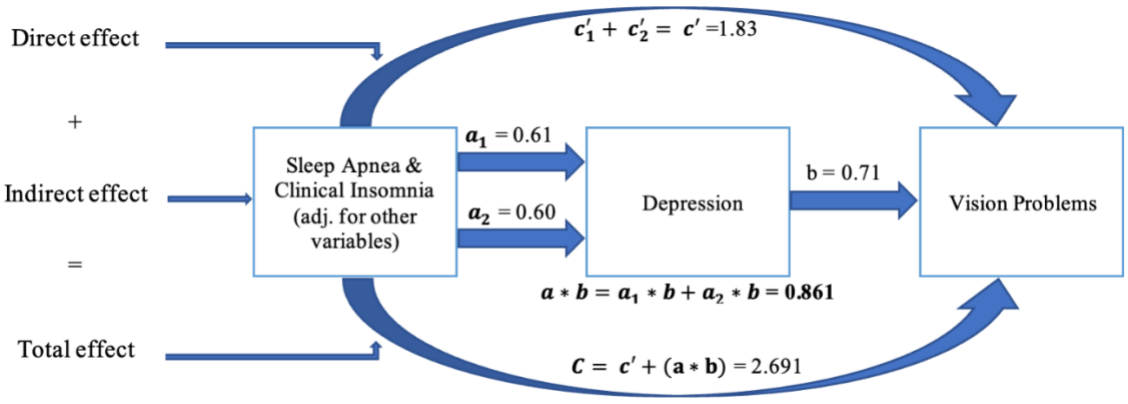

Figure 4.6: Mediation Analysis: Relationship among Sleep Disorders, Depression and Vision Problems

The ratio of indirect effect to total effect (RIT= 0.32) and indirect effect to direct effect (RID = 0.47), calculated as below, revealed a medium-sized mediation effect. These findings showed that about 32% of the effect of sleep disorders on vision problems was mediated by depression which was 47 times as large as the direct effect.

RIT = Ratio of Indirect effect to total effect = a*b/C = 0.861/2.691 = 0. 319

RID = Ratio of the indirect effect to the direct effect = a*b/c' = 0.861/1.83 = 0.47

CHAPTER 5: DISCUSSION

This chapter will initially summarize the findings and then focus on the prevalence of vision problems among First Nations in Canada. Then, I discuss the relationship between sleep disorders and vision problems and compare the findings with previous research. Later, I discuss the findings from mediation analysis and significant interactions. Finally, risk factors associated with vision problems will be discussed.

5.1 Summary and Interpretation of Results

The "Assess, Redress, Re-assess: Addressing Disparities in Sleep Health among First Nations People" is an ongoing cohort study in partnership with two Cree First Nation communities. The baseline data constituted the foundation of my thesis, which examined the association between sleep disorders and vision problems among First Nations people living in on-reserve communities in rural Saskatchewan. To address our research questions, we applied Health Canada's Population Health Framework in our study.

We used the secondary data of an ongoing cohort study to examine the association between sleep disorders and vision problems among First Nations people living in on-reserve communities in rural Saskatchewan. This cross-sectional study estimated the prevalence of vision problems among First Nations people and showed the relationship between self-reported doctor-diagnosed sleep disorders, including sleep apnea, clinical insomnia and ESS, and vision problems. Vision problems were more prevalent among participants with sleep apnea, clinical insomnia, and ESS as compared to individuals not self-reporting/diagnosed with these sleep disorders. However, sleep deprivation and STOP-BANG scores failed to show a significant association with vision problems in the current study.

Other significant risk factors for vision problems were increasing age, female sex, less than secondary school education, unemployment status, and a history of attending residential school. Additionally, we found that smoking in the house, high BMI, PTSD, multimorbidity, and restless leg were significantly associated with vision problems. Further analysis revealed three significant interactions: BMI and residential schools, BMI and ESS, and multimorbidity and sex. Most participants who reported vision problems were females and had two or more co-morbidities. Moreover, depression mediated the relationship between sleep disorders and vision problems, which accounted for 32% of this association.

5.2 Prevalence of Vision Problems

The current study estimated the prevalence of vision problems among First Nations people at 18.71%. This value is considerably higher than the 5.4% reported from a national Canadian survey on visual disability and the 1.4% reported from 2018-2019 CHMS data, both of which were general population estimates [12,13]. We do not have previous data on the prevalence of vision problems among First Nations people to check the trends and compare values. However, our estimated value is within range of the prevalence of vision problems reported among Indigenous people in Australia (10.0% to 93.0%) and the United States (11.1% to 28.5%) [9,11]. In addition, the prevalence among Indigenous people may vary across different First Nation communities depending upon the presence of associated risk factors such as age and the geographical area.

Certain eye diseases are strongly associated with chronic health conditions; for instance, diabetic retinopathy is a complication of diabetes, and uveitis can be associated with rheumatoid arthritis [185,186]. The prevalence of diabetes is high among First Nations people in Canada [187]. Likewise, the evidence shows a high prevalence of rheumatoid arthritis among First Nation populations of central Canada [186,188]. With high rates of associated chronic health conditions, there is an increased likelihood of vision problems in these communities. The current study aimed to bring researchers and policy makers' attention to focus on vision problems among First Nations communities in Canada that may be associated with sleep disorders.

5.3 Sleep Disorders and Vision Problems

My findings demonstrated that participants who reported sleep apnea had vision problems about three times more compared to their counterparts which was consistent with previous studies [189–191]. A recent meta-analysis published that OSA increased the risk of glaucoma 1.5 times, non-arteritic ischemic optic neuropathy 3.6 times, and diabetic retinopathy 1.6 times [189]. Similarly, another publication supports the association of untreated OSA with ocular diseases [190]. The same study considered the range of eye diseases involving eyelid issues due to optic neuropathies to retinal vascular disorders. These studies suggested sleep apnea as a potential risk factor for several eye diseases.

A recent study examined the association between dry eyes syndrome and sleep disorders [191]. Researchers employed Ocular Surface Disease Index (OSDI) questionnaire along with PSQI, ISI, ESS, and the STOP-BANG questionnaire. Their findings showed a relationship

between dry eye syndromes and sleep disorders. As per these results, the ESS score, ISI, and PSQI were significantly correlated with the OSDI score. However, the STOP-BANG score was not statistically correlated with the OSDI score. Our results are in support of these findings. Our findings showed that clinical insomnia increased the risk of vision problems about two times, and with every unit increase of ESS likelihood of vision problems increased by 1.11.

Moreover, the present study showed the same trend regarding STOP-BANG, which was not statistically significant. Nevertheless, unlike the earlier study, my findings showed an insignificant association between PSQI and vision problems [191]. My outcome variable included all ocular diseases, unlike previous studies, which only considered dry eyes syndrome.

Another publication conducted a systematic review and meta-analysis to find the sleep outcome associated with dry eye diseases. It revealed that patients with dry eyes had higher ESS and PSQI. Additionally, the researcher concluded that patients with dry eye disease had a higher incidence, prevalence, and severity of sleep disorders [192]. Likewise, a case-control study was conducted to compare the thickness of different inner layers of the eye between patients with primary insomnia and their control match [193]. The results showed the thinning of retinal nerve fibre layers and inner plexiform layers, and the thickness of the choroid was correlated with the severity of insomnia. The retinal and choroidal thicknesses are considered biomarkers of many ocular diseases that may indicate neurodegeneration and glaucoma [194,195].

Although most of these studies considered only one eye disease/disorder as outcome variable, all previous publications were consistent with current study findings. Sleep disorders like sleep apnea and insomnia are associated with reduced brain function, blood flow, or glucose metabolism [8–11]. Similarly, hypoxia, microvascular and autonomic dysfunction are known to cause degeneration of retinal and choroidal layers, which affect corneal thickness [196–199]. These conditions may lead to vision-threatening eye diseases, such as diabetic retinopathy, glaucoma, and ischemic optic neuropathy.

5.4 Mediation Analysis Findings

The present study explained the two paths in the relationship between sleep disorders and vision problems. According to our results, one direction is that sleep disorders may directly produce vision problems; the other path explains that sleep disorders indirectly cause vision problems due to sequential consequences, i.e. sleep disorders cause depression, and depression cause vision problems. In other words, sleep disorders and vision problems may relate to each

other due to a common cause which was depression in our study population. Based on the findings, depression accounted for about 32% of the relationship between sleep disorders and vision problems. Moreover, the causal relationship intensified by depression was 47 times larger than the direct relationship.

The results in this thesis were consistent with previous studies that reported persistent sleep disturbances can cause mental health issues such as anxiety and depression [104,200]. Moreover, about 90% of patients suffering from depression complain about sleep problems, including insomnia, restless leg syndrome, and sleep apnea [201]. Many studies have demonstrated that the relationship between depression and sleep disorders, specifically chronic insomnia, is reciprocal [159,200,202]. Depression can re-occur in the case of chronic insomnia and other sleep disturbances; these chronic health issues occur side-by-side. Sleep disorders can cause daytime fatigue, poor performance at work/education, and irritability. The lower productivity can cause agitation and diminished interest in everyday activities, and mood changes can be observed subjectively and objectively, further escalating sleep issues [202].

A recent study assessed the association between several sleep characteristics and depression among high school students in Korea [203]. This study explored the risk of depression on sleep characteristics, including morningness or eveningness preference, sleep duration (weekday and weekend), weekend catch-up sleep duration, perceived sufficiency of sleep, daytime sleepiness, snoring, sleep apnea (self-reported), and sleep environment. The results revealed that students who preferred to wake up till late (eveningness) and reported insufficient weekday sleep were more prone to develop depression; moreover, female gender, higher BMI, snoring, sleep apnea, internet addiction, non-optimal environment, and excessive or insufficient sleep duration sleep, were some of the other risk factors of depression. This study apprehends to understand the sleep characteristics of adolescents that could lead to the onset of depression later in life.

Evidence has shown that depression is associated with various systematic diseases such as cardiovascular conditions, diabetes, obesity, and metabolic disorders [19,204–207]. Many studies reported that psychological distress, for instance, depression, is associated with eye diseases [208,209]. The study examined the association between anxiety and depression with primary open-angle Glaucoma [208]. Hospital Anxiety Depression Scale (HADS) was used to measure pressure and depression, and Glaucoma was categorized as mild, moderate, and severe. The study

results showed that HADS scores for anxiety and depression increased with the severity of Glaucoma.

A recent systematic review provided evidence of an association between different eye diseases and the prevalence of anxiety and depression [181]. The study showed a significant difference in the prevalence of depression among patients with eye diseases compared to healthy-eye individuals. The researchers reported a 25% pooled prevalence of depression among patients with eye diseases. These results revealed a higher prevalence among dry eyes patients, followed by Glaucoma, AMD, and cataract. Likewise, a study investigated the sleep quality and mood status (anxiety and depression) characteristics of the ocular surface [210]. The researcher reported that patients with poor sleep quality showed irregular ocular surface characteristics; anxiety and depression aggravated this irregularity.

Previous studies have shown the relationship between depression and eye diseases; however, longitudinal studies are required to establish the directionality. Moreover, like sleep disorders, there is a possibility of a bilateral relationship between vision problems and depression, i.e. one causes the other. Nevertheless, the higher cortisol levels in depression can explain the mechanism that causes vision problems. Research has shown persistently higher cortisol levels among depressed persons [211]. This change in cortisol pattern enhances the sympathetic nervous system, which can cause dilated pupils, which allows an immense amount of light to enter the eyes. Prolonged exposure to ample light may damage the retinal layers sensitive to light, producing a state auspicious to several eye diseases [212].

In the above studies, researchers emphasized managing psychological health issues such as depression, anxiety, and chronic eye diseases for a good prognosis and proper treatment that reduces the likelihood of vision problems. Furthermore, sleep disorders contribute to the progression of depression; the research investigators underscored the management of depression and sleep disturbances to elevate the symptoms of these chronic health issues. Individuals with sleep disorders feel fatigued, irritable, sad, and pessimistic, and cognitive disorders such as depression can create a vicious cycle; therefore, properly managing these chronic conditions together can optimize overall well-being. According to recent evidence, cognitive behavioural therapy and chronotherapy are preferred over pharmacological treatments that can effectively improve sleep architecture [213]. However, it is essential first to rule out and treat sleep-related breathing disorders to vitalize sleep health. In addition, focusing on sleep hygiene, including a

bedroom environment (comfortable, dark, and noise-free), reduction of screentime, and avoiding caffeinated beverages can remarkably improve sleep quality [214].

5.5 Significant Interactions

Participants who attended residential schools were two times more likely to have vision problems compared to those who did not. Several studies showed that attending residential school impacted the physical health outcome among Aboriginal people [215–217]. The study used the scoping review of existing articles on residential school attendance and its effect on all four components of health as described by the Indigenous Medicine Wheel [216]. The investigators incorporated eye health outcome articles in physical health, including cataracts, glaucoma, blindness, or severe vision problems that were unable to be corrected with spectacles. According to their finding, the residential school negatively impacted health outcomes for attendees and transmitted them to the next generation. Likewise, the same results were reported in another publication stating that residential school attendance is a significant factor in health disparities between Indigenous and non-Indigenous people in Canada [215]. Likewise, the research reported that residential school attendance induced poor health outcomes among Indigenous people by limiting access to socio-economic resources [217].

Nonetheless, in our findings, the residential school showed interaction with BMI. A longitudinal study assessed the association of self-reported and actigraphy sleep efficiency, i.e., duration and continuity, with BMI and showed an inverse relationship between the two variables. The study reported that decreased sleep efficiency was linked with higher BMI, especially among women [218]. The association of higher BMI with sleep disorders and low sleep efficiency was well established in previous studies [219–221]. Similarly, a recent study assessed the morphometric indices among morbid obese and healthy individuals [222]. These findings showed the signs of neuropathy and retinopathy among morbid obese concluding that the increased risk of glaucoma and glaucomatous optic neuropathy is associated with obesity [222]. Another cross-sectional study conducted in China assessed the association between BMI and visual impairment among school-going children and found a significant relationship between higher BMI and increased prevalence of visual impairment [223]. According to their findings, children with overweight/obesity were 16 times more likely to have visual impairment than normal or underweight children after adjusting for age and sex.

Nevertheless, my study showed that individuals with higher BMI who attended residential school were less likely to develop vision problems. This was a distinctive finding since residential school and higher BMI were individually associated with vision problems in our study (in univariable analysis). A study that used repeated Aboriginal surveys from 1991 to 2001 found that among those who attended residential schools, overall adult height increased and body weight decreased. [224]. The study further examined the underlying policies that directly impacted this change and found that this would result from selection criteria and tighter health regulations of residential schools implemented in the 1960s. The selection for enrollment was based on those most vulnerable, such as children with chronic conditions who otherwise did not have access to healthcare [224]. This could explain why the children in residential schools with better healthcare access might have better visual outcomes despite having higher BMI. This area of study requires further research and clarity of the pathways involved.

Research has shown that BMI is an effect modifier in the relationship between ESS and vision problems [99,225]. A previous study assessed the relationship between EDS and sleep apnea and considered a vast array of predisposed factors [99]. The results showed substantial progress in the prevalence of EDS at the overweight threshold (BMI = 28). In addition, depression and diabetes were strongly associated with EDS. The study concluded that patients with the complaint of EDS should also be assessed for depression and metabolic syndrome with or without the presence of sleep apnea. Another study explored the factors affecting quality of life among those with sleep disorders and identified BMI, higher ESS and other co-existing diseases as having a detrimental impact [225].

The above studies were suggestive of a correlation between higher ESS and higher BMI. Relating to vision problems, a study assessed the association between retinitis pigmentosa and daytime sleepiness; their finding revealed that patients with retinitis pigmentosa had higher daytime sleepiness scores and reduced alertness compared to individuals with normal eyesight [226]. On the contrary, a study examined the relationship between primary glaucoma, sleep quality, and daytime sleepiness [133]. The results showed that primary closed-angle glaucoma is associated with poor sleep quality; however, no significant association was found with daytime sleepiness. We could not find any study exploring the association between vision problems and sleep disorders with the interaction between BMI and ESS. There was a significant correlation between the participants' BMI and ESS, as an increase in the ESS shows an interaction between

the two variables. Particularly, the probability of having vision problems among BMI groups differs with variations in the ESS.

Our results showed that females were more prone to vision problems compared to males, which was consistent with previous studies. A systematic review and meta-analysis conducted in sub-Saharan Africa in 2015 showed that the age-standardized prevalence of blindness and moderate to severe vision impairment was higher among females than males [227]. Another systematic review and meta-analysis revealed the global causes of vision impairment and blindness [228]. In this meta-systematic review, investigators included population-based data from 98 countries. This study showed that the common causes of blindness and vision impairment in women were cataracts, uncorrected refractive error, and diabetic retinopathy; on the other hand, in men were glaucoma and corneal opacities. Furthermore, leading causes of blindness and vision impairments were uncorrected refractive errors and cataracts, suggesting females were affected more globally.

Multimorbidity was found to have existed in all age groups since certain chronic diseases share common risk factors that systematically co-occur [229,230]. We observed an interaction between multimorbidity and sex. The probability of having vision problems was increased three times more among females with two or more chronic conditions. Our results were consistent with previous research [231]. A cross-sectional study to estimate eye disease prevalence and risk factors among patients with OSA [231] reported that patients with OSA had more eye diseases than the general population. Furthermore, a significant gender difference was associated with glaucoma. The study adjusted for various chronic diseases and showed that females were at greater risk of developing glaucoma with severe OSA.

Likewise, another recent study examined the association between cataracts and multimorbidity and reported the prevalence of these two conditions among Spanish adults [232]. This study defined multimorbidity as the presence of two or more chronic conditions, as I defined in this thesis, Chapter 3, section 3.6.2.2. Moreover, researchers considered several chronic conditions that were included in our research, such as hypertension, cardiac diseases, chronic pain, asthma, chronic bronchitis, COPD/emphysema, diabetes, thyroid disease, stroke, and kidney disease. Their finding showed a significant relationship between cataracts and multimorbidity; this association was significant between different sex and age groups. In addition, female participants were more frequent to have cataracts. A systematic review using 39

publications from 12 countries reported age, female, and lower socio-economic status as determinants of multimorbidity [233].

Considering sleep disorders and multimorbidity, a study examined the independent relationships of sleep disturbances, including insomnia, trouble falling asleep, difficulty staying asleep, daytime tiredness, and hours of daily sleep, with multimorbidity among community-dwelling older adults [79]. The study's sex-specific findings revealed that all insomnia symptoms were significantly associated with multimorbidity among women after adjusting for all covariates. The above research indicated that female participants were more prone to chronic conditions and co-morbidities than males, which was coherent with our findings.

5.6 Other Predictors of Vision Problems

Our study population comprised more than half of adults between the age of 18 years to 39 years, about 54.25%. Our findings showed a dose-response relationship between age groups and vision problems, i.e., with an increase in age, the odds of having vision problems increased. in multivariable analysis, the risk of developing vision problems was highest among adults aged 60 years and older (OR_{adj}. 5.84, CI: 2.43 – 14.06, p-value <0.001). Many studies explored age-related vision impairment, consistent with our results [234,235]. The previous study showed severe visual impairment with ≥65 years of age based on age-stratified analyses; it concluded that the prevalence and incidence of visual impairment worsen with age, thus reducing the vision-related quality of life [234]. The same can also be explained as many chronic ocular diseases such as glaucoma, cataract, AMD, and retinopathies advance with age. An eye health longitudinal survey reported the major causes of vision loss among Aboriginal people of western Australia [236]. This study recruited participants 16 years of age and older and suggested that most of the vision loss causes were preventable. However, the study displayed age as a continuous variable, with the mean age of 42 years on their first visit.

Research has shown that attaining secondary school or higher education is protective against vision problems [237,238], and we found similar results with multivariable analysis. A recent national eye health survey report by the Centre for Eye Research Australia and Vision 2020 Australia published that the age-adjusted prevalence of vision impairment and blindness was three times more among indigenous people compared to non-indigenous people [237]. While the years of educational attainment were significantly higher in non-Indigenous participants (p<0.001) than in Indigenous people [237]. We observed similar findings suggesting that higher

education acted protective against vision problems. According to the article published in Canada, the general-public with higher educational had higher knowledge about the three most common eye diseases; cataract OR 1.8 (95% CI: 1.3-2.5), glaucoma OR 1.8 (95% CI: 1.3-2.5), and age-related macular diseases OR 2.13 (95% CI: 1.45- 3.15) [238].

Another socio-economic factor was employment; our findings showed that having some income source was protective against developing vision problems. Other studies reported coherent results. The study showed the prevalence and risk factors of visual impairment and blindness and showed that unemployment increased visual impairment by 3.3 times (95% CI: 1.7–6.3) [239]. Likewise, other studies were suggestive of lower income/ unemployment with increased risk of vision impairment or vision loss [240,241].

Numerous studies reported low socio-economic determinants of health as significant risk factors for vision loss [240–242]. According to these studies, being women, increasing age, low education attainment, and unemployment or limited income were significantly associated with impaired eye health. These results are consistent with our findings. In general, Aboriginal people have low socio-economic status and high prevalence of poor health outcomes compared to general Canadian population [58]. A study conducted in Canada analyzed the uveitis outcome and its characteristics between Aboriginal First Nations and non-aboriginal uveitis patients. The results demonstrated the early onset of disease, bilaterality, and higher complications among Aboriginal First Nations) compared to non-aboriginal people [243].

Relating to lifestyle factors such as cigarette smoking and tobacco smoking, the univariable analysis was insignificant; however, live smoking in the house appeared to be a significant factor in the univariable and multivariable analysis. According to results, individuals exposed to live smoking at home were 1.8 times more likely to have vision problems than their counterparts. These findings are consistence with the study that analyzed exposure to environmental smoke and ocular disease [244]. The study findings revealed that exposure to environmental tobacco smoke (indoor air pollutants) is significantly associated with ocular diseases such as cataracts, uveitis, macular degeneration, and dry eye syndrome. Another study conducted a systematic review on passive smoking reported seven studies that showed the association between environmental tobacco smoke and eye diseases, including refractive errors, cataracts, AMD, and Grave ophthalmopathy [245]. The investigators suggested including the

environmental tobacco smoke on eye diseases research in the future since the available literature on this relationship is inadequate.

Nevertheless, previous research established the association between smoking exposure and sleep disorders. A recent study exploring the association between modifiable lifestyle factors, including active and passive smoking, and the risk of OSA showed an inverse relationship [246]. Their findings suggested that a healthy lifestyle might lower the OSA risk. The study findings showed that men who never smoked and were exposed to smoking at the workplace had higher odds of having shorter sleep duration than those who were never exposed to smoking at work [247]. Similarly, studies reported that cohabiting with smokers increased the risk of having sleep disturbances [248,249]. Passive smoking is a significant problem in many Indigenous communities.

Restless leg syndrome, the urge to move the leg primarily occurs in the evening while sitting or lying in bed, is a common sleep disorder that interferes with sleep [250]. Studies suggest the presence of family history or genetic influence as a clinical diagnosis of restless leg symptoms [250,251]. The co-occurrence of restless leg syndrome with sleep apnea and insomnia was also indicated in previous research [252]. Restless leg syndrome delays sleep onset or duration and reduces sleep quality.

Results of our study showed that the risk of having vision problems with restless syndrome increased by around two times. The pathophysiology of restless leg syndrome is not fully understood, but research showed sympathetic overactivity is associated with the restless leg; nonetheless, the symptoms showed marked improvement with stimulation of the dopamine system [253,254]. Research evidence indicated that a hypodopaminergic state and sympathetic overactivity could cause structural changes in the retinal and choroidal layers, respectively [255,256].

We can relate our results with previous studies that examined the association between morphological alterations in the inner layers of the eye and restless leg syndrome [257–259]. These studies used the optical coherence tomography (OCT) technique to analyze structural changes in the optic nerve head, retinal layers, and macular among patients with restless leg syndrome. As discussed before, the thickness of retinal and choroidal layers is considered the biomarker of many ocular diseases [194]. Therefore, we can say that thinning of these ocular

layers may indicate the presence of chronic ocular conditions that can cause irreversible vision loss.

A case-control study investigated the association between restless leg syndrome and retinal layers thickness and found a significant association between these variables [257]. Using the OCT technique, this study revealed that most retinal layers were thinner among cases compared to the control group. Furthermore, Pearson correlation was applied to check the disease duration and severity. Results showed a statistically significant negative correlation between the length of the disease and the thickness of macular and retinal layers [257].

Similarly, a study examined the structural changes in retinal nerve fibre layers and optic nerve in patients with restless leg syndrome [258]. The results showed statistically significant alterations among retinal and macular layers with restless leg syndrome. There was a thickness reduction in the inner ocular layers compared to healthy controls. However, there was no significant difference in optic nerve parameters. Likewise, another case-control study showed that choroidal thickness was linked with restless leg syndrome [259]. However, the difference between retinal and macular thickness was statistically insignificant among patients with restless legs and healthy individuals.

Nevertheless, a recent case-control study assessed the relationship between the thickness of choroidal and retinal layers and restless leg syndrome and showed contradictory results to the above studies [260]. The results showed a statistically insignificant relationship between the thickness of inner ocular layers and the duration of diseases. However, these studies used a small sample size, and the authors suggested replicating the study using a larger sample size for further investigation.

Finally, our results showed that patients with PTSD are 3.5 times more likely to develop vision problems than those without PTSD ($p = 0.002$). Previous studies discussed the development of PTSD with visual impairment [49,261], whereas fewer studies discussed PTSD as a risk of any chronic ocular condition. A longitudinal study examined the frequency, and associated risk factors of severe dry eye symptoms among US veterans [262]. The study results revealed a progression in dry eye symptoms after one year, and associated risk factors were sleep apnea, insomnia, depression, non-ocular pain, and medications such as antianxiety and analgesics. Multivariable analysis showed that the risk increased with sleep apnea to 3.8-folds,

with Dry Eye Questionnaire 5 score ≥12 to 1.15-folds and with PTSD risk increased to 1.01-folds with p-values, 0.05, 0.02, and 0.02, respectively [262].

Likewise, a recent study assessed the relationship between dry eye symptoms and ocular and non-ocular parameters [263]. The investigators hypothesized that symptoms of dry eye are linked more strongly with non-ocular conditions such as pain, depression, and PTSD compared to ocular parameters. A statistically significant relationship between dry eye symptoms and non-ocular conditions (PTSD and pain) was observed based on correlation and regression techniques. However, the relationship between dry eye symptoms and ocular parameters (tear film measures) was statistically insignificant [263].

Another study examined the association between PTSD and the development of central serous chorioretinopathy (CSCR) (a retinal eye disease) among men veterans [264]. The study found a statistically strong association between PTSD and CSCR (OR = 9.433; 95% CI: 2.28–39.09, p = 0.002). Other risk factors were sleep apnea, heart disease, smoking, and using steroids. However, the above studies of PTSD were conducted on veterans, and most of the sample size comprised of men, thus were not representative of the general population.

PTSD affects the mind, body, and emotions; furthermore, blurry vision, slurred speech, and inability to think properly are some of the symptoms of PTSD once stimulated [265]. Evidence suggests that when triggered, individuals with PTSD relive their traumatic experiences, which hinder normal brain function [266]. First Nation communities had experienced psychiatric distress due to the cultural disruption and historical trauma of residential schooling. Despite tremendous progress, Indigenous people in Canada still suffer from health inequalities, and colonization history makes them more vulnerable to chronic health conditions than the rest of Canadians [267]. Therefore, it is essential to have a holistic approach to managing chronic diseases rather than a disease-specific approach when treating these health conditions.

The current study also collected data on Apnea Hypopnea Index (AHI), the clinical variable used to assess the severity of sleep apnea. However, it was only collected for a subgroup of 230 participants and from one Cree community; thus, we did not include AHI in this study.

Several other sleep health-related questions were asked from participants to get the sleep history, patterns/ trends, participants' usual sleep habits during the past month, and reasons for having trouble sleeping in the past month. However, these sleep health patterns and habits were

beyond the scope of this study and we did not include these data in the final analysis. The next section discussed the overall strengths and limitations of the current study.

5.7 Study Strengths and Limitations

5.7.1 Study Strengths

To the best of my knowledge, current prevalence rates of vision problems among First Nations in Canada is unknown. Also, few studies examined the association between sleep disorders and vision problems among Indigenous people; most of the data I found was from studies in Australia. The current study provided an estimate of the prevalence of vision problems among First Nations living in on-reserve communities in Saskatchewan. In addition, it was the first of its kind to examine the association between sleep disorders and vision problems among First Nation people in Canada. I included several sleep health-related variables to assess the relationship; furthermore, I recognized the associated risk factors for vision problems among First Nation people.

The current study used the population health framework approach and appropriate statistical techniques, including logistics regression and gsem with Bootstrap variance estimation method, to achieve the study's objectives. In addition, our findings determined the baseline data for various sleep disorders and vision problems and provided detailed information on individual, contextual factors, and other covariates.

I conducted a mediation analysis to explore the causal path in the relationship between sleep disorders and vision problems among First Nation people. Depression played a mediator role in the relationship, and our findings explained the direct and indirect path from sleep disorder to health outcome, i.e., vision problems. Exploring mediators or finding pathways is critical concerning the public health perspective. This will help the policy makers or program developers build interventional programs that are indispensable for a holistic approach that targets the risk factors or coexisting health conditions for preventing vision problems from occurring or slowing down the onset of vision problems.

The study was conducted in collaboration with university researchers, community partners, and First Nation community Councillors. Everyone incorporated their expertise in the designing, planning, and implementation stages. The survey questionnaire was developed in consultation with Community leaders for cultural appropriateness. Furthermore, the research

assistants were recruited from the communities and trained to spread the word about the ongoing survey through various strategies, and the interviewer-administered survey was conducted.

5.7.2 Study Limitations

The current study has several limitations. First, the study design was cross-sectional and therefore, could not determine temporality between sleep disorders and vision problems. Thus, longitudinal studies are required to establish whether a cause-effect relationship exists. Second, all variables, including outcome and predictor variables, were self-reported, which can increase vulnerability to differential (e.g., recall bias, social desirability) and non-differential misclassification errors.

Third, the sample size was large enough to compute appropriate statistical tests and accomplish the objectives with adequate statistical power. However, a larger sample size would have allowed for a more nuanced investigation of statistical interactions among risk factors. Fourth, a large fragment of data was missing for important variables (e.g., life stress); therefore, I could not include these variables as potential confounders and/or effect modifiers.

Last, it was difficult to make comparisons between my study results and the broader research literature due to the measurement of the dependent variable. Most of the research reviewed in this thesis was clinical (i.e., association was assessed for specific eye disease with any sleep disorder, for instance, the sleep apnea and glaucoma). Also, regarding outcome variables, different investigators used different variables (i.e., visual impairment, visual morbidity, or vision disability). Moreover, I used secondary data to achieve the study objectives and could not change the questionnaire to include more vision-related variables.

CHAPTER 6: CONCLUSION

6.1 Conclusion

The findings of this thesis suggest that the prevalence of vision problems among First Nations People in Canada is higher than the general population. Also, there is a relationship between sleep disorders and vision problems among First Nation people in rural Saskatchewan. This association was strongest for sleep apnea, followed by clinical insomnia and ESS (excessive daytime sleepiness). However, my results were unable to support a statistically significant relationship between STOP-BANG and sleep deprivation. Other significant risk factors for vision problems were age, sex, education, employment, residential school attendance, PTSD, restless leg, BMI, and multimorbidity. Furthermore, depression may be one of the mechanisms linking sleep disorders with vision problems.

More in-depth studies are required to determine the directionality of depression and vision problems, the role of colonization on sleep disorders and vision problems, and lifestyle factors on these chronic health conditions. Moreover, longitudinal studies are required to better understand underlying mechanisms and establish a cause-effect relationship between these chronic health conditions.

6.2 Recommendations and Future Directions

The current study estimated the prevalence of vision problems in two First Nations communities. Future data on the incidence and prevalence of vision problems are required to determine trends and patterns of vision problems among Indigenous people. Moreover, data from other provinces and territories of Canada are required to determine the prevalence of vision problems and associated risk factors in First Nations communities.

The current study was designed as cross-sectional and cannot determine the causality between sleep disorders and vision problems. Longitudinal studies are recommended to establish the cause-and-effect relationship. Our study identified several areas to explore in-depth. Firstly, to find out the prevalence of the most common sleep disorders and vision-threatening eye problems among the First Nation population in Canada. The history of colonization, deeply rooted among Indigenous people in Canada, is a significant factor that creates the health inequality gap between Indigenous and non- Indigenous health. It is imperative to sub-analyze

the surveys based on indigeneity or Indigenous people; thus, estimating the prevalence of sleep disorders would help to advocate for sleep health needs in Canada.

Secondly, to explore the underlying causes or risk factors of sleep disorders and vision problems among the First Nation population. Investigating the risk factors for these chronic health conditions will help policymakers to develop health programs targeting the areas to focus on to eliminate risk factors. Furthermore, research will help understand First Nation people's needs, barriers, and challenges, especially in on-reserve communities. For instance, the reasons for delayed diagnosis or treatment can be addressed while the development of health programs, therefore, targeting the areas to overcome these challenges.

Thirdly, our findings reported some unanticipated interactions, such as residential schooling and BMI, which should be explored further to understand their impact on First Nation population health. In addition, our study collected limited information on vision problems. Future studies should be tailored to collect more comprehensive data on vision problems, for instance, the severity of the ocular condition, duration and level of impairment that would help us comprehend the most common eye diseases and reasons for vision loss among First Nation people living on on-reserve communities.

Fourthly, the current study examined the role of depression as a mediator; other potential mediators, including perceived-life stress and type 2 diabetes, should be investigated in the relationship between sleep disorders and vision problems, which we were unable to explore because of the small sample size and missing data. Moreover, longitudinal studies are required to establish the directionally between depression and vision problems and understand the underlying mechanisms thoroughly.

Fifthly, the current study should be replicated with a larger sample size since the data for a few important variables, such as perceived-life stress, alcohol consumption and screentime, was missing, which were significant as per literature. Although previous research demonstrated that smoking status and physical activity significantly impact sleep disorders and vision problems, our results showed insignificant results. Therefore, repetition of this study with a larger sample size is warranted to understand the impact of these crucial lifestyle factors on these chronic health conditions.

Lastly, the collaboration between researchers, health professionals, policymakers, and First Nations community leaders is imperative for all future research and program design. This

will ensure addressing the underlying factors which impact the health of the First Nations population, such as housing and access to healthcare; furthermore, considering the novel needs and identifying the challenges will help in designing comprehensive community-centric healthcare programs. In addition, the engagement of First Nation people and support of health service delivery will optimize successful outcomes and sustainability.

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