THE INCIDENCE OF VISUAL IMPAIRMENT, ITS RISK FACTORS, AND ITS MOBILITY CONSEQUENCES:

THE CANADIAN LONGITUDINAL STUDY ON AGING

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ABSTRACT

INTRODUCTION: Canada has yet to conduct high quality, prospective, population-based surveys that measure incident visual impairment, its risk factors, and adverse consequences, creating an unmet need to obtain more rigorous analysis in this regard

QUESTIONS: What is the 3-year incidence of visual impairment in each province? What are the risk factors for the 3-year incidence of visual impairment? Do they include geographic, sociodemographic, lifestyle, social, health and healthcare factors? Does vision loss increase the odds of balance problems after three years?

METHODS: Baseline and 3-year follow-up data were used from the Canadian Longitudinal Study on Aging. The Comprehensive Cohort included 30,097 adults ages 45-85 years old recruited from 11 sites across 7 provinces. Presenting binocular visual acuity was measured using the Early Treatment of Diabetic Retinopathy Study chart. Incidence of VI was defined as the development at follow-up of visual acuity worse than 20/40 in those with acuity better than or equal to 20/40 at baseline. Balance was measured using the one-leg balance test. Those who could not stand on one leg for at least 60 seconds were classified as having failed the test. Participants were asked about the self-report of a diagnosis of cataract, macular degeneration, or glaucoma.

RESULTS: 3.88% (95% Confidence Interval (CI) 3.61, 4.17) of Canadian adults developed VI over a 3-year period. There was a high degree of variability in the incidence between Canadian provinces with a low of 1.42% in Manitoba and a high of 7.33% in Nova Scotia. Uncorrected

refractive error was the leading cause of incident VI. Risk factors for incident VI included older age (odds ratio (OR)=1.07, 95% CI 1.06, 1.07), Black race (OR=2.64, 95% CI 1.36, 5.14), lower household income (OR=1.73 for those making less than $20,000 per year, 95% CI 1.24, 2.40), current smoking (OR=1.78, 95% CI 1.37, 2.32), and province. Of the 12,158 people who could stand for 60 seconds on one leg at baseline, 18% were unable to do the same at follow-up 3 years later. After adjustment for demographic and health variables, those with worse visual acuity (per 1 line) were more likely to fail the balance test at follow-up (OR=1.15, 95% CI 1.10, 1.20). Those with a report of a former (OR=1.59, 95% CI 1.17, 2.16) or current cataract (OR=1.31, 95% CI 1.01, 1.68) were more likely to fail the test at follow-up.

CONCLUSION: The incidence of visual impairment is common in older Canadian adults, varies markedly between provinces, and is largely due to treatable causes. Risk factors for VI suggest sub-groups that may benefit from interventions to improve access to eye care. These data provide longitudinal evidence that vision loss increases the odds of balance problems over a 3-year period. Efforts to prevent avoidable vision loss are needed as are efforts to improve the balance of visually impaired people.

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ABBREVIATION LIST

Age-Related Eye Diseases Study	AREDS
Age-Related Macular Degeneration	AMD
Berg Balance Scale	BBS
Body Mass Index	BMI
Canadian Community Health Survey	CCHS
Canadian Community Health Survey– Healthy Aging	CCHS- HA
Confidence Interval	CI
Canadian Longitudinal Study on Aging	CLSA
Canadian National Institute for the Blind	CNIB
Canadian Ophthalmological Society	COS
Data Collection Site	DCS
Early Treatment of Diabetic Retinopathy Study	ETDRS
The Frailty and Injuries: Cooperative Studies of Intervention Technique	FICSIT-4
Falls in Older people with Cataracts	FOCUS
Functional Reach	FR
Get Up and Go	GUGT
Gross Domestic Product	GDP
International Classification of Diseases-10	ICD-10
Life-Space Mobility	LSM
Logarithm of the Minimum Angle of Resolution	LogMAR
Log Angeles Latino Eye Study	LALES
Odds Ratio	OR
Random Digit Dialing	RDD
United States	US
Visual Acuity	VA
Visual Impairment	VI
Vision Impairment Balance and Mobility	VISIBILITY
World Health Organization	WHO

CHAPTER 1: INTRODUCTION

PROBLEM AT HAND

Globally, those aged 65 and over are growing at a rate faster than all other age groups.[1] In 2014, there were over 6 million Canadians aged 65 years or older, representing 15.6% of Canada's population.[2] By 2030, it is estimated that older adults will number over 9.5 million and make up 23% of Canadians.[3] The challenges of an aging Canadian society will require continued efforts to improve the health, well-being and independence of older adults in later life.

The frequency of vision loss increases with age.[4] This is because many eye diseases like cataract, age-related macular degeneration, and glaucoma are more common in older age. Other common causes of vision loss are uncorrected refractive error and diabetic retinopathy. Cataract and uncorrected refractive error are avoidable causes of vision loss since they can be corrected by surgery or eyeglasses.

According to a statistic reporting in 2011 by the National Coalition for Vision Health, 1 in 9 Canadians develop irreversible vision loss by age 65, and by age 75 1 in 4 Canadians develop irreversible vision loss.[5] Reportedly, the most common causes of visual impairment (VI) globally are uncorrected refractive error, cataracts, age-related macular degeneration, and glaucoma.[6]

With these anticipated increases in vision loss due to the growing aging population, Canada needs to prepare and develop eye care policies that can protect Canadians from avoidable VI and

treat irreversible VI. However, in order to develop these policies, there is an unmet need to generate data on the frequency and severity of visual impairment in Canadians, its risk factors, and its adverse consequences.

In a recent report, the prevalence of visual impairment in Canadian adults aged 45-85 years old was 5.7%.[7] The prevalence of VI proportionally increased with age, to a high of 16% among adults aged 75-85 years. Within this report, refractive error was the leading cause of VI in Canada, whereas older age, lower-income, province, smoking, diabetes, and memory problems were also associated risk factors with the prevalence of VI.[7] To date, Canada has no data on the incidence, or new onset, of developing VI. In contrast, many other countries have conducted high quality, prospective, population-based surveys to measure incident VI.[8–11]

In addition to understanding the incidence of VI, it is also important to understand the potential consequences of VI. For example, maintaining mobility in older age is critical to staying healthy and independent; however, mobility could be compromised with incident VI.[12,13] Objective measures such as the ability to balance on one leg, activities of daily living, walking, and climbing stairs have been used as measures of physical function in the elderly.[14] Evidence shows that those with lower measures of physical function at baseline had lower scores in the four-year follow-up.[14] Likewise, people with vision loss reported having more difficulty with mobility tasks than their non-visually impaired counterparts.[13] However, longitudinal research to better understand the risks of mobility loss in those with VI is needed.

In this context, it is important to know the incidence of VI each year for the purpose of eye care policy planning and to compare ourselves to other countries. Furthermore, understanding the

risk factors for the incidence of VI can help indicate which sub-groups might benefit from interventions to reduce the risk of VI. Finally, understanding the adverse consequences of VI in everyday, such as on balance, is useful to understand how vision loss can have a significant impact on the quality of life for older adults.

OBJECTIVES

The objective of this research is to estimate the three-year incidence of VI, its risk factors, and its relationship with balance. By leveraging longitudinal data from the Canadian Longitudinal Study on Aging Comprehensive Cohort, we are able to satisfy the following aims:

Aim 1. Determine the 3-year incidence of VI in each province.

Aim 2. Determine the risk factors for 3-year incidence of VI including geographic, sociodemographic, lifestyle, social, health and healthcare factors..

Aim 3. Determine whether baseline VI is associated with potentially adverse consequences such as the 3-year onset of balance problems among those with baseline VI.

SIGNIFICANCE OF STUDY

Prospective data collected by the CLSA offer a unique opportunity to examine the incidence of VI in Canada for the first time and to better understand its risk factors and potential consequences. Our project will provide novel and essential data to allow eye care professionals, health policy planners, and low vision rehabilitation providers to more adequately prepare for the

needs of the aging population and identify groups at highest risk. These data will also help us to understand the downstream consequences of vision loss and their impact on balance.

THESIS ORGANIZATION

This section outlines the organization of this manuscript-based thesis. The **first chapter** provides an introduction to the problem leading into the objectives and significance of the study. The **second chapter** involves an in-depth description on vision, visual impairment, and its determinants and methods of measuring visual functions. Then, the **third chapter** involves an in-depth description on the current literature involving the association between balance and vision. **Chapter four** will involve a description of the data source including a description of the dataset, sampling, study population, and data collection methods. Meanwhile, **chapter five** will be a brief summary of the literature. Then, **chapter si**x defines the conceptional framework and methods of this thesis submission. **Chapters seven and eight** will consist of the first and second manuscripts, respectfully. Chapters nine through eleven will be the discussion, references, and appendices, respectfully.

CHAPTER 2: VISION

WHAT IS VISION?

One's ability to see is the result of a complex process orchestrated by several different tissues. An inside look of the eye is shown in Appendix F1. Each eye constantly adjusts the amount of light it lets in to transmit electrical signals to the brain to produce images. [15] The outer covering of the eyeball (or the white of the eye) consists of a tough, white layer called the sclera. The sclera and front of the eye are covered by a thin, transparent membrane called the conjunctiva.[15] The conjunctiva also covers the moist back surface of the eyelids and eyeballs.[15,16] The conjunctiva helps lubricate the eye by producing mucus and tears.[16]

Light enters the eye through the **cornea** and the **pupil**, the curved layer in front of the iris and the black hole in the center of the iris, respectfully.[17,18] The **iris** is the circular-coloured area of the eye.[19] The curved feature of the cornea serves as a protective outer layer for the front of the eye and also helps focus light onto the retina.[15] The **retina** is a thin layer of tissue that line the back of the inside of the eye which takes light and converts it into chemical and nervous signals to be interpreted by visual centers in the brain.[15,20] The retina contains the light-sensing cells called photoreceptor cells that contain cones and rods and the blood vessels that nourish them.[15,20] **Cones** are active at higher light levels and are capable of colour vision; meanwhile, **rods** are responsible for vision at low light levels.[15,21,22] The most sensitive part of the retina is a small area called the **macula**, which has millions of tightly packed cones to make the visual image detailed.[23]

The iris can dilate or constrict to control the amount of light that enters the eye.[24,25] The iris plays a key role in controlling the amount of light that accesses the retina by either dilating or constricting the pupil.[25] The iris will enlarge or dilate the pupil to allow more light into the eye when the environment is dark; otherwise, the iris will shrink or constrict the pupil and allows less light into the eye when the environment is bright. [26,27] The diameter of the pupil is controlled by the action of the pupillary sphincter muscle and dilator muscle inside the iris.[24]

Similarly, the lens is responsible for focusing light onto the retina and is invisible to the naked eye.[24] The muscle attached to the lens can make the lens change depth to focus on objects of different distances.[28] The lens will become thicker to focus on nearby objects and thinner to focus on distant objects.[28] **Binocular vision** is vision using two eyes with overlapping fields of view, allowing a good perception of depth.[15,21] After the retina converts light into chemical and nervous signals, the optic nerve will transport these signals from each eye and cross in the optic chiasm and also will continue to the back of the brain.[15] In this context, each half of the brain receives information for from both visual fields of both eyes, enabling binocular vision.[15] See Appendix F2 for the anatomy of optic chiasm.

MEASURING VISUAL FUNCTION: VISUAL ACUITY

Visual function describes how well the eye and visual system performs in order to see clearly.[29] When considering the complexity of vision, there are many different aspects of visual functioning.[30] This thesis will focus on visual acuity. **Visual acuity (VA)** measures the examinee's ability to distinguish small details with precision and refers to the clarity of vision or the "resolving power of the eye".[31] VA is the most commonly used test to assess visual function.[32,33] To test VA,

the examinee is tasked to read letters or symbols on a chart. The examinee reads the chart from the top down and their score is compared to someone with normal vision (20/20 vision on the Snellen fraction).[34]

The figures or letters on an acuity chart are traditionally known as "optotypes".[35] In the case of the traditional Snellen chart, the optotypes are in the form of block letters.[36] Block letters have a simple geometry in which the thickness of the lines equals the thickness of the white spaces between lines and the thickness of the gap in the letter "C" and the height and width of the optotype (letter) is five times the thickness of the line.[32,37]

Around 1850, however, major changes started to happen in ophthalmology, causing for it to later be called the Golden Age of Ophthalmology and make ophthalmology the first organ-oriented specialty.[38] It was within this time that the Snellen chart was developed and quickly adopted worldwide.[32]

The Snellen chart (Figure 1) was introduced in 1862 by Herman Snellen and has since been adopted as an accepted tool for measuring VA in the clinic.[34] The Snellen chart contains eleven lines of block letters. The first line in the Snellen chart is one very large letter, which may have letters such as E, H, or N and, subsequent rows have increasing numbers of letters that decrease in size (Figure 1).[32,34]

While the Snellen chart is still widely used in the clinic, it has its limitations. The Snellen chart has poor reliability and reproducibility.[38] For example, Gibson *et al.* noted that 13% of

measurements on eyes displayed discrepancies of two lines of more, even on repeated testing.[39] Additionally, the chart also has fewer letters at the top of chart, resulting in less precise measurements and less repeated testing in those with severe VI.[40] Certain letters (such as C, D, O, G, E) are harder to read than others (A, J, L), making the analysis inconsistent.[40]

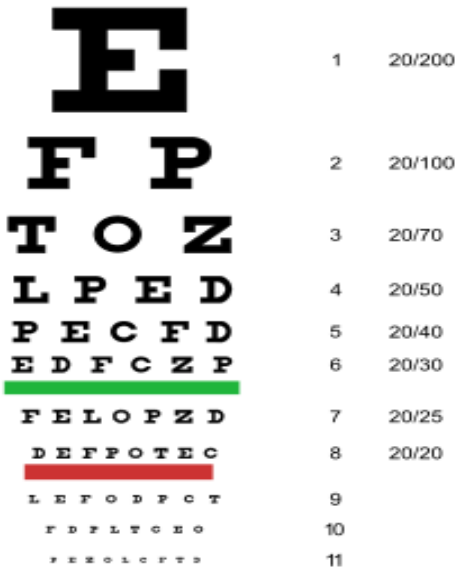

Figure 1: Snellen Chart (developed in 1862) as a measure of visual acuity.[41]

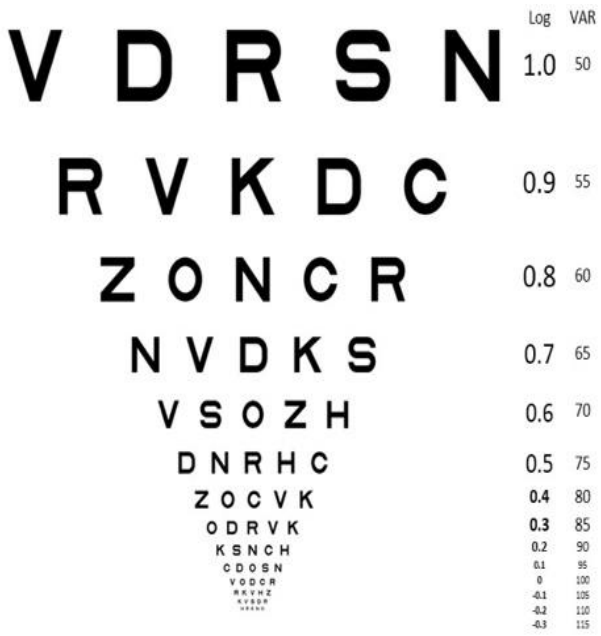

Figure 2: LogMAR chart (developed in 1976) as a measure of visual acuity.[41]

Figure adapted from: [41]

Another design problem of the Snellen chart is that the spacing between each row of letters and between letters has no systematic relationship to the width and height of letters,[40] and the

number of letters increases in each row from top to bottom of the chart, causing letters to be crowded at the bottom.[37] As such, the letters crowded at the bottom are limiting proper assessment in two ways: 1) It makes the task more disproportionally difficult with unwelcomed crowding at the bottom and 2) those with worse VA scores are tested with fewer letters than those with better visual acuity due to earlier termination of the VA test.[40]

Newer **logMAR charts**, also called a Bailey-Lovie chart or an Early Treatment Diabetic Retinopathy Study Chart (ETDRS), shown in (Figure 2), which have been created that have negated the disadvantages of the Snellen chart.[37] This chart was developed in 1976, is more widely used by ophthalmology researchers and incorporates recommendations made by the Committee on Vision of the American National Academy of Sciences.[32,37]

One advantage of the LogMAR chart is the test task being is the same level of difficulty at each size level on the chart.[37,42] Such standardization of the test task entails the use of letters of equal legibility (such as S, D, K, H, N, O, C, V, R, and Z), an equal number of letters in each row and, uniform between-letter and between-row spacing.[37,42] Combined with test task standardization, there is a logarithmic progression of letter size in each line.[43] For example, at a distance of 4 m, the top line will give a score of 1.0; however, each line below will give a score 0.1 log unit less than the line above (see Figure 2 for example). Therefore, each of the five letters in each row counts for a score of 0.1/5 = 0.02 log units.[37]

Both the logMAR and Snellen chart determine VA through one's ability to read the lowest line possible and both charts compare scores to someone with perfect vision (6/6 in meters or 20/20 in feet).[40] Although many practitioners use examination rooms designed for Snellen charts at 6m and the logMAR test distance is 4m, thankfully, this problem can be solved by a very simple conversion factor.[40,42,43] The regular geometric design of the optotypes in the logMAR allows easy conversion for other non-standard distances and also into the Snellen equivalent, which negates one of the major disadvantages of the Snellen chart and helps with combining scores done at different test distances.[37]

Given this information, logMAR charts have negated the disadvantages of the Snellen chart and allow greater standardization of VA assessment.[40] This makes logMAR charts very useful for research and for clinical practice - making the logMAR chart now the gold standard measure of visual acuity around the world.[44,45]

VISUAL IMPAIRMENT AND ITS CAUSES

Visual impairment (VI) is based on the loss of VA and refers to the degree of impairment to see small details.[45,46] Most North American researchers define VI as binocular VA of worse than 20/40.[47] However, there are two major classifications used to define VI with different VA thresholds (refer to Table 1.0). The VI equivalent adopted by the World Health Organization (WHO), which draws from the International Classification of Diseases-10 (ICD-10) to classify VI, is presenting VA worse than 20/70 but equal or better than 20/200.[45] For this work and

corresponding manuscripts in this thesis submission, the North American (NA) criteria were used, which is presenting VA worse than 20/40 (0.301 logMAR) with habitual distance correction (i.e., their regular glasses or contacts worn) in place.[44] The most common causes of VI globally are uncorrected refractive error at 66%, cataracts at 16.4%, age-related macular degeneration at 10.9%, and glaucoma at 3.1%.[44,48]

Table 1.0: Classification of Visual Impairment (VI): WHO vs. North American

WHO			**North American**		
Category	**Worse than**	**Equal to or better than**	**Category**	**Worse than**	**Equal to or better than**
Mild or no visual impairment		20/60 (0.5)	**No visual impairment**		20/40 (0.3)
Moderate visual impairment	20/60 (0.501)	20/200 (1)	**Visual impairment**	20/40 (0.301)	20/200 (1)
Severe visual impairment	20/200 (1.01)	20/400 (1.3)	**Blindness**	20/200 (1.01)	
Blindness		No light perception (4.0)			

* Units are in feet and (logMAR), table adapted from: [44]

Refractive error

Refractive error happens when an eye is misshapen, preventing the precise focusing of light rays on the right place on the retina (the light-sensitive tissue at the back of the eye).[49] Uncorrected refractive error is when inadequate attempts have been made to correct it. Refractive errors can happen naturally because the eyeball grows or reduces in length, the cornea may change shape, or part of the aging process.[50] The four most common types of refractive errors are myopia, hyperopia, presbyopia, and astigmatism.[50] **Myopia** (near or short-sightedness) (Appendix F3.1)

causes far away images to appear blurred, while images up close appear clear.[51] Myopia can occur when the distance between the cornea and the retina is too long or the cornea is too curved.[51] Therefore, it causes light to focus in front of the retina, instead of on the surface of the retina.[51] In contrast, **hyperopia** (far or long-sightedness) (Appendix F3.2) occurs when the distance between the cornea and the retina is too short causing for light to focus behind the retina.[52] Hyperopia causes blurred images that are close-up to appear blurred and far away images to appear clear.[52] While hyperopia can occur at any age, **presbyopia** is an age-related condition with an effect similar to hyperopia with close up images appearing blurry due to increasing rigidity in one's lenses with increasing age.[53] Finally, **astigmatism** is when the cornea has asymmetric curvature (ex. football shape) causing the image to focus unevenly on the retina and the image to appear distorted.[54] Fortunately, there are simple solutions that are available to correct the refractive error, including eyeglasses, contact lenses, or refractive surgery.[50]

Cataracts

Cataracts are the global leading cause of treatable blindness, accounting for at least 34% of cases of blindness.[55] A cataract refers to the clouding of the eye lens, making it incredibly difficult for light rays to pass through and focus on the retina, making vision appear blurry. If left untreated it could lead to a loss in vision.[55,56] The concept of clouding the lens is not largely understood, however, experts explain that the lens of the eye is made up of several proteins and certain factors can cause denaturation of that protein and lead to its opacification.[57] With increasing age, these proteins may clump together and cloud small areas of the lens making it difficult to see.[58] Many chronic diseases, such as diabetes[59] and hypertension[60] may play a role in the incidence of cataracts. In addition, behavioural factors such as heavy alcohol intake,[61,62] sunlight

exposure,[63,64] lower body mass index (BMI),[65] and cigarette smoking[66] may also contribute to cataract formation. Fortunately, cataract is treatable, and its surgery is one of the most perfected surgeries in the world.[67] Patients can opt to have the cataractous lens removed and replaced with a clear synthetic version if they are experiencing significant impairment in vision from cataracts. [67]

Age-related macular degeneration (AMD)

Age-related macular degeneration (AMD) is the leading cause of permanent blindness in North American adults over the age of 55 years.[68] The macula is responsible for detailed central vision and is the most central part of the retina, representing the inner layer at the back of the eye.[69] However, when the macula degenerates, it causes the center of your vision to blur while peripheral (side) vision remains unaffected.[70] There are two types of AMD; dry (geographic atrophy) and wet (choroidal neovascularization).[71] Anti-vascular endothelial growth factor injections are currently the gold standard treatment for wet AMD; however, there is currently no effective treatment for dry AMD.[72] Evidence from the Age-Related Eye Diseases Study (AREDS) trial indicated that taking an antioxidant plus zinc supplement slowed the progression to advanced AMD.[73] Other preventive strategies, such as dietary modifications, have been investigated but the evidence is not sufficient.[74]

Glaucoma

Glaucoma, which is often associated with elevated intraocular pressure, is an eye disease in which the degeneration of the optic nerve can lead to loss of vision or blindness.[75,76] Glaucoma is the leading cause of irreversible blindness worldwide.[76] Glaucoma often progresses with

minimal or no symptoms so that it often goes undetected until the optic nerve already has been irreversibly damaged.[77] Depending on whether the aqueous fluid can access the drainage angle or not, glaucoma can be categorized into either open-angle (can access the drainage angle) or narrow-angle (cannot access the drainage angle) glaucoma.[75,78] Treatment for glaucoma can involve surgery, laser treatment, or medication.[79] However, due to the irreversible nature of this disease, professionals recommend early detection and prevention as the best strategy to avoid glaucomatous vision loss.[75] Eye drops with medication aimed at lowering intraocular pressure are usually attempted as a first line of defense to control glaucoma.[80]

DETERMINANTS OF PREVALENCE OF VISUAL IMPAIRMENT

There are several risk factors reported related to the prevalence of VI. Lower personal income,[7] and lower socioeconomic status[81] have been correlated with the prevalence of VI. Studies have shown significant variability in the prevalence of VI by ethnic and geographic background.[82,83] Behavioural factors, like cigarette smoking, are associated with a higher risk of development of age-related eye diseases, especially cataracts and AMD.[7,84]

Comorbid health conditions, such as diabetes and high blood pressure, have been associated with VI.[60,85]Memory problems were also associated with prevalent VI.[7] Most eye diseases demonstrate a positive correlation between VI and chronological age.[7,86] Additionally, differences in eye care policies are potentially creating large provincial differences in the prevalence of VI.[7] While the national average of VI was 5.7% (5.4-6.0 95% CI) in Canada, researchers observed that the prevalence of VI ranged from a low of 2.4% in Manitoba to a high

of 10.9% in Newfoundland and Labrador.[7] These variations may be due to differences in eye-care policies, which is discussed in later sections.

Although research has investigated the risk factors associated with the prevalence of VI, and the incidence of VI and its risk factors has yet to be explored in a Canadian population.

INCIDENCE OF VISUAL IMPAIRMENT

Although information about the prevalence provides insight about the present burden of VI in Canada, having data on the incidence of VI is important to understand how the risk of VI is changing over time and to provide more rigorous evidence about the temporal relationship in the investigation of risk factors for VI. Having data on the incidence of VI will be helpful to inform policymakers and develop plans to meet the future demands for VI rehabilitation services, especially in Canada where the large majority of the population are older adults. In order to estimate the incidence, it is ideal to use high-quality, prospective, population-based surveys.[87]

Several population-based studies around the world have investigated the incidence of VI. First, **the Beaver Dam study** was one of the earliest population-based studies on VI and report data on both nursing home and community dwelling participants.[88] The study recruited a population of 4,926 adults, between the ages of 43 and 86 years old, from Beaver Dam, Wisconsin.[88] Incidence of VI was defined as best-corrected VA of poorer than 20/40 at a 5-year follow-up in the better eye with one or both eyes being 20/40 or better at baseline.[88] This study concluded an overall 5-year incidence of 1.4%, varying from 0.1% in persons 50–54 years of age to 14.6% in those 85 years of age and older.[88] Early epidemiological studies of VI only used best-

corrected visual acuity rather than presenting visual acuity. Therefore, they excluded any VI due to uncorrected refractive error, which we now know is the leading cause of VI.[55]

Los Angeles Latino Eye Study (LALES), which included 4,658 participants adult Latinos and Hispanics aged 40 years and older, reported the 4-year incidence of presenting binocular VI. Participants underwent ophthalmic examinations using the standard ETDRS protocol.[87] The 4-year incidence was ascertained by VA of ≥20/40 at baseline and a follow-up <20/40. LALES found that the 4-year incidence of presenting binocular VI was 2.9%.[8] The study also found an annual incidence of VI in Latinos and Hispanics to be higher than the reported non-Hispanic white persons in the US, highlighting the need for increased screening and intervention programs among this sub-population.[8]

In **the Reykjavik Eye Study**, researchers examined the five-year incidence of VI in adults 50 years and older in the Icelandic population.[89] All participants underwent an exclusive ophthalmological examination including best corrected VA.[89] According to the United States (US) criteria, the five-year incidence of bilateral VI was 3.49% (95% CI 2.24-4.74) for this population.[89]

You et al. estimated the cumulative five-year incidence of VI in older Chinese adults in the **Beijing Eye Study** of 2006.[11] This study included 3,251 subjects who had participated in 2001 and then returned for re-examination (99.9% follow-up). VA was measured using presenting VA (including uncorrected or under corrected refractive error) and VI was defined using the US criteria for VI (VA<20/40 in the better-seeing eye). Researchers in this study reported an incidence of

presenting VI of 3.8% (+/-0.3%) with under corrected refractive error being the major cause (76% of cases). [11]

The Melbourne study in Australia estimated the 5-year incidence of VI using a study population of 3,040 people aged 40 years and older. Distance and near vision were measured using standard logMAR charts. VI was defined if bilateral presenting VA was <20/40 at follow up and ≥20/40 at baseline. The study found a 4.22% incidence of VI over 5 years with undercorrected refractive error accounting for 50% of cases of VI.[90]

To summarize, the incidence rates vary from 1.4 to 3.8%.[8,11,89–91] However, most of these reported studies only reported the best-corrected VA. Therefore, uncorrected refractive error as a cause of VI is excluded from these reports and thus their estimates are likely an underestimation of truthful incident VI. Additionally, different methods of measurement, different target cohorts, different eye care policies in each country, different ethnicities, and different time periods may contribute to variations found between studies.

Although many countries, including those reported above, have reported the incidence of VI in their sub-population, Canada has no data on the incidence of VI.

EYE CARE POLICIES IN CANADA

An understanding of the thirteen interlocking provincial health insurance plans can help researchers gain an understanding of why there may have been provincial differences on the prevalence of VI. We will determine if similar provincial differences are found in the incidence of

VI. Despite Canada's health care system being based on universal health coverage, universal eye health coverage does not apply in Canada.[92] The government only covers medically necessary vision- related costs, such as treatments for eye injury and various eye diseases (e.g., cataract, glaucoma, and diabetic retinopathy).[93] However, provinces within Canada vary and each province covers a different range of eye-care costs.

For example, for a large majority of Canadians they are required to pay out-of-pocket for primary eye-care services, such as eye examinations and spectacles.[93] In this regard, despite advocacy efforts by key stakeholders in eye health, Canada is still very much behind making relevant policy shifts in terms of addressing the structural barriers of nationwide coverage for eye-care services.[92] In order for Canada to meet the WHO's goal of universal eye health, Canada must face the inescapable reality of unmet eye care needs.[93]

Barriers to accessing nationwide eye-care coverage is explained in a scoping review on existing Canadian policy on vision care low vision services.[94] This review explains that barriers accessing nationwide eye-care may include the gap between ongoing growth in demand and limited resources for vision services,[95] the lack of cooperation between providers,[96] limited awareness on existing rehabilitation benefits and availability,[97,98] and a need to promote greater compliance with referrals on the behalf of the consumer.[98] The source also does not fail to imply the ongoing need for low vision services with Canada's aging population.[99] For example, there are gaps in coverage for routine preventative screenings, improper reimbursement to skilled eye care professionals providing low vision services thus creating a scenario where they no longer willing

to provide them, and individually providing low vision services who don't have certain demands will not have the resources if the demand were to increase.[100]

Although Canada has not yet established nationwide eye care coverage, provinces within Canada have established coverage for certain routine examinations for those ≤18 and ≥ 65 years old, but there is inter-provincial variability on what is covered and how often (refer to Table 2) for provincial information on specific coverage on the seven provinces with CLSA data collection sites). Unfortunately, despite recommendations by the Canadian Ophthalmological Society (COS) to see an ophthalmologist or optometrist every year, some high-risk groups (e.g., patients 60+ with a family history of eye disease) are not currently covered.[101,102] To summarize, different eye care coverage policies may explain some of the provincial discrepancies in the prevalence of VI.

Table 2: Coverage of routine eye exams by seven provinces included in the CLSA

ALBERTA[103]	Routine examinations are covered annually for individuals ≤18 or ≥65
BRITISH COLUMBIA[104]	Routine examinations are covered annually for individuals ≤18 or ≥65
MANITOBA[105]	Routine examinations are covered bi-annually for individuals <19 or >64

NEWFOUNDLAND AND LABRADOR[106]	No provincial vision care coverage. Only a $55 contribution for those on income support once every 36 months for adults.
NOVA SCOTIA[107]	Routine examinations are covered bi-annually for individuals <10 or >65
ONTARIO[108]	Routine examinations are covered annually for individuals <20 or >65
QUEBEC[109]	Routine examinations are covered annually for individuals <17 or >65

ECONOMIC CONSEQUENCES OF VISUAL IMPAIRMENT

A report by the Canadian National Institute for the Blind (CNIB) and COS found the financial cost of vision loss in Canada to be estimated at $15.8 billion in 2007, around 1.19% of Canada's gross domestic product (GDP).[110] As Canada covers medically necessary vision costs, this breaks down to $500 for every Canadian or $19,370 for every Canadian with vision loss in 2007.[110] The financial cost of vision loss is most likely much larger since this report was published in 2009. This report also projected that by 2032, the number of Canadians with vision is expected to double.[110] Based on current projections, the financial expenditures associated with vision loss would cost Canadians $30.3 billion by 2032.[110]

However, 75% of vision loss is avoidable, preventable, or treatable.[110] If we provided proper medical care for avoidable vision loss and thus prevented medically necessary vision-related expenses, millions of dollars could be saved annually.[111] A return of close to $5 for every

dollar invested can be achieved.[112] However, this return doesn't even consider the indirect costs, thus making it an underestimation of the actual return.[111] Therefore, it is imperative that indirect costs be taken into equation when evaluating the economic-benefit of vision-loss prevention programs.

CHAPTER 3: BALANCE AND VISION

WHAT IS BALANCE

Balance is formally defined as the "state in which the body is in equilibrium", where it depends on the body's ability to neutralize forces such as gravity by counter forces, so that the result of all forces acting is zero. [113] Balance is divided into static (ability to maintain a base of support with minimal movement) and dynamic (the ability to perform a task while maintaining a stable position).[114] Balance is an important pre-requisite for functionality because it is vital to the performance of activities of daily living (ADL).[114]

The visual system, the vestibular system, and the somatosensory system are three systems responsible for the maintenance of proper balance.[113] These systems work together to take information from the environment and send that information to our brain to maintain an upright position.[113,115] For example, a change in your body position or base of support would receive feedback from these systems by feedback and feedforward mechanisms. Additionally, while balance is considered a whole-brain phenomenon, some key structures in maintaining balance are the cerebellum, basal ganglia, and thalamus, which are likely implicated in balance disorders.[116]

Balance is a type of umbrella concept in that several different motor skills are required to maintain balance and each can be challenged.[114] Balance can be subcategorized into postural control of involuntary movements, on a stationary base, in voluntary movements, and in perturbations from outside.[114] The subdivision of balance enables us to challenge these motor skills to different degrees. For example, to test the ability to keep a position, for example, one could ask the individual to keep his balance with a decreasing base of support.

MEASURES OF BALANCE

Measuring shortfalls in one's balance allow clinicians to determine if their patient is at risk of a fall, as well as guide intervention.[117] Some tests which assess balance in older adults include the "Get Up and Go" Test (GUGT), the Berg Balance Scale (BBS), and the Functional Reach (FR).[118–120] The GUGT uses five items to challenge an elderly's sense of balance.[120] The (BBS) also tests varying levels of balance by assessing the participant in 14 different tasks.[120] Meanwhile, the FR test evaluates the maximum distance an elderly person can reach forward while standing at a fixed position.[119]

However, for the purpose of this thesis, the one-legged balance test was used. The one-legged balance test is a significant and easy-to-administer predictor of injurious falls.[121] In one study, it was the strongest individual predictor.[121] Evidence demonstrates that the standing balance test has the ability to capture balance impairments that signify increased fall risk in community-dwelling older adults.[122] The standing balance test requires the participant of interest to stand with

one leg raised to the calf level for up to 60 seconds.[123] The inter-rater reliability of the standing balance test is good.[124]

IMPORTANCE OF BALANCE TO FALLS

Performance deficits or difficulties in balance increase with age and are often the first signs of further functional decline.[125] To prevent disability, it is important to identify people who are not yet disabled but who are at risk (potentially those visually impaired) for disability progression in the near future. For this purpose, knowledge of the temporality and causality between VI and balance is of importance.

Balance has evidently been associated with an increased risk of falling.[126] Although a fall can seem like a minor disturbance in one's day-to-day life, it can seriously impact a person's life physically, psychologically, emotionally, and financially if the person is an older adult.[127] Falls are very common with 17-30% of the population having experienced a balance disorder during their lifetime,[128] and 30% of the population 65 and older experiencing at least one fall annually,[129] and of these, 50% will fall again.[129] The consequences of these falls may range from a few bruises, to hospitalization, institutionalization, or even death.[127] Therefore, researching balance is an important consideration for research, practice, and policy in aging, and one's mobility is a strong indicator of one's quality of life.[130,131]

RISK FACTORS FOR POOR BALANCE

Knowledge of risk factors for poor balance is important so interventions can be placed among these sub-groups to further prevent declines in one's balance. Many risk factors for poor

balance have already been identified. For example, increasing age has been associated with difficulty maintaining a stable position.[132] This may be due to decreased muscular strength and endurance with age,[113] resulting in more difficulty maintaining balance on uneven surfaces.[127] Body mass index (BMI) has also been associated with postural dysfunction for many reasons. With excess body fat, the skeleton will carry more weight than intended and create an exaggerated lumbar lordosis, thus distorting the normal alignment of the body.[113]

Medical conditions associated with balance disorders are listed in *Table 3*.[133–137] Factors such as alcohol consumption, exhaustion, previous history of falls, body pain, and having at least one comorbidity have been significantly associated with poor balance.[138,139] Medical conditions are found to be the strongest predictor of poor balance for many reasons, such as causing diminished strength, limited range of motion, poor posture, decreased sensory perception, fatigue, deformity, and decreased awareness.[140]

Table 3: Medical Conditions and Risk Factors Associated with Gait and Balance Disorders

Affective disorders and psychiatric conditions	**Neurological Disorders**
Depression	Cerebellar dysfunction or degeneration
Fear of falling	Delirium
Sleep disorders	Dementia
Substance abuse	Multiple Sclerosis
Cardiovascular Diseases	Myelopathy
Arrythmias	Normal pressure hydrophalus

Congestive heart failure	Parkinson disease
Coronary artery disease	Stroke
Orthostatic hypotension	Vertebrobasilar insufficiency
Peripheral arterial disease	Vestibular disorders
Infectious and metabolic diseases	**Sensory Abnormalities**
Diabetes mellitus	Hearing impairment
Hepatic encephalopathy	Peripheral neuropathy
Human immunodeficiency virus – associated neuropathy	Visual impairment
Hyper and hypothyroidism	Other
Obesity	Other acute medical illnesses
Tertiary syphilis	Recent hospitalization
Uremia	Recent surgery
Vitamin B_{12} Deficiency	
Musculoskeletal disorders	
Cervical spondylosis	
Gout	
Lumbar spinal stenosis	
Muscle weakness or atrophy	
Osteoarthritis	
Osteoporosis	
Podiatric conditions	

Table derived from [133–136,140,141]

BALANCE AND VISION LOSS

This thesis will focus on the role of vision and eye disease on balance. The correlation between balance and VI has been described in some cross-sectional research.;[142–148] For example, Vafaei et al. conducted a study using the CLSA baseline dataset to determine the relationship between VA and standing balance.[148] The 1-leg standing test was used to assess balance, where the time the person stood without putting the raised leg down or losing balance was recorded for up to 60 seconds and VA was measured using the ETDRS chart at 2m.[149] The study found that having a 1-line worse score on the VA test was associated with 23% higher odds of being unable to stand for at least 60 seconds after adjusting for variables such as age, sex, education, province, BMI, and diabetes mellitus (OR = 1.23, 95% CI = 1.20-1.26) in a logistic regression model.[148]

Furthermore, Thomas et al. sought to cross-sectionally determine the attributes, including VI, associated with balance performance.[142] The study included 364 participants from the Boston Rehabilitative Impairment Study of the Elderly (Boston Rise) between 65 and 94 years of age. VA was measured using a Snellen chart and, a score of 20/50 or worse was defined as VI. The Frailty and Injuries: Cooperative Studies of Intervention Technique FICSIT-4 balance scores were assessed for standing balance. After conducting a bivariate linear regression model of association, a strong association was found between VI and balance ($p = 0.003$).[142]

Additionally, Sorbello at al. examined the cross-sectional association between varying levels of VA and physical performance in older adults 50 years of age or older.[143] Baseline data

from the Falls in Older people with Cataracts (FOCUS) and the Vision Impairment Balance and Mobility (VISIBILITY) (studies were combined to include a comprehensive study population of varying ranges of vision. Physical performance had three measures: gait speed, standing balance, and sit to stand. The study found that in this cohort of older adults with compromised vision of both better or worse eye, VA was associated with poorer standing balance ($p = .006$ and $p = .004$, respectively).[143] No association with overall physical performance was found. [143]

In another study by Wilson et al., researchers in this study investigated the association of the combined and individual sensory association (visual system, the vestibular system, and the somatosensory system) with balance.[144] The study included data from 1,662 participants between the age of 40 to 85 years of age from the 2003-2004 National Health and Nutrition Examination Survey. Vision was objectively measured, while balance was measured using a modified Romberg test of standing on a firm and compliant support surface and involved the participants' ability to stand under 4 different conditions. A multivariable logistic regression showing association between sensory impairment and reported odds of having difficulty with falling was reported. VI (vs. normal vision) was associated with 5.59 increased odds of perceived difficulty with falling (95% CI = 0.98–31.99, $p = 0.05$).[144] Additionally, a multivariable logistic regression model looking at the association between sensory impairment and odds of functional balance were reported; however, no association was found.[144]

Freeman et al. identified the visual factors associated with various levels of balance from 1,505 individuals from the Salisbury Eye Evaluation population-based cohort study.[147] Measures of visual function, such as acuity, contrast sensitivity, visual fields, and motion detection were

obtained. Balance was assessed by participants completing a series of timed standing tasks that increased in difficulty. They found that worse motion detection threshold scores and worse visual field scores were associated with worse balance. [147]

Willis et al. sought to compare balance measures in individuals with normal vision, VI, and uncorrected refractive error.[146] A total of 4,590 adults 40 years of age or older who had participated in the National Health and Nutrition Examination Survey in 2001 though 2004 were included.[146] Presenting VA for each eye was assessed using an autorefractor containing built-in VA charts. Participants whose better-eye presenting VA was 20/40 or better were classified as normal vision. Those whose better-eye presenting VA was worse than 20/40 but better-eye refractometer VA was 20/40 or better were characterized as having uncorrected refractive error. Those whose better-eye VA was worse than 20/40 after autorefraction were classified as having VI.[146] Measured with eyes closed on a foam surface, multivariable models demonstrated higher rates of balance loss with VI-associated vision loss ($p = .02$) and with uncorrected refractive error-associated vision loss ($p = .04$). These findings demonstrate how visual inputs are an important system that maintains the effectiveness of vestibular balance.[146]

There are only three known longitudinal studies have looked at the impact of vision loss to the long-term consequences of balance problems. However, two of the three longitudinal studies show no association. The first study, conducted by Baloh et al. (2003), measured VA and balance scores in 59 normal older subjects and conducted yearly follow-up examinations on balance dysfunction. The study only found weak correlations between VA and balance.[150] The second

study, conducted by Kulmala et al. (2012), found a similar change in lower extremity function (including standing balance) between those with VI and those with good vision among a group of 313 women aged 63-75 years at the three-year follow-up time-point.[151] However, these studies are limited in providing concrete results due to their small sample size. The only known study which found associations between visual function and balance was conducted by Salive et al. (1994), where 3,133 older residents were followed up 15 months later. The study found an association between VI and the onset of limitations in a composite mobility measure that included balance.[152] In this regard, the conflicting results suggest there is a need for more rigorous analysis to examine this issue.

Therefore, due to limited longitudinal research and some conflicting study findings, there is a need to confirm this hypothesis in a larger, longitudinal, prospective, nationwide survey such as the CLSA. Very limited research has looked at the impact of vision loss on the long-term consequence of balance problems and its temporality and causality of VI on balance and balance on VI. More conclusive information on the long-term consequence of VI can accentuate the importance of preventing vision loss.

CHAPTER 4: DATA SOURCE: CANADIAN LONGITUDINAL STUDY ON AGING (CLSA)

OVERVIEW

The Canadian Longitudinal Study on Aging (CLSA) was an initiative designed to build research on the many factors that may affect healthy aging over the life course.[153] The longitudinal design of the CLSA enables the inter-and transdisciplinary study of the onset of health outcomes and allows researchers to make projections about the aging process.[153]

The CLSA is a large, national, prospective cohort study.[153] For the purpose of this research, we will be using the Comprehensive Cohort of the CLSA, which recruited 30,097 randomly selected Canadians aged 45-85 years of age between the years of 2010 and 2015 and will ultimately have a 20-year follow-up period with data collected every three years.[154] This cohort of the CLSA contains an in-home interview (questionnaires and tests) and a visit to one of the 11 Data Collection Sites (DCS) across seven Canadian provinces (Victoria, Vancouver, Surrey, Calgary, Winnipeg, Hamilton, Ottawa, Montreal, Sherbrooke, Halifax, and St. John's).[154]

SAMPLING, RECRUITMENT, AND RESPONSE RATES

Recruitment into the CLSA cohort had a total of three sampling frames: (1) a subset from Statistics Canada's Canadian Community Health Survey-Healthy Aging (CCHS-HA); (2) from registries of provincial health care systems; and (3) using a Random Digit Dialing (RDD) strategy (which generates telephone numbers at random) of landline telephones.[154] Weighting efforts were

made to oversample certain areas to ensure these groups are properly represented in the CLSA. Those who initially replied to a request to participate in the CLSA, the pre-recruit group, was about 45%. Whereas those who actually completed a baseline assessment and underwent in-home interviews and a visit to a DCS was only 10% of the pre-recruit group.[154] Sampling weights were calculated for the Comprehensive Cohort to account for the complex sampling methodology and ensure representativeness with the target population.[154]

ETHICS

We have already received approval to access CLSA data for this project. We have obtained ethics approval from the University of Ottawa for these analyses.

CHAPTER 5: SUMMARY OF PROJECT

Canada has yet to report a population-based estimate of the incidence of VI and its associated risk factors. With changing demographics in Canada and provincial differences in healthcare, there is an unmet need to determine which sub-groups and provinces may be the most at risk for incident VI.. This epidemiological information will help guide eye care policies and create interventions for those most at risk. Roughly 75% of vision loss is avoidable, preventable, or treatable, and thus targeted outreach of at-risk groups could potentially prevent vision loss.

This study will also provide novel longitudinal data on the consequence of VI on mobility, specifically balance. Previous studies have been mainly cross-sectional and therefore unable to assess the impact of VI on balance over time. Using baseline and follow-up data from the CLSA, we can estimate the 3-year incidence of VI in each province, its associated risk factors, as well as determine whether baseline VI is associated with potentially adverse consequences such as balance problems.

CHAPTER 6: CONCEPTUAL FRAMEWORK

The conceptual framework used to formulate specific aims 2 and 3 and to guide the data analysis is shown in Figure 4 below. After reviewing the available literature and considering biological plausibility, we have identified four categories of potential risk factors for VI that can be evaluated in the CLSA. These include **sociodemographic variables,**[155,156] **lifestyle** factors, [157,158] **social** factors, [157,158] and **health** factors.[159]

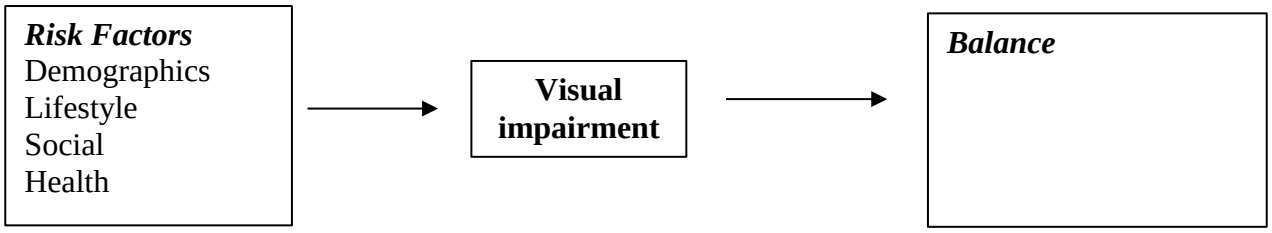

Figure 3: Conceptual framework for aims 2 and 3 of thesis.

We propose a framework for how vision loss may affect the risk of developing balance problems. The relationships between VI and balance may be **confounded** by demographic variables, diet, smoking, comorbid conditions, or disability. They may be **modified** by factors like age, sex, health status, income, hearing impairment, and other factors. For example, vision may be more related to balance difficulty in women than men, in older adults compared to middle-aged adults, or only in those with certain chronic health conditions (like peripheral vascular disease, as has been reported previously).[42] **The availability of longitudinal data will help us to disentangle the temporality of these effects**.

CHAPTER 7: MANUSCRIPT ONE: INCIDENCE OF VI

Purpose: Answer thesis objective 1 &2

Required Ethics Approval: : Ethics approval was received April 28, 2020, Following review by The University of Ottawa Office of Research Ethics and Integrity.

Title: The 3-Year Incidence of Visual Impairment and its Risk Factors in Canada: The Canadian Longitudinal Study on Aging

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Contributions:

- ZK contributed to the analysis, the interpretation of the data, and drafting the manuscript.
- MJA, RB, and MJK contributed to the interpretation of the results and the revision of the manuscript.
- EEF contributed to the acquisition, analysis, and interpretation of the data and the revision of the manuscript.
- All authors gave final approval for the version to be published and agree to be accountable for all aspects of the work.

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ABSTRACT

Objective: Determine the 3-year incidence of visual impairment (VI) in Canada and its risk factors.

Design: Prospective 3-year cohort study

Participants: Data from 23,973 adults taking part in the Canadian Longitudinal Study on Aging Comprehensive Cohort baseline and 3-year follow-up exams were included.

Methods: Inclusion criteria included being 45 to 85 years of age, community-dwelling, and living near one of the 11 data collection sites across 7 Canadian provinces. Presenting binocular visual acuity was measured using the Early Treatment of Diabetic Retinopathy Study chart. Incidence of VI was defined as the development at follow-up of visual acuity worse than 20/40 in those with acuity better than or equal to 20/40 at baseline.

Results: 3.88% (95% Confidence Interval (CI) 3.61, 4.17) of Canadian adults developed VI over a 3-year period. There was a high degree of variability in the incidence between Canadian provinces with a low of 1.42% in Manitoba and a high of 7.33% in Nova Scotia. Uncorrected refractive error was the leading cause. Risk factors for incident VI included older age (odds ratio (OR)=1.07, 95% CI 1.06, 1.07), Black race (OR=2.64, 95% CI 1.36, 5.14), lower household income (OR=1.73 for those making less than $20,000 per year, 95% CI 1.24, 2.40), current smoking (OR=1.78, 95% CI 1.37, 2.32), and province.

Conclusion: The incidence of visual impairment is common in older Canadian adults, varies markedly between provinces, and is largely due to treatable causes. Risk factors for VI suggest sub-groups that may benefit from interventions to improve access to eye care.

Keywords: incidence, visual impairment, CLSA, Canada, acuity, vision

INTRODUCTION

We previously published the first national, population-based estimate of the prevalence of visual impairment in Canada using baseline data from the Canadian Longitudinal Study on Aging (CLSA). We reported that visual impairment affected 5.7% of community-dwelling Canadians ages 45-85 years old [1]. Canada has no population-based data on the incidence of visual impairment from research using a visual acuity chart. Incidence data are important because they tell us about the risk of becoming visually impaired and can allow us to better establish the temporality of risk factors with the onset of visual impairment, which is useful for inferring causality. Many other developed countries have conducted prospective, population-based surveys that have measured the incidence of visual impairment [2-5]. The CLSA study [6], a population-based prospective cohort study of 30,097 people ages 45-85 years old, gives us the opportunity for the first time to measure the 3-year incidence of visual impairment and its risk factors.

METHODS

Study Design

We performed a prospective analysis of the 30,097 adults in the CLSA Comprehensive Cohort [6]. We focused on adults in the Comprehensive Cohort because they undertook a visual acuity test. Participants were recruited from provincial health registries and random digit dialing. Stratified sampling was used to ensure adequate representation of various demographic groups. Strata within a province were defined by age group, sex, and distance from the data collection site.

Baseline recruitment was between 2010 and 2015 and the follow-up was completed between 2013 and 2018. The follow-up rate was very high at 92%.

Study Population

Adults had to meet the following inclusion criteria: between the ages of 45 and 85 years old, community-dwelling, and living within a 25-50 km radius of one of the 11 data collection sites in 7 provinces (Victoria, Vancouver, Surrey, Calgary, Winnipeg, Hamilton, Ottawa, Montreal, Sherbrooke, Halifax, and St. John's). People were excluded from the CLSA if they were in an institution, living on a First Nations reserve or settlement, were a full-time member of the Canadian Armed Forces, did not speak French or English, or had cognitive impairment. Participants gave written informed consent. Ethics approval was obtained from the Research Ethics Board of the University of Ottawa.

Data Collection

Data were collected either from an in-home questionnaire or from questionnaires or procedures performed at a data collection site. CLSA personnel at all sites underwent a detailed training session.

Visual Acuity, Eye Disease, and Eye Care Use

The CLSA used an illuminated Early Treatment of Diabetic Retinopathy Study (ETDRS) visual acuity letter chart at a 2 meter distance to assess vision [7]. Participants wore their normal correction for distance, if any. Visual acuity was measured in three ways: binocular, by eye, and by eye with pinhole. Pinhole correction entails having the participant stare through an occluder with small holes in it, which remove the large majority of refractive error. Incident visual impairment was defined as the development of binocular visual acuity worse than 20/40 at follow-up in those who had binocular acuity equal to 20/40 or better at baseline. This definition is frequently used in North American research because people begin to experience difficulty at this point and driving laws often require this level of acuity [1,8]. Participants were also asked at baseline and at follow-up if a doctor had ever told them that they have cataracts, glaucoma, or macular degeneration. The incidence of each eye disease was defined as the presence of a diagnosis at follow-up and the absence of that same diagnosis at baseline. Eye care use was assessed at baseline by asking "During the past 12 months, have you had contact with an ophthalmologist or optometrist about your health?".

Demographic, Health and Lifestyle Data

Demographic information on age, sex, income, education, and race/ethnicity were collected. Household income was assessed by asking, "What is your best estimate of the total household income received by all household members, from all sources, before taxes and deductions, in the past 12months?". Participants were defined as having high blood pressure, diabetes, or a memory problem if they reported ever having a physician diagnosis of those conditions. A current smoker was defined as a person who reported smoking at least 100 cigarettes

and currently smokes daily or occasionally while a former smoker was someone who reported smoking at least 100 cigarettes in life but had not smoked in the last 30 days.

Statistical Analysis

The primary outcome was the 3-year incidence of VI. To determine the proportion of VI due to refractive error, we took 1- (incidence of VI using pinhole-corrected visual acuity / the incidence of VI using presenting visual acuity) at each age group using data from the right eye. Demographic, health, and lifestyle variables were compared by VI status. Differences were tested using the chi-square test. Multiple logistic regression was used to determine independent risk factors for incident VI. Variables were included in the regression model if they had a P-value less than 0.2 in unadjusted analyses. The complex survey design was accounted for in all analyses. Stata SE Version 16 (College Station, Texas) was used. To estimate the number of people in Canada who developed VI, data were used from Statistics Canada [9].

RESULTS

Of the 30,097 people in the baseline sample, 27,765 provided data at follow-up (92%). Of the 27,765 people, 2,102 were missing data on binocular visual acuity at either baseline or follow-up or both leaving 25,663 with visual acuity data at both time points. Of the 25,663, 1,690 had VI at baseline and therefore were excluded since they were not eligible for incident VI leaving 23,973 adults in our final sample. Those missing data on visual acuity were older, had lower household income, and were more likely to currently smoke than those who were not missing data ($P<0.01$) (data not shown).

The incidence of VI was 3.88% (95% CI 3.61, 4.17) (Table 1). However, there was substantial heterogeneity in the incidence rates for the 7 provinces that were included in the CLSA. Manitoba had the lowest incidence of VI at 1.42% (95% CI 1.05, 1.92) while Nova Scotia had the highest incidence at 7.33% (95% CI 6.32, 8.49) (Table 1).

The leading cause of incident VI was uncorrected refractive error (Figure 1). Using data from the right eye, uncorrected refractive error was responsible for 77% of VI in the youngest age group while it was responsible for 48% in the oldest age group (66% overall). Results were similar using data from the left eye (data not shown).

The 3-year incidence rates of self-reported eye disease are shown for each province and for the whole CLSA population in Table 2. Incident cataract was reported in 10.38% of people, incident glaucoma in 1.93%, and incident AMD in 1.68%. The provincial results were fairly homogeneous with the exception of a higher incidence of glaucoma in Quebec at 2.85%.

In Tables 3-4, the incidence of VI is presented by demographic, lifestyle, and health factors. Older age was strongly related to the incidence of VI as 2.00% of those ages 45-54 years developed VI while 10.44% of those 75-85 developed VI. There was not a statistically significant sex difference as about 4% of both men and women developed VI (P=0.06). Race/ethnicity was not statistically significantly associated with incident VI although Black Canadians had a higher incidence compared to white (7.07% versus 3.98%) (P=0.19). Other factors that were associated with a higher incidence included lower education, urban or semi-urban residence, lower household income, current smoking, high blood pressure, and Type 2 diabetes (P<0.05).

In a multiple logistic regression model, five variables were statistically significantly related to incident VI after adjustment (Table 5). Older age was associated with incident VI (OR=1.07, 95% CI 1.06, 1.07). The self-report of Black race was associated with incident VI (OR=2.64, 95% CI 1.36, 5.14). Those with lower household income had a greater risk of incident VI. The highest odds was in those making less than $20,000 per year (OR=1.73, 95% CI 1.24, 2.40). Current smokers had a higher odds of incident VI (OR=1.78, 95% CI 1.37, 2.32). Finally, province of residence remained statistically significantly related to incident VI ($P<0.05$). Adjusting for the use of eye care did not affect the provincial results (data not shown).

In Table 6, using the age-specific incidence rates of VI and multiplying them by the age-specific population size, we estimated that the total number of people in Canada between the ages of 45-85 years old who developed VI over a 3-year period was 670,232 people.

DISCUSSION

The incidence of VI was 3.88% (95% CI 3.61, 4.17) in the CLSA study population, a population-based sample of Canadians from 7 different provinces. There was substantial heterogeneity in the incidence of VI between provinces with Nova Scotia having the highest incidence and Manitoba having the lowest. Risk factors for VI included older age, Black race, lower household income, current smoking, and province. We estimate that 670,232 people between the ages of 45-85 years old in Canada developed VI over a 3-year period. Uncorrected refractive error was the single leading ocular cause of incident VI as it was responsible for 66%. Cataract was the most commonly reported incident eye disease.

Refractive error and cataract are entirely treatable. Refractive error can be corrected by eyeglasses, contact lenses, or refractive surgery while cataract can be treated by cataract surgery. The first step to treatment, though, is to see an eye care professional. We previously reported that certain groups are less likely to regularly access eye care including smokers, those with less education, and those with lower household incomes [10]. Other causes of VI often include age-related macular degeneration (AMD) and glaucoma [11]. AMD and glaucoma can often be effectively managed by intraocular pressure-lowering drops (glaucoma), intraocular injections of anti-angiogenesis agents (AMD), or surgery (glaucoma).

We found substantial heterogeneity in the provincial incidence of VI, similar to our previous finding of provincial heterogeneity in the prevalence of VI in Canada [1]. The provinces of Manitoba, Ontario, and Quebec had the lowest incidence of VI, while Alberta, British Columbia, Newfoundland and Labrador, and Nova Scotia had the highest incidence. Age differences between the provinces did not explain these differences. One possible explanation is that eye care coverage differs by province, although Nova Scotia, which had the highest incidence of VI, does provide coverage for the cost of an eye exam for adults ages 65 years and older. Furthermore, adjusting for a report of having used eye care in the last year did not affect the results. Other possible explanations could include provincial differences in household income, education, or smoking rates. However, when we adjusted for these variables in our model, province was still statistically significantly associated with the incidence of VI. It is possible that residual confounding exists for these variables or there are other omitted variables that might explain these differences (e.g. private insurance for eye care, cataract surgery waitlists).

Besides province, we identified 4 other variables that were risk factors for incident VI: Black race, household income, current smoking, and older age. People who self-identified as Black had a 2.64 higher odds of becoming visually impaired compared to people who self-identified as white after adjustment for potentially confounding variables such as income, education, and province. We must caution that this estimate is based on a relatively small number of people in the sample who identified as Black (n=191). Therefore, the estimate may be somewhat unstable (i.e. driven by a small number of people and more subject to residual confounding). Nevertheless, it was statistically significant. Other studies have also reported ethnic differences in the incidence [2] or prevalence of VI [2,8,12] and other eye diseases [12]. Efforts are ongoing to better understand the reasons for these differences including social, biological, ocular, and genetic factors [13-16]. Lower household income was also associated with the odds of VI in a dose-dependent manner such that the lower the income, the higher the odds. Eye care can be expensive as the cost of glasses and contact lenses are not typically covered under provincial health insurance. Cataract surgery can also have uncovered costs such as for special intraocular lenses, eye drops, and the cost of transportation for pre and post-op visits. Other studies have also reported an association with income [1,17,18]. Current smokers had a higher odds of VI. Several eye diseases, including certain types of cataract and AMD, and unmet refractive need are related to current smoking [19-21]. Also, smokers often seek preventive eye care less often than non-smokers [10]. Finally, older age was associated with a higher odds of VI, which is well documented in the literature [2,22].

To our knowledge, this is the first population-based estimate of the incidence of VI based on direct measurement of visual acuity in Canada. This publication allows comparison to the rest of the world. The 3-year incidence of VI in the CLSA using binocular presenting visual acuity with a 20/40 cutoff was 3.88%. When comparing to other studies, it is ideal to compare to other studies that used binocular presenting visual acuity with the same cutoff. The CLSA estimate of

3.88% is higher than the Los Angeles Latino Eye Study, which found a 2.9% incidence of VI over 4 years in a population of adults ages 40 and older [2]. It is also higher per year than the Melbourne VIP Study in Australia, which found a 4.22% incidence of VI over 5 years—a two year longer time period than the CLSA [23]. Our work may be useful in meta-analyses that attempt to estimate the global burden of VI [24].

There are some limitations of this work that should be acknowledged. First, although visual acuity was measured by trained personnel using an ETDRS chart, there was no optometric or ophthalmologic exam in the CLSA. The self-report of eye disease was not confirmed by an eye care professional or by a medical chart. Second, visual acuity was missing for 2,102 people precluding us from measuring incidence. Those missing data were older, had lower household income, and were more likely to be current smokers—all risk factors for VI—indicating their absence may have led to an underestimate of the true incidence of VI. Therefore, our estimate of VI should be considered conservative. Third, our results may not be generalizable to provinces not included in the CLSA Comprehensive Cohort or to those not included in the inclusion criteria.

In conclusion, these novel Canadian incidence data, in conjunction with the recently published prevalence data [1], will be helpful to eye care professionals, low vision rehabilitation providers, and healthcare policy planners. The leading causes of VI of refractive error and cataract are entirely treatable indicating that much VI is avoidable. Furthermore, the risk factors for VI that we identified indicate that there are certain sub-groups that might benefit from interventions to reduce the risk of VI. There is much that can be done to prevent avoidable vision loss both in Canada and in the world [25,26].

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Table 1: 3-year incidence rates of visual impairment by province

Province	**Incidence of VI** **% (95% CI)**
Alberta (n=2,297)	6.07 (5.09, 7.23)
British Columbia (n=4,832)	5.55 (4.93, 6.25)
Manitoba (n=2,610)	1.42 (1.05, 1.92)
Newfoundland & Labrador (n=1,642)	6.45 (5.36, 7.74)
Nova Scotia (n=2,340)	7.33 (6.32, 8.49)
Ontario (n=5,386)	2.10 (1.76, 2.52)
Quebec (n=4,866)	2.38 (1.99, 2.84)
CLSA (n=23,973)	3.88 (3.61, 4.17)

VI=visual impairment; CLSA=Canadian Longitudinal Study on Aging

Figure 1: Proportion of visual impairment due to refractive error by age group.

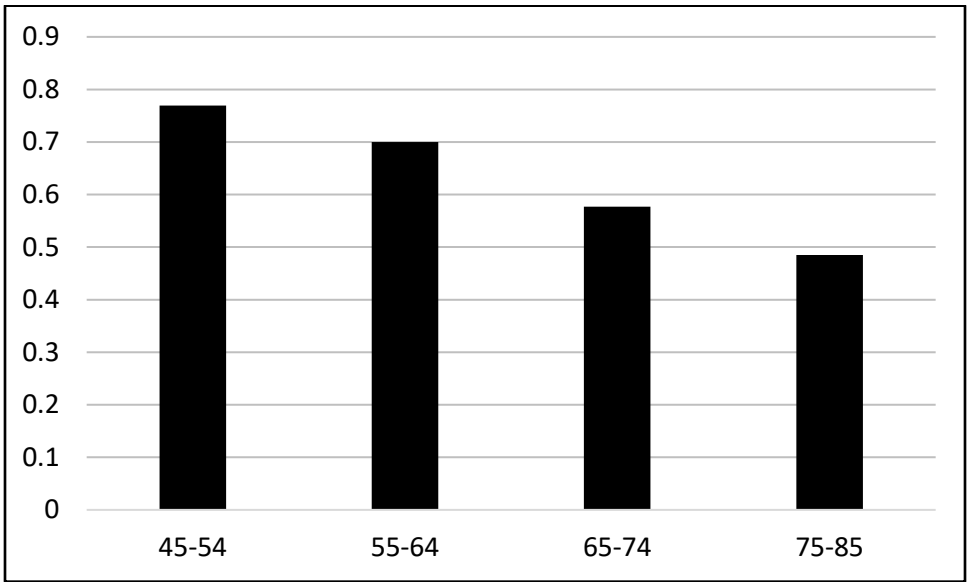

Table 2: Three-year incidence of self-reported eye disease by province

Site	Alberta %	BC %	Manitoba %	NF & L %	Nova Scotia %	Ontario %	Quebec %	CLSA %
3-Year Incidence of Cataract	10.14	11.26	8.53	9.19	11.13	10.22	10.20	10.38
3-Year Incidence of Glaucoma	1.22	1.57	1.72	0.95	1.28	1.74	2.85	1.93
3-Year Incidence of AMD	1.69	1.88	1.99	1.32	0.95	1.63	1.53	1.68

VI=visual impairment; BC=British Columbia; NF & L=Newfoundland and Labrador;
CLSA=Canadian Longitudinal Study on Aging
AMD=age-related macular degeneration

Table 3: Incidence of visual impairment by demographic factors (n=23,973 unless noted)

	Incident VI n=1,217 (%)	**No Incident VI n=22,756 (%)**	**P-Value**
Age Group, Years			
45-54 (n=6,547)	2.00	98.00	
55-64 (n=8,308)	3.59	96.41	<0.01
65-74 (n=5,760)	6.70	93.30	
75-84 (n=3,358)	10.44	89.56	
Sex/Gender			
Male (n=11,887)	3.75	96.25	0.06
Female (n=12,086)	4.24	95.76	
Race/Ethnic Group			
White (n=22,675)	3.98	96.02	0.19
Black (n=191)	7.07	92.93	
Asian (East, South, SE) (n=515)	4.58	95.42	
Aboriginal (n=283)	3.01	96.99	
Other (n=309)	2.91	97.09	
Education*			
More than Bachelor's (n=5,420)	3.78	96.22	<0.01
Bachelor's Degree (n=5,931)	3.08	96.92	
Less than Bachelor's (n=12,583)	4.56	95.44	
Residence*			
Urban, Semi-urban (n=21,696)	4.09	95.91	<0.01
Rural (n=1,992)	2.76	97.24	
Household Income Per Year			
≥$100,000 (n=8,923)	2.46	97.54	<0.01
$50,000 - $100,000 (n=8,064)	4.71	95.29	
$20,000 - $50,000 (n=4,605)	6.08	93.92	
<$20,000 (n=993)	6.70	93.30	
Refused/Don't Know (n=1,388)	5.26	94.74	

*n missing: education (n=39), residence (n=285);
Other=Arab and West Asian, Latin American, and Other

Table 4: Incidence rates visual impairment by lifestyle and health factors (n=23,973 unless noted)

	Incident VI (%)	**No Incident VI (%)**	**P-Value**
Smoking*			
Never (n=11,601)	3.49	96.51	<0.01
Former (n=10,460)	4.39	95.61	
Current (n=1,828)	5.21	94.79	
High Blood Pressure*			
No (n=15,467)	3.54	96.46	<0.01
Yes (n=8,406)	4.95	95.05	
Diabetes*			
None (n=19,960)	3.80	96.20	<0.01
Type 1 (n=125)	3.72	96.28	
Type 2 (n=1,985)	6.12	93.88	
Suspect/Neither Type (n=1,684)	4.12	95.88	
Memory Problems*			
No (n=23,592)	3.98	96.02	0.27
Yes (n=328)	5.13	94.87	

*n missing: Smoking (n=84), High blood pressure (n=100), Diabetes (n=219), Memory problems (n=53)

Table 5: Variables and their independent association with the incidence of visual impairment using multiple logistic regression

	Incidence of VI n=23,278 Adjusted Odds Ratio*	**95% CI**
Age, Per 1 Year	1.07	1.06, 1.07
Female Sex	1.07	0.93, 1.24
Race/Ethnicity		
White	1.00	
Black	2.64	1.36, 5.14
Asian	1.33	0.82, 2.17
Aboriginal	0.98	0.50, 1.91
Other	0.72	0.35, 1.44
Education		
More than Bachelor's	1.00	
Bachelor's Degree	0.86	0.69, 1.07
Less than Bachelor's	1.01	0.84, 1.21
Household Income Per Year		
≥$100,000	1.00	
$50,000 - $100,000	1.43	1.18, 1.73
$20,000 - $50,000	1.52	1.22, 1.90
<$20,000	1.73	1.24, 2.40
Refused/Don't Know	1.30	0.95, 1.78
Rural vs Non-Rural	0.84	0.62, 1.12
Smoking		
Never	1.00	
Former	1.11	0.96, 1.28
Current	1.78	1.37, 2.32
Diabetes		
None	1.00	
Type 1	0.94	0.42, 2.07
Type 2	1.21	0.97, 1.50
Suspect/Neither Type	0.95	0.74, 1.22
High Blood Pressure	0.96	0.83, 1.11
Province		
Alberta	1.00	

British Columbia	0.76	0.60, 0.96
Manitoba	0.16	0.11, 0.22
Newfoundland & Labrador	0.89	0.67, 1.17
Nova Scotia	1.02	0.79, 1.32
Ontario	0.25	0.19, 0.33
Quebec	0.26	0.20, 0.34

*Adjusted for all variables in table and also for the complex study design

Table 6: Estimated numbers of people ages 45-85 years who developed visual impairment over a 3-year period by province and for Canada overall

Site	Alberta	BC	Manitoba	NF & L	Nova Scotia	Ontario	Quebec	Canada
% with Incident VI by Age								
45-54	3.49	3.30	0.24	2.82	3.14	1.07	1.01	2.00
55-64	5.59	4.86	1.08	6.53	7.08	1.59	2.09	3.44
65-74	13.18	9.95	2.91	9.30	14.60	2.96	3.56	6.52
75-85	18.45	14.33	4.73	22.87	17.64	6.91	6.69	9.93
Population Size by Age								
45-54	561,872	714,515	171,381	83,245	140,133	2,036,191	1,161,851	5,165,682
55-64	507,709	698,766	165,221	85,556	148,176	1,864,176	1,205,689	4,979,010
65-74	292,842	489,618	109,875	63,176	108,810	1,273,948	852,226	3,392,368
75-85	156,307	263,777	61,767	29,150	56,410	732,047	466,496	1,756,880
Estimated New Cases of VI In 3 Years								
45-54	19,609	23,579	411	2,348	4,400	21,787	11,735	103,314
55-64	28,381	33,960	1,784	5,587	10,491	29,640	25,199	171,278
65-74	38,597	48,717	3,197	5,875	15,886	37,709	30,339	221,182
75-85	28,839	37,799	2,922	6,667	9,951	50,584	31,209	174,458
45-85	115,425	144,055	8,315	20,476	40,728	139,721	98,481	670,232

VI=visual impairment; BC=British Columbia; NF & L=Newfoundland and Labrador

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CHAPTER 8: MANUSCRIPT TWO

Purpose: Answer thesis objective 3

Required Ethics Approval: : Ethics approval was received April 28, 2020, Following review by The University of Ottawa Office of Research Ethics and Integrity.

Title: Vision, Eye Disease, and the Onset of Balance Problems: The Canadian Longitudinal Study on Aging

Authors: Zaina Kahiel, BSc, Alyssa Grant, MSc, Marie-Josée Aubin, MD, MSc, MPH, Ralf Buhrmann, MD, PhD, Marie-Jeanne Kergoat, MD, Ellen E. Freeman, PhD

Contributions:

- ZK contributed to the analysis, the interpretation of the data, and drafting the manuscript.
- MJA, RB, and MJK contributed to the interpretation of the results and the revision of the manuscript.
- EEF contributed to the acquisition, analysis, and interpretation of the data and the revision of the manuscript.
- All authors gave final approval for the version to be published and agree to be accountable for all aspects of the work.

Status: Submitted to American Journal of Ophthalmology.

Vision, Eye Disease, and the Onset of Balance Problems: The Canadian Longitudinal Study on Aging

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Short Title: Vision and Balance Problems
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ABSTRACT

Purpose: To understand the relationship between visual impairment, self-reported eye disease, and the onset of balance problems.

Design: Population-based prospective cohort study

Methods: Baseline and 3-year follow-up data were used from the Canadian Longitudinal Study on Aging. The Comprehensive Cohort included 30,097 adults ages 45-85 years old recruited from 11 sites across 7 provinces. Balance was measured using the one-leg balance test. Those who could not stand on one leg for at least 60 seconds failed the balance test. Presenting visual acuity was measured using the Early Treatment of Diabetic Retinopathy Study chart. Participants were asked about a previous diagnosis of cataract, macular degeneration, or glaucoma. Logistic regression was used.

Results: Of the 12,158 people who could stand for 60 seconds on one leg at baseline, 18% were unable to do the same 3 years later. For each line worse of visual acuity, there was a 15% higher odds of failing the balance test at follow-up (odds ratio (OR)=1.15, 95% confidence interval (CI) 1.10, 1.20) after adjustment. Those with a report of a former (OR=1.59, 95% CI 1.17, 2.16) or current cataract (OR=1.31, 95% CI 1.01, 1.68) were more likely to fail the test at follow-up. AMD and glaucoma were not associated with failure on the balance test.

Conclusion: These data provide longitudinal evidence that vision loss increases the odds of balance problems over a 3-year period. Efforts to prevent avoidable vision loss are needed as are efforts to improve the balance of visually impaired people.

Keywords: balance, visual impairment, cataract, glaucoma, age-related macular degeneration, CLSA

INTRODUCTION

Balance is critical to successful aging as studies have found that poor balance is associated with an increased risk of falls, nursing home admission, and mortality [1-3]. Balance is regulated by multiple systems including the visual system, the vestibular system, and the proprioceptive system. Studies have reported that the visual system takes on a more important role in maintaining postural control in older age [4,5]. Yet, visual impairment becomes much more common in older age, [6] which may leave visually impaired older adults without adequate postural control.

Many cross-sectional studies have indicated a relationship between impaired vision and worse balance. For example, many population-based studies have reported an association between various measures of visual function (e.g. visual acuity, visual field, motion detection threshold) and balance problems [7-12]. Other clinical research studies have found that patients with glaucoma, cataract, or age-related macular degeneration had worse balance [13-17]. All of these studies have been cross-sectional in design, which can lead to reverse causality.

To our knowledge, only 3 longitudinal studies have reported on vision and the onset of balance problems. Two of them have shown no association [18,19] while one found an association between visual impairment and the onset of a composite mobility measure that included balance [20]. There is a need for more longitudinal data that examine this issue. Data from the Canadian Longitudinal Study on Aging (CLSA) provide an opportunity to investigate how visual impairment or eye disease are associated with the risk of developing balance problems.

METHODS

Study Design

The CLSA is a population-based prospective cohort study. We focused on the 30,097 adults in the Comprehensive Cohort of the CLSA because they visited a data collection site and undertook a visual acuity test. Participants were recruited from provincial health registries and through the use of random digit dialing. For those recruited using provincial health registries, letters introducing the study were sent to randomly chosen, age-eligible persons. Consent forms to be returned were enclosed. For those recruited through random digit dialing, a random sample of landline telephone numbers was selected for a given geographic area. Once a call was answered, eligibility was established and consent was obtained. Stratified sampling was used to ensure adequate representation of various demographic groups. Strata within a province were defined by age group, sex, and distance from the data collection site. Baseline data were collected between 2010 and 2015 and the follow-up data were collected between 2013 and 2018. The follow-up rate was 92%. Written informed consent was obtained from all participants. Research Ethics Board approval was received in July 2010 from all affiliated sites. Ethics approval from the Office of Research Ethics and Integrity at University of Ottawa was received for the present analysis in May 2019.

Study Population

To be eligible, adults were required to meet the following inclusion criteria: between the ages of 45 and 85 years old, community-dwelling, and living near one of the 11 data collection

sites in 7 provinces (Victoria, Vancouver, Surrey, Calgary, Winnipeg, Hamilton, Ottawa, Montreal, Sherbrooke, Halifax, and St. John's). People were excluded from the CLSA if they were in an institution, living on a First Nations reserve or settlement, were a full-time member of the Canadian Armed Forces, did not speak French or English, were not a Canadian citizen or permanent resident, or had cognitive impairment at baseline.

Data Collection

Data were collected from two locations: an interviewer-administered questionnaire given at home or from procedures performed at a data collection site. All CLSA personnel underwent detailed training sessions to standardize the data collection process.

Balance Assessment

The one-leg balance test was used to measure standing balance. This test has shown good reliability [21] and is predictive of injurious falls [2] and incident disability [22]. Those who were unable to stand unassisted or who used a cane or walker regularly were excluded from this assessment. Participants were asked to remove their shoes, stand one meter away from the wall, and lift their right leg to the calf while placing their hands on their waist. The timer started when the foot left the ground. It stopped when the foot touched the ground, when the participant lost balance and/or touched the wall, or once 60 seconds had passed. This assessment was then repeated for the left leg. Participants were given the opportunity to practice their stance before the official assessment. The better time of the right and left legs was used. A person was classified as having failed the balance test if they could not stand for 60 seconds.

Visual Acuity and Eye Disease

At baseline, an illuminated Early Treatment of Diabetic Retinopathy Study (ETDRS) visual acuity letter chart at a 2-meter distance was used to assess binocular and monocular visual acuity. Participants wore their normal correction for distance, if any. Visual acuity was scored as the number of letters read correctly which were then converted to the log of the minimum angle of resolution (logMAR). A logMAR of 0.0 is normal (20/20) while a logMAR of 1.0 indicates blindness (20/200). At baseline, participants were also asked if a doctor had ever told them that they have the following conditions: cataract, glaucoma, or macular degeneration. Those who reported a history of cataract were asked a second question about whether they currently had a cataract. Those who said no were assumed to have had the cataract(s) removed by surgery. Those who were not sure if their cataract(s) had been removed were analyzed as a separate group.

Demographic, Health, and Lifestyle Data

At baseline, data were collected on demographic, health, and lifestyle data. Sociodemographic information on age and sex were collected by self-report. Body mass index (BMI) was calculated by taking measured weight (kilograms) and dividing by height (in meters^2). BMI was categorized into underweight (<20kg/m^2), normal weight (20-24kg/m^2), overweight (25-29kg/m^2), and obese (>=30kg/m^2) in order to examine non-linearity. Limitations in activities of daily living (ADL) were based on the number of activities that participants could only do with help or were unable to do at all. Some examples of activities included getting dressed, eating, walking, and getting out of bed. A participant who needed help with or was unable to do 1 or more activities was classified as having ADL limitations.

Participants were defined as having diabetes or stroke if they reported ever having a physician diagnosis of those conditions. A current smoker was defined as a person who reported smoking at least 100 cigarettes and currently smokes daily or occasionally. A former smoker was someone who reported smoking at least 100 cigarettes in life but had not smoked in the last 30 days.

Statistical Analysis

A longitudinal analysis was done using data from both baseline and follow-up. The primary outcome was the inability to stand for 60 seconds at follow-up. In order to examine the new onset of balance problems at follow-up, the analysis was restricted to those who were able to stand for 60 seconds at baseline. Baseline characteristics of those who did not attempt the balance test at follow-up were compared to those who did attempt the balance test. Also, baseline characteristics of those who were unable to stand for 60 seconds at follow-up (defined as a failure) were compared to those who were able to stand for 60 seconds (defined as passing). For both of these comparisons, chi-square tests (for categorical data) and t-tests (for continuous data) were used. Multiple logistic regression models were used to determine whether the baseline visual acuity or eye disease variables were independently related to failing the balance test after adjustment for baseline variables including age, sex, smoking status, BMI, diabetes, ADL limitations, stroke history, and province. Binocular visual acuity was entered in the model as a continuous variable. Glaucoma and AMD were entered as dichotomous variables (no, yes). Cataract was entered into the model as a 4-category indicator variable (never, past, current, status unknown). The complex survey design was accounted for in all analyses by incorporating information on sample weights and strata using the svy commands in Stata SE Version 16 (College Station, Texas).

RESULTS

In Figure 1, a flow chart is provided to illustrate who is included in the analysis sample. Of the 30,097 people in the Comprehensive Cohort at baseline, 27,765 provided follow-up data 3 years later (92%). Of these 27,765 people, 26,475 attempted the balance test at baseline with 12,929 passing it. Of the 12,929 who passed the baseline balance test, 12,158 attempted it at follow-up, which is our analysis sample. Those who did not attempt the balance test at follow-up were older, more likely to be women, more likely to smoke, to be obese, to have diabetes, to have ADL limitations, and to have suffered a previous stroke (Table 1). They were also more likely to have worse visual acuity, to have had a cataract, age-related macular degeneration (AMD), and glaucoma (Table 1).

In Table 2, the characteristics of those who passed and failed the balance test at follow-up are provided. Of the 12,158 people who could stand for 60 seconds on one leg at baseline, 18% were unable to do the same at follow-up 3 years later after adjusting for the complex survey design. Those who were older, smoked, were obese, had diabetes, ADL limitations, or stroke were more likely to fail the balance test at follow-up.

The visual and eye disease characteristics of those who passed and failed the balance test are presented in Table 3. Those who failed the balance test at follow-up had worse baseline visual acuity compared to those who passed ($P<0.001$). All three eyes diseases at baseline were associated with failing the balance test at follow-up including having a past or current cataract, or AMD, or glaucoma, ($P<0.001$).

Worse baseline binocular visual acuity was associated with failing the balance test at follow-up after adjustment using multiple logistic regression (Table 4). For each line worse of visual acuity (0.1 logMAR), there was a 15% higher odds of failing the balance test at follow-up

(OR=1.15, 95% CI 1.10, 1.20) after adjusting for age, sex, smoking status, BMI, diabetes, ADL limitations, stroke history, and province. Other risk factors for failing the balance test were older age, female sex, current smoking, higher BMI, diabetes, and ADL limitations ($P<0.05$).

As shown in Table 5, both having a cataract in the past (OR=1.59, 95% CI 1.17, 2.16) and having a current cataract (OR=1.31, 95% CI 1.01, 1.68) were associated with failing the balance test at follow-up. Those who were unaware if their cataract had been removed or not did not have a higher odds of failing the balance test (OR=1.08, 95% CI 0.90, 1.30). AMD (OR=1.05, 95% CI 0.73, 1.50) and glaucoma (OR=1.17, 95% CI 0.87, 1.58) were not associated with failure on the balance test after adjustment.

Binocular visual acuity remained statistically significantly associated with failing the balance test at follow-up even after adjusting for the self-report of cataract, AMD, and glaucoma (OR=1.15, 95% CI 1.10, 1.20). Furthermore, cataract surgery remained associated with balance even after adjusting for binocular visual acuity (OR=1.61, 95% CI 1.18, 2.19) or the difference in visual acuity between the left and right eyes (OR=1.47, 95% CI 1.08, 2.01).

DISCUSSION

We found that visual acuity was associated with failing the balance test even after adjusting for a self-report of cataract, glaucoma, or AMD indicating that other ocular factors may affect balance. We also found that people who reported a history of cataract, whether it had been removed or not, were more likely to fail the balance test 3 years later. Surprisingly, we did not find that AMD or glaucoma were associated with failure on the balance test although it may have been due to their self-reported nature or because most cases were very mild or early stage.

Visual acuity was associated with failing the balance test even after adjusting for cataract, AMD, and glaucoma indicating that uncorrected refractive error may be driving this association.

Uncorrected refractive error, the leading cause of vision loss in the world [23], has been previously found to be associated with balance. Willis *et al* found using cross-sectional data that both visual impairment due to uncorrected refractive error and visual impairment due to causes other than uncorrected refractive error were related to failure on a balance test [7]. Our result that poorer visual acuity is associated with worse balance is in agreement with Salive *et al*, a longitudinal study [20], and with several cross-sectional studies [7,8,11]. However, two longitudinal studies did not demonstrate this association [18,19].

Cataract was also associated with failing the balance test. Perhaps counter-intuitively, we found that those who had a cataract removed had the highest odds of failing the balance test followed by those who had a cataract still in the eye. Cataract surgery not only removes the cataract but can also largely correct refractive error in that eye by inserting an intraocular lens of the correct power. There are several potential reasons that might explain why we found that cataract surgery was associated with worsening balance. First, there is a period between first-eye and second-eye cataract surgery that can leave a person with very different refractive powers between their two eyes. This can be corrected with glasses. If people are reluctant to pay for new glasses during this period and instead choose to wait until after the second-eye cataract surgery, they may go through a period of time with unequal refractive powers between eyes and impaired stereopsis, which may lead to worse balance [24]. However, adjusting for the difference in visual acuity between the two eyes did not eliminate the association between cataract removal and the onset of balance problems. Second, even after second eye cataract surgery, a person may still have some post-operative refractive error that could not be completely corrected. For example, a large European study found that the absolute mean biometry prediction error after cataract surgery was 0.42D [25]. Of those advised by their surgeons to obtain spectacles for distance correction, 77% did so [26]. However, adjusting for visual acuity did not reduce the

association between cataract removal and the onset of balance problems**.** Third, there may be other ocular differences in people who have had cataract surgery that may affect their balance. Although we adjusted for AMD and glaucoma, and the association remained unchanged, we did not have data on measures of visual function other than acuity like contrast sensitivity, visual field, or motion detection. Finally, people who have had cataract removal may differ in other health-related ways that affect balance. However, adjusting for ADL disability, diabetes, and stroke did not meaningfully change the association. We are ultimately unable to determine the reason why people with cataract removal were more likely to develop balance problems.

Our research findings on cataract are supported by previous work that found that cataract simulation leads to worse postural control [27]. Furthermore, several studies have examined cataract surgery and either balance, postural sway, or falls. Our finding that cataract and cataract removal are associated with worse balance is in agreement with Meuleners *et al* [28], a retrospective cohort study of over 28,000 people receiving bilateral cataract surgery in Australia. They found that injurious falls requiring hospitalization were twice as likely in between first and second-eye cataract surgery and even 34% more likely during the two years after second-eye cataract surgery compared to the two-year period before first-eye surgery. However, our results are in disagreement with several studies that have evaluated balance or falls after cataract surgery. For example, Harwood *et al* conducted a randomized controlled clinical trial in which people who needed first-eye cataract surgery were randomized either to expedited surgery (4 week wait) or routine surgery (12 month wait) [29]. The researchers did not find a difference between the groups for the first fall but they did find that the expedited group had lower risks of a second fall or any fracture after 12 months of follow-up. Our findings are also in disagreement with some observational studies [30-32].

Strengths of our research included the use of longitudinal data, the measurement of visual acuity, and a large population-based sample from across Canada. The use of longitudinal data allows us to ensure that the vision loss occurred before the onset of the decline in balance. Thus, reverse causality cannot be driving the estimate of the association. A limitation was that eye disease was based on self-report, which is known to have limited sensitivity [33,34]. We also only had data on visual acuity, but not other measures of visual function like contrast sensitivity, visual field, and motion detection that may be relevant to balance. We did not know whether a person had one cataract or two or which eye(s) the cataract was in. Furthermore, missing data was a limitation. Some people did not know if they had had their cataract removed or not. We examined this group separately and did not find that they had a higher odds of failing the balance test. Some people were missing data on balance at either baseline or follow-up. Given they were more likely to have risk factors for poor balance and they were more likely to have vision loss and eye disease, it is likely that our results are underestimates of the true associations. Finally, our results may not generalize to those people not included in the CLSA such as those living in nursing homes.

To conclude, visual impairment and having had a cataract removed or a cataract in the eye were associated with the onset of balance problems. These findings suggest that more attention needs to be paid to balance problems in people with vision loss. Interventions to improve balance in groups with irreversible vision loss should be considered [35,36].

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Figure 1: Flow chart of participants included in the analysis

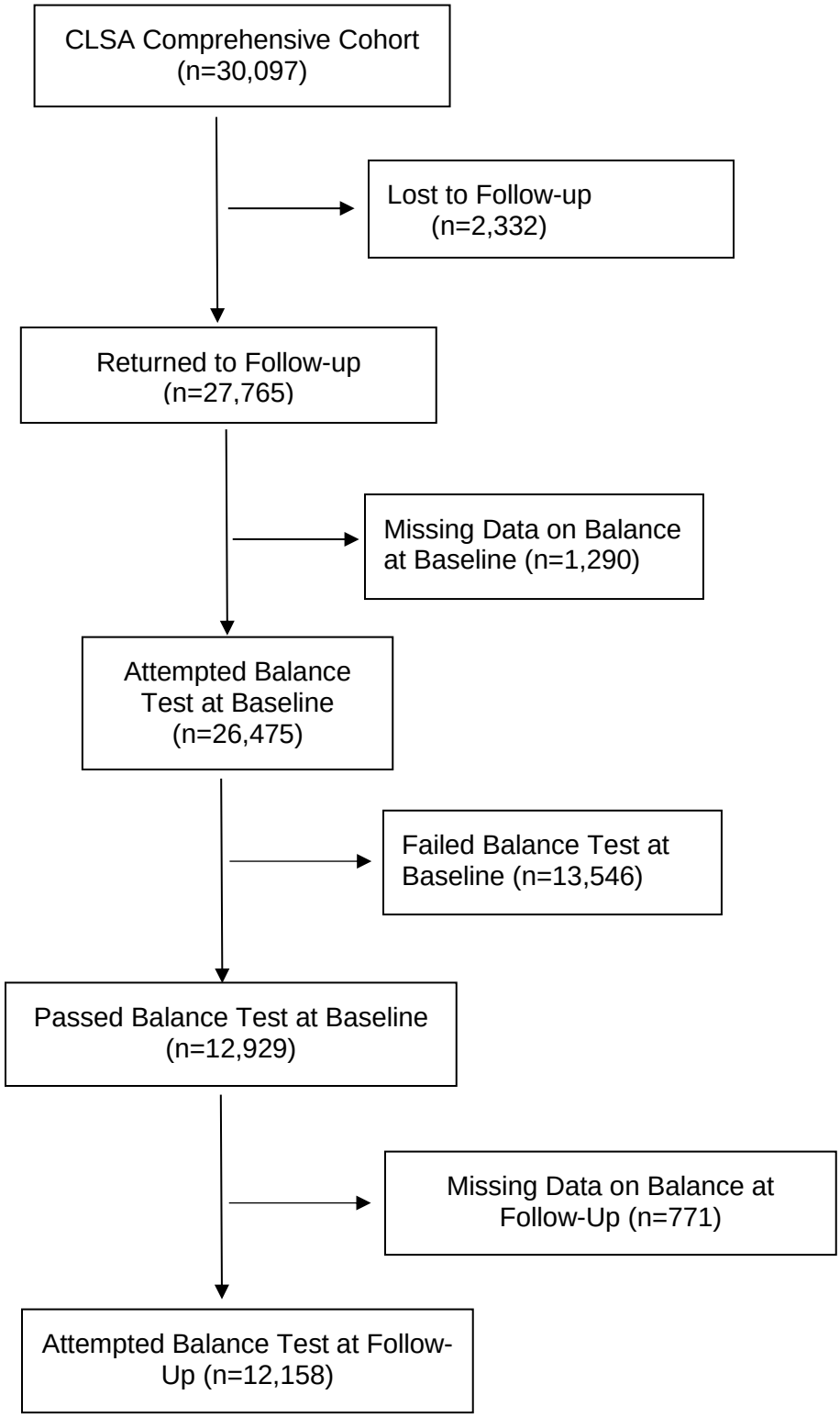

Table 1: Descriptive characteristics of those who attempted versus did not attempt the balance test at follow-up.

Baseline Exposures	**Attempted Balance Test at Follow-Up n=12,158 Mean (SD) or %**	**Did Not Attempt Balance Test at Follow-Up n=17,939 Mean (SD) or %**
Age, Years	55.2 (6.4)	63.5 (11.3)
Sex		
Male (n=14,777)	52%	46%
Female (n=15,320)	48%	54%
Smoking		
Never (n=14,236)	55%	45%
Former (n=13,186)	38%	44%
Current (n=2,572)	7%	11%
Body Mass Index		
<20 kg/m^2 (n=421)	3%	2%
20-24 kg/m^2 (n=4,333)	35%	22%
25-29 kg/m^2 (n=5,050)	42%	38%
>=30 kg/m^2 (n=2,348)	20%	38%
Diabetes		
No (n=10,833)	90.3%	79.7%
Type 1 (n=36)	0.3%	0.8%
Types 2 (n=494)	3.6%	11.9%
Neither/Suspect (n=728)	5.8%	7.6%
ADL Limitations		
No (n=11,763)	97.4%	87.2%
Yes (n=366)	2.6%	12.8%
Stroke		
No (n=12,072)	99.5%	97.8%
Yes (n=68)	0.5%	2.2%
Visual Acuity, logMAR	-0.02 (0.12)	0.05 (0.17)
Cataract		
Never (n=10,396)	90.6%	67.1%
Past (n=262)	1.4%	7.2%
Current (n=420)	2.6%	7.1%
Status Unknown (n=853)	5.4%	18.6%

AMD No (n=11,879) Yes (n=233)	 98.5% 1.5%	 95.3% 4.7%
Glaucoma No (n=11,845) Yes (n=283)	 98.1% 1.9%	 94.2% 5.8%

SD=standard deviation; ADL=activities of daily living

Table 2: Descriptive characteristics of participants by ability to pass the balance test.

Baseline Exposures	**Passed Balance Test at Follow-Up n=9,528 Mean (SD) or %**	**Failed Balance Test at Follow-Up n=2,630 Mean (SD) or %**
Age, Years	54.2 (6.2)	59.4 (9.2)
Sex Male (n=6,304) Female (n=5,854)	 53% 47%	 52% 48%
Smoking Never (n=6,410) Former (n=4,896) Current (n=822)	 56% 37% 7%	 48% 43% 9%
Body Mass Index <20 kg/m^2 (n=421) 20-24 kg/m^2 (n=4,333) 25-29 kg/m^2 (n=5,050) >=30 kg/m^2 (n=2,348)	 3% 37% 42% 18%	 3% 26% 42% 29%
Diabetes No (n=10,833) Type 1 (n=36) Types 2 (n=494) Neither/Suspect (n=728)	 91.5% 0.2% 2.9% 5.4%	 84.8% 0.7% 6.8% 7.7%
ADL Limitations No (n=11,763) Yes (n=366)	 98% 2%	 95% 5%
Stroke No (n=12,072) Yes (n=68)	 99.6% 0.4%	 99.0% 1.0%

SD=standard deviation; ADL=activities of daily living

Table 3: Vision and eye disease descriptive characteristics of participants by ability to pass the balance test.

Baseline Exposures	Passed Balance Test at Follow-Up n=2,630 Mean (SD) or %	Failed Balance Test at Follow-Up n=9,528 Mean (SD) or %	P-value
Visual Acuity, logMAR	-0.03 (0.13)	0.02 (0.16)	<0.001
Cataract			
Never (n=10,396)	92%	82%	
Past (n=262)	1%	3%	<0.001
Current (n=420)	2%	5%	
Status Unknown (n=853)	4%	10%	
AMD			
No (n=11,879)	99%	98%	<0.001
Yes (n=233)	1%	2%	
Glaucoma			
No (n=11,845)	98%	97%	<0.001
Yes (n=283)	2%	3%	

SD=standard deviation; logMAR=log of the minimum angle of resolution; AMD=age-related macular degeneration

Table 4: Multiple logistic regression results of relationship between visual acuity and failure on the balance test.

Baseline Exposures	Failed Balance Test at Follow-Up n=11,973 Adjusted OR*	95% CI
Visual Acuity, Per 1 Line	1.15	1.10, 1.20
Age, Per Year	1.11	1.10, 1.12
Sex		
Male	1.00	
Female	1.20	1.08, 1.34

Smoking		
Never	1.00	
Former	1.05	0.94, 1.17
Current	2.04	1.67, 2.50
Body Mass Index		
<20 kg/m^2	1.08	0.79, 1.48
20-24 kg/m^2	1.00	
25-29 kg/m^2	1.51	1.32, 1.71
>=30 kg/m^2	2.98	2.56, 3.48
Diabetes		
No	1.00	
Type 1	3.82	1.72, 8.47
Types 2	1.64	1.31, 2.06
Neither/Suspect	1.22	0.99, 1.51
ADL Limitations		
No	1.00	
Yes	2.01	1.53, 2.64
Stroke		
No	1.00	
Yes	1.87	0.88, 3.98

OR=odds ratio; CI=confidence interval; ADL=activities of daily living

*Also adjusted for province.

Table 5: Multiple logistic regression results of relationship between cataract and the failure of the balance test

Baseline Exposures	**Failed Balance Test at Follow-Up n=11,793 Adjusted OR***	**95% CI**
Cataract		
Never	1.00	
Cataract Was Removed	1.59	1.17, 2.16
Cataract Still in Eye	1.31	1.01, 1.68
Cataract – Status Unknown	1.08	0.90, 1.30
Age, Per Year	1.11	1.10, 1.12
Sex		
Male	1.00	
Female	1.24	1.11, 1.39

Smoking		
Never	1.00	
Former	1.07	0.96, 1.20
Current	2.14	1.74, 2.62
Body Mass Index		
<20 kg/m^2	1.12	0.82, 1.54
20-24 kg/m^2	1.00	
25-29 kg/m^2	1.50	1.32, 1.70
>=30 kg/m^2	2.96	2.54, 3.45
Diabetes		
No	1.00	
Type 1	3.72	1.69, 8.18
Types 2	1.65	1.31, 2.07
Neither/Suspect	1.20	0.97, 1.49
ADL Limitations		
No	1.00	
Yes	1.94	1.48, 2.54
Stroke		
No	1.00	
Yes	2.04	0.97, 4.30

OR=odds ratio; CI=confidence interval; ADL=activities of daily living

*Also adjusted for province.

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CHAPTER 9: DISCUSSION

To estimate the incidence of VI, its risk factors, and potential consequences with balance among people aged 45 to 85 years in Canada, this work sought to answer three objectives. This discussion section includes findings to all three aims, comparison of results to previous literature, strengths and limitations, and future directions given the implications of our research.

FINDINGS FOR THE RESEARCH AIMS

Aim 1) Determine the 3-year incidence of VI.

The incidence of VI was 3.88% (95% CI 3.61, 4.17) in the CLSA study population, a population-based sample of Canadians from 7 different provinces. Older age was strongly related to the incidence of VI as 2.00% of those ages 45-54 years developed VI while 10.44% of those 75-85 developed VI. Incident cataract was reported in 10.38% of people, incident glaucoma in 1.93%, and incident AMD in 1.68%. Manitoba had the lowest incidence of VI at 1.42% (95% CI 1.05, 1.92) while Nova Scotia had the highest incidence at 7.33% (95% CI 6.32, 8.49).

Aim 2) Determine the risk factors for 3-year incidence of VI including geographic, sociodemographic, lifestyle, health and healthcare factors.

Risk factors for VI included older age, Black race, lower household income, current smoking, and province. Uncorrected refractive error was the single leading ocular cause of incident VI as it was responsible for 66%. Cataract was the most commonly reported incident eye disease. Other factors that were associated with a higher incidence included lower education, urban or semi-urban residence, lower household income, current smoking, high blood pressure, and Type 2 diabetes ($P<0.05$).

Aim 3) Determine whether baseline VI is associated with the onset of balance problems.

Worse visual acuity was associated with failing the balance test after adjustment using multiple logistic regression. For each line worse of visual acuity (0.1 logMAR), there was 15% higher odds of failing the balance test at follow-up (OR=1.15, 95% CI 1.10, 1.20) after adjusting for age, sex, smoking status, BMI, diabetes, ADL limitations, stroke history, and province. Visual acuity remained statistically significantly associated with balance even after adjusting for cataract, AMD, and glaucoma (OR=1.15, 95% CI 1.10, 1.20). We found that people who reported a history of cataract, whether it had been removed or not, were more likely to fail a one-leg balance test 3 years later.

COMPARISON WITH OTHER FINDINGS

As research investigating incident VI, its risk factors, and the consequences of VA and worsening balance has already been investigated in other cohorts, validating these findings in the CLSA Comprehensive Cohort is of importance.

Incidence of VI and its Risk Factors

Previous research which conducted longitudinal analysis on the incidence of VI varied between 1.4% to 3.8%, respectfully.[8,11,89,91] This variation will largely depend on different nationalities, ethnicities, different follow-up periods, and different modes of measurement. Canada's incidence rate of 3.88% (95% CI 3.61, 4.17) in the CLSA study population as an estimate of national VI is just outside the range found in previous research. However, this study included uncorrected refractive error whereas most other studies included best-corrected VA. Therefore, our best estimate of best-corrected VI would actually be substantially lower if the analysis was limited to best correct VI, as uncorrected refractive error accounted for 66% of incidence VI cases in Canada. Although our estimate is an over-estimate in comparison to other research, it highlights the prevalence of uncorrected refractive error in Canada and the importance of seeing an eyecare professional on an annual basis.

In concordance with previous studies, we were able to confirm associations between older age,[7,160] lower income,[7] current smoking,[7,66,84] and type 2 diabetes with VI.[59] We also found higher odds of VI in Black populations, as found in the LALES study.[87] This highlights the importance of putting extra interventions for certain sub-groups at risk.

In the second manuscript, for each line worse of VA (0.1 logMAR), there was 15% higher odds of failing the balance test at follow-up. Our research is supported by the Salive at al, longitudinal study, [161] and also with several cross-sectional studies.[162–167] In this context, vision loss is a risk factor for mobility decline. Therefore, it is important to develop programs and funding around preventing vision loss to further prevent mobility decline.

STRENGTHS

The large population-based sample, the prospective design, and the measurement of VA are strengths of this study. Given the large sample size, we were able to have a strong power level to detect a certain size odds ratio (80% power for risk factors for the 3-year incidence of VI and 100% statistical power in detecting the relationship between VI and change in balance). The large sample size also allowed us to assess groups that often are too small and therefore underpowered to study like certain ethnic groups, people making low incomes, or current smokers. The use of longitudinal data allowed us to determine the incidence through selecting a cohort which did not have VI at baseline and seeing if they developed VI in three years. Longitudinal data also allowed us to ensure that vision loss occurred before the onset of declining balance. Visual acuity was measured using an ETDRS chart rather than by self-report.

LIMITATIONS

Although the CLSA is one of the largest, national, prospective cohort studies ever conducted in Canada,[149] this work is not void of limitations. General limitations in both works were that record of prevalent eye diseases were based on self-report, which is known to have limited sensitivity.[168,169] Self-report of eye disease was not confirmed by an eye care professional or by a medical chart. Therefore, there may be some misclassification or undercount of the prevalence of eye diseases in this study. Finally, missing data and the low-response rate were also limitations in this study.

SIGNIFICANCE AND IMPLICATIONS

This was the first report of the incidence of VI in Canada. Most other studies which have reported the incidence of VI have different demographic, socio-demographic, lifestyle, social, health and healthcare factors than Canada. In order to prepare for the eye-care needs of the aging population and to meet the future demands for VI rehabilitations services, this information is vital to policymakers. In addition, information about the risk factors associated with VI will potentially allow policymakers to understand if potential sub-groups need special interventions or extra support, such as those belonging to lower-income households.

Although Nova Scotia covers annual eye-examinations among those over 65 years of age,[107] Nova Scotia had the highest incidence of VI of 7.33% (95% CI 6.32, 8.49). Certain efforts should be made to look at the appropriateness of the services provided and its utilization and awareness in Nova Scotia and other provinces. One potential reason may be due to low usage of eye care services and in turn increasing awareness and informing the public on the potential consequences of VI may help mitigate these effects. However, this was not confirmed

when referring to eye care utilization in Canada. In a report by Aljied et al., the crude eye care utilization was 56.3% (95% CI 54.2-58.3%).[170] As the highest eye care utilization was in Ontario (62%) and the lowest was in Newfoundland and Labrador (50%), [170] there is still some ambiguity and need for further investigation as to why Nova Scotia may be experiencing the highest incidence rates in Canada. Finally, in order to reduce the incidence rates in Canada in the future, there is a need for more public awareness campaigns on the causes and consequences of VI so that vision loss can be prevented and thus be able to improve older adults' quality of life.

Finding that vision loss causes a 3-year decline in standing balance communicates how vision loss is not an isolated event and can often affect different aspect central to healthy aging. As 75% of vision loss is preventable,[110] these findings highlight the importance of prevention and early detection. Additionally, as the financial cost of vision loss in Canada was estimated at $15.8 billion in 2007,[110]prevention and early detection have major implications even for Canada's economic GDP.

FUTURE DIRECTIONS

Future studies should try to determine whether certain sub-groups which were excluded from the study were actually at a higher risk of VI than those in the Comprehensive Cohort of the CLSA. For example, those living on a First Nations reserve or settlement, who were a full-time member of the Canadian Armed Forces, did not speak French or English, or had cognitive impairment were excluded from the study. However, those living in a reserve or settlement, a member of the Armed Forces, those with language deficiencies, and those with cognitive

deficiencies face unique challenges that may actually put them at a greater risk of VI. Within this context future studies should look at these smaller groups and determine if they had a higher risk of VI.

Secondly, the CLSA will follow these subjects over a 20-year period and will follow-up every three years and determining the 6-year and 9-year incidence of VI may provide more information on the average time of onset of vision problems. The COVID-19 pandemic may lead to a greater incidence in VI in the future since many people may be avoiding or unable to receive eye care. Over time, policy changes may occur in eye-care coverages, certain interventions to reduce vision loss may be implemented, and more active efforts for early treatment creates merit to investigate how these policy modifications might change the onset of vision problems over time.

CONCLUSION

This thesis suggests that the incidence of VI in Canada is 3.88% and its risk factors are older age, Black race, lower household income, current smoking, and province. Uncorrected refractive error was the leading cause of incident VI as it accounts of 66% of cases. Worse VA was associated with failing the balance test, where each line worse of VA had 15% higher odds of failing the balance test at follow-up. We found that people who reported a history of cataract, whether it had been removed or not, were more likely to fail a one-leg balance test 3 years later. Taken together, these findings suggest that VI is an ongoing problem in the Canadian aging population and affects other aspects of healthy aging. Prevention, early detection, and proper eye-care services can help mitigate these effects.

CHAPTER 10: REFERENCES

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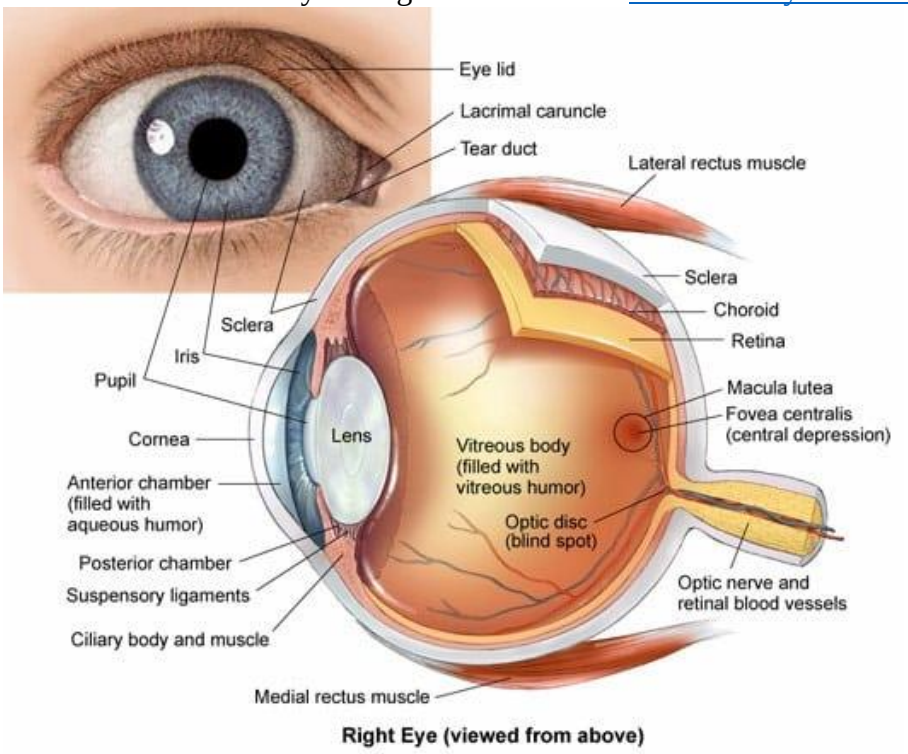
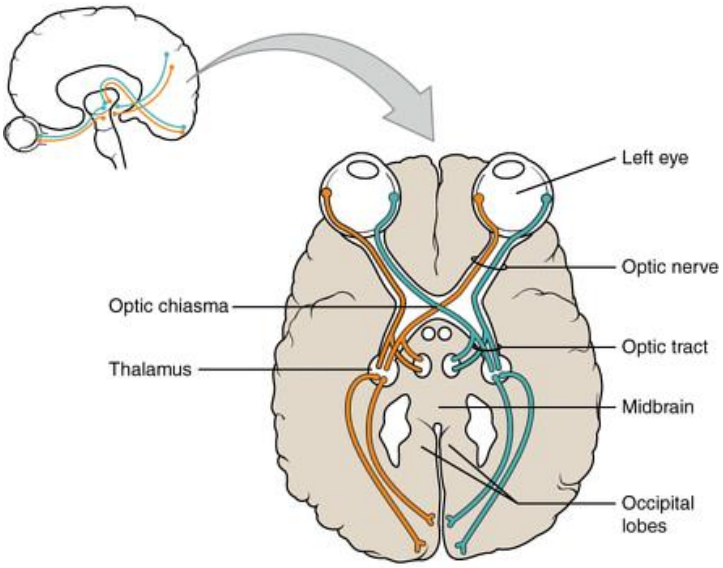
ANATOMIES

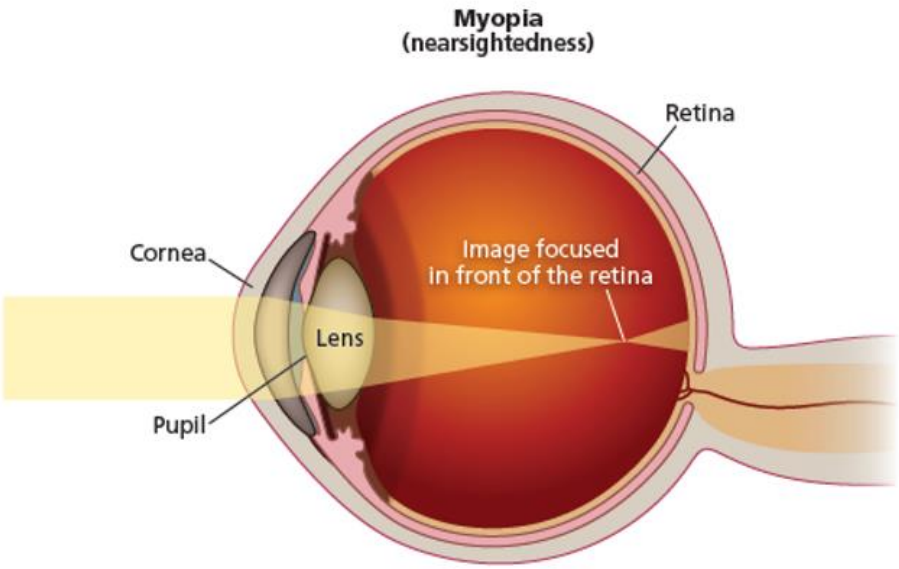
F1: Inside look of the eye. Image taken from the Columbia Eye Clinic.



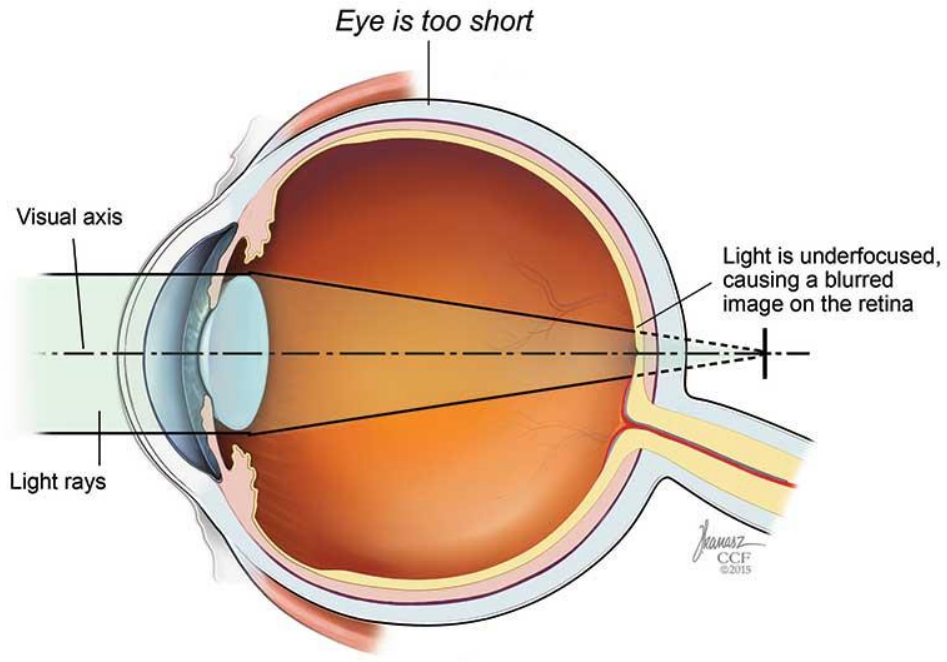
F2: Optic Chiasm. Image Taken from Radiopaedia articles.



F3.1: Myopia (near or short sightedness). Image taken from Iris



F3.2: Hyperopia (far or long sightedness). Image taken from Cleveland Clinic



ETHICS APPROVAL

28/04/2021

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

CERTIFICAT D'APPROBATION ÉTHIQUE | CERTIFICATE OF ETHICS APPROVAL

Numéro du dossier / Ethics File Number	H-05-19-4466
Titre du projet / Project Title	The Incidence of Visual Impairment, its Risk Factors, and its Mobility and Health Consequences
Type de projet / Project Type	Recherche de professeur / Professor's research project
Statut du projet / Project Status	Renouvelé / Renewed
Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)	29/05/2019
Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)	28/05/2022

Équipe de recherche / Research Team

Chercheur / Researcher	Affiliation	Role
Ellen FREEMAN	Département d'épidémiologie et santé publique / Department of Epidemiology and Public Health	Chercheur Principal / Principal Investigator
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Alyssa GRANT	Département d'épidémiologie et santé publique / Department of Epidemiology and Public Health	Étudiant-chercheur / Student-researcher
Zaina KAHIEL		Étudiant-chercheur / Student-researcher

Conditions spéciales ou commentaires / Special conditions or comments

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Université d'Ottawa

Bureau d'éthique et d'intégrité de la recherche

University of Ottawa

Office of Research Ethics and Integrity

Le Comité d'éthique de la recherche (CÉR) de l'Université d'Ottawa, opérant conformément à l'*Énoncé de politique des Trois conseils* (2014) et toutes autres lois et tous règlements applicables, a examiné et approuvé la demande d'éthique du projet de recherche ci-nommé.

L'approbation est valide pour la durée indiquée plus haut et est sujette aux conditions énumérées dans la section intitulée "Conditions Spéciales ou Commentaires". Le formulaire « Renouvellement ou Fermeture de Projet » doit être complété quatre semaines avant la date d'échéance indiquée ci-haut afin de demander un renouvellement de cette approbation éthique ou afin de fermer le dossier.

Toutes modifications apportées au projet doivent être approuvées par le CÉR avant leur mise en place, sauf si le participant doit être retiré en raison d'un danger immédiat ou s'il s'agit d'un changement ayant trait à des éléments administratifs ou logistiques du projet. Les chercheurs doivent aviser le CÉR dans les plus brefs délais de tout changement pouvant augmenter le niveau de risque aux participants ou pouvant affecter considérablement le déroulement du projet, rapporter tout évènement imprévu ou indésirable et soumettre toute nouvelle information pouvant nuire à la conduite du projet ou à la sécurité des participants.

The University of Ottawa Research Ethics Board, which operates in accordance with the *Tri-Council Policy Statement* (2014) and other applicable laws and regulations, has examined and approved the ethics application for the above-named research project.

Ethics approval is valid for the period indicated above and is subject to the conditions listed in the section entitled "Special Conditions or Comments". The "Renewal/Project Closure" form must be completedfour weeks before the above-referenced expiry date to request a renewal of this ethics approval or closure of the file.

Any changes made to the project must be approved by the REB before being implemented, except when necessary to remove participants from immediate endangerment or when the modification(s) only pertain to administrative or logistical components of the project. Investigators must also promptly alert the REB of any changes that increase the risk to participant(s), any changes that considerably affect the conduct of the project, all unanticipated and harmful events that occur, and new information that may negatively affect the conduct of the project or the safety of the participant(s).

Ethics COORDINATOR
Coordonnateur de l'éthique / Ethics Coordinator
Pour/For **Daniel LAGAREC** Président(e) du/ Chair of the **Comité d'éthique de la recherche en sciences de la santé et sciences / Health Sciences and Sciences Research Ethics Board**

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DATA ACCESS AGREEMENT

CLSA Access Agreement

This agreement is entered into this 2 February, 2017 (the "**Effective Date**"), at Hamilton, Ontario.

McMaster University, a University incorporated by special act of the Province of Ontario, Canada, with a main address at 1280 Main Street West, McMaster Innovation Park, Suite 309A, Hamilton, Ontario, Canada, L8S 4K1 ("**McMaster**") is the host institution of the Canadian Longitudinal Study on Aging ("***CLSA***").

AND

University of Ottawa, with a main address at **3042-800 King Edward, Ottawa, Ontario K1N 6N5("Approved User *Institution*")**

WHEREAS:

A. Dr. Parminder Raina (McMaster University) is the Lead Investigator for the CLSA funded by a grant from the Canadian Institutes of Health Research (CIHR) and is responsible for the academic obligations under this Agreement

B. Dr. Ellen Freeman (the "Approved User") is an associate professor at the Institution, where he/she carries or wishes to carry out a study entitled "The Prevalence of Visual Impairment, Its Risk Factors, and Its Consequences in Canada", for which access to CLSA samples or data (or both) will be required.

C. The document titled "CLSA Data and Sample Access Policy and Guiding Principles" attached as Schedule A is an integral part of this agreement. All obligations contained therein are part of this agreement.

The parties hereto agree as follows:

1. Definitions

"Agreement" means this CLSA *Access Agreement.*

"DSAC" means the CLSA's Data and Sample Access Committee.

"**Study**" means the **CLSA Data and/or Biospecimen Request Application** described in Schedule B attached hereto.

"Transferred Materials" means the CLSA data and/or the biological samples described in Schedule B attached hereto.

2. Sample and Data Security.

2.1 Security measures specified in Schedule C attached hereto will apply to all Transferred Materials. The Approved User undertakes to respect these security measures during the Study and afterwards, during storage of Transferred Materials where necessary.

2.2 The Approved User shall agree to the audit of his/her research facility by McMaster to ensure the security and confidentiality of Transferred Materials. These audits may be conducted with reasonable prior notice. Any discrepancies between the security measures specified in Schedule C and what is found at the Institution's research facility will have to be corrected within 60 days of notice by McMaster. The costs associated with these audits will be supported by McMaster.

2.3 Transferred Materials, including any copies thereof, may only be used for the Study described in Schedule B and may not be disclosed, transmitted or shipped to anyone except employees working directly with the Approved User or co-investigators including co-applicants or other personnel from other institution(s), indicated in the Study who will require direct access to the CLSA Data and who agree to be bound by the terms of this Agreement or to persons expressly designated in writing by McMaster. The Approved User shall retain control of the Transferred Material at all times. It is the responsibility of the

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