Functional Status, Postural Stability and Falls among Older Adults with Glaucoma

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The work contained in this thesis has not been previously submitted to meet requirements for an award at this or any other higher education institution.

To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made.

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Abstract

Visual impairment is an important contributing factor in falls among older adults, which is one of the leading causes of injury and injury-related death in this population. Visual impairment is also associated with greater disability among older adults, including poorer health-related quality of life, increased frailty and reduced postural stability. The majority of this evidence, however, is based on measures of central visual function, rather than peripheral visual function. As such, there is comparatively limited research on the associations between peripheral visual function, disability and falls, and even fewer studies involving older adults with specific diseases which affect peripheral visual function, the most common of which is glaucoma.

Glaucoma is one of the leading causes of irreversible vision loss among older adults, affecting around 3 per cent of adults aged over 60 years. The condition is characterised by retinal nerve fibre loss, primarily affecting peripheral visual function. Importantly, the number of older adults with glaucomatous visual impairment is projected to increase as the ageing population grows.

The first component of the thesis examined the cross-sectional association between glaucomatous visual impairment and health-related quality of life (Study 1a), functional status (Study 1b) and postural stability (Study 1c) among older adults. A cohort of 74 community-dwelling adults with glaucoma (mean age 74.2 ± 5.9 years) was recruited and completed a baseline assessment. A number of visual function measures was assessed, including central visual function (visual acuity and contrast sensitivity), motion sensitivity, retinal nerve fibre analysis and monocular and binocular visual field measures (monocular 24-2 and binocular integrated visual fields (IVF): IVF-60 and IVF-120). The analyses focused on the associations between the outcomes measures and severity and location of visual field loss, as this is the primary visual function affected by glaucoma.

In Study 1a, we examined the association between visual field loss and health-related quality of life, measured by the Short Form 36-item Health Survey (SF-36). Greater binocular visual field loss, on both IVF measures, was associated with lower SF-36 physical component scores, adjusted for age and gender (Pearson's r =|0.32| to |0.36|, p<0.001). Furthermore, inferior visual field loss was more strongly associated with the SF-36 physical component than superior field loss. No association was found between visual field loss and SF-36 mental component scores.

The association between visual field loss and functional status was examined in Study 1b. Functional status outcomes measures included a physical activity questionnaire (Physical Activity Scale for the Elderly, PASE), performance tests (six-minute walk test, timed up and go test and lower leg strength) and an overall functional status score. Significant, but weak, correlations were found between binocular visual field loss and PASE and overall functional status scores, adjusted for age and gender (Pearson's r =|0.24| to |0.33|, p<0.05). Greater inferior visual field loss, independent of superior visual field loss, was significantly associated with poorer physical performance results and lower overall functional status scores.

In Study 1c, we examined the association between visual field loss and postural stability, using a swaymeter device which recorded body movement during four conditions: eyes open and closed, on a firm and foam surface. Greater binocular visual field loss was associated with increased postural sway, both on firm and foam surfaces, independent of age and gender (Pearson’s r =|0.44| to |0.46|, p <0.001). Furthermore, inferior visual field was a stronger contributor to postural stability, more so than the superior visual field, particularly on the foam condition with the eyes open. Greater visual field loss was associated with a reduction in the visual contribution to postural sway, which underlies the observed association with postural sway.

The second component of the thesis examined the association between severity and location of visual field loss and falls during a 12-month longitudinal follow-up. The number of falls was assessed prospectively using monthly fall calendars. Of the 71 participants who successfully completed the follow up (mean age 73.9 ± 5.7 years), 44% reported one or more falls, and around 20% reported two or more falls. After adjusting for age and gender, every 10 points missed on the IVF-120 increased the rate of falls by 25% (rate ratio 1.25, 95% confidence interval 1.08 - 1.44) or every 5dB reduction in IVF-60 increased the rate of falls by 47% (rate ratio 1.47, 95% confidence interval 1.16 - 1.87). Inferior visual field loss was a significant predictor of falls, more so than superior field loss, highlighting the importance of the inferior visual field area in safe and efficient navigation.

Further analyses indicated that postural stability, more so than functional status, may be a potential mediating factor in the relationship between visual field loss and falls. Future research is required to confirm this causal pathway. In addition, the use of topical beta-blocker medications was not associated with an increased rate of falls in this cohort, compared with the use of other topical anti-glaucoma medications.

In summary, greater binocular visual field loss among older adults with glaucoma was associated with poorer health-related quality of life in the physical domain, reduced functional status, greater postural instability and higher rates of falling. When the location of visual field loss was examined, inferior visual field loss was consistently more strongly associated with these outcomes than superior visual field loss. Insights gained from this research improve our understanding of the association between glaucomatous visual field loss and disability, and its link with falls among older adults. The clinical implications of this research include the need to include visual field screening in falls risk assessments among older adults and to raise awareness of these findings to eye care practitioners and adults with glaucoma. The findings also assist in developing further research to examine strategies to reduce disability and prevent falls among older adults with glaucoma to promote healthy ageing and independence for these individuals.

Publications and Presentations

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List of Abbreviations

6MW	Six-minute walk
ABS	Australian Bureau of Statistics
ADL	Activities of daily living
AFV	Attentional field of view
AGIS	Advanced Glaucoma Intervention Study
AIHW	Australian Institute of Health and Welfare
BMI	Body mass index
CI	Confidence intervals
COP	Centre of pressure
CS	Contrast sensitivity
dB	Decibel
ICF	International Classification of Functioning, Disability and Health (ICF) framework
IOP	Intraocular pressure
IRR	Incident rate ratio
IVF-60, IVF-120	Integrated visual field (60 degree) / (120 degree)
LLS	Lower limb strength
MCS	Mental component score
OCT	Optical Coherence Tomographer
PASE	Physical Activity Scale for the Elderly
PCS	Physical component score
QOL	Quality of life

RNFL	Retinal nerve fibre layer
SF-36, SF-12	Short-form Health Survey 36-item, 12-item
TUGT	Timed-up and go test
US	United States
VA	Visual acuity
VFQ-25	25- item Visual Function Questionnaire
VIF	Variance inflation factor
VSR	Visual stability ratio
WHO	World Health Organization

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Chapter 1: Introduction

Older adults comprise the fastest growing segment of the Australian population (Australian Bureau of Statistics, 2002), similar to trends in developed countries across the world. Over the next 20 years, a quarter of the population will be aged over 65 years, including a four-fold increase in those aged over 85 years (Australian Bureau of Statistics, 2002). The number of older adults with visual impairment will increase significantly over the coming years, given that the prevalence of visual impairment is strongly associated with increasing age (Wang et al., 2000a; Weih et al., 2000; Australian Institute of Health and Welfare, 2005). This trend is consistent across the developed world, and will dramatically change the patterns of eye disease, visual impairment and blindness in the future. By the year 2020, the World Health Organization estimates that the number of people with visual impairment across the world will double (World Health Organization, 2004). In developed nations, including Australia, the main causes of visual impairment include under-corrected refractive error and eye diseases, primarily cataracts, macular degeneration, glaucoma, and diabetic retinopathy (Wang et al., 2000a; Weih et al., 2000).

Visual impairment causes a high burden of disease and disability among older adults. In particular, visual impairment impacts on an individual's visual, social, physical and psychological functioning, and increases the risk of a number of adverse health outcomes. Epidemiological studies have found significant associations between visual impairment and an increased risk of falls and fractures (Coleman et al., 2007; Freeman et al., 2007; Coleman et al., 2009), frailty (Klein et al., 2003a; Klein et al., 2006), depression (Hayman et al., 2007; Tournier et al., 2008), motor vehicle crashes (Owsley & McGwin, 1999), nursing home placement (Klein et al., 2003b; Wang et al., 2003) and mortality (Freeman et al., 2005; Pedula et al., 2006).

Preserving the health and independence of older adults with visual impairment is a challenge, and strategies are needed to reduce the burden of visual impairment, particularly with the ageing of the population. The burden of visual impairment is highlighted by Javitt et al (2007), who explored the annual health costs based on health claims in over 600,000 adults in the United States between the years 2000 and 2003. Individuals with visual impairment coded in their medical records spent on average USD $3000 more on non eye-related costs each year than those with no vision loss. It was estimated that around one third of these costs were attributed to injury, depression, skilled nursing facility utilisation and admission to long-term nursing care facilities.

Research into the associations between visual impairment and disability or falls have largely focused on general populations or heterogeneous eye-disease groups, with a predominant focus on central visual function. There are, therefore, comparatively few studies that have examined the associations between peripheral visual function and disability or falls, or have involved older adults with specific diseases which affect peripheral visual function, such as glaucoma, which is the leading cause of peripheral visual field loss in the older population (Ramrattan et al., 2001).

Glaucoma is a chronic progressive eye disease, and is a leading cause of irreversible vision loss and blindness among older adults in the Western world (Quigley & Broman, 2006; Leske, 2007). It is estimated to affect around 3 per cent of the Australian population aged 60 years or older (Rochtchina & Mitchell, 2000; Weih et al., 2001), and around 66 million people worldwide, with over 5 million people bilaterally blind from the condition (Gupta, 2005; Quigley & Broman, 2006). Age is a key risk factor for glaucoma, and estimates in the United States indicate that the number of adults with glaucoma will increase by 50 per cent by the year 2020, due to the growth of the ageing population (Friedman et al., 2004). Glaucoma leads to irreversible loss of visual function, affecting peripheral visual function in the early stages of the disease. Owing to this and the slow progression of the disease, around half of the population with glaucoma remains undiagnosed and unaware of their condition (Weih et al., 2001; Friedman et al., 2004).

The purpose of this research was to expand on previous research, which has been very limited in scope, by examining the association between visual impairment and functioning (health-related quality of life, functional status and postural control) and the development of adverse health outcomes (falls) among older adults with glaucoma. This is important, as falls can result in serious physical and psychological consequences. Moreover, this research specifically examined the association between the severity and location of glaucomatous visual field loss and these outcomes, using a range of standardised procedures for measuring central and peripheral visual function.

The International Classification of Functioning, Disability and Health (ICF) framework (World Health Organization, 2001) provides a common language and classification to better understand the complex process in which glaucoma may impact on functioning and disability. In the ICF, human functioning is viewed as the product of the interaction between a person's body functions or structures, activities and participation, influenced also by contextual factors (environmental and personal). The ICF uses *functioning* as the umbrella term to describe positive aspects referring to body functions/structures, activities and participation, while *disability* refers to the negative aspects, referred to as impairments, limitations and restrictions.

The ICF framework, and how it is viewed in the broad context of this thesis, is presented in Figure 1-1. This thesis examines the links between glaucoma and bodily functions and structures, activities and participation, and how disability may lead to other adverse health conditions, in particular falls. The consequences of falls are a frequent and important cause of further disability among older adults, due to their impairment on body functions/structure, activity limitations and participation restriction. Ultimately, falls among older adults with glaucomatous visual impairment has the potential to negatively impact on their health and well-being, increases the risk of mortality, and places heavy demands on the healthcare system. Therefore, the prevention of falls in this population is of paramount importance, with the overall goal being to maintain the capacity of these individuals to live independently and to function well.

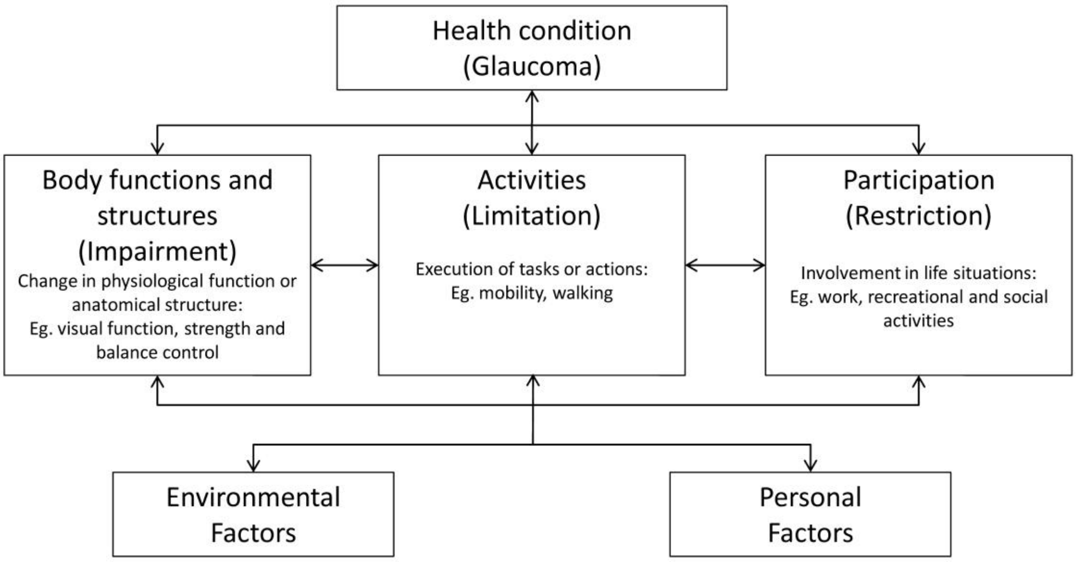

Figure 1-1: Interactions between components of the International Classification of Functioning, Disability and Health (World Health Organization, 2001)

The research outcomes arising from this thesis provides important insights into the association between glaucoma and disability among older adults, and its relationship with falls. The findings also assist in guiding future research to develop strategies to promote and maintain functioning and reduce the risk of falls in this population. The promotion of healthy ageing in populations with visual impairment is critical to maintain or enhance their health, independence and quality of life into older age.

The thesis is structured as follows:

Chapter 2 provides a review of glaucoma and its impact on visual function. This chapter includes a review of the literature which has examined the associations between visual impairment and eye disease on health-related quality of life, functional status, postural stability and falls. A concise review of glaucoma or visual field loss studies is presented, as the introductions of the relevant chapters provide a comprehensive review of this literature.

Chapter 3 describes the study design, procedures used to recruit study participants and common methodology used throughout the thesis. This chapter also reports the baseline socio-demographic, health, medical and visual function characteristics of the study cohort.

The following four chapters present the research examining the association between vision impairment and health-related quality of life (**Chapter 4**), functional status (**Chapter 5**), postural stability (**Chapter 6**), and falls (**Chapter 7**), among the cohort of older adults with glaucoma. Each chapter presents a review of the research pertaining to glaucoma or visual field loss, the outcome measure methodology, and the results and discussion of the findings.

Finally, **Chapter 8** presents an overview and summary of the major findings of the thesis. The strengths and limitations of the research are presented along with the clinical implications of the findings. Recommendations for further research in this area are presented in this chapter.

Chapter 2: Literature Review

2.1 Overview

This chapter provides an overview of the epidemiology of glaucoma, its impact on visual function and current treatments. In addition, this chapter reviews the literature examining the impact of visual impairment from a range of eye diseases on health-related quality of life, functional status, postural stability and falls among older adults, to provide a background to the research. A concise review of studies assessing associations between visual field loss and glaucoma and these outcomes is presented, while a comprehensive review of this literature is provided in the introduction section of the relevant chapters which follow.

Glaucoma is a major cause of irreversible vision impairment (Friedman et al., 2004), and is the leading cause of visual field loss among older adults (Ramrattan et al., 2001). Emerging evidence shows that glaucomatous visual impairment increases the risk of adverse health outcomes, which emphasises the need for further research to better understand the impact of glaucoma on the overall health and well-being of older adults. Bramley et al (2008) retrospectively examined health claims of over 180,000 adults with glaucoma aged over 65 in the United States. Adults with glaucomatous vision loss coded in their medical records were nearly 60 per cent more likely to experience falls, injury and fractures, and were twice as likely to be placed in a nursing home, compared to those with no vision loss.

The pathway in which glaucoma may cause disability among older adults can be illustrated using the ICF framework, outlined in the Chapter 1 (Figure 1-1). Glaucoma results in retinal nerve fibres loss, with subsequent visual impairment, particularly peripheral visual function. This visual impairment may initiate restriction in participation in recreational and social activities due to mobility difficulties. This may lead to subsequent de-conditioning of other body functions, for example muscle function or balance control, resulting in functional limitations and disability. Clearly, this is a complex process which is likely to occur over time, and our current understanding of this is limited. Moreover, a number of these aspects of disability have been identified as risk factors for falls among older adults with visual impairment, which are a frequent and significant cause of further physical and psychological disability in this population.

2.2 Glaucoma

2.2.1 Definition

The term glaucoma refers to a group of diseases with diverse clinical presentations, yet all characterised by progressive optic nerve atrophy leading to irreversible vision loss. Primary open-angle glaucoma is the most common form of the disease, representing around 90% of all cases (Gupta, 2005). Primary open-angle glaucoma differs from other forms of the disease, which include congenital, narrow-angle, pigmentary and secondary glaucoma, as the anterior-chamber angles are open and there is an absence of any other known mechanisms (Gupta, 2005). To avoid confusion, the term glaucoma will refer to the primary-open angle form of the condition for the remainder of this thesis. In glaucoma, the progressive degeneration of retinal ganglion cells leads to nerve fibre layer loss, characteristic optic disc changes and often reduced visual field sensitivity. Like many eye diseases, the clinical picture of glaucoma can differ between affected individuals in terms of the extent of structural and functional vision loss, treatment modalities and symptoms.

The diagnosis of glaucoma involves assessment of the structural characteristics of the optic nerve head, measurement of intraocular pressure (IOP), and assessment of central and peripheral visual function using standard automated perimetry. Although raised IOP is an important risk factor for glaucoma, patients can still present with IOP within the statistically normal range, known as normal-tension or low-tension glaucoma (Shields, 2008). Irrespective of IOP, the disease is diagnosed by the presence of structural changes at the optic nerve head and/or functional perimetric visual field defects. Changes in optic nerve head structure and appearance are generally believed to precede reductions in visual field sensitivity (Quigley et al., 1982; Kerrigan-Baumrind et al., 2000), although this is not always the case. Recent advances in imaging technologies allow for objective and quantitative structural assessment of the retinal nerve fibres entering the optic nerve head, using non-invasive optical techniques, such as optical coherence tomography. The glaucomatous loss of neural axons results in thinning of the retinal nerve fibre layer, and the extent and location of these defects have been shown to correlate quantitatively with peripheral visual function (Bowd et al., 2006; Ajtony et al., 2007).

2.2.2 Epidemiology and risk factors

According to Australian studies, it is estimated that around 3 per cent of the population aged 60 years or older have glaucoma, and these studies predict that over 300,000 Australians will have glaucoma by the year 2030 (Rochtchina & Mitchell, 2000; Weih et al., 2001). The prevalence of glaucoma in Australia is similar to other developed countries. Estimates in the United States suggest that glaucoma affected more than 2 million individuals in the year 2004, and that this number will increase by 50 per cent by the year 2020 (Friedman et al., 2004). The marked rise in numbers can be attributed to the ageing of the population, in addition to advances in diagnostic technology for glaucoma detection.

A major concern is that the rate of undiagnosed glaucoma remains high, even in developed countries including Australia. In various population studies, around half of the participants who have glaucoma are undiagnosed and therefore unaware that they have the disease (Tielsch et al., 1991; Mitchell et al., 1996; Weih et al., 2001; Friedman et al., 2004). The rate of undiagnosed glaucoma in the Los Angeles Latino Eye Study was 75%, which also raises concerns about the provision of eye-care services to various socio-economic and ethnic populations (Varma et al., 2004). In a European longitudinal study, only 37 per cent of adults with glaucoma detected at the 5

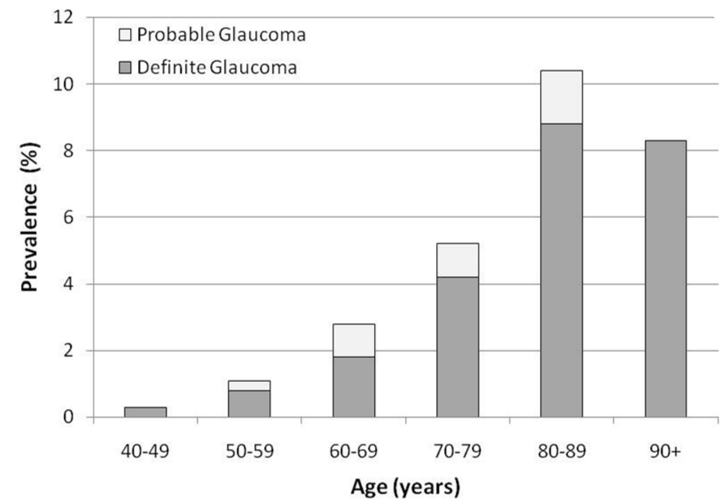

Figure 2-1: The prevalence of glaucoma in Australia, data from Weih et al (2001)

year follow-up examination were receiving treatment (de Voogd et al., 2005). A considerable amount of research continues to examine strategies to increase the early detection and treatment of glaucoma, which will assist in reducing the numbers of older adults with severe glaucomatous visual impairment.

Age is associated with an increased risk of developing glaucoma. In Australian studies, the prevalence of glaucoma rises from around 2 per cent in those aged 60 to 69 years to around 8 per cent in those aged 80 years and older (Rochtchina & Mitchell, 2000; Weih et al., 2001), as shown in Figure 2-1. Similarly, 5 year incidence of glaucoma in both Australian and European studies increases from around one per cent of adults aged 40 to 49 years to between three and 11 per cent in those aged 80 years and older (Mukesh et al., 2002; de Voogd et al., 2005).

There are a number of additional factors associated with the development of glaucoma. A meta-analysis by Rudnicka (2006) reported that men were more likely than women to have glaucoma. There may be a protective role of oestrogens in the prevention of glaucoma, but the evidence remains unclear (de Voogd et al., 2008). Other risk factors for glaucoma include a family history of the disease, which increases the risk four-fold (Tielsch et al., 1994). Racial variations have also been reported, as the prevalence of glaucoma is

3 to 6 times higher in African Americans than in whites (Weinreb & Khaw, 2004; Wadhwa & Higginbotham, 2005; Rudnicka et al., 2006). Research also suggests a systemic vascular role for the development of glaucoma, which may relate to vascular perfusion to the optic nerve head, as associations have been reported with systemic hypertension (Tielsch et al., 1995; Muskens et al., 2007; Leske et al., 2008) and diabetes (Bonovas et al., 2004).

2.2.3 Impact of glaucoma on visual function

The progressive degeneration of retinal nerve fibres from glaucoma leads to reductions in visual function, and the extent of nerve damage determines the severity of visual function loss. Primarily, glaucoma results in the reduction in peripheral visual field sensitivity and is the leading cause of visual field loss in the older population (Ramrattan et al., 2001). In its early stages, reduced visual field sensitivity often goes unnoticed by the patient, and can be asymptomatic until it encroaches on central vision. Owing to this and the gradual progression of the disease, a significant proportion of the population with glaucoma is undiagnosed and remains unaware of their condition (Weih et al., 2001; Friedman et al., 2004). Central vision can also be affected in advanced stages of glaucoma, resulting in loss of visual acuity, contrast sensitivity and depth perception. There is evidence that other visual functions may be affected by glaucoma, such as motion sensitivity. The following sections outline the impact of glaucoma on these visual functions.

2.2.3.1 *Peripheral visual function*

Visual field sensitivity is the primary visual function affected by glaucoma, and the use of computerised automated perimetry is the accepted standard for assessing visual field sensitivity. Conventional white-on-white perimetry measures light detection thresholds (in decibels) at various locations across the visual field, using a white stimuli on a white background. Other perimetry strategies have been reported to detect glaucoma earlier than conventional white-on-white perimetry, such as short wavelength automated perimetry

(Bengtsson & Heijl, 2006) and frequency doubling technology (Sample et al., 2000), but these strategies are less widely used in clinical practice. In the clinical setting, visual field sensitivity is frequently measured within the central 30 degree radius from fixation, although a wide variety of programs and strategies are available. Areas within the visual field where sensitivity is reduced, relative to age-matched levels, are referred to as visual field defects. The extent or depth of visual field defects can range from early loss of sensitivity (relative defect) to total loss of sensitivity (absolute defect). Severity of glaucomatous visual field loss is often reported using the average difference across the field from age-matched sensitivity, known as the mean deviation.

The early stages of glaucoma result in either superior or inferior hemifield defects, in the form of paracentral, nasal step or arcuate defects, which reflect the unique anatomical distribution of the retinal nerve fibres. With progression of the disease and greater loss of retinal nerve fibres, the extent and depth of visual field defects increase and can extend across both superior and inferior hemifields. In a study of 245 glaucoma patients, Hoffman et al (2006) reported a slight predominance for defects to occur in the superior hemifield compared to inferior hemifield (40% and 30%, respectively), as it is believed that the inferior optic nerves are structurally more susceptible to glaucomatous damage. It was also found that visual field defects between eyes more often corresponded within the same hemifield, compared to opposite hemifields. A study by Lee et al (2003), however, showed little variation in the distribution of superior and inferior hemifield defects, when the visual field defects in the worse eye of 104 glaucoma patients were examined. Around 29% had superior field defects, 32% had inferior field defects, and 39% had combined superior and inferior defects.

2.2.3.2 *Central visual function*

More advanced glaucoma results in reductions in central visual function due to loss of central retinal nerve fibres. Visual acuity is a measure of resolution thresholds for high-contrast, high spatial frequency targets, and is the most commonly measured central vision function. In a study of 113 glaucoma patients, Sukumar et al (2009) reported significant correlations between visual acuity and visual field 24-2 mean deviation (r=-0.43).

Contrast sensitivity is also impaired with more advanced glaucoma. Contrast sensitivity is a measure of contrast thresholds across a range of spatial frequencies, with a peak threshold around 4 cycles per degree (Schwartz, 2004). There are various techniques for measuring contrast sensitivity, most of which measure central contrast sensitivity near the peak of the contrast sensitivity function. Hawkins et al (2003) reported significant correlations between Pelli-Robson letter contrast sensitivity and visual field 24-2 mean deviation (r=0.57) among 144 adults with glaucoma. Significant, but weaker, correlations were found between visual acuity and mean visual field sensitivity (r=-0.32).

2.2.3.3 ***Additional visual functions***

Glaucoma is also reported to affect other visual functions. Studies have shown that stereoacuity is impaired in participants with glaucoma (Essock et al., 1996; Gupta et al., 2006), most likely due to asymmetries in visual field loss between eyes leading to changes in cortical binocular neural processing. In an experimental study using visual evoked potentials, adults with glaucoma were shown to have impairment in stereoscopic vision compared to control subjects (Bergua et al., 2004). Recently, glaucoma patients were shown to exhibit significant deficits in eye–hand coordination compared with the age-matched normally sighted controls (Kotecha et al., 2009).

Motion sensitivity may also be impaired among glaucoma patients. Glaucoma has been reported to preferentially affect the motion sensitivity neural pathways (Falkenberg & Bex, 2007), and motion sensitivity may be a promising diagnostic measure in the early detection of glaucoma (Bullimore et al., 1993). McKendrick et al (2005) showed significant impairments in motion sensitivity in areas of the visual field, classified as normal by conventional perimetry, among adults with glaucoma. Their findings suggest that the pathways controlling motion detection are preferentially affected by glaucoma, prior to changes in other visual functions. These studies, however, remain experimental and comparisons between studies are difficult due to the variety of motion sensitivity tests used (Shabana et al., 2003).

2.2.4 Treatment

Current medical and surgical treatments for glaucoma are centred on lowering IOP, which is currently the only proven treatable risk factor in slowing the progression of glaucoma (Heijl et al., 2002). The primary goal of treatment is to preserve remaining vision by preventing further retinal nerve fibre degeneration and visual field loss. There are no known preventative measures for glaucoma, but early detection and treatment reduces the risk of disease progression (Burr et al., 2007).

Topical medications are usually the first stage of treatment to reduce intraocular pressure (Friedman et al., 2005), which act on either decreasing the formation of aqueous humour or increasing the draining of aqueous humour in the eye. Until recently, beta-blockers were the most commonly prescribed medications (Weih et al., 1998; Kirwan et al., 2002), but there is a shift towards newer topical medications, such as the prostaglandin analogues and alpha adrenergic agonists. Recent studies in Europe and the US show that more than half of the topical glaucoma treatments include these newer medications (Strutton & Walt, 2004; van der Valk et al., 2005). But the use of topical beta-blockers is still widespread and is unlikely to discontinue as they are often used in conjunction with the newer classes of medications, especially in those whose glaucoma cannot be adequately controlled with a single medication. For example, around 70 per cent of all participants in a UK study were using at least one prostaglandin analogue, 50 per cent were using at least one topical beta-blocker, and 25 per cent were using both agents (Tattersall et al., 2006).

The topical medications used to lower IOP are not without potential systemic side effects, which can include fatigue, dizziness or sedation (Novack et al, 2002). These medications are systemically absorbed through the highly vascular tear drainage system. Up to 80% of the active ingredient has been reported to reach the systemic circulation (Labetoulle et al., 2005), due to large drop volumes and high doses of the active ingredients. The chronic nature of glaucoma may result in long-term systemic exposure to these active ingredients.

Of the currently available topical treatments, topical beta-blockers are reported to have considerable side-effects that can impact on the health and well-being of users. Topical beta-blockers act by decreasing the formation of aqueous humour in the eye which reduces the IOP, but systemic absorption can also act on the heart tissue receptors and bronchial tissue receptors (Tattersall et al., 2006). Topical beta-blocker use results in bradycardia, lowering the heart rate in the resting state (Tattersall et al., 2006) and during exercise (Nieminen et al., 2005), which has the potential to reduce blood oxygen levels, increasing fatigue, dizziness and risk of syncope. In addition, topical beta-blocker use has been shown to result in increased bronchial constriction and reduced airflow, which may not be completely reversible on withdrawal of the medication (Gandolfi et al., 2005), and can lead to increased fatigue and dizziness. Even selective topical beta-blockers, which are reported to have fewer bronchial side-effects, have been linked to the risk of airway obstruction in patients with no previous respiratory history (Kirwan et al, 2004).

Glaucoma can also be treated using surgical and laser procedures, including trabeculotomies and trabeculectomies, which reduce IOP by artificially increasing drainage of the aqueous humour through the trabecular meshwork by means of laser or surgical tissue removal. These procedures are commonly performed on patients who exhibit poor response, tolerance or compliance with medical therapy (Gaskin et al., 2006). These procedures, however, are not always successful and are not without adverse effects (AGIS Investigators, 2002). Trabeculectomy procedures are associated with increased risk of cataract formation (AGIS Investigators, 2001), and many patients remain on long-term topical medications following these procedures (Ederer et al., 2004).

While the majority of patients with glaucoma are successfully treated and retain good vision throughout the remainder of their life, disease progression still occurs in up to 20% of patients (Chen, 2003; Zahari et al., 2006; Musch et al., 2009). The success of glaucoma treatment depends on patient compliance, and often the compliance and adherence to treatment among glaucoma patients is low (Deokule et al., 2004; Shaw, 2005). Compliance can be a challenge for glaucoma patients, as the disease often requires lifelong topical medical therapy, regular eye examinations to monitor intraocular pressure, optic disc appearance and visual fields, and can be relatively asymptomatic, especially in its early stages (Kulkarni et al., 2008). In addition, poor adherence to glaucoma topical medications has been linked to a range of factors, some of which include low patient education, cost of medications and side effects (Friedman et al., 2008).

2.3 Health-related quality of life (QOL)

There are many diseases or health conditions, including eye diseases, that can affect a person's health-related quality of life (QOL), which refers to "the extent to which patients' perceived physical and mental functioning is affected on a day-to-day basis by a chronic disease" (Centers for Disease Control and Prevention). Health-related QOL encompasses aspects of physical, emotional and social functioning, and is an important component of older adults' overall quality of life (Bowling, 2005), and is fundamental to successful ageing (Spirduso et al., 2005). With the predicted rise in the number of older adults living with glaucoma, it is important to characterise the personal burden of the disease by understanding of how glaucomatous visual impairment affects the health-related QOL of older adults.

Interest in general health-related QOL measures in health research has led to the development of questionnaires which examine the physical, emotional and social aspects associated with a disease. These multidimensional instruments measure the impact of health problems on general health status, and allow for a common metric to compare between different diseases. A number of well validated, generic health-related QOL instruments are available, which have been used across a wide range of populations and disease groups, such as the Short-Form 36-Item and 12-Item Health Survey (SF-36, SF-12) and the Euro-QOL (EQ-5D).

These generic health-related QOL measures differ to vision- or disease-specific QOL questionnaires. Vision-specific QOL questionnaires assess the impact of an eye disease on vision-related tasks, and examples of these include the Activities of Daily Vision Scale, Vision Activity Questionnaire, National Eye Institute Visual Function Questionnaires (VFQ-51, VFQ-25), and Impact of Visual Impairment Instrument (Spaeth et al., 2006). Glaucoma-specific instruments have also been developed, particularly for use in glaucoma clinical trials to examine treatment or intervention effects on quality of life (Janz et al., 2001). Example of these include the Glaucoma Symptom Scale, Glaucoma Quality of Life and the Glau-QoL (Spaeth et al., 2006). Compared to the generic health-related QOL instruments, these vision- or glaucoma-specific instruments tend to be more sensitive to changes in visual function, given their emphasis on vision-related tasks.

The impact of visual impairment on vision- or disease-specific QOL has been well documented in the literature. Compared to normally sighted individuals, those with visual impairment report poorer vision-specific QOL, based on central vision loss (Globe et al., 2004; Chia et al., 2006a; Varma et al., 2006) or visual field loss (Gutierrez et al., 1997; Sherwood et al., 1998; McKean-Cowdin et al., 2007; Freeman et al., 2008b). Similarly, greater severity of visual impairment has been associated poorer vision-specific QOL, according to central visual function (Valbuena et al., 1999; Mangione et al., 2001; Chia et al., 2006a) or peripheral visual function (Gutierrez et al., 1997; Mangione et al., 2001; Jampel et al., 2002a; McKean-Cowdin et al., 2007).

As a considerable amount of research has examined the impact of visual impairment on vision- and disease-specific QOL among adults with glaucoma, this area is not explored in this thesis. The purpose of this research, however, was to examine the association between visual impairment and general health-related QOL among older adults with glaucoma. Previous research has not focused on older adults with glaucoma, and the association between visual impairment and health-related QOL in this population has not been well described.

2.3.1 Visual impairment and health-related QOL

Visual impairment can negatively impact on aspects of general health-related QOL, such as physical, emotional and social functioning (Chia et al., 2004; Langelaan et al., 2007). There are a number of reasons for this, including the diagnosis itself, the loss of visual function, and the costs, inconvenience and side-effects associated with treatment (Severn et al., 2008). This is not surprising, given that many daily activities which are central to the lives of older adults are highly dependent on vision, for example reading, walking, driving and participating in social and recreational activities.

The impact of visual impairment on health-related QOL is comparable to that of other major medical conditions. Chia et al (2004) compared age and sex standardised physical and mental component SF-36 summary scores with a range of medical conditions. The impact of visual acuity loss on the mental health domain was greater than that of diabetes, stroke or arthritis. Although the impact of visual acuity loss on the physical domain was milder, its effect was similar to that of arthritis, asthma and diabetes. Langelaan et al (2007) assessed general health-related QOL, using the EuroQol (EQ-5D) questionnaire, among 128 adults with a range of eye diseases attending a low-vision clinic. The health-related QOL in this population was poorer compared to other chronic conditions such as diabetes, coronary syndromes, and hearing impairments.

It can be difficult, however, to establish if decrements in health-related QOL among older adults with visual impairment are due to their vision loss or other co-morbidities, particularly as they often report concomitant co-morbidities (van Nispen et al., 2009). Furthermore, there may be common underlying risk factors or ageing markers between visual impairment and co-morbidity, as research has reported links between many sensory deficits, for example visual impairment and hearing impairment (Chia et al., 2006b). Previous research, however, has demonstrated significant associations between vision impairment and health-related QOL, even following adjustment for other potential factors which may influence health-related QOL in older populations (Wang et al., 2000b; Chia et al., 2004).

There is clear evidence that central vision loss is associated with poorer health-related QOL among older adults. In a study of 3,154 adults aged 49 years and older, participants with non-correctable bilateral visual acuity loss (n=66) reported poorer scores on most SF-36 subscales and the mental component score, compared to those with good visual acuity, even after adjustment for demographic and medical factors (Chia et al., 2004). The SF-36 physical component scores were lower in those with visual acuity loss compared to those with good visual acuity; however, this failed to reach statistical significance. Similar trends were noted in an earlier study which examined the health-related QOL among adults with moderate to severe non-correctable unilateral visual acuity loss (n=79), although the associations were weaker compared to those with bilateral visual acuity loss (Chia et al., 2003). This suggests that bilateral visual impairment has a stronger impact on health-related QOL than unilateral visual impairment. In another study, Wang et al (2000b) reported that adults with reduced visual acuity in the better eye were more likely to report low self-rated health, assessed by a single question rating their overall health (excellent, good, fair, or poor).

There are studies, however, that have found no association between health-related QOL and central vision loss. Varma et al (2006) found that participants with moderate to severe bilateral visual acuity loss (n=101), defined as worse than 6/24, reported lower SF-12 physical and mental component summary scores, but these were not statistically different from those with no vision impairment (n= 4,272). The lack of significant findings may be due to their relatively young cohort (mean age 55 years), compared to Chia et al (2004) (mean age 67 years), as age is strongly associated with poorer health-related QOL (Chia et al., 2003).

Central vision loss also negatively impacts on the psychological well-being of older adults. In a study of adults aged 75 years and older with visual acuity of 6/24 or worse, nearly one in three were identified as potentially depressed

(Hayman et al., 2007). Tournier et al (2008) examined clinical coded records among older adults aged 65 years and older, and found that adults diagnosed with either moderate visual impairment, severe vision impairment or blindness were more likely to suffer with depression compared to those with no visual impairment.

Studies have also reported significant associations between health-related QOL and vision-related QOL measures. Swamy et al (2009) found that older adults with lower VFQ-25 also reported lower SF-36 physical and mental summary scores, although these correlations were not strong (r=0.30 and 0.26, respectively). Similarly, Mangione et al (1998) reported significant correlations between the majority of the VFQ-51 subscales and SF-36 physical and mental summary scores, but these correlations were generally low (r<0.3). These studies indicate that health-related QOL measures are different from, and independent of, vision-related QOL measures, yet there are some aspects that overlap between the two measures.

2.3.2 Visual field loss and health-related QOL

Research has shown that adults with visual field loss report poorer health-related QOL, compared to those with normal vision. This association has been confirmed in population studies comprising adults with visual field loss from any cause (McKean-Cowdin et al., 2007) and glaucoma (McKean-Cowdin et al., 2008). Small clinical studies also report similar findings (Sherwood et al., 1998; Wilson et al., 1998).

There is, however, inconsistent evidence regarding whether severity of visual field loss is associated with poorer health-related QOL. McKean-Cowdin et al (2007) found that greater visual field loss from any cause, using the mean deviation score in the better-eye, was significantly associated with lower SF-12 physical and mental component scores in their cohort of 5,213 adults aged over 40 years. This relationship, however, was not confirmed in a follow-up study when analyses were confined to 213 participants with glaucoma (McKean-Cowdin et al., 2008). Some clinical studies have reported weak correlations between severity of visual field loss and health-related QOL (Parrish et al., 1997; Iester & Zingirian, 2002), whereas others have not found any such association (Jampel et al., 2002a; Jampel et al., 2002b).

A limitation in these studies is the limited focus on older adults, even though older adults are particularly susceptible to more chronic conditions and health problems than their younger counterparts. As such, the association between glaucomatous visual impairment and health-related QOL among older adults has not been well described. A detailed review and discussion of this literature is presented in Chapter 4, along with the rationale for the research.

2.4 Frailty and functional status

Visual impairment has also been linked with frailty among older adults, which is an important clinical and public health challenge. While there is no accepted definition of frailty, it is often described as a syndrome of declining physiological reserves, with associated loss of functional abilities and further illness and disability (Puts et al., 2005; Ensrud et al., 2007; Fairhall et al., 2008). The condition is characterised by observable functional declines in the body, particularly weight loss, exhaustion, low energy expenditure, slowness and weakness (Ensrud et al., 2007; Rockwood et al., 2007; Fairhall et al., 2008). Frailty increases vulnerability to a number of adverse outcomes, particularly falls (Ensrud et al., 2007), fractures (Ensrud et al., 2007), hospitalisation (Cesari et al., 2009) and institutionalization (Fried et al., 1998; Rockwood et al., 2007).

Moreover, frailty has been linked to increased risk of mortality among older adults. In the Beaver Dam Study, frailty among older adults, defined by poor physical function, was associated with increased mortality over the 4 years of the study (Klein et al., 2005a). Similarly, adults classified as frail in the Cardiovascular Health Study had an increased risk of mortality when compared to non-frail adults (Fried et al., 1998). Cesari et al (2009) recently reported that poor results on physical performance tests, including timed gait and repeated chair stands, were predictive of mortality during the 7 year follow-up of 3,024 well-functioning adults aged over 70 years.

While the prevalence of frailty varies according to different frailty definitions, approximately 50% of adults aged over 65 years show some signs of frailty. Like most health conditions, there is a spectrum of frailty, ranging from early (pre-frail) to more advanced levels. Functional or capability measures are used as indicators or markers of frailty, and the presence of multiple markers is often used to classify frail adults. The Cardiovascular Health Study, comprising of adults aged 65 years and older, defined frailty as three or more of the following markers: weight loss, muscle weakness, poor endurance/energy, slowness and low physical activity (Fried et al., 2001). In their study, 7 per cent of the cohort exhibited 3 or more frailty criteria, 47 per cent between 1 and 2 criteria and 46 per cent had none. Using similar markers of frailty, the Canadian Study of Health and Aging, comprising of adults aged 70 years and older, found that 17 per cent were considered to be frail and 36 per cent as pre-frail (Rockwood et al., 2007). It is possible that the true prevalence rate of frailty may be even higher, as cross-sectional studies are likely to under-report the rates of frailty, as frail, ill participants tend be under-represented in these studies.

Age is strongly associated with an increased prevalence of frailty. In the Cardiovascular Health Study, the prevalence of frailty increased from 4% in those aged 65 to 74 years, to 25% among those aged 85 years and older (Fried et al., 2001). In a study of 9,704 older women aged 65 years and older, the prevalence of impaired self-reported function, defined as difficulty performing three or more activities of daily living, was approximately four times higher in women 85 years or older than in those aged 65 to 69 years (Ensrud et al., 1994).

Reduced physical function is an important underlying component of frailty, and correlates significantly with greater functional limitations and disability among older adults (Guralnik et al., 2000; McAuley et al., 2007). Sarcopenia, which is the loss of skeletal muscle mass and strength that occurs with age, underlies the resulting weakness, exhaustion, slowness and low physical activity among frail adults (Spirduso et al., 2005). Physical activity and exercise may postpone or reverse the effects of sarcopenia, given the associated improvement in muscle mass and strength (Roubenoff, 2000; Snijders et al., 2009). Deshpande et al (2008) found that activity restriction among older adults significantly predicted disability in the performance of daily living tasks and lower extremity physical function over a period of three years. As such, early detection and prevention of frailty may be an important measure to improve health and well-being among older populations.

Physical activity had been shown to improve functional capacity and delay the onset of frailty among older adults (Keysor, 2003; Spirduso et al., 2005; Pahor et al., 2006), as well as providing other positive health outcomes including reduced risk of cardiovascular disease, some cancers and depression (World Health Organization, 2003). Furthermore, physical activity decreases the risk of chronic disease morbidity, which is a major risk factor for disability (Penedo and Dahn, 2005). Conversely, physical inactivity is known to be a risk factor for further disability (Mor et al., 1989; Boyle et al., 2007), predicts declines in mobility performance (Buchman et al., 2007) and is associated with increased mortality (Landi et al., 2008). Physical inactivity was estimated to have caused 6 per cent of the total disease burden among Australian males and 8 per cent among females in 1996 (Mathers et al., 1999).

2.4.1 Visual impairment, frailty and functional status

Cross-sectional population studies have demonstrated significant associations between visual impairment and functional status or frailty. Klein et al (2003a) reported that older adults with reduced visual acuity or contrast sensitivity, compared to those with good vision, were more likely to be frailer, based on a number of frailty markers (gait time, peak expiratory flow rate, handgrip strength, chair stand). In a study of 2,781 older adults, those with impaired visual acuity demonstrated lower levels of functional performance for various performance measures, which included walking speed, chair stands, stair climbs and standing balance, compared to those with good visual acuity (Laitinen et al., 2007).

The ability to carry out activities of daily living (ADL), which correlates with physical function (McAuley et al., 2007), is reduced among adults with visual impairment. In a study of 9,704 older white women, Ensrud (1994) showed that those with poor visual acuity were more likely to report disability, defined as difficulty in performing three or more functional activities. Similarly, West (1997) found that binocular visual acuity loss, worse that 6/12, was significantly associated with self-reported reduction in social activities, ADL and mobility among 2,520 older men and women.

Research has also shown that vision impairment predicts further functional decline in older adults. Wallhagen (2001) reported that older adults with moderate or greater levels of self-reported vision impairment were more likely to report declines in self-rated health, difficulties with activities of daily living and physical performance difficulties at a 12 months follow up. Similarly, Lin (2004) showed that reduced visual acuity at baseline, defined as worse than 6/12 binocularly, was significantly associated with functional decline 4 years later, based on self-reported abilities on activities including walking, climbing stairs, preparing meals, shopping, and doing housework.

Frailty has been linked to a number of eye diseases. Klein et al (2006) reported that the presence of age-related cataracts was associated with frailty measures (gait time, peak expiratory flow rate, handgrip strength, chair stand), even after controlling for visual acuity loss and systemic co-morbidities. This suggests that visual functions other than visual acuity are associated with frailty. In a similar study, weaker handgrip strength was associated with age-related macular degeneration (AMD) in men, but no associations were found for women (Klein et al., 2005b). No other measures of frailty, such as gait time, peak expiratory flow rate, and chair stand, were associated with AMD in either men or women.

There is evidence that visual field loss is associated with functional limitations among older adults, based on physical health-related QOL measures. As reported earlier in this review, participants with visual field loss from any cause reported poorer physical health-related QOL, measured by the SF-12, compared to those with no visual field loss (McKean-Cowdin et al., 2007). However, no association between SF-12 physical function and glaucomatous visual field was found in a follow-up study (McKean-Cowdin et al., 2008).

Few studies, however, have examined the association between functional performance measures and visual field loss or glaucoma. In a case-control study assessing falls and driving outcomes, the mean “timed up and go” times for the glaucoma participants were significantly slower than the age-matched controls (Haymes et al., 2007), although no differences were noted for self-reported physical activity levels. In a population study examining mobility performance, stair climbing speed among older participants with bilateral glaucoma was slower than those without glaucoma, but these differences were not statistically significant (Friedman et al., 2007). A detailed discussion of studies examining associations between glaucoma, visual field loss and functional status is provided in Chapter 5.

Physical activity can improve functional capacity among older adults (Keysor, 2003; Spirduso et al., 2005), yet little is known about the impact of visual impairment on physical activity among older populations. Furthermore, the relationship between physical activity and visual field loss remains unknown, as there is no previous research in this area. Visual impairment may be a barrier for participating in physical activity, due to difficulties in safe navigation and obstacle avoidance. Activity restriction may lead to physical de-conditioning, reduced functional status and ultimately frailty. Further research is required to better understand this potential pathway.

Physical activity programs among visually impaired populations, however, may be problematic and even possibly harmful. Campbell et al (2005) examined whether a strength and balance training programme was beneficial in reducing falls among community dwelling adults (aged 75 years and older) with visual acuity of 6/24 or worse. The exercise programme, which the authors had previously shown to be of benefit among general community dwelling groups, was not successful in reducing the rate of falls in this population. In fact, the rate of falls was greater in those receiving the exercise programme, although not significantly so.

Functional status may play a role in mediating the relationship between vision impairment and mortality among older adults, which is well established in the literature (Klein et al., 1995; McCarty et al., 2001; Freeman et al., 2005; Knudtson et al., 2006; Pedula et al., 2006; Cugati et al., 2007). Vision impairment has been linked with functional status declines (Klein et al., 2003a; Klein et al., 2006), and reduced functional status or frailty are also associated with an increased risk of mortality (Fried et al., 1998; Klein et al., 2005a). It is also possible that visual impairment and frailty may share a common biological or ageing factor.

Recent studies provide some insights into possible underlying factors in the relationship between vision impairment and mortality. Using US National Health Survey and mortality data (n=135,581), Christ et al (2008) reported that severe self-reported visual impairment was directly associated with an increased risk of mortality compared with no vision impairment. In addition, structural equation models found that reduced physical function, based on self-reported physical disability and health, was a significant mediating factor between visual impairment and mortality. In another recent study, disability in walking demonstrated a significant indirect pathway for the association between visual impairment and mortality, using structural equations modelling techniques in a cohort of 3,654 adults aged over 49 years (Karpa et al., 2009). Despite some of the limitations in these studies, they provide valuable insights into the potential pathways which may lead to mortality in visually impaired populations.

2.5 Postural stability

2.5.1 Postural sensory systems

The maintenance of postural stability is a highly complex skill which ensures the body remains upright during standing and walking activities. Postural stability is defined as the ability to maintain the position of the body within stability limits, which vary according to task complexity (Lord et al., 2007). For example, the limits of stability when standing with two feet on the ground are greater than when standing with only one foot on the ground. When the body's centre of mass extends beyond the stability limits, then overbalancing or even falling is likely to occur.

The regulation of postural stability relies on a complex sensorimotor control system resulting from the integration of three sensory systems in the central nervous system: the visual, vestibular and somatosensory (lower-limb, neuromusculo-skeletal) systems. This control system generates appropriate motor responses based on the input from these sensory systems to quickly and accurately respond to balance perturbations. The postural control system works under continually changing task and environmental conditions, for example changes in movement and direction, and variations in lighting and flooring conditions. As a result, the relative contribution to postural control of the three sensory systems changes according to the environmental conditions. For example, maintaining stability on an unstable surface requires greater visual and vestibular contribution due to lowered somatosensory input, while maintaining stability under dim lighting conditions requires greater vestibular and somatosensory contribution due to reduced visual input (Lord et al., 1991). Importantly, if the remaining sensory systems are unable to compensate due to particular sensory impairments, then the ability to effectively maintain postural stability becomes increasingly difficult.

2.5.2 Assessment of postural stability

Assessment of postural stability determines the capacity of an individual to maintain their centre of mass within their limits of stability. Researchers have used a wide range of techniques to assess postural stability, ranging from high-tech laboratory-based measures, such as electronic force plates measuring the centre of pressure (COP) displacement, to low-tech clinical-based measures, such as measuring the ability to perform standing balance tests. In addition, postural stability can be measured under various conditions, including stationery upright stance, leaning tasks, stepping tasks or even during postural stress tests which assess postural responses to external perturbations (Lord & Menz, 2002; Piirtola & Era, 2006; Lord et al., 2007).

No one sway measure completely reflects the complex nature of postural stability, due to the many inherent intrinsic and extrinsic factors which contribute to the variability of these measures (Hageman et al., 1995). Depending on the technique, deficits in the postural control system may be reflected in greater amounts of postural sway while performing balance tasks, or the inability to perform standing balance tests, although there is a lack of standardised test protocols and outcomes measures between studies (Era et al., 2006). For example, studies using electronic force plates report changes in COP displacement as an indicator of balance, yet there is little consistency in the outcomes measures reported. Commonly used measures include the amplitude, mean, root-mean-square and speed of the mediolateral (ML) and anteroposterior (AP) COP displacement, as well as path length and area of COP displacement (Piirtola & Era, 2006). Studies that comprise of standing balance tests use the ability to perform tasks of increasing difficulty as an indicator of balance performance (Freeman et al., 2008a), but these measures can have marked ceiling effects among adults younger than 60 years of age (Era et al., 2006).

2.5.3 Postural stability and ageing

Normal ageing increases postural sway due to declines in the sensory systems which mediate postural control (Manchester et al., 1989; Woollacott, 2000; Era et al., 2006), along with changes in the efficacy of the central nervous system to integrate this sensory information (Manchester et al., 1989). In the visual system, normal ageing results in reductions in visual function (Haegerstrom-Portnoy et al., 1999) due to an estimated loss of around 5% of optic nerve fibres per decade of life (Sing et al., 2000). The somatosensory system also experiences neuromuscular changes, particularly reductions in muscle mass (Hughes et al., 2001) and neural awareness or proprioception (Shaffer & Harrison, 2007). Similarly, vestibular function becomes impaired with age, with an estimated 20% loss of vestibular ganglion neurons by the age of 60 years (Park et al., 2001). Lastly, ageing is associated with changes in the neural pathways, particularly slowing of reaction times, which can result in delays in awareness and reactions to postural perturbations (Callisaya et al., 2009).

Furthermore, a number of diseases have been reported to impair postural stability among older adults, due to further impairment of the postural sensory systems. For example, postural stability is reduced among adults with visual impairment, such as cataracts (Schwartz et al., 2005) and macular degeneration (Wood et al., 2009). Similarly, adults with significant vestibular impairment demonstrate greater postural instability compared to controls (Sturnieks et al., 2008). Postural stability is also significantly impaired in conditions which affect lower limb sensation and motor control, such as diabetes (Sturnieks et al., 2008) and Parkinson's Disease (Contin et al., 1996).

2.5.4 Consequences of postural instability

There are important consequences of postural instability, the most serious of which are falls. Individuals with greater postural instability are more likely to fall due to the inability to recover from postural perturbations or maintain balance during difficult balance situations. Cross-sectional studies, which classify fallers and non-fallers based on their previous falls history, have shown that fallers demonstrate greater amounts of sway compared to non-fallers. Cho et al (2004) showed that adults reporting previous falls demonstrated poorer balance control, based on a range of step and standing balance tests, compared to those reporting no previous falls.

Stronger evidence of the link between postural instability and falls is provided by prospective studies. Maki et al (1994) found that greater postural sway, measured using an electronic force plate, was a significant predictor of falls among 100 older adults during the 12 month follow-up. Similarly, in a population study of 2,375 older adults, the odds of experiencing a fall in the 12 month follow-up was 35 per cent higher among participants with poor balance (unable to stand with feet side-by-side with eyes open for 30 seconds), compared to those able to maintain balance (Freeman et al., 2007).

Recent research also indicates that poor balance is a significant predictor of hospitalisation and mortality among older adults. In a study of 3,024 well-functioning adults aged over 70 years, Cesari et al (2009) reported that individuals with poor balance at a baseline examination, based on timed standing balance tests, were more likely to be hospitalised or suffer mortality during the 7 year follow-up, compared to those with good balance. The link between poor balance and these adverse events may be due to injurious falls, or poor balance may be an important marker of poor overall general health.

2.5.5 Visual contribution to postural stability

The visual system is an important sensory contributor to postural control through the provision of critical information and visual feedback on the body's position in relation to its surroundings. The importance of vision for postural control is easily demonstrated by measuring postural sway with the eyes closed, which removes all visual cues. This condition elicits around 2 to 3 times greater postural sway than with the eyes open, as shown in experimental studies involving younger participants (Paulus et al., 1984) and in population studies of adults aged 30 years and over (Era et al., 2006).

The Romberg quotient can be used to quantify the visual contribution to postural stability, and is calculated as the ratio of the amount of sway with eyes closed to eyes open (Turano et al., 1993). This ratio is usually greater than one, as postural stability is generally more stable with the eyes open than eyes closed. Studies show examples of individuals who demonstrate visual destabilization, where stability with eyes open is lower than with eyes closed (Turano et al., 1993; Cornilleau-Peres et al., 2005), although this is uncommon. Another method to quantify the visual contribution to postural sway is the stabilization ratio, which is reported to have less variability and a normal distribution compared to the Romberg quotient (Cornilleau-Peres et al., 2005). The stabilization ratio differs to the Romberg quotient, as it quantifies the relative change in sway with eyes open, referenced to sway with eyes closed. For example, a stabilisation ratio of 0.2 means that the visual input reduces the extent of postural sway by 20 per cent.

The reliance on visual information for the maintenance of postural stability increases with age, which acts to compensate for the age-related deterioration in the somatosensory and vestibular systems (Woollacott, 2000; Choy et al., 2003; Era et al., 2006). Adults aged 85 years or more have been shown to sway up to 38 per cent more on eye closure compared to those aged 50-60 years (Pyykko et al., 1990). Recent studies have shown that this increased visual reliance occurs in women as early as 50 years (Choy et al., 2003). Balance may be compromised if the balance system does not adapt to this increased visual reliance. Indeed, one study demonstrated that individuals who experienced previous falls had less reliance on visual information for balance than those who did not (Turano et al., 1994).

This increased reliance on visual information for maintenance of postural stability with increasing age has important implications given the increased prevalence of vision impairment with age. Ocular diseases that result in impaired vision decrease the visual contribution to postural control. Research has shown that the visual contribution to postural control is reduced among individuals with central field loss (Turano et al., 1996) and visual field loss from retinitis pigmentosa (Turano et al., 1993), compared to age-matched controls with normal vision. Shabana et al (2003) also demonstrated that visual field loss from glaucoma was significantly associated with a reduction in the visual contribution to postural control, by an amount which correlated with the severity of visual field loss.

2.5.6 Vision impairment and postural stability

It is well documented that postural stability among individuals with normal vision is impaired in the presence of simulated vision impairment, including refractive blur (Paulus et al., 1984; Anand et al., 2002; Anand et al., 2003a, 2003b), cataract blur (Anand et al., 2003a) and visual field restriction (Paulus et al., 1984; Berencsi et al., 2005).

Importantly, older adults with visual impairment exhibit greater postural sway, due to the reduction in the visual contribution to postural stability and the age-related changes in their remaining postural sensory systems. Schwartz et al (2005) found that postural stability was significantly improved among older adults following cataract surgery. Older adults with macular degeneration have also been shown to exhibit greater magnitudes of sway compared to age-matched control subjects, particularly under conditions of reduced somatosensory feedback (Elliott et al., 1995; Turano et al., 1996). Recent research has also indicated that greater severity of macular degeneration is associated with greater levels of postural instability (Wood et al., 2009).

To date, only one study has examined the association between visual field loss from glaucoma and postural stability (Shabana et al., 2005). In this study, postural sway of glaucoma participants, based on measures of force platform sway velocities, did not differ from age-matched controls, nor was associated with severity of visual field loss. This may be due to their young sample, aged 40 to 66 years, who demonstrated greater somatosensory contributions to postural stability to maintain steady stance, as compared to the controls. Given the limited research, it remains unclear if glaucomatous visual field loss impacts on postural stability among older adults. This is discussed further in Chapter 6.

2.6 Falls

2.6.1 The problem of falls

Falls are common adverse events experienced by many older adults and can result in serious physical and psychological consequences. Despite recent progress, many risk factors for falls have not been adequately studied or remain unexplored (Rubenstein, 2006). With the ageing of the population, the burden of falls will significantly impact on society. As such, there is a vital need to improve our understanding of the underlying risk factors for falls, so effective evidence-based interventions can be developed and targeted towards older adults at risk of falls.

Epidemiological studies undertaken in community settings indicate that around one in three adults aged over 65 years experience at least one fall each year, and around half of these experience multiple falls (Tinetti et al., 1988; Coleman et al., 2007; Freeman et al., 2007). Freeman et al (2007) monitored falls, for an average of 17 months, among 2,375 community-dwelling older adults aged 65 years and older, and reported that 29 per cent of participants reported at least one fall. In a study of 761 adults aged 70 years and over, 35 per cent of participants reported at least one fall during the 12 month follow up (Campbell et al., 1989). Many older adults also report more than one fall each year. In a study of 4,071 older women aged 70 years and older, Coleman et al (2007) reported that 16 per cent of women experienced at least two falls during the 12-month follow up.

The incidence of falls is even higher among frailer populations. A recent study monitored falls among frail community-dwelling adults aged over 70 years, who were recruited from local hospital outpatient aged care services (Cumming et al., 2007). During the 12-month follow up, 58 per cent reported at least one fall, 34 per cent reported two or more falls and eight per cent reported a fracture. The rate of falls in nursing homes is also high, where as many as 60 per cent of residents experience at least one fall each year (Lord et al., 2003a). This can be attributed to the older, frailer and more cognitively impaired population which resides in this setting.

The proportion of older adults who fall each year increases with age. In a retrospective study, the proportion of participants reporting a previous fall increased from around 24 per cent of those aged 60-69 years to around 41 per cent of those aged 80 years and over (Lord et al., 1994). Another study reported that the proportion of participants who reported two or more falls rose from around five per cent of those aged 60-69 to 24 per cent of those aged 80 years and over (Klein et al., 2003a).

2.6.2 Consequences of falls

The consequences of falls place significant physical, emotional and financial burdens on individuals, communities and the health sector. A fall can result in physical injury, fear of falling and activity restriction, in addition to the financial costs associated with treatment and rehabilitation following an injurious fall.

Falls account for more than 40 per cent of injury-related deaths and approximately one per cent of all deaths in Australians aged 65 and over. Falls are the leading cause of injury-related deaths, followed by motor vehicle accidents and suicide (Dunn et al., 2002). Around 20 per cent of falls result in injury requiring medical treatment (Tinetti et al., 1988; Koski et al., 1998), while hip fractures are associated with high mortality rates (20 to 30 per cent within 12 months of the fall) (Davidson et al., 2001; Rosell & Parker, 2003), and those who recover from a fall often have persistent pain and reduced mobility (Davidson et al., 2001). In 2002, more than 1,300 Australians aged 65 or older died as a result of a fall (Kreisfeld et al., 2004) and more than 55,000 older Australians were hospitalised for injuries sustained from falling during the financial year 1999-2000 (Helps et al., 2002).

There are also important psychological consequences associated with falling, even in the absence of physical injury. Falls can lead to fear of falling, which produces anxiety and depression about self-sufficiency and independence (Legters, 2002). Fear of falling has also been linked with deteriorating health, which leads to reduced quality of life and independence (Cumming et al., 2000). Around a quarter of older individuals report restricting their activities following a fall (Nevitt et al., 1989), and falls are a strong predictor of nursing home admission (Tinetti & Williams, 1997; Cumming et al., 2000).

The financial and economic costs associated with injurious falls are considerable. An Australian study estimated that the average cost of a fall requiring presentation to an emergency department was around AUD $4,500 in 1999, of which 80 percent comprised hospital costs, 16 per cent community costs and four per cent personal costs (Hall & Hendrie, 2003). In Australia alone, falls and related injuries resulted in direct medical costs of around $500 million in 2001, and this is likely to increase three-fold by 2051 (Moller, 2003). There are also indirect costs associated with falls which have yet to be measured, for example costs associated with institutionalisation following falls.

2.6.3 Risk factors for falls

Falls are seldom due to a single cause, and epidemiological studies in community-dwelling older adults have identified many contributing factors for falls. Findings from these studies guide effective strategies to identify adults who are at risk of falling, and enable risk factors to be targeted to assist in the prevention of future falls.

There are a number of well established risk factors associated with falling among community-dwelling older adults (Tinetti et al., 1988; Close, 2001; Moylan & Binder, 2007). Some of these factors include:

- *Socio-demographic factors*: older age, female gender, previous history of falls, living alone;

- *Non-specific physiological or functional factors*: postural sensory impairment (visual, vestibular and somatosensory impairment), lower-limb muscle weakness;
- *Specific medical risk factors*: Parkinson's disease, stroke, depression, cognitive impairment and arthritis;
- *Medications*: Use of central nervous system agents (such as psychotropics and antidepressants); use of multiple medication use (polypharmacy).
- *Environmental factors*: Use of inappropriate footwear, poor environmental lighting, trip hazards and slippery or uneven surfaces.

A Cochrane review examining interventions for preventing falls indicated that targeting modifiable risk factors can be beneficial in reducing falls among community-dwelling older adults (Gillespie et al., 2003). Successful interventions have included exercise programmes to improve muscle strength and balance, home hazard assessment and modification, and withdrawal of psychotropic medications. Even though some risk factors may not be modifiable, individuals with these factors may benefit from interventions targeting other risk factors, such as education and awareness to promote changes in behaviour, exercise programmes to improve functional capacity or home hazard modification.

2.6.4 Falls research methodology

One of the complexities with falls research is the numerous methodological variations, which makes comparisons between studies difficult. These variations include study populations (sample size, age, gender, ethnicity, level of frailty), designs (cross-sectional, longitudinal, case-control), and outcome measures (any falls, multiple falls, injurious falls). Hip fracture studies are also often included within the area of falls research, as 90 per cent of hip fractures occur as a result of falls (Marks et al., 2003).

The methodological quality of studies varies according to how falls data is collected. Retrospective falls studies rely on participants reporting on falls which occurred prior to risk factor assessment, generally in the previous 12 months. An important limitations of these studies is recall bias, as up to 30 per cent of older adults do not recall previous falls (Cummings et al., 1988). In addition, these studies can be limited by selection bias, as adults who suffered previous falls resulting in hospitalisation, institutionalisation or mortality, are not represented. The gold standard in falls research is prospective monitoring of falls, usually for a minimum of 12 months. Prospective studies provide better data quality due to greater accuracy in reported falls (Hauer et al., 2006), less selection bias and causality can be established as risk factors are measured prior to the occurrence of any falls.

2.6.5 Visual impairment and falls

There is a growing body of literature which links vision impairment or eye disease to an increased falls risk among older adults. Early population studies drew attention to the higher rate of falls among participants with vision impairment (Tinetti et al., 1988; Nevitt et al., 1989). Similarly, research from accident and emergency departments reported significant links between adults presenting due to falls and vision impairment (Jack et al., 1995; Close et al., 1999). In one study, over half of the adults attending a geriatric emergency department, mostly due to falls, presented with binocular visual acuity of 6/18 or worse (Jack et al., 1995). In a similar study, Close et al (1999) reported that 59 per cent of patients presenting to an emergency department due to falls had a presenting visual acuity of 6/12 or worse. Falls occur commonly among older adults with visual impairment. A prospective 12 month study of 391 older adults with visual acuity worse than 6/24 reported that 48 per cent of participants experienced a fall and 25 per cent experienced multiple falls (Campbell et al., 2005).

A considerable amount of falls research has centred on measures of visual acuity, given its universal recognition and ease of measurement. A number of large-scale population studies have shown that visual acuity loss increases the risk of falls, despite the limitations in retrospective falls research. Klein et al (1998) found that older adults presenting with binocular visual acuity of 6/7.5 or worse were twice as likely to report more than two falls in the previous year. Similar studies reported that older adults presenting with binocular visual acuity worse than 6/9 were approximately twice as likely to report multiple falls in the previous year (Ivers et al., 1998; Klein et al., 2003a).

More recent prospective falls studies also support the association between reduced visual acuity and increased risk of falls. Coleman and colleagues (2007) showed that women aged over 65 years, whose visual acuity had decreased by two or more lines in the previous four to six years, were 43 per cent more likely to have multiple falls in the following year than women whose visual acuity had reduced by less than two lines over the same period. The risk of multiple falls was even greater (74 per cent more likely) when baseline acuity was worse than 6/12. In a study of 416 adults aged between 75 and 80 years, participants with moderate visual acuity loss, between 6/12 to 6/20 in the better-eye, were more likely to suffer injurious falls, according to hospital data, during the 10 year follow-up compared to those with normal vision (Kulmala et al., 2008).

Visual impairment may also compound other risk factors for falls among older adults. In a prospective study, reduced distance visual acuity (worse than 6/20) was a significant risk factor for incident injurious falls among older adults requiring assistance with daily living tasks (n=222), but not among independently functioning adults (n=151) (Koski et al., 1998). In a recent study, Kulmala et al (2009) reported that older women with combined visual acuity loss (worse than 6/7.5) and hearing impairment (threshold in the better ear worse than 21 dB) were more likely to fall, more so than visual acuity loss alone.

Studies also report significant links between reduced visual acuity and prospective fractures. Ivers et al (2003) found that reduced visual acuity (6/18 or worse) was associated with hip fractures during the two year follow-up, even after adjusting for other health and visual functions measures. Similarly, Dargent-Molina et al (1996) showed that women who had habitual visual acuity of 6/15 or worse were nearly twice as likely to suffer a hip fracture than those with visual acuity better than 6/9. The Framingham study reported that hip fractures were more likely if visual acuity was worse than 6/9 in either eye (by 1.7 times), and more so if binocular visual acuity was 6/30 or worse (by 2.2 times) (Felson et al., 1989).

Similar findings are also reported in retrospective fracture studies. Klein et al (1998) reported that the risk of any previous hip fracture was nearly 4 times more likely if visual acuity was 6/7.5 or worse. In a follow-up study, Klein et al (2003b) found that adults presenting with visual acuity worse than 6/12 were nearly twice as likely to have experienced any fracture in the previous 5 years. Cummings et al (1995), however, failed to find any association between visual acuity and prospective hip fractures in a study of 9,516 women aged 65 years or older. Recent studies indicate that visual acuity is not a strong predictor of hip fractures among older women (Coleman et al., 2009), which may explain Cummings' findings. This is discussed in detail later in this review.

While visual acuity has long served as the primary visual function test, eye diseases can affect multiple components of visual function, including contrast sensitivity, peripheral field sensitivity, stereoacuity and other non-standard aspects of visual function (Rubin et al., 1997). A measure of visual acuity alone provides limited information about the level of performance on these other aspects of visual function.

Research has shown that visual functions such as visual field loss, rather than visual acuity, are better visual predictors of safe and efficient mobility among visually impaired older adults, which refers to their ability to travel independently within the environment (Lovie-Kitchin et al., 1990). In these studies, speed and obstacle contact are often used as measures of performance within mobility courses. Individuals with visual field loss, from a range of eye diseases, are shown to walk more slowly (Haymes et al., 1996; Geruschat et al., 1998; Turano et al., 1999; Hassan et al., 2002; Turano et al., 2004), and experience more obstacle contacts (Geruschat et al., 1998; Turano et al., 2004). As visual function measures other than visual acuity are important for safe navigation and obstacle avoidance, it is important to consider these visual functions in relation to falls risk.

Recent large population studies measuring prospective falls provide the best evidence linking vision impairment with falls among older adults. Visual field loss, rather than visual acuity or contrast sensitivity loss, was the strongest predictor of falls in these studies (Coleman et al., 2007; Freeman et al., 2007). In one study, severe binocular visual field loss increased the risk of multiple falls by 50% (Coleman et al., 2007), while in another study, a 10% loss of visual field increased the risk of falling by 8% (Freeman et al., 2007). In a recent prospective study, older women with severe binocular visual field loss were 66% more likely to experience a hip fracture during the 8 year follow-up (Coleman et al., 2009). In contrast, measures of visual acuity and contrast sensitivity loss were not associated with an increased risk of hip fracture. These were well designed studies that provide strong evidence that visual field loss, rather than central vision loss, is linked to an increased risk of falling. Chapter 7 presents a detailed discussion of these studies.

Contrast sensitivity has also been associated with falls, although the findings are equivocal. A possible explanation of the contradictory findings is the diversity of contrast sensitivity measures used in these studies. Poor contrast sensitivity has been linked to retrospective falls (Ivers et al., 1998) and hip fractures (Klein et al., 1998), while others have failed to find similar associations (Klein et al., 2003a). De Boer and colleagues (2004) showed that low-frequency contrast sensitivity loss, measured by Vistech charts, increased the likelihood of a prospective falls, but not for fractures. Two fracture studies using the Vistech charts have also demonstrated that loss of low-frequency contrast sensitivity increases the risk of hip fracture among older women (Cummings et al., 1995; Wainwright et al., 2005). However, these findings should be interpreted with some caution, since the reliability of Vistech charts is reportedly low (Reeves et al., 1991).

Similarly, findings regarding the association between depth perception, or stereoacuity, and falls have been inconsistent. One study showed that reduced stereoacuity, defined as 200 seconds of arc or worse on the Randot test, doubled the risk of multiple falls (Nevitt et al., 1989). In contrast, other studies have failed to support these findings, for either stereoacuity assessed by the Randot test (Friedman et al., 2002) or according to asymmetry in visual acuity between the eyes (Klein et al., 2003b). Several studies have linked poor depth perception using the Howard-Dohlman test with increased risk of hip fracture (Cummings et al., 1995; Wainwright et al., 2005). However, prospective studies have failed to find that poor depth perception increases hip fracture risk, based on Randot test performance (Dargent-Molina et al., 1996) or asymmetry in visual acuity between eyes (Felson et al., 1989).

There is also evidence that self-reported visual disability measured by vision-related QOL instruments, as a proxy measure for objective measures of vision, is associated with falls. In a study of 143 adults with a range of eye diseases, Activities of Daily Vision Scale (ADVS) scores were significantly lower among those reporting a previous fall (Kamel et al., 2000). Using a cut-off of score of 90, the ADVS showed 67% sensitivity in identifying previous fallers. Among participants with glaucoma (n=29), this cut-off had a 100% sensitivity in correctly identifying fallers, yet displayed low specificity (42%). Despite the small sample size and retrospective falls measures, the findings suggest that in the absence of objective vision measures, these indirect measures of visual function may be useful in assessing falls risk among older adults with various eye diseases including glaucoma. Prospective studies are yet to confirm this link.

Research has shown significant links between a number of eye diseases and increased likelihood of falls and fractures, which is not surprising given the considerable evidence showing that impaired visual function increases the risk of these events. However, comparisons between studies are made difficult due to variations eye disease classification (self-report through to ophthalmic assessment), level of disease severity and study designs.

Large population studies have found that the likelihood of falls is greater among older adults with cataracts (Ivers et al., 1998; McCarty et al., 2002; Ivers et al., 2003), diabetic retinopathy (Ivers et al., 2001) and glaucoma (Dolinis et al., 1997; Ivers et al., 2003; Lamoureux et al., 2008). Although macular degeneration is a leading cause of irreversible vision loss (Wang et al., 2000a; Weih et al., 2000), little is known about the relationship between macular degeneration and falls. In contrast, various studies have also failed to demonstrate significant links with falls or fractures among those with cataracts (Felson et al., 1989), diabetic retinopathy (Ivers et al., 1998; Ivers et al., 2000) and glaucoma (Grisso et al., 1991; Ivers et al., 2000; Coleman et al., 2004). As the aims of this research are focused on glaucoma, Chapter 7 presents an extensive discussion of findings from studies examining the risk of falls among adults with glaucoma.

2.6.6 Visual attention and falls

There is emerging evidence that the attentional field of view (AFV) may be a factor which influences safe navigation and mobility among older adults. The AFV is the extent of the visual field over which a person can simultaneously extract and process central and peripheral visual information (Owsley & Ball, 1993). Two forms of AFV measures are commonly used, the first of which determines processing speed in a given visual area, while the second determines visual field extent for a fixed processing speed (Clay et al., 2005). The task complexity of these measures range from divided attention tests (a single central and peripheral target), to more cognitively demanding selective attention tests (the addition of peripheral distracting targets). Thus, AFV measures are influenced by visual functioning, as well as higher-order visual/cognitive processes (Clay et al., 2005).

It is well known that the AFV reduces with increasing age (Kosslyn et al., 1999; Haegerstrom-Portnoy, 2005). In addition, studies of older adults have reported that reduced AFV performance is associated with reductions in functional performance, particularly relating to driving (Owsley et al., 1998; Wood et al., 2006) and mobility performance (Broman et al., 2004; Leat & Lovie-Kitchin, 2008).

Not surprisingly, the loss of peripheral visual function is likely to negatively impact on the AFV, due to a reduced ability to detect peripherally located objects. Leat & Lovie-Kitchin (2006) found that the AFV, when corrected for visual field defects, did not differ between visually impaired adults with a range of eye diseases and age-matched controls.

Poor AFV performance has been linked to greater mobility difficulties. Broman et al (2004) found that divided attention was an independent predictor of obstacle collisions on a mobility course among 1,504 older adults. This association remained significant even when adjusted for visual field loss. In a study of 342 community-dwelling older adults, reduced AFV was associated with poorer scores on balance confidence, balance and gait problems, and mobility assessment, but not for previous falls or physical activity levels (Owsley & McGwin, 2004). Leat & Lovie-Kitchin (2008) found that AFV measures were associated with mobility performance (mobility errors and walking speed) among 35 subjects with visual impairment, from a range of eye diseases. These associations, however, were weak when adjusted for visual field loss. It remains unclear, however, if AFV is associated with increased risk of falls due to a lack of evidence.

2.6.7 Mediating factors between visual field loss and falls

The precise mechanisms underlying the relationship between vision impairment and falls among older adults remain unclear because of limited previous research. Insights into these aspects are important for guiding future falls prevention interventions among visually impaired older adults. The most likely mechanism is the reduction in safe and efficient navigation and obstacle avoidance which results from visual impairment (Lovie-Kitchin et al., 1990; Hassan et al., 2002; Turano et al., 2004). Reduction in safe navigation and obstacle avoidance is likely to increase the risk of tripping on hazards or inappropriate foot placement, and hence, increase the risk of falls.

Other factors may also contribute to the causal pathway between visual impairment and falls, such as postural stability or functional status, although there is no supporting evidence in the literature. Visual impairment is associated with greater postural instability among older adults (Elliott et al., 1995; Turano et al., 1996; Schwartz et al., 2005), and postural instability is a known risk factor for falls (Vellas et al., 1997; Freeman et al., 2007).

Similarly, declines in functional status or greater levels of frailty have been linked to vision impairment (Klein et al., 2003a; Klein et al., 2006), and are associated with an increased risk of falls (Ensrud et al., 2007). However, many of these associations are cross-sectional in nature, which limit the ability to establish causality.

Falls among older adults with visual impairment may also be an underlying mechanism in the pathway between vision impairment and mortality (Freeman et al., 2005; Pedula et al., 2006). Serious falls injuries, such as hip fractures, are associated with visual impairment (Coleman et al., 2009), and are associated with higher risk of mortality (Davidson et al., 2001; Rosell & Parker, 2003). Although this area of research is beyond the scope of this thesis, it remains to be established whether the relationship between vision impairment and mortality is in part due to these injurious falls.

2.7 Overall rationale and research questions

Among older populations, glaucoma is a leading cause of vision impairment (Weih et al., 2001), and is the leading cause of visual field loss (Ramrattan et al., 2001). With the ageing of the population and the high rate of undiagnosed glaucoma (Weih et al., 2001; Friedman et al., 2004), the number of older people living with glaucomatous visual impairment will rise accordingly and the personal and economic impact of the disease will increase.

Studies have reported significant associations between visual impairment, disability and falls among general population cohorts or heterogeneous disease groups. Much of this research, however, is based on measures of central vision loss, primarily visual acuity. As such, there is limited research on disability and falls outcomes in populations with visual field loss or glaucoma, and even less in older age groups.

The primary aim of this research was to evaluate the relationship between visual impairment and prospective falls in a cohort of older adults with glaucoma. The secondary aims were to investigate the cross-sectional associations between visual impairment and health-related QOL, functional status and postural sway in this cohort, and to determine whether these factors contribute to falls. An important consideration in the design of the study was the use of standardised central and peripheral visual function measures, including integrated visual field measures to provide estimates of binocular visual field extent. Furthermore, validated and standardised outcome measures were incorporated into the research, including prospectively measured falls. The findings of this research provide important insights into the links between glaucomatous visual field loss and disability among older adults, and its association with falls.

The following primary research questions are addressed in this thesis:

Q1. Is there an association between the severity and location of visual field loss and health-related quality of life among older adults with glaucoma?

Q2. Is severity and location of visual field loss associated with functional status among older adults with glaucoma?

Q3. Is there an association between the severity and location of visual field loss and postural sway among older adults with glaucoma?

Q4. Does the severity and location of visual field loss predict falls among older adults with glaucoma?

Hypotheses specific to these research questions are presented in the relevant chapters.

Chapter 3: Study Design, Methods and Baseline Characteristics

This chapter outlines the recruitment procedures and common methods employed throughout the component chapters. The methodologies pertinent to the outcome measures for each component are described in detail in the relevant chapters. This chapter also reports on the baseline socio-demographic, health, medical and visual function characteristics of the study participants.

3.1 Study design

To address the research questions posed in Section 2.7 of this thesis, a single study was conducted. The thesis is structured as two components, the first of which examined the cross-sectional association between visual field loss and health-related QOL, functional status and postural stability from baseline data. These are presented as separate chapters, referred to as Studies 1a, 1b and 1c. The second component examined the association between visual field loss and prospective falls based on a longitudinal study design. This is presented as a single chapter, referred to as Study 2. This study also incorporated outcome measures assessed in the earlier studies, to examine possible mediating factors in the relationship between visual field loss and falls. A schematic of the study design is outlined in Figure 3-1.

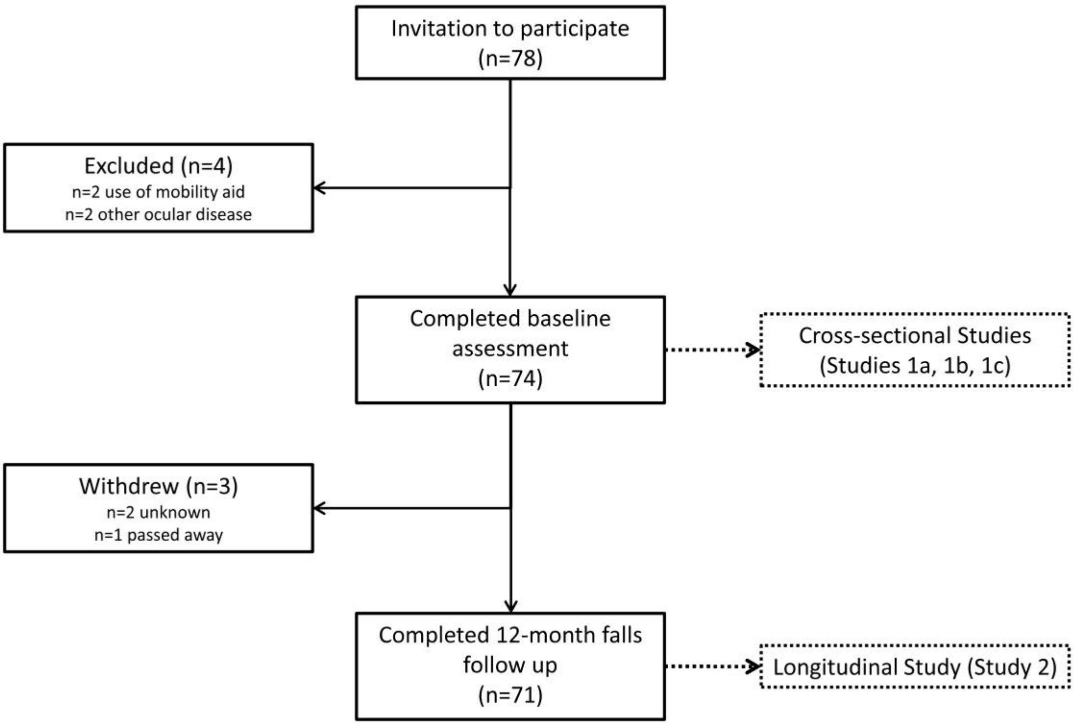

Figure 3-1: Schematic of the study design

3.2 Participants

3.2.1 Study recruitment

The recruitment strategy targeted older adults with glaucoma during the period of June 2006 and January 2008. Potential participants were identified by clinical record reviews using the Queensland University of Technology Optometry Clinic database, or from referrals from optometrists and ophthalmologists in private practice. The study was also advertised to potential participants through notices published in Glaucoma Australia newsletters, local newspapers and flyers distributed at local retirement villages.

3.2.2 Eligibility criteria

A number of inclusion and exclusion criteria were established prior to participant recruitment to ensure that the study cohort was consistent with the research hypotheses.

The inclusion criteria and the rationale were as follows:

- Adults aged over 60 years. The incidence of falls and prevalence of glaucoma increases significantly among older adults aged over 60.
- Living independently in the community. The focus of the study was on community dwelling older populations. Older adults requiring assistance with daily living (i.e. in nursing homes or age-care facilities) represent a different population, often older and frailer, and were outside the scope of the study.
- Being treated for primary open angle glaucoma. While there are other types of glaucoma (such as angle-closure, secondary, and developmental glaucoma), the focus of this study was on older adults with primary open-angle glaucoma, which represents around 90% of glaucoma cases (Gupta, 2005).

The exclusion criteria and the rationale were as follows:

- Any significant ocular or visual pathway disease leading to visual field loss, other than primary open angle glaucoma, to limit the cohort to a specific eye-disease population.
- Unable to speak English.
- Unable to walk unaided, i.e. without any walking aids. The use of walking devices assists in the prevention of falls, which would likely distort the relationship between vision impairment and falls.
- A diagnosis of Parkinson's disease, chronic dizziness or vestibular disease. Individuals with these conditions experience a high rate of falling and may distort the study findings.

- Presence of significant impairment of cognitive function assessed using the Mini-mental State Examination (see Section 3.5, Cognitive status). Screening for cognitive impairment ensured that eligible participants were capable of providing informed consent, accurate recall and timely completion of the monthly fall calendars.

The study investigator contacted potential participants over the telephone to conduct a screening interview to confirm eligibility for inclusion into the study. The telephone screening questions are presented in Appendix 1. Eligible participants were sent a letter of invitation to participate in the study, and with their acceptance to participate, a baseline testing appointment was scheduled.

3.3 Baseline assessment procedures

Participants met with the study investigator once during the study for a baseline assessment session. The baseline assessment consisted of a single 2-hour session which was conducted at the Queensland University of Technology Kelvin Grove campus. All assessments were conducted by the study investigator who is a registered optometrist.

3.4 Socio-demographic, health and medical data

Participants completed a structured self-administered baseline questionnaire developed by the investigators that collected a number of socio-demographic, health and medical variables (see Appendix 2).

3.4.1 Socio-demographic data

The socio-demographic variables included age, gender, country of birth, current living arrangements, completed education level, current employment status and source of household income. Additional information was collected on current driving status (yes, no, never), smoking status (non-smoker, former smoker or current smoker) and alcohol intake (abstainers, light drinkers and heavy drinkers).

Smoking status was categorized into three groups: (a) non-smoker (having never smoked or smoked less than 100 cigarettes (or equivalent amount of tobacco) in his/her lifetime), (b) former smoker (having smoked at least 100 cigarettes in his/her lifetime and had given up smoking before the study examination) and (c) regular smoker. Alcohol intake was estimated by calculating the daily equivalent number of standard drinking units (one bottle of beer, one glass of wine, or one unit of spirit) habitually consumed, according to his/her reported number and frequency of consumption. Participants were classified into three groups, based on Australian alcohol guidelines for males and females (National Health and Medical Research Council, 2001): (a) abstainers; (b) light drinkers (less than 3 standard drinks per day but more than none) and (c) heavy drinkers (3 or more standard drinks per day).

3.4.2 Health and medical data

3.4.2.1 *Current medication use*

The baseline questionnaire collected details on currently used medications, including prescription, non-prescription and vitamins. All prescription drugs were coded according to the therapeutic classifications used by Australian MIMS Online (www.mims.com.au), a web-based pharmaceutical database (Appendix 3).

Medications were coded into the following groups for analyses, based on previous literature (Tinetti et al., 1988; Hartikainen et al., 2007):

- Total number of prescription medications;
- Polypharmacy (defined as use of four more medications);
- Use of any central nervous system drug;
- Use of any hypnotics, sedatives and anti-anxiety agents (including benzodiazepines);

- Use of any antidepressants;
- Use of any cardiovascular drug;
- Use of any oral beta-adrenergic blocking agents;
- Use of any endocrine system drug;
- Use of any respiratory system drug.

3.4.2.2 *Self-reported co-morbidities*

Participants were asked if they suffered from a number of medical and health conditions on the baseline questionnaire. The medical conditions were derived from previous vision research (Globe et al., 2005), and included: arthritis, cancer, diabetes mellitus, hypertension, cardiovascular disease (angina, heart attack), hearing impairment, history of stoke, history of hip fracture, and incontinence. To summarize the impact of co-morbid medical conditions, a count of these self-reported chronic medical conditions was used as the co-morbidity index, which has been shown to be an accurate method of quantifying co-morbidity (Globe et al., 2005).

3.4.2.3 *Glaucoma medical information*

Information was collected regarding current and past glaucoma treatments from the baseline questionnaire. Information was also collected on disease duration and laterality. Based on previous research, the use of topical anti-glaucoma medications was dichotomously coded into either the use of topical medications including beta-blockers or the use of topical medications other than beta-blockers.

3.4.3 Previous falls and fear of falling

Participants were asked to report the number of falls they had experienced in the previous 12 months, defined as coming to rest inadvertently on the ground or other lower level, but not due to an external force. Participants who reported one or more previous falls in the previous 12 months were classified as a “previous faller”, while those who reported no previous falls were classified as a “previous non-faller”. If previous falls were reported, participants were asked if any injuries were incurred as a result of the fall/s.

Two yes/no questions were asked to obtain data pertinent to fear of falling and activity restriction, based on previous studies (Friedman et al., 2002): “Are you worried or afraid of falling, except in a high place?” and “Do you limit any activities due to fear of falling?” These simple dichotomous questions show good general reliability in measuring fear of falling and activity restriction (Jorstad et al., 2005), without the need for comprehensive questionnaires measuring specific fall-related psychological outcomes.

3.4.4 Body mass index

Body weight was measured using an analogue portable scale while participants were dressed in light clothing (i.e. no shoes, sweaters, jackets, or belts) to the nearest kilogram. Standing height was assessed to the nearest centimetre using a wall mounted tape measure with shoes removed. Body mass index (BMI) was calculated on measured weight (in kilograms) divided by measured height (in metres) squared.

3.5 Cognitive status

Cognitive status was assessed using the Mini-Mental State Examination (MMSE) (Folstein et al., 1983), which is widely used in health research (West et al., 1997; Coleman et al., 2007; Cumming et al., 2007). This instrument consists of an interviewer-administered questionnaire which detects and quantifies the degree of cognitive impairment based on assessments of memory, recall and response.

The test is scored on a scale ranging from 1 to 30, where higher scores indicate better cognitive status. Participants scoring less than 23 in the present study were excluded due to potential difficulties with providing informed consent, accurate recall of events and ability to complete the monthly falls calendars. This cut-off score was based on previous studies comprising older populations (Folstein et al., 1983; Clarke et al., 1991; Cullen et al., 2005).

3.6 Visual function assessment

3.6.1 Screening eye examination

All participants underwent an eye examination performed by the investigator, which included ocular history, slit-lamp biomicroscopy and ophthalmoscopy to confirm eligibility for the study. The ocular history assessed any previous ocular or medical history that may have resulted in any vision loss, for example corneal scarring or stroke. The anterior eye segment was assessed for corneal and other media opacities. Any lenticular opacification was graded according to the LOCS III scale (Chylack et al., 1993). Participants with mild, early cataracts on clinical examination were included in the study. A significant cataract was defined as LOCS III nuclear opalescence greater than 3.0 and/or cortical cataract greater than 3.0 and/or posterior subcapsular cataract greater than 2.0 (Nirmalan et al., 2004). The posterior eye segment was assessed for any retinal or macular diseases, other than primary open angle glaucoma. All habitually worn spectacles (for both distance and near vision) were measured and recorded.

3.6.2 Visual Acuity

A Bailey-Lovie high-contrast letter chart was administered at 6 metres with a chart luminance of 160 candela/m^2. The chart consists of lines of five high-contrast letters (95% Weber contrast), with each successive line decreasing in angular size by 0.1 log units in minimum angle of resolution (logMAR) (Bailey & Lovie, 1976).

Monocular visual acuities were measured using participants' presenting distance refractive correction. Participants were directed to begin reading the letters at the top of the chart and to continue reading down the chart until at least three of the five letters on a line were called incorrectly. Participants were given additional time to respond and were encouraged to guess. Visual acuity was recorded as the total number of letters read correctly, with a weighting of -0.02 log units per letter, converted to logMAR units (Bailey & Lovie, 1976).

As the testing battery involved a number of different visual function measures, only monocular, rather than binocular, measures of visual acuity were measured to minimise fatigue and learning effects. As binocular visual acuity can be estimated from measures of monocular visual acuity in the better-eye (Rubin et al., 2000), and is well represented with better eye measures among older adults (Schneck et al., 2010), visual acuity in the better-eye and worse-eye was used in the analyses, corresponding to the eyes with the lower and higher logMAR scores respectively. This approach is consistent with key studies in this area (Ivers et al., 1998; Coleman et al., 2007; Freeman et al., 2007; Coleman et al., 2009).

3.6.3 Contrast sensitivity

The Pelli-Robson contrast sensitivity letter chart (Clement Clarke International Ltd) was selected to assess contrast sensitivity, due to its extensive use in vision and falls research. The Pelli-Robson chart comprises letters that are arranged in groups of three each having the same contrast. In total, there are eight rows, with two triplets per row, with each successive triplet decreasing in contrast from the top to the bottom of the chart in steps of 0.15 log units. The contrast of the triplets ranges from 0.00 (highest contrast letters) to 2.25 log units (lowest contrast letters). Each letter subtends 3 degrees at the recommended viewing distance of 1 metre (Pelli et al., 1988). This corresponds to a spatial frequency of around 1 cycle per degree (Bradley et al., 1991), near the peak of the contrast sensitivity function. The chart luminance was 83 cd/m^2, within the recommended range of 60 to 120 cd/m^2 (Woods & Wood, 1995).

Monocular contrast sensitivities were measured using participants' presenting distance refractive correction, plus a working distance lens of +0.75DS (Elliott et al., 1991). Participants were instructed to read the letters starting with the high contrast letters at the top of the chart and to continue reading letters until no letters in a given triplet were read correctly. Participants were given additional time to respond and were encouraged to guess.

To improve reliability in the scoring, each correctly identified letter was scored a value of 0.05 log units and a call of “O” for “C” was accepted as correct (Elliott et al., 1990; Elliott et al., 1991). Log contrast sensitivity was calculated by recording the total number of letters read correctly, subtracting three and multiplying by 0.05. As was the case for the visual acuity data, contrast sensitivity in the better-eye and worse-eye was used in analyses, corresponding to the eyes with the higher and lower logCS scores respectively.

3.6.4 Stereoacuity

Random dot stereotests are generally considered the gold standard for measuring near stereoacuity, as they contain no monocular clues and depth can only be perceived by the detection of the disparities between the sets of random dots presented to the two eyes (Garnham & Sloper, 2006). Of the commercial random dot stereotests available, the TNO test was chosen for its ease of administration and ability to measure stereoacuity thresholds (Simons, 1981).

The TNO test (Laméris Instrumenten BV, Utrecht, The Netherlands) uses random dot stimuli with red-green glasses to separate the images presented to each eye. Participants are presented with 12 test plates at six different disparity levels (two at each level). The corresponding retinal disparities in this test range from 15 to 480 seconds of arc. Testing was performed at the recommended viewing distance of 40 centimetres while participants wore their habitual near correction with even overhead fluorescent lighting (approximately 350 lux).

Participants were asked to identify the missing sector at the four possible orientations for each test plate, beginning with the largest disparity plates

(480 sec arc). If the two largest disparity plates were incorrectly identified, stereoacuity was recorded as “absent”. For correct responses, plates of increasing difficulty (smaller disparity) were presented, and stereoacuity was defined as the smallest level of disparity at which both test plates were correctly identified. As a considerable proportion of participants’ stereoacuity was coded as absent, stereoacuity was dichotomised into absent (worse than 480 sec arc) or present (480 sec arc or better) for analyses.

3.6.5 Monocular visual field assessment

Visual field testing was performed separately for each eye with the Humphrey Field Analyzer model 750 (Carl Zeiss-Meditec, Dublin, CA, USA) using conventional white-on-white perimetry. In all cases, the optimal lens correction for the working distance of the perimeter was placed before the tested eye, and the fellow eye occluded. Although many of the participants were experienced at performing visual field testing, a number of reliability criteria were set to ensure accurate visual field measurements. Testing was repeated if there were more than 33% fixation losses, false-positive or false-negative responses (Johnson et al., 2002).

Two visual field testing programs were selected for the purpose of generating integrated binocular visual field plots, which is discussed in detail in Section 3.6.6. The 24-2 program was chosen due to its extensive use in clinical settings (Gaskin et al., 2006), large glaucoma clinical trials (AGIS Investigators, 1994; Zahari et al., 2006) and previous functional outcome studies (Turano et al., 1999). This program is faster and less variable than the 30-2 program (Khoury et al., 1999). The 81-point screening program was selected due to its use in a number of prominent quality of life, mobility and falls studies (Jampel et al., 2002a; Broman et al., 2004; Turano et al., 2004; Freeman et al., 2007; Friedman et al., 2007; Freeman et al., 2008b). The following sections discuss these programs in detail.

For this research, the central visual field area was defined according to the anatomical width of the fovea, which subtends approximately 4.5 degrees in diameter of visual area (Nolan et al., 2008). The peripheral visual field area was defined as the remaining region of visual field. For the remainder of this thesis, the term visual field loss is used synonymously with a reduction in visual field sensitivity.

3.6.5.1 ***24-2 threshold fields***

Monocular threshold field sensitivity was measured using the 24-2 SITA-standard strategy with conventional test parameters (Goldmann size III stimulus, 31.5 apostilb or 10 cd/m^2 white background). From central fixation, this procedure measures visual field sensitivity to 21 degrees superiorly and inferiorly, 27 degrees nasally and 21 degrees temporally, with a spacing of 6 degrees between adjacent test points (Figure 3-2).

For each visual field location, a deviation from the normal age matched value in decibels (dB) is calculated and presented in a total deviation plot, based on the normative database provided by the manufacturer. Positive decibel values indicate a better-than-average sensitivity, while negative values indicate a worse-than-average sensitivity. The in-built software calculates the average deviation across the visual field, known as the mean deviation (MD), which provides an overall indicator of disease severity. Visual field sensitivity in the better-eye and worse-eye was used in the analyses, corresponding to the eyes with the more positive and more negative MD scores respectively. The monocular 24-2 fields were also used to create an integrated visual field, as discussed in section 3.6.6.

3.6.5.2 ***81-point screening fields***

Monocular visual fields were assessed using an 81-point single intensity screening program (24dB, Goldmann size III stimulus with 31.5 apostilb or 10 cd/m2 white background). For this program, the optimal lens correction for the 30 cm working distance of the perimeter was placed before the tested eye during testing of the central 20 degrees, and then removed for the remaining peripheral field testing.

In this screening program, a point is counted as missed if the participant cannot see that point with the single-target intensity of 24dB. From central fixation, 81 visual field locations are assessed to 38 degrees superiorly, 55 degrees inferiorly, 44 degrees nasally and 58 degrees temporally, with various spacing between adjacent test points (Figure 3-3). These monocular fields were not included in analyses, as these were used to generate an integrated visual field, as outlined in section 3.6.6.

3.6.6 Integrated visual fields

Functional activities, for example reading, walking and driving, are performed binocularly. Unlike measures of central visual function, where binocular visual function can be closely inferred from monocular measures (Rubin et al., 2000), this is more challenging for measures of peripheral visual function. The use of better-eye monocular field tests to estimate binocular visual field measures can misrepresent the actual extent of binocular visual field, as the visual sensitivity of overlapping areas of visual field can vary between eyes. For example, extensive inferior visual field loss in one eye may correspond to normal visual field in the fellow eye. Therefore, careful consideration was given to the use of visual field measure in this research to provide an appropriate estimation of participants' binocular visual field extent.

Ideally, binocular threshold visual field sensitivity should be measured with both eyes open; however, this is problematic in the clinical setting. It requires the accurate binocular correction of near refractive errors for the close working distance (Herse, 1992), and it can be difficult to reduce the likelihood of lens or trial frame rim defects during testing. Moreover, it does not allow for fixation to be monitored and older patients often report diplopia due to the close working distance.

Esterman (1982) developed a screening program to estimate binocular visual field extent, using a Goldmann size III white stimulus with an single-target intensity of 10 dB to examine 120 visual field locations, extending 140 degrees horizontally and 85 degrees vertically. Testing is performed binocularly, using the patient's own spectacles. This program, however, is limited as the relatively bright stimulus results in considerable ceiling effects, particularly among patients with early to mild visual field defects (Jampel et al., 2002a). Furthermore, the one level screening strategy does not determine threshold sensitivity, nor is there any provision for fixation monitoring during testing.

An approach gaining popularity is the integration of monocular field tests into a single representation a patient's binocular field of view, known as integrated visual fields (IVF) (Nelson-Quigg et al., 2000; Owen et al., 2008). This technique is based on using values from the most sensitive eye for each corresponding field location to generate a binocular visual field plot. These measures have been used widely in recent studies assessing functional outcomes, including quality of life, mobility, falls and driving (Jampel et al., 2002b; Coleman et al., 2007; Freeman et al., 2007; Friedman et al., 2007; Freeman et al., 2008b; Coleman et al., 2009; Keay et al., 2009).

The IVF approach was included for use in the present study, due to its use in previous studies and its ability to generate threshold estimates of the binocular visual field. In total, two IVFs were generated for each participant. The following sections provide details of these measures.

3.6.6.1 *Integrated 60-degree field (IVF-60)*

The monocular 24-2 threshold visual field tests were merged using the IVF approach. Binocular field sensitivity at each given location was defined as the most sensitive of the corresponding left and right monocular mean deviation field values from the total deviation plot (Nelson-Quigg et al., 2000; Owen et al., 2008). From central fixation, this integrated binocular field approximately extends 20 degrees superiorly and inferiorly, and 30 degrees left and right (Figure 3-2). As the total horizontal extent was approximately 60 degrees, this integrated field was termed IVF-60. A mean deviation score (in dB) for the IVF-60 was calculated as the average of all test locations across the total field area. Based on field points above and below horizontal midline, mean deviation scores were also calculated for the superior and inferior field areas respectively.

3.6.6.2 *Integrated 120-degree field (IVF-120)*

The monocular 81-point screening field tests were merged using the IVF approach. A point in the integrated field was counted as missed if the participant could not see that point in both the left and the right eye, and was counted as seen if at least one eye could see that point (Broman et al. 2004; Turano et al. 2004; Freeman et al. 2007). From central fixation, this integrated binocular field extends approximately 38 degrees superiorly, 55 degrees inferiorly and 58 degrees left and right (see Figure 3-3). As the total horizontal extent was approximately 120 degrees, this integrated field was termed IVF-120.

The IVF-120 consists of a total of 96 points, comprising 46 points superiorly and 50 points inferiorly. An overall IVF-120 score was calculated from the total number of points missed across the total field area. Based on field points above and below horizontal midline, scores were calculated for the superior and inferior field areas respectively.

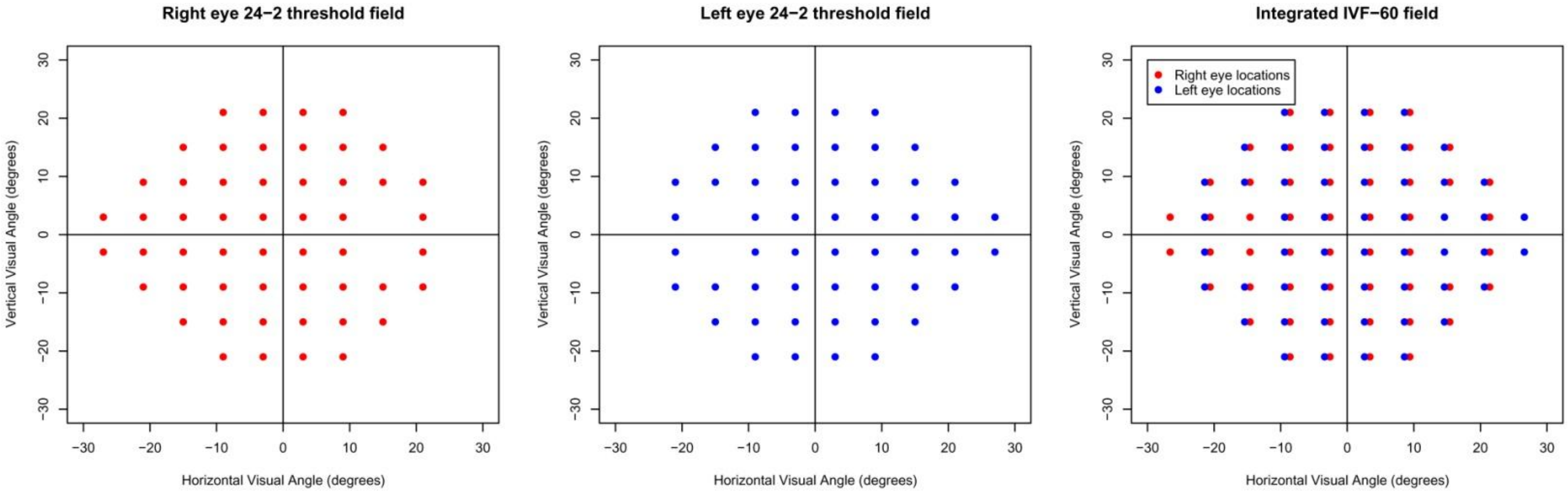

Figure 3-2: Right and left monocular 24-2 and integrated binocular visual field (IVF-60)

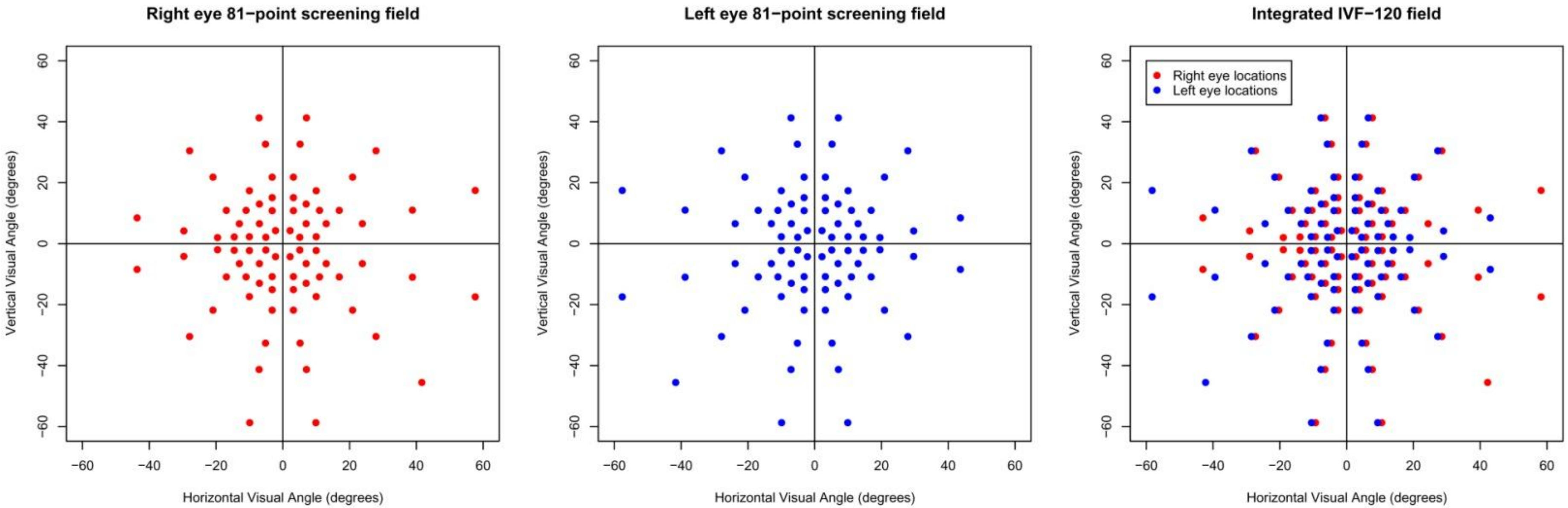

Figure 3-3: Right and left monocular 81-point screening and integrated binocular visual field (IVF-120)

3.6.7 Retinal nerve fibre layer analysis

An objective measure of glaucomatous nerve damage was also included in this study, in addition to the subjective visual function measures. Given that damage to the retinal nerve fibre layer (RNFL) in glaucoma can often precede functional reduction in the visual fields (Hoffmann et al., 2006). Furthermore, subjective visual field measures are influenced by patient variability and assess a limited portion of total peripheral visual function, often the central 30 degrees from fixation.

Retinal nerve fibre layer (RNFL) analysis was undertaken using the Stratus Optical Coherence Tomographer (OCT) 3000 (software version 4.0.5, Carl Zeiss Meditec, Dublin, CA). Using scanning laser technology and the optical properties of the RNFL, the OCT quantifies the thickness of the RNFL at various locations around the optic nerve and is a rapid and reproducible test (Zangwill et al., 2001). The technology has been shown to reproducibly detect damage in tissue thickness with a sensitivity of around 10 microns (El Beltagi et al., 2003).

As the OCT equipment only became available after the commencement of the research, RNFL data were available for a subset of participants. Poor quality scans also meant that some data were not included for analyses, as only well-focused, centred scans with signal strength greater than 6 using the Fast RNFL Thickness 3.46 Scan protocol were included (Leung et al., 2008).

The average RNFL in each eye, in microns, was recorded. RNFL thickness in the better-eye and worse-eye was used in the analysis, corresponding to the eyes with the thicker and thinner RNFL respectively. Unlike the IVF measures, superior and inferior RNFL estimates could not be estimated from the OCT assessment. Figure 3-4 presents an example of an OCT plot, and the corresponding monocular 24-2 visual field plot. Red segments on the OCT plot represent areas of significantly thinner RNFL than age-matched controls. Black squares in the lower 24-2 plots represent points where sensitivity is significantly worse than age-matched average sensitivity.

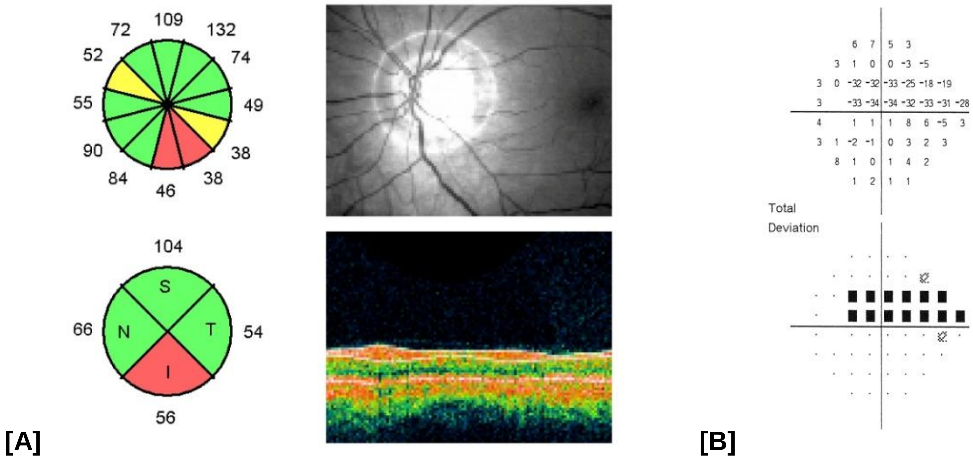

Figure 3-4: Example of [A] OCT scan and [B] corresponding 24-2 threshold visual field plot.

3.6.8 Motion sensitivity

A motion sensitivity test was included in the study, as motion sensitivity has been shown to be affected by glaucoma (Silverman et al., 1990; Bullimore et al., 1993; Shabana et al., 2003) and has been associated with reduced postural stability among older adults (Freeman et al., 2008a). Motion sensitivity was assessed using a computer generated motion sensitivity program, designed by Wood and Bullimore (1995).

A computer screen, placed 3.2m from the participant, presents a large square of random dots subtending 4.0 degree diameter. An inner square of dots within this larger square, subtending 2.9 degree diameter, is displaced (in degrees per second) in one of the four cardinal directions (up, down, left or right). For each presentation, participants report the perceived direction of movement (forced-choice), and the displacement of the following presentation is increased or decreased, in a two down, one up staircase procedure. The program determines the minimum perceived displacement threshold, in degrees per second, based on the average of the last four reversals.

3.6.9 Attentional field of view

Attentional field of view (AFV) measures were included as explanatory factors in the longitudinal falls study (Chapter 7), because previous studies have reported significant associations between AFV and mobility (Broman et al., 2004; Owsley & McGwin, 2004; Leat & Lovie-Kitchin, 2008). Participants' attentional field of view (AFV) was measured binocularly using a computerised test developed at QUT (Wood & Troutbeck, 1995; Wood et al., 2006). Participants were seated 27cm in front of a computer monitor, wearing their habitual single vision distance correction and optically corrected for the test distance. Standard room illumination was provided by overhead fluorescent lighting.

This AFV test consists of central discrimination task (presence or absence of a circle) while simultaneously performing a peripheral discrimination task (localising a triangle). The peripheral triangle can be located in one of 24 possible locations along the 8 cardinal directions on 3 annular rings, subtending 11, 20 and 28 degrees respectively from central fixation. It is estimated that the size of the targets subtend 3.4 degrees, or approximately 6/244 (Leat & Lovie-Kitchin, 2006).

In the absence of any peripheral distractors, the test is a measure of divided attention (AFV_{DIV}). A further level of complexity is introduced with the presence of peripheral distractors, consisting of 47 shaded squares, and is a measure of selective attention (AFV_{SEL}). Figure 3-5 shows some example screenshots of the divided and selective attention tasks. The display duration was constant (90 milliseconds), followed by a random masking pattern to minimise the formation of an afterimage.

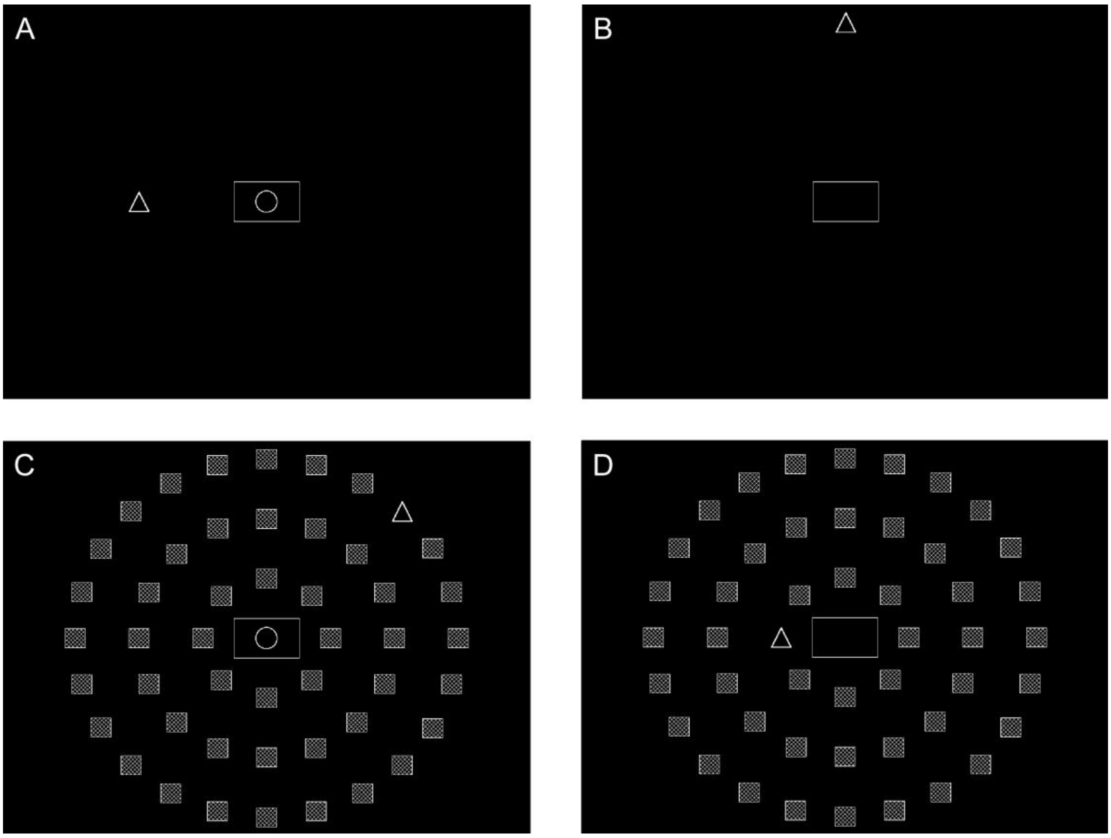

Figure 3-5: Attentional field of view tasks. Divided attention = central and peripheral task, with no peripheral distracters [images A & B]. Selective attention = central and peripheral task, with peripheral distracters [image C & D].

A response was considered **correct** when both the central and peripheral targets were correctly identified and **incorrect** when the central target was correctly identified while the peripheral target was incorrectly identified. A central error was recorded when the central target was incorrectly identified, indicating central inattentiveness, and was retested until a correct response was recorded. The locations of incorrect responses for each of the 24 peripheral positions were recorded, along with the overall sum of incorrect responses. The superior and inferior field scores were calculated as the sum of incorrect responses in the respective hemifields, excluding the horizontal midline target locations.

3.6.10 Vision-related quality of life

The National Eye Institute 25-Item Visual Function Questionnaire (VFQ-25) was used to assess impairment in vision-related functioning (Mangione et al., 2001). This is a widely used and well validated questionnaire that is a condensed and improved version of the original 51-item questionnaire (Mangione et al., 1998).

The self-administered 25-item questionnaire assesses 12 domains: (i) self-rated general health, (ii) overall vision, (iii) difficulty with near vision activities, (iv) difficulty with distance vision activities, (v) limitations in social functioning because of vision, (vi) role limitations because of vision, (vii) increased dependency because of vision, (viii) mental health limitations caused by vision, (ix) driving difficulties, (x) limitations with peripheral vision, (xi) limitations in colour vision and (xii) ocular pain.

Scores were calculated according to the developers' guidelines (Mangione et al., 2001). The subscales scores are an average of the items in the subscale transformed to a 0 to 100 scale, where 100 represents the highest level of functioning or minimal subjective impairment and 0 represents the lowest. The overall composite score for the VFQ-25 is an unweighted average of the responses to all subscale scores, excluding the general health question. The composite score ranges from 0 to 100, where 100 represent the highest level of functioning or minimal subjective impairment and 0 the lowest. The distribution of the VFQ composite score was normalised using a logarithmic transform using the formula TVFQ-25=ln (101-VFQ-25), in which TVFQ-25 and VFQ-25 are the transformed and untransformed values of the composite scale, respectively (McKean-Cowdin et al., 2007; McKean-Cowdin et al., 2008).

3.7 Statistical considerations

3.7.1 Sample size analysis

The sample size estimates were guided by the numbers of participants required to address the hypothesis of the longitudinal falls study (Study 2), as this was the main focus of this research. These calculations were based on a two-sample test comparing means (Chow & Liu, 2004). To detect a minimum difference of 5 points in the binocular integrated visual field measure (IVF-120) between fallers and non-fallers as statistically significant (two-tailed hypothesis at 5% level of significance), with 80% power, would require 58 persons per group. This estimate assumes that the standard deviation of binocular visual field scores (IVF-120) is around 10 units (Freeman et al., 2007). As previous studies indicate 1 in 3 older adults will experience a fall each year (Tinetti et al., 1988; Coleman et al., 2007; Freeman et al., 2007), it is likely that the ratio of non-fallers to fallers will be 2:1. To account for unequal sampling probability, the target sample size was increased by 10%. A total cohort of 135 participants would be needed to obtain an 80% power to detect a 5 point difference on binocular visual field scores between non-fallers and fallers.

It was also important to ensure that the above sample size would be sufficient to address the hypotheses for the cross-sectional studies (Studies 1a, 1b and 1c). Studies have reported significant correlations between visual field loss and health-related QOL measures (SF-36) in the order of r= 0.20 to 0.30 (Jampel et al., 2002a; McKean-Cowdin et al., 2007). In addition, Shabana et al (2005) demonstrated significant correlations between visual field loss and visual stability ratio between r= 0.30 to 0.40. The smallest correlation that could be identified with a power of 80% using a sample size of 135 participants was r=0.24. Alternatively, to identify a correlation of r=0.30, a sample size of 83 participants would be required to provide 80% power to discover a significant difference from the null hypothesis at the 0.05 significance level.

3.7.2 Statistical analyses

Statistical analyses were performed using SPSS (version 16.0, SPSS, Chicago, IL), R (version 2.6.0) and Microsoft Excel Version 2007 (Microsoft Corporation, 1997). The significance criterion was set at p=0.05, and all tests were two-tailed.

Descriptive statistics (including mean, standard deviation, range and proportions, as appropriate) were calculated for all variables. Distributions of these variables were examined for normalcy using histograms, normal quantile-quantile plots and box plots with outliers. Normally distributed continuous data were summarised using mean and standard deviation (SD) statistics. Continuous data not normally distributed were summarised using median statistics. Nominal data were presented as counts and percentages.

Specific statistical analyses undertaken for each data set are detailed in the relevant chapters. Given the exploratory nature of this study, multiple adjustments are not strictly required and are overly conservative, and can potentially mask important findings (Perneger, 1998; Bender & Lange, 2001). Therefore in our analyses, p-values were not adjusted for multiple comparisons; however, the possibility of chance findings due to type I errors must be considered when interpreting our results.

All linear regression models were assessed for model fit and residuals examined to confirm the model assumptions of normality, linearity and homoscedasticity. Multicollinearity was assessed in regression models using the collinearity diagnostics in SPSS based on the variance inflation factors (VIF). A VIF value greater than 10 provides evidence of multicollinearity (Chatterjee et al., 2006).

3.7.3 Potential confounding factors

By definition, confounding factors are significantly associated with both the outcome and explanatory variables, but do not lie on the causal pathway (Woodward, 2005). It was considered a priori that age and gender would be important potential confounding factors. Age is associated with an increased the risk of glaucoma (Rochtchina & Mitchell, 2000; Weih et al., 2001) and falls (Ivers et al., 1998; Klein et al., 2003b; Freeman et al., 2007). In addition, gender differences have been reported for glaucoma risk (Rudnicka et al., 2006) and falls (Ivers et al., 1998; Tromp et al., 2001; Freeman et al., 2007). As such, these factors were included as confounding variables in all analyses, regardless of their statistical significance with the visual function and outcome measures.

Systematic assessment of other potential confounding factors was performed and is presented in Appendix 4. The following demographic, health and medical variables were evaluated as confounding factors: smoking status (non-smoker, former smoker or current smoker), alcohol intake (abstainers, light drinkers and heavy drinkers), medication use (central nervous system, hyponotics/sedatives, antidepressants, cardiac, oral beta-blockers, endocrine, respiratory, number of medications and polypharmacy) and some self-reported medical conditions (diabetes, hearing impairment, heart disease, hypertension and co-morbidity index). Several variables were not considered as potential confounding variables, such as arthritis and body mass index, because these variables may be in the causal pathway between vision field loss and the outcome measures.

For the correlation analyses, the variables were tested for confounding based on a criteria of $p<0.20$ for the bivariate association between the outcome measures (health-related QOL, functional status and postural sway) and the key explanatory variables (IVF measures) (Maldonado & Greenland, 1993). This liberal criteria for $p<0.20$ for inclusion of covariates is required, since statistical power was not ensured for these correlations. As the majority of these variables failed to meet the criteria for confounding, none were included as confounding variables to avoided over-fitting the models given the small sample size in the study.

For the longitudinal falls analyses, the variables were tested for confounding based on the change-in-estimate criteria using a value of 10 per cent (Maldonado & Greenland, 1993). As none of these variables demonstrated greater than 10 per cent change in the rate ratio estimates when included in the regression models between visual field loss and falls, they were not included as confounding variables in analyses.

3.8 Ethical approval

The Queensland University of Technology Human Research Ethics Committee granted ethical clearance for this study in October 2005 (QUT Reference Number 4189H) and the investigation was conducted in accordance with the tenets of the Declaration of Helsinki.

3.9 Data entry and quality control

A number of measures were employed to ensure optimal data quality and accuracy in data entry and analysis. These measures include:

- Use of standardised data collection instruments and procedures wherever possible;
- Careful inspection of returned questionnaires and forms for completeness and consistency;
- Use of a single examiner and interviewer for data consistency;
- Random checking of paper based data with the computerised database (minimum 10 per cent, with minimal errors encountered); and
- Carefully controlled data checking, coding and cleaning procedures. These procedures are detailed in Appendix 5.

3.10 Baseline characteristics of the study cohort

3.10.1 Study population

In total, a convenience sample of 78 community-dwelling individuals, aged over 62 years of age and being treated for open-angle glaucoma, were invited to participate in this study. Four participants failed to meet the inclusion criteria when assessed at the baseline visit. Reasons for exclusion included the inability to walk unaided (n=2) and the presence of other significant ocular disease (n=2). In total, 74 participants were eligible to participate and completed the baseline assessment. During the 12-month follow-up period, one participant passed away, and two withdrew from the study, leaving a total of 71 participants who completed the prospective falls assessment. A summary of the recruitment and data collection process is presented in Figure 3-1. In total, 150 adults were approached to participate in the study, identified from the various recruitment sources. Although the sample size calculations estimated that 135 participants were required, this target was not achievable within the study period, due to the strict inclusion and exclusion criteria of the study, along with difficulties in attending the campus due to transport limitations.

3.10.2 Socio-demographic, health and medical characteristics

The group of 35 (47%) women and 39 (53%) men had a mean age of 74.2 years (SD 5.9) ranging from 62 to 90 years (Table 3-1). Female participants were similar in age to the male participants (74.3 ± 6.3 and 74.2 ± 5.5 years respectively, t = -0.08, p=0 .94).

Participants reported a median of two non-ocular co-morbidities (range none to 5); the four most frequently cited were arthritis (51%), hearing impairment (39%), hypertension (39%) and heart disease (30%) (Table 3-2). The majority of participants (76%) were taking some form of cardiac medication, followed by endocrine medications (32%). In terms of the self-rated general health of the participants, 30 participants (41%) reported very good or excellent health, 36 (49%) reported good health and 8 (11%) reported poor health (data not shown).

The median duration of glaucoma reported was 9 years, ranging from 1 to 56 years. The majority of participants were being treated bilaterally (92%), and 14 (19%) reported having had previous glaucoma surgery. The treatment of glaucoma in all but one participant was by means of topical anti-glaucoma medications. Of these, 27 (36%) were using two or more topical preparations (data not shown, range 1 to 3 medications) and 22 (30%) were using a topical beta-blocker medication.

In the previous year, 26 (35%) participants reported experiencing at least one fall and 7 (10%) reported two or more falls (range 1-6). Of these, 4 (5%) participants reported an injury arising from the previous fall/s. Fear of falling was reported in 16 (22%) participants and 12 (16%) reported some restriction in their activities due to fear of falling.

Table 3-1: Baseline socio-demographic characteristics of participants (n=74)

Mean age, years (sd)	74	± 5.9			
Range	62 - 90				
Female, n (%)	35	(47.3%)			
Country of Birth, n (%)					
Australia	53	(71.6%)	**Current Employment Status, n (%)**		
United Kingdom	13	(17.6%)	Retired	53	(71.6%)
Europe	2	(2.7%)	Employed full-time	1	(1.4%)
Asia	1	(1.4%)	Employed part-time	3	(4.1%)
North America	1	(1.4%)	Home Duties	4	(5.4%)
Other	4	(5.4%)	Missing	13	(17.6%)
Accommodation, n (%)			**Primary Household Income, n (%)**		
House	52	(70.3%)	Salary or wage	4	(5.4%)
Unit	18	(24.3%)	Superannuation, investments	38	(51.4%)
Other	4	(5.4%)	Any form of pension	19	(25.7%)
Living Arrangements, n (%)			Missing	13	(17.6%)
With spouse	54	(73%)	**Current driver, n (%)**	62	(83.8%)
Alone	16	(21.6%)	**Smoking Status, n (%)**		
With relatives	2	(2.7%)	Non-smoker	47	(63.5%)
Other	2	(2.7%)	Former smoker	26	(35.1%)
Education Completed, n (%)			Current smoker	1	(1.4%)
University/College Degree	26	(35.1%)	**Alcohol Consumption, n (%)**		
Trade/Technical Certificate	11	(14.9%)	Abstainer	21	(28.4%)
Secondary High School	31	(41.9%)	Light drinker	50	(67.6%)
Primary School	6	(8.1%)	Heavy drinker	3	(4.1%)

Notes: sd = standard deviation;

Table 3-2: Baseline health and medical characteristics of participants (n=74)

	Prevalence	
Medical co-morbidities, n (%)		
Arthritis	38	(51.4%)
Cancer	20	(27%)
Diabetes	9	(12.2%)
Hearing impairment	29	(39.2%)
Heart disease	22	(29.7%)
Hypertension	29	(39.2%)
History of hip fracture	3	(4.1%)
Incontinence	8	(10.8%)
History of stroke	1	(1.4%)
Other	5	(6.8%)
Co-morbidity index, median (range)	2	(0 - 5)
Number of medications, median (range)	4	(1 - 12)
Use of four or more medications, n (%)	47	(63.5%)
Systemic medication use, n (%)		
Use of central nervous system medication	10	(13.5%)
Use of sedatives or hypnotics	5	(6.8%)
Use of antidepressants	6	(8.1%)
Use of cardiac medication	56	(75.7%)
Use of oral beta-blocker	11	(14.9%)
Use of endocrine medication	24	(32.4%)
Use of respiratory medication	5	(6.8%)
Median duration of glaucoma, years (range)	9	(1-56)
1-5 years, n (%)	26	(35.1%)
5-10 years, n (%)	12	(16.2%)
More than 10 years, n (%)	27	(36.5%)
Missing	9	(12.2%)
Glaucoma Laterality, n (%)		
Unilateral	6	(8.1%)
Bilateral	68	(91.9%)
Number of topical glaucoma medications, median (range)	1	(0 - 3)
Glaucoma medication use, n (%)†		
Use of a topical beta-blocker medication	22	(29.7%)
Use of other topical glaucoma medications	66	(89.2%)
Previous glaucoma surgery, n (%)		
Yes	14	(18.9%)

† Totals do not equal 100% due to multiple medications use

3.10.3 Vision Function Characteristics

Among the 74 participants assessed at baseline, 14 (19%) did not wear any distance correction, 9 (12%) used single-vision distance spectacles, 1 (1%) wore contact lenses, and 50 (68%) wore multifocal spectacles. Of the multifocal wearers, the majority wore bifocals (n=33), followed by progressive lenses (n=15) and trifocals (n=2).

The baseline visual function characteristics of the 74 participants are presented in Table 3-3. There are missing data for some visual function measures, as some participants were unable to complete the motion perception tests (n=3), incomplete VFQ-25 questionnaires (n=2) and poor quality OCT scans (n=17). The AFV characteristics of the cohort are presented in Chapter 7.

The cohort comprised a heterogeneous group regarding severity of glaucoma. The mean severity of binocular visual field loss was -4.10 dB (range 1.59 dB to -28.23 dB) for the IVF-60, and 32 points missed (range 6 to 96) for the IVF-120. Three participants had presenting habitual visual acuity in the better eye worse than 6/12 (data not shown).

Many of the visual function measures were significantly correlated, as shown in Table 3-4. Central visual function measures of visual acuity and contrast sensitivity were highly correlated with each other (r = -0.61 to -0.83). With more advanced glaucoma, both central and peripheral visual function are affected, evidenced by the significant correlations between VA better-eye and IVF measures (r= |0.44| to |0.53|) and between CS better-eye and IVF scores (r= |0.71| and |0.79|). The correlations between IVF and worse-eye measures (VA, CS and 24-2) were generally weaker compared to better-eye measures.

Greater IVF loss was significantly associated with poorer motion detection scores (r=|0.35| to |0.36|) and stereoacuity (r=|0.49| to |0.52|). The integrated visual field measures were highly inter-correlated (r=|0.72| to |0.93|) (data presented in Appendix 6).

Table 3-3: Baseline visual function characteristics of participants (n=74)

Visual function	N	Better-eye		Worse-eye		Binocular	
Visual Acuity (logMAR), mean ± sd, (range)	74	0.06 ± 0.13	(-0.26 to 0.52)	0.21 ± 0.26	(-0.1 to 1.4)		
Contrast Sensitivity (logCS), mean ± sd, (range)	74	1.54 ± 0.17	(0.65 to 1.7)	1.44 ± 0.29	(0.25 to 1.7)		
Stereopsis, n (%)							
present	61					61	(82.4%)
absent	13					13	(17.6%)
Dot Motion (log deg/sec), mean ± sd, (range)	71					-1.38 ± 0.24	(-1.868 to -0.795)
Visual Field Sensitivity (dB), mean ± sd, (range)	74	-4.29 ± 6.39	(-28.01 to 1.29)	-8.66 ± 8.55	(-31.99 to 0.81)		
RNFL (µm), mean ± sd, (range)	57	83.8 ± 19.0	(42.33 to 128)	73.0 ± 18.4	(38.92 to 116.17)		
IVF-60 (dB), mean ± sd, (range)							
total field	74					-4.10 ± 6.28	(-28.23 to 1.59)
lower field	74					-3.52 ± 6.28	(-28.36 to 2.75)
upper field	74					-4.67 ± 7.02	(-28.96 to 3.25)
IVF-120 (points missed), mean ± sd, (range)							
total field	74					32 ± 21	(6 to 96)
lower field	74					17 ± 12	(2 to 46)
upper field	74					15 ± 11	(1 to 50)
VFQ-25 score, median (range)	72					87.9	(26.36 to 100)

Notes: sd = standard deviation; MAR = minimum angle of resolution; CS = contrast sensitivity; dB = decibel; RNFL = retinal nerve fibre layer; IVF = integrated visual field; VFQ-25 = Visual Function Questionnaire

Table 3-4: Pearson's correlations between vision measures, according to [A] better-eye and [B] worse-eye scores†

[A]	VA better-eye	CS better-eye	Stereo-acuity	Motion sensitivity	24-4 better-	IVF-60 overall	IVF-120 overall
VA better-eye	1						
CS better-eye	-0.61 **	1					
Stereoacuity	0.36 **	-0.65 **	1				
Motion sensitivity	0.38 **	-0.48 **	0.41 **	1			
24-4 better-eye	-0.52 **	0.77 **	-0.49 **	-0.37 **	1		
IVF-60 overall	-0.53 **	0.79 **	-0.52 **	-0.36 **	0.99 **	1	
IVF-120 overall	0.44 **	-0.71 **	0.49 **	0.35 **	-0.91 **	-0.93 **	1
VFQ-25 composite	0.34 **	-0.53 **	0.36 **	0.22	-0.54 **	-0.54 **	0.52 **

[B]	VA worse-eye	CS worse-eye	Stereo-acuity	Motion sensitivity	24-4 worse-	IVF-60 overall	IVF-120 overall
VA worse-eye	1						
CS worse-eye	-0.83 **	1					
Stereoacuity	0.59 **	-0.71 **	1				
Motion sensitivity	0.45 **	-0.47 **	0.41 **	1			
24-4 worse-eye	-0.53 **	0.72 **	-0.55 **	-0.28 *	1		
IVF-60 overall	-0.64 **	0.70 **	-0.52 **	-0.36 **	0.86 **	1	
IVF-120 overall	0.57 **	-0.66 **	0.49 **	0.35 **	-0.86 **	-0.93 **	1
VFQ-25 composite	0.40 **	-0.46 **	0.36 **	0.22	-0.42 **	-0.54 **	0.52 **

Notes: * $p<0.05$; ** $p<0.01$; VA = visual acuity; CS = contrast sensitivity; IVF = integrated visual field; VFQ-25 = Visual Function Questionnaire (transformed scale).
† n=74, with the exception of VFQ-25 (n=72);

3.11 Summary

In summary, this chapter described the recruitment procedures and common methods used throughout the thesis. The baseline demographics and visual function characteristics of the study population were also presented. The following four chapters present the findings from the cross-sectional studies (Studies 1a, 1b and 1c) and the longitudinal falls study (Study 2).

Chapter 4: Visual Impairment and Health-Related Quality of Life among Older Adults with Glaucoma [Study 1a]

4.1 Introduction

Visual impairment may affect health-related QOL due to a number of reasons, which include the diagnosis itself, the loss of visual function, its impact on functional activities, and the costs, inconvenience and side-effects associated with treatment (Severn et al., 2008). It follows, therefore, that visual impairment from glaucoma would negatively impact on the health-related QOL of older adults. However, this relationship has not been well explored in the previous literature.

As outlined in the literature review, there is a growing body of literature that has examined health-related QOL as a means of understanding the broader impact of eye disease. However, these studies have focused on the impact of visual acuity loss or self-reported vision loss on health-related QOL (Chia et al., 2004; Langelaan et al., 2007). Visual field loss has received comparatively little attention in previous research, and its association with health-related QOL is less well understood, particularly among older adults. The remainder of this introduction reviews the literature which has examined the association between glaucoma or visual field loss and health-related QOL.

4.2 Glaucoma, visual field loss and health-related QOL

There is consistent evidence that has demonstrated that adults with glaucoma or visual field loss report poorer levels of general health-related QOL, compared to those with normal vision. In the Los Angeles Latino Eye

Study (LALES) of adults aged over 40 years, McKean-Cowdin et al (2007) demonstrated that adults with moderate to severe bilateral visual field loss from any cause (n=340), defined as a mean deviation in both eyes worse than -6dB, reported significantly lower SF-12 scores compared to adults without visual field loss (n=2,886), in both the physical and mental components (by 3.7 and 2.8 units, respectively). The study also indicated that health-related QOL is not significantly affected until glaucoma becomes bilateral, as adults with moderate to severe unilateral visual field loss (n=77), reported similar SF-12 scores to those without visual field loss.

In a follow-up study comprising of the same LALES cohort, McKean-Cowdin et al (2008) examined health-related QOL scores among adults with visual field loss from glaucoma (n=180), defined as a mean deviation in a merged binocular field worse than -2dB. Compared to participants without glaucoma (n=2,821), those with bilateral glaucoma reported lower SF-12 scores, but only in the physical component of the SF-12 (by 2.1 units). The results of the follow-up study were weaker than their earlier study (McKean-Cowdin et al., 2007), most likely due to the less stringent criteria of visual field loss (-2 dB compared with -6 dB) and the smaller sample size.

Case-control studies have shown that individuals with glaucoma report poorer health-related QOL compared to controls with normal vision. Sherwood et al (1998) found that patients aged over 40 years with glaucoma (n=54) reported lower scores on the Medical Outcome Study 20-item questionnaire in 5 of the 6 subscales, when compared to age-matched controls (n=54). The specific subscales which differed significantly between glaucoma and control groups included physical functioning, role functioning, mental health, general health and social functioning. The study, however, did not examine the association between severity of visual field loss and these subscales in the glaucoma group.

In a similar study, Wilson (1998) compared SF-36 subscale scores between a group of glaucoma patients (n=121), whose mean deviation in the better eye averaged -9.4 dB (range 1.7 dB to -27.7 dB), and a normally sighted control group (n=135). Individuals with glaucoma reported significantly lower scores in six of the eight domains, notably in the subscales for physical functioning (by 4.55 units) and role limitation-physical (by 4.83 units). Interestingly, mental health scores were significantly higher among those with glaucoma (by 0.51 units). There were some notable limitations, however, as the control group was significantly younger than the glaucoma group (mean age 44.8 and 69.8 years, respectively), and the analyses did not include the SF-36 physical or mental component scores.

Gutierrez (1997) compared SF-36 scores between 147 glaucoma patients, with a mean glaucoma severity score of 5.3 ± 5.9 units in the better eye, and 25 controls with normal vision, aged over 30 years (average age not reported). Participants with glaucoma reported lower scores on all 8 SF-36 subscales, but the differences failed to reach statistical significance. These findings were limited by the uneven group sizes, along with the control group being significantly younger, by 15 years on average, than the glaucoma participants. The study also did not calculate either of the SF-36 physical or mental component scores.

4.3 Severity of visual field loss and health-related QOL

It is unclear, however, whether severity of visual field loss is related to declines in health-related QOL. Comparisons between studies are difficult due to the use of a variety of health-related QOL instruments, visual field measures and variations in the study populations. At best, the expected associations between severity of visual field and health-related QOL are not likely to be strong, given that outcomes from health-related QOL instruments are influenced by additional health-related factors, and are not likely to be considerably influenced by changes in visual function. Despite this, previous studies have reported associations between the severity of visual field loss and health-related QOL.

The best evidence, to date, is shown in a population-based study comprised of 5,213 adults aged over 40 years (McKean-Cowdin et al., 2007). In this study, greater visual field loss from any cause, using the better-eye mean deviation scores, was associated with lower physical and mental SF-12 component scores. The association was slightly stronger on the physical component than the mental component (linear regression coefficient (B) 0.23 vs 0.21, respectively). However, the results were not supported in a follow-up study when the analysis was limited to adults with glaucoma (n=213) (McKean-Cowdin et al., 2008). No significant associations were found between visual field loss (mean deviation in the better-eye) and either the SF12 physical (B coefficient 0.16; p=0.128) or mental (B coefficient 0.28; p=0.056) component scores. It is likely that the disparity in the findings of the latter study is due to the smaller sample size compared to the former study.

The findings from smaller clinical studies are also mixed. Parrish et al (1997) examined SF-36 scores among 147 glaucoma participants (mean age 70; range 15-92). Weak but significant correlations were found between a number of SF-36 domains and binocular Esterman field scores, most notably between subscales for physical function (r=-0.25), role physical (r=0.26) and role emotional (r=-0.21). Iester et al (2002) reported a significant correlation between mean deviation in the worse eye and SF-36 scores (r=0.40) among 77 glaucoma participants (mean age 62±5 years; range not reported). The study, however, is limited by the lack of findings based on the SF-36 summary scores, or the better eye visual field measures.

Jampel et al (2002b) reported low correlations between SF-36 subscale scores and binocular Esterman scores (highest correlation with physical function, r=0.18) or better-eye MD (highest correlation with social function, r=0.20), in a study of 191 glaucoma participants (mean age 72 years; range 26–92). In another study by Jampel (2002a), low correlations were found on a range of monocular and binocular visual field tests and SF-36 subscales among 101 glaucoma patients (mean age 69 years; range 32-90). The strongest correlate was found between merged binocular fields and the role-physical domain (r=0.21). In contrast, Wilson et al (1998) failed to demonstrate any associations between SF-36 subscale scores and mean deviation in the better-eye in a cohort of 121 participants with glaucoma (mean age 70 ± 13 years; range not reported). The study, however, did not examine these associations using the SF36 summary scores.

An area of research that has received little attention is the relationship between field loss location and health-related QOL. Severity of central and inferior visual field loss have been shown to correlate significantly with reduced mobility performance among visually impaired individuals (Lovie-Kitchin et al., 1990; Turano et al., 2004). The loss of inferior visual field may impact on health-related QOL, particularly if difficulties in mobility result in restriction in social and recreational participation, with subsequent declines in functional capacity. However, this association remains unexplored, as no previous studies have examined the association between visual field loss location and health-related QOL.

There is little evidence in the literature to suggest that glaucomatous visual field loss affects the psychological well-being among older adults. Skalicky et al (2008) reported no significant association between visual field loss and depression, using the Geriatric Depression Scale, among 165 participants with glaucoma. Visual field loss was not a significant predictor of depression, using the Center for Epidemiologic Studies Depression Scale, in a study of 121 patients with open-angle glaucoma (Wilson et al., 2002), nor in study of 607 newly diagnosed glaucoma patients (Jampel et al., 2007).

4.4 Rationale for the study

In summary, there is evidence that adults with glaucoma report poorer health-related QOL compared to controls, although it remains unclear if greater severity of visual field loss is associated with poorer health-related QOL. Variations in the study cohorts and the use of different methods to assess health-related QOL may explain the equivocal findings. In addition, there appears to be limited evidence to suggest that visual field loss negatively impacts on psychological well-being of older adults.

The age groups examined in these previous studies vary considerably, some including participants aged as young as 15 years of age. Older adults experience significant declines in physical function (Fried et al., 2001; Rockwood et al., 2007), and have higher rates of chronic illness and comorbidites than their younger counterparts. There is, however, limited research into the association between glaucoma and health-related quality of life specifically among older populations. It is possible that the impact of glaucomatous vision impairment on health-related quality of life among older populations may be significantly greater than younger populations, yet remains to be explored. Thus, the current study sought to examine the association between severity and location visual field loss and health-related QOL in a cohort of older adults with glaucoma.

4.5 Study aims and hypotheses

Using a cohort of community-dwelling older adults with glaucoma (n=74), the aim of the research was to examine the cross-sectional relationship between severity and location of visual field loss and health-related QOL, based on the Short Form 36-item Health Survey (SF-36).

The hypotheses of the research (expressed as alternate hypotheses) described in this chapter are that:

- Greater visual field loss is associated with poorer self-reported health-related QOL;
- Greater visual field loss in the inferior field region is associated with poorer self-reported health-related QOL.

4.6 Additional methods

4.6.1 Health-related QOL outcome measures

4.6.1.1 *Short form 36-item health survey (SF-36)*

The Australian version of the Medical Outcomes Study Short Form 36-item Health Survey Version 2 (SF-36) was used to assess general health-related QOL (Ware & Sherbourne, 1992). This is a well-known generic, multi-dimensional health status instrument. It was selected because it has been well-validated and has standardized normal values (Ware & Sherbourne, 1992; Hawthorne et al., 2007). In addition, it has been widely used in vision research and has been shown to be a valid and reliable instrument among older populations (Chia et al., 2006c). Excellent test-retest reliability of the SF-36 summary scores has been reported in studies among older adults, with reliability estimates greater than 0.73 (Haywood et al., 2005).

The self-administered 36-item questionnaire assesses eight dimensions (subscales) of health and wellbeing: (i) physical functioning (PF), (ii) role limitation due to physical problems (RP), (iii) bodily pain (BP), (iv) general health perceptions (GH), (v) vitality (VI), (vi) social functioning (SF), (vii) role limitation due to emotional problems (RE) and (viii) mental health (MH). These subscales are scored from 0 (representing worst possible health state) to 100 (representing best possible health state) by coding, summating and transforming relevant item scores, according to the recommended guidelines and algorithms. The subscales are standardized using a Z-score transform based on Australian population SF-36 normal values (Hawthorne et al., 2007).

The eight subscales are used to create two summary measures: the physical component score (PCS) and the mental component score (MCS), weighted by established factor score coefficients (Hawthorne et al., 2007). The subscale and summary scores are standardized to a T-score (mean = 50, standard deviation = 10). Scores greater than 50 indicate better-than-average quality of life and scores below 50 indicate worse-than-average quality of life.

4.6.2 Statistical analysis

As most of the SF-36 subscales were not normally distributed, the bivariate associations between the subscales scores and visual function measures were assessed using Spearman rank-correlations.

Pearson's correlations were used to examine the bivariate relations between the continuous predictor variables and SF-36 PCS and MCS scores; point biserial correlations were used to examine relations between the categorical variables and SF-36 PCS and MCS scores. Further analyses adjusted for age and gender. P-values were not adjusted for multiple comparisons, as reported in Section 3.7.2.

The associations between integrated visual field loss (IVF-60 and IVF-120) and SF-36 PCS were assessed using linear regression models, adjusted for age and gender. No further analyses were undertaken using the SF-36 MCS scores, because of the lack of bivariate associations with the visual function measures.

To examine the independent association between SF-36 PCS and location of visual field loss, the superior and inferior field integrated field measures were considered together in a regression model, adjusted for age and gender. These models were examined separately for the IVF-60 and IVF-120 measures. Multicollinearity was assessed using the collinearity diagnostics in SPSS based on the variance inflation factors (VIF).

4.7 Results

4.7.1 Description of study cohort

The socio-demographic, health, medical and visual characteristics of the 74 participants have been described in Chapter 2.

4.7.2 Severity of visual impairment and health-related QOL

The distributions of the SF-36 raw and normalised subscales and summary scores are presented in Table 4-1. Few participants had scale scores of 0, while many of the scales were positively skewed towards higher scores. The normalised SF-36 subscale scores ranged from 46.3 ± 9.4 for physical function to 50.4 ± 8.9 for vitality. Of the summary scores, participants reported lower PCS and higher MCS scores (46.8 ± 8.5 and 50.7 ± 10.2, respectively).

Table 4-1: Raw and normalised SF-36 subscale and summary scores (n=74)

	Raw Scores					Normed Scores				
Scale	**Mean**	**SD**	**Median**	**Min**	**Max**	**Mean**	**SD**	**Median**	**Min**	**Max**
Physical Function	76.6	20.6	85	10	100	46.3	9.4	50.2	15.9	57.0
Role Physical	77.1	24.1	84.38	0	100	47.1	9.6	50.0	16.4	56.2
Bodily Pain	68.8	19.3	72	22	90	46.4	9.1	47.9	24.4	56.4
General Health	70.4	17.9	72	22	100	49.3	8.2	50.1	27.2	62.8
Vitality	62.1	18.5	62.5	6.25	100	50.5	8.9	50.7	23.6	68.7
Social Function	87.2	19.2	100	25	100	50.4	8.6	56.2	22.6	56.2
Role Emotional	88.1	18.7	100	8.33	100	48.0	10.7	54.8	2.4	54.8
Mental Health	80.4	16.6	85	20	100	49.9	9.8	52.6	14.3	61.4
SF-36 PCS	-	-	-	-	-	46.8	8.5	48.2	24.5	62.6
SF-36 MCS	-	-	-	-	-	50.7	10.2	53.4	6.7	70.7

Notes: SD = Standard Deviation; SF-36 = Short-form 36-item survey; PCS = Physical Component Score; MCS = Mental Component Score

The bivariate correlations between the SF-36 subscales and vision variables are presented in

Table 4-2. Only 2 of the 8 SF36 subscales showed significant associations with several visual function measures, and the correlations in these cases were relatively weak (r=|0.24| to |0.34|). Greater overall visual field loss (24-2 better-eye, IVF-120) and inferior visual field loss (IVF-60 and IVF-120) was associated with lower role physical scores. In addition, greater overall visual field loss (24-2 better-eye and IVF-60) was associated with lower general health scores. Significant correlations were also found between VFQ-25 composite score and 6 of the 8 SF-36 subscales (r=-0.29 to -0.42).

The unadjusted and adjusted correlations for the association between visual function and SF-36 summary scores are shown in Table 4-3. In the age and gender adjusted analyses, lower scores on the SF-36 PCS scores were associated with reduced central visual function (VA better-eye r=-0.30; CS better-eye r=0.33) and overall visual field loss (24-2 better-eye r=0.35; IVF-60 r=0.36; IVF-120 r=-0.32). The inferior field integrated scores were more strongly associated with lower PCS scores than the superior field scores (IVF60 inferior r=0.36; IVF-120 inferior r=-0.35). Only the VFQ-25 composite score was significantly associated with SF-36 MCS scores.

The results from linear regression models controlling for age and gender are presented in Table 4-4. Each decibel reduction in total IVF-60 was associated with a 0.50 unit decrease in PCS scores (Model 1), while each 10 points missed on the total IVF-120 was associated with a 1.28 units decrease in PCS score (Model 3). When both the superior and inferior fields were considered together in a model, the inferior fields were more strongly associated with PCS scores, particularly in the IVF-120 model (Model 4), whereas the superior field estimates fell short of statistical significance. Each 10 points missed on the IVF-120 inferior field was associated with a 3 units decrease in PCS score. While a similar trend was noted for IVF-60, this failed to reach statistical significance.

Table 4-2: Spearman's correlations between visual function measures and SF-36 subscales scores†

	SF-36 Subscales							
Vision Measure	**Physical Function**	**Role Physical**	**Bodily Pain**	**General Health**	**Vitality**	**Social Function**	**Role Emotion**	**Mental Health**
Visual Acuity (logMAR)								
better-eye	-0.06	-0.08	0.06	-0.01	0.09	0.14	0.11	0.14
worse-eye	-0.06	-0.21	0.08	0.02	0.09	0.14	-0.06	0.12
Contrast Sensitivity (logCS)								
better-eye	0.10	0.08	-0.20	0.13	0.09	0.04	0.00	-0.05
worse-eye	0.04	-0.01	**-0.28** *	0.13	0.01	-0.08	-0.05	-0.18
Stereoacuity (present/absent)	-0.15	-0.09	0.15	-0.09	-0.11	-0.10	-0.08	0.10
Motion sensitivity (log deg/sec)	0.11	-0.06	0.19	-0.02	0.02	0.13	-0.13	-0.03
Visual Field Sensitivity (dB)								
better-eye	0.10	**0.25** *	-0.10	**0.28** *	0.13	0.15	0.06	0.09
worse-eye	0.05	0.13	-0.11	0.17	0.07	0.18	0.13	0.01
RNFL (µm)								
better-eye	-0.14	0.11	-0.11	0.26	0.16	0.15	-0.02	-0.03
worse-eye	-0.20	0.02	-0.07	0.21	0.10	0.11	-0.06	-0.14
IVF-60 (dB)								
overall field	0.09	0.22	-0.14	**0.24** *	0.12	0.14	0.06	0.07
inferior field	0.15	**0.25** *	-0.13	0.22	0.16	0.14	0.19	0.11
superior field	0.05	0.20	-0.12	0.19	0.09	0.13	0.01	0.04
IVF-120 (points missed)								
overall field	-0.12	**-0.24** *	0.06	-0.19	-0.09	-0.15	-0.03	-0.07
inferior field	-0.22	**-0.26** *	0.02	-0.14	-0.09	-0.15	-0.11	-0.08
superior field	-0.07	-0.20	0.10	-0.16	-0.06	-0.13	0.02	-0.04
VFQ-25 composite	-0.15	**-0.33** **	-0.07	**-0.42** **	**-0.31** **	**-0.41** **	**-0.29** *	**-0.37** **

Notes: Bold values indicate significant correlations; *p<0.05; **p<0.01; † n=74, with the exception of RNFL (n=57) and VFQ-25 (n=72); SF-36 = Short-form 36-item survey; RNFL = Retinal Nerve Fibre Layer; IVF = Integrated Visual Field; VFQ-25 = Visual Function Questionnaire.

Table 4-3: Pearson's correlations between visual function measures and SF-36 summary scores†

	Unadjusted		Age and gender adjusted	
	Physical Component	**Mental Component**	**Physical Component**	**Mental Component**
Visual Acuity (logMAR)				
better-eye	**-0.30** **	0.10	**-0.30** *	0.12
worse-eye	**-0.29** *	0.02	**-0.27** *	0.05
Contrast Sensitivity (logCS)				
better-eye	**0.31** **	0.07	**0.33** **	0.05
worse-eye	**0.24** *	-0.02	**0.24** *	-0.05
Stereoacuity (present/absent)	-0.15	-0.01	-0.14	0.03
Motion sensitivity(log deg/sec)	0.11	-0.12	0.14	-0.08
Visual Field Sensitivity (dB)				
better-eye	**0.29** *	0.17	**0.35** **	0.17
worse-eye	0.20	0.06	**0.25** *	0.06
RNFL (µm)				
better-eye	0.15	0.02	0.11	0.01
worse-eye	0.02	-0.01	0.07	-0.01
IVF-60 (dB)				
overall field	**0.30** **	0.14	**0.36** **	0.15
inferior field	**0.33** **	0.18	**0.36** **	0.17
superior field	**0.24** *	0.10	**0.31** **	0.11
IVF-120 (points missed)				
overall field	**-0.29** *	-0.09	**-0.32** **	-0.08
inferior field	**-0.35** **	-0.14	**-0.35** **	-0.12
superior field	-0.20	-0.03	**-0.25** *	-0.03
VFQ-25 composite	**-0.30** **	**-0.30** **	**-0.29** *	**-0.29** *

Notes: Bold values indicate significant correlations; *p<0.05; **p<0.01; † n=74, with the exception of RNFL (n=57) and VFQ-25 (n=72); SF-36 = Short-form 36-item survey; RNFL = Retinal Nerve Fibre Layer; IVF = Integrated Visual Field; VFQ-25 = Visual Function Questionnaire (transformed scale);

Table 4-4: Association between visual field measures and SF-36 physical component scores (linear regression, adjusted for age and gender; n=74)

Model	Predictor Variables	B coefficient (95% CI)		Beta	p-value	VIF
1	IVF-60 overall field (per dB)	**0.50**	**(0.19 to 0.8)**	**-0.37**	**0.002**	
2	IVF-60 inferior field (per dB)	0.42	(-0.06 to 0.91)	-0.32	0.088	2.72
	IVF-60 superior field (per dB)	0.09	(-0.36 to 0.53)	-0.07	0.707	2.91
3	IVF-120 overall field (per 10 points)	**-1.28**	**(-2.17 to -0.39)**	**-0.32**	**0.006**	
4	IVF-120 inferior field (per 10 points)	**-3.01**	**(-5.64 to -0.38)**	**-0.39**	**0.028**	2.48
	IVF-120 superior field (per 10 points)	0.38	(-2.15 to 2.91)	0.05	0.769	2.57

Notes: Bold values indicate significant correlations; SF-36 = Short-form 36-item survey; IVF = Integrated Visual Field; CI = Confidence Interval; VIF = Variance Inflation Factor

The VIF values calculated in the linear regression models ranged from 2.48 to 2.91 suggesting some variance inflation due to multicollinearity between the superior and inferior field variables. While the results should be interpreted with some care, none of the VIF values were greater than 10. An alternative analysis to support these findings using factor analysis is presented in Appendix 7.

4.8 Discussion

In this cross-sectional study of older adults, greater severity of glaucomatous visual impairment was associated with poorer self-reported health-related QOL in the physical component. In particular, participants with greater visual field loss reported lower scores for the SF-36 PCS. Furthermore, participants with greater visual field loss in the inferior region reported lower SF-36 in the physical component, independent of the severity of superior VFL. No significant association between SF-36 scores in the mental domain and glaucomatous visual impairment was found.

To the author’s knowledge, this is the first study to examine the association between severity and location of visual field loss and health-related QOL exclusively in an older cohort of glaucoma patients. It is well known that age is associated with reductions in overall physical function and increased prevalence of chronic illness and co-morbidities (Fried et al., 2001; Rockwood et al., 2007) and our findings indicate that visual field loss is associated with reductions in health-related quality of life among older populations, particularly in the physical domains. The mechanism of this relationship, albeit speculative, is that visual field loss may initiate restriction of activity and participation due to mobility difficulties, which in turn may lead to functional limitations and disability which are reflected in the poorer SF-36 physical domain scores. Because of the cross-sectional nature of our data, we are unable to establish the causal direction; however, it is likely that visual field loss reduces self-reported physical function, rather than the reverse.

A number of SF-36 subscales were significantly correlated with severity of visual field loss in the present study, particularly role physical and general health. It is difficult to compare our findings with previous studies, given the variation in cohort characteristics, particularly in the age-range and level of vision impairment. Despite this, our findings support previous studies, demonstrating weak but significant correlations, particularly with the role physical SF-36 subscale. Parrish et al (1997) reported weak but significant correlations between visual field loss and physical function, role physical and role emotional (r between -0.21 and -0.26), while Jampel et al (2002a) found the strongest correlation between binocular visual field loss and role physical SF-36 subscale (r=0.21).

In this study, greater visual field loss was significantly associated with lower SF-36 PCS scores. Similarly, McKean-Cowdin et al (2007) found significant correlations between SF-12 PCS scores and 24-2 mean deviation in the better-eye, from all causes (B coefficient= 0.23), which is comparable to the association between SF-36 PCS and IVF-60 in the current study (B coefficient = 0.50). Direct comparison is difficult, however, due to differences in the visual field measures and health-related QOL instruments.

As expected, the associations between health-related QOL and vision impairment were weak, as generic health-related QOL surveys are not strongly influenced by changes in visual function. While health-related QOL must be viewed in context of other significant health issues faced by this population (Chia et al., 2004), our findings demonstrated small but detectable decrements in physical health-related QOL among older adults, which vary according to the severity of visual field loss.

The independent associations between the various visual function measures and health-related QOL were not examined in the present study. Strong correlations were found between central and peripheral visual function, which was expected as advanced glaucoma affects multiple visual functions. Therefore, visual acuity and contrast sensitivity were also significantly correlated with SF-36 PCS in the present study. We cannot rule out that these visual functions may also influence health-related QOL among older adults with glaucoma.

In contrast, previous studies have failed to demonstrate significant associations between visual field loss and health-related QOL (Gutierrez et al., 1997; Parrish et al., 1997; Wilson et al., 1998; McKean-Cowdin et al., 2008; Muir et al., 2008). An important point of difference is the focus on older adults in the present study, where the level of physical functioning and co-existing conditions are likely to differ to that of younger adults, which may exacerbate the effect of visual impairment on health-related QOL.

After adjusting for age and gender, severity of IVF-120 inferior visual field loss was shown to be significantly associated with lower SF-36 PCS scores, independent of superior visual field loss. The association between PCS scores and IVF-120 inferior visual field loss was more than double that of the overall IVF-120 score (B coefficient -3.01 vs. -1.28, respectively). This is the first study to demonstrate a significant relationship between inferior field loss and self-reported physical function. While the findings of this study are cross-sectional in nature, it is likely that loss of inferior visual field results in physical activity restriction due to mobility difficulties (Lovie-Kitchin et al., 1990; Turano et al., 2004), which in turn may lead to subsequent declines in physical function. Additional research is needed to confirm these findings using a longitudinal study design.

We found small, but significant, correlations between the VFQ-25 component and the SF-36 summary scores, both in the physical and mental domains. While these correlations were not strong (r<0.3), they reflect that lower perceived visual function is linked with poorer perceptions of general health. This is consistent with previous studies (Mangione et al., 1998; Swamy et al., 2009), confirming that health-related QOL is independent to vision-related QOL, yet there are overlapping aspects of these measures. Massof et al (2007) reported significant correlations between VFQ-25 and SF-36 summary scores among a group of low vision patients, more so in the physical than mental domains (r=0.49 and 0.32, respectively).

In the present study, no association was found between the mental component of the SF-36 and visual field loss. Similarly, McKean-Cowdin (2008) found no significant associations between visual field sensitivity in the better-eye and SF-12 mental component scores among the 213 glaucoma participants. Furthermore, previous studies have not demonstrated significant links between depression and glaucoma (Wilson et al., 2002; Jampel et al., 2007; Skalicky & Goldberg, 2008). Visual field loss may not be an important contributor to depression among older adults, due to the limited awareness of visual field loss.

The only visual factor associated with SF-36 mental component scores in the present study were VFQ-25 composite scores. This is consistent with previous studies which have shown significant associations between depression and vision-related QOL, but not with clinical measures of visual function. Jampel (2007) showed significant associations between depression and Visual Activities Questionnaire among glaucoma participants, but not with visual acuity or visual field. Similarly, Skalicky et al (2008) reported that depression scores were associated with Glaucoma Quality of Life scores, but not visual acuity or visual field loss. In a study of participants with visual acuity worse than 6/24, depressive symptomatology was associated with Visual Function-14 scores, but not visual acuity (Hayman et al., 2007).

The cross-sectional nature of this study makes it difficult to provide clinical guidance as to the point in disease progression at which glaucoma impacts on self-reported physical function. This is an area that would benefit from further research using longitudinal methods to better understand the impact of glaucoma on functional status.

One potential limitation of the present study is that item response theory (IRT) using Rasch analysis was not conducted to validate the use of the SF-36 tool in this population. Rasch analysis is a psychometric technique used to transform ordinal data into equal interval measures expressed as a linear scale, and evaluates an instrument's unidimensionality and item relevancy (Massof & Ahmadian, 2007; Lamoureux et al., 2009). The sample size in the present study, however, was not powered to examine the psychometric properties of the SF-36 tool in this population, although the use of this technique is warranted for further research. In addition, we do not anticipate that the main conclusions of the study would vary considerably if Rasch analysis was applied, given that the psychometric reliability and validity of the SF-36 has been extensively studied among diverse patient groups (McHorney et al., 1993; McHorney et al., 1994).

The strengths of this study include extensive assessment of different vision components, including the use of binocular integrated fields, and the use of a well-validated and widely used general health-related QOL instrument. There are, however, a number of limitations which include the small sample size and cross-sectional study design. Chapter 8 provides additional discussion on a number of strengths and limitations pertaining to all of the studies presented in this thesis, along with the implications arising from the findings.

4.9 Conclusion

In this study of community-dwelling older adults with glaucoma, greater visual field loss was associated with poorer health-related QOL in the physical domain. In addition, greater visual field loss in the inferior field area was significantly associated with lower self-reported physical health-related QOL, more so than superior visual field loss. No associations were found between visual field loss and health-related quality of life in the mental domain.

The results provide important insights into the association between glaucomatous vision impairment and health-related QOL among older adults, and expand our understanding of the personal burden of glaucoma. Older populations face many health issues that can impact on their health-related QOL (Chia et al., 2004), and visual field loss is one factor which may influence their health-related quality of life. Further research is needed to refine our understanding of the longitudinal impact of visual impairment on health-related QOL among older adults with glaucoma.

Chapter 5: Visual Impairment and Functional Status among Older Adults with Glaucoma [Study 1b]

5.1 Introduction

Frailty, as indicated by the presence of declines in health, functional status or capacity, affects around 10 per cent of the older population, with as many as 40 per cent demonstrating early signs of the condition (Fried et al., 2001; Rockwood et al., 2007). The prevalence of frailty increases with age, and increases vulnerability to a number of adverse health outcomes, including falls (Ensrud et al., 2007), fractures (Ensrud et al., 2007), institutionalization (Fried et al., 1998; Rockwood et al., 2007) and mortality (Klein et al., 2005a; Rockwood et al., 2007; Cesari et al., 2009).

The literature review presented research showing that reduced visual acuity has been linked to poor performance in physical markers of frailty (Klein et al., 2003a; Laitinen et al., 2007) and reduced functioning for daily activities (Ensrud et al., 1994; West et al., 1997). Furthermore, reduced visual acuity has been shown to predict future declines in self-rated health and functional status (Wallhagen et al., 2001; Lin et al., 2004). Despite these links between functional status declines and visual acuity loss, its association with visual field loss or glaucoma is not well understood due to the limited research in this area.

5.2 Glaucoma, visual field loss and functional status

Few studies have examined the association between functional status and visual field loss or glaucoma. Two studies have investigated aspects of functional status among older adults with glaucoma compared to controls with normal vision, although their findings are limited by a number of methodological factors, including the use of crude outcome measures and study designs.

Friedman et al (2007) examined stair climbing speed, measured as the time to ascend and descend a flight of stairs at their normal rate, as part of a population mobility study of adults aged 65 years and over. Although stair climbing speed was slower in those with bilateral glaucoma (n=74) compared to those without glaucoma (n=1,064), these differences were not statistically significant. Stair climbing speed also did not differ between those with unilateral glaucoma (n=76) compared to those without glaucoma. The association between severity of field loss and stair climb performance was not examined in the study, and the conclusions are limited by the crude, non-standardised outcome measure.

In a retrospective case-control study assessing falls and driving outcomes, Haymes et al (2007) reported poorer functional mobility, measured using the "timed up and go" test, in a group of 48 glaucoma participants compared to 47 controls (11±3 versus 10±2 seconds, respectively; p=0.01). The study also reported physical activity levels in the glaucoma and control groups, using the PASE questionnaire, but no differences were found. The findings are limited by the small sample size, and methodological shortcomings of the retrospective case-control study design, which is more susceptible to selection bias compared to other epidemiological study designs.

Systemic vascular factors may also contribute to declines in functional status among older adults with glaucoma, given the reported links between glaucoma and cardiovascular disease, such as atherosclerosis and peripheral arterial disease (Jeganathan et al., 2009). There may be a possible common underlying pathophysiological mechanism, such as an inflammatory process, although these associations are not well established in the literature. It remains unclear if these underlying vascular factors influence functional status among older adults with glaucoma.

5.3 Rationale for the study

In summary, the association between glaucomatous vision impairment and functional status or frailty is poorly understood due to limited previous research. There is a need for research to better understand this relationship, to facilitate future strategies to minimise and/or reverse the physical functional declines in this population. Frailty poses a serious threat to the health of older adults, increasing the risk of falls, fractures, institutionalisation and mortality (Fried et al., 1998; Klein et al., 2005a; Ensrud et al., 2007; Rockwood et al., 2007; Cesari et al., 2009). The current study, therefore, sought to examine the association between severity and location visual field loss and functional status in a cohort of older adults with glaucoma.

5.4 Study aims and hypotheses

Using a cohort of community-dwelling older adults with glaucoma (n=74), the aim of the research was to examine the cross-sectional relationship between severity and location of visual field loss and functional status, based on the range of performance-based and self-reported functional measures.

The hypotheses of the research (expressed as alternate hypotheses) described in this chapter are that:

- Greater visual field loss is associated with declines in functional status;
- Greater visual field loss in the inferior field region is associated with declines in functional status.

5.5 Additional methods

5.5.1 Functional status outcome measures

The functional status tests were selected to represent a broad range of measures associated with frailty according to previous research. Prominent studies among older adults have included muscle weakness, poor endurance, slowness and low physical activity as markers of frailty (Fried et al., 2001; Rockwood et al., 2007). Standardised and validated instruments were selected to quantify these components, and careful consideration was given to tests which would be suitable for use in a clinical setting.

The selected functional status measures are outlined below. Performance-based tests of physical function included lower limb strength (muscle weakness), the six minute walk test (endurance) and the timed-up and go test (slowness). The Physical Activity Scale for the Elderly (PASE) questionnaire was used to assess self-reported physical activity levels. A novel overall functional status score was devised from these individual measures, based on equal weighting from all components.

5.5.1.1 ***Timed up and go test (TUGT)***

The Timed Up and Go Test (TUGT) is a quick, reliable and widely used tool for assessing the basic level of functional mobility among older adults (Podsiadlo & Richardson, 1991). Good test-retest reliability of the TUGT among older adults has been demonstrated in previous studies (intraclass correlation coefficient = 0.97-0.99) (Podsiadlo & Richardson, 1991; Steffen et al., 2002) and it has been reported to accurately discriminate between fallers and non fallers among older adults (Shumway-Cook et al., 2000). Scores on this test represent the time, measured in seconds, for a participant to rise from a chair, walk a distance of 3 m at their “usual walking pace”, turn around, walk back to the chair and sit down. Following one practice trial, the average time of two tests was used as the final measure. Longer TUGT times reflect poorer functional mobility performance.

5.5.1.2 *Six-minute walk test (6MW)*

The six minute walk test (6MW) is a widely used physical performance measure in clinical research to assess overall mobility and physical functioning in older populations (Duncan et al., 1993; Lord & Menz, 2002). It is a practical and simple test in which the distance a participant can quickly walk along a level path for a period of 6 minutes is measured, and has demonstrated excellent test-retest reliability among older adults (ICC = 0.95) (Steffen et al., 2002). The level of exertion required for the test is sub-maximal, as participants choose their own intensity level of exercise and are allowed to stop and rest during the test (American Thoracic Society, 2002).

The walkway used for this test was a level indoor corridor measuring 25 metres in length. The corridor was well-lit with standard overhead fluorescent lighting, climate controlled and free of any floor or peripheral obstacles. Prior to the test, a set of standardised instructions were given to participants: “to walk as quickly as you can for six minutes so that you cover as much ground as possible”. They were informed that they could slow down or rest if necessary during the test. When a participant reached the end of the corridor, they were instructed to turn around and continue walking back in the opposite direction. During the test, the examiner remained at one end of the corridor to assist if necessary whilst also timing the test with a stopwatch. The total distance travelled in the 6 minutes to the nearest metre was recorded. Longer 6MW distances reflect better physical performance.

5.5.1.3 *Lower limb strength (LLS)*

Overall muscle mass and strength is an important component of physical function and frailty (Fried et al., 2001; Klein et al., 2005a). In this study, a marker of muscle strength was obtained by measuring lower limb strength (LLS) using a spring gauge dynamometer, which measured the isometric strength of the knee extensor muscles (quadriceps). Spring gauge dynamometers have previously been demonstrated to be a reliable, inexpensive instrument for the measurement of isometric strength in lower limb musculature, with good test-retest reliability (Pearson’s correlation =

0.75) (Lord et al., 1991; Lord et al., 2003b), and their measurements have a high correlation with those attained through strain gauge (handheld) dynamometers (Bohannon, 1998).

Testing was performed on the participants' dominant leg. Leg dominance was ascertained according to the leg which participants' reported that they would self-select to kick a ball. Participants were seated on a 65cm high chair with hips and knees flexed to 90 degrees. The spring gauge was attached just above ankle and with the posterior leg of the chair (Figure 5-1). A soft foam pad was placed between strap and leg for comfort. Participants were asked to extend their dominant leg smoothly and as forcefully as possible against the strap, generating maximum quadriceps force. The maximum force value (in kg force) was obtained from a peak detector on the gauge. After one familiarisation attempt, three maximum voluntary contractions were completed and the maximum score was recorded as lower limb strength. Higher LLS scores reflect stronger lower limb musculature.

Figure 5-1: Lower limb strength assessment

5.5.1.4 *Physical activity levels*

A standardised, previously validated, instrument was used to quantify participant's self-reported level of physical activity, measured by the Physical Activity Scale for the Elderly (PASE). This self-administered 10-item questionnaire was developed around activities specific for older populations, as opposed to general population instruments which focus solely on sport or recreational activities (Washburn et al., 1993). Good test-retest reliability for the PASE among older adults has been demonstrated, with a 3–7 week test-retest correlation coefficient of 0.75 for self-administration of the PASE (Washburn et al., 1993). The PASE asks respondents about typical activities performed by older adults and has been shown to be a valid and reliable instrument reflecting true energy expenditure (Schuit et al., 1997). The PASE score is based on a range of leisure, household, and occupational activities that have been performed in the seven days prior to assessment. The activities include light, moderate and strenuous sport/recreational activities, muscle strength/endurance exercises, light and heavy housework, home repairs, lawn work or yard care, caring for another person, and work for pay or as a volunteer.

The PASE score is derived by multiplying the amount of time spent on each activity (hours/week) or participation in an activity (yes/no) by specific item weights, and summed over all activities (Appendix 8). Item weights have been determined based on measures of daily energy expenditure and self-reported physical activity (Washburn et al., 1993). Higher PASE scores reflect greater activity levels.

5.5.1.5 *Overall functional status score*

A novel overall functional status score was derived to capture the functional performance of individual participants compared with the whole group. Z-scores for each of the four functional status measures (were calculated and adjusted accordingly so that more positive scores indicated better functional performance. For each participant, the mean of these Z-scores was calculated, with equal weighting assigned for all measures, to provide an overall functional status score. More positive status scores reflect better overall functional status.

The overall functional status score formula, defined in Equation 1, was calculated using the converted Z score values of the six minute walk (6MW), timed up and go (TUGT), lower limb strength (LLS) and physical activity scale for the elderly (PASE).

Equation 1: Functional status score = $(Z_{6MW} - Z_{TUGT} + Z_{LLS} + Z_{PASE}) / 4$

5.5.2 Statistical analysis

To examine the bivariate relationships between the visual function variables and functional status scores, Pearson's correlations were used for continuous visual function variables and point biserial correlations for categorical visual function variables. Additional analyses adjusted for age and gender. P-values were not adjusted for multiple comparisons, as reported earlier in Section 3.7.2.

The association between integrated visual field loss (IVF-60 and IVF-120) and functional status scores were examined using linear regression models, adjusted for age and gender. To examine the independent association between functional status scores and location of visual field loss, the superior and inferior field integrated field measures were considered together in a regression model, adjusted for age and gender. These models were examined separately for the IVF-60 and IVF-120 measures. Multicollinearity was assessed using the collinearity diagnostics in SPSS based on the variance inflation factors (VIF).

5.6 Results

5.6.1 Description of study cohort

The socio-demographic, health, medical and visual characteristics of the 74 participants have been described in Chapter 3.

5.6.2 Severity of visual impairment and functional status

The distributions of the functional status score are presented in Table 5-1. These measures were strongly correlated with each other (Appendix 9). Longer six-minute walk distance was associated with faster TUGT score ($r=-0.70$), stronger leg strength ($r=0.36$) and higher PASE scores ($r=0.32$). Stronger leg strength was also associated with higher PASE scores ($r=0.30$).

Table 5-1: Mean scores for the functional status outcome measures (n=74)

	Mean	SD	Median	Min	Max
Six-minute Walk distance (metres)	503	69	508	342	650
Timed-Up and Go Test (seconds)	10.11	1.95	9.69	6.75	15.30
Lower Limb Strength (kg)	19.39	7.78	18.00	6.00	44.00
PASE (weighted score)	128.68	52.50	120.77	37.86	301.29
Overall functional status (z-score)	0.00	0.71	0.05	-1.74	1.62

Notes: SD = standard deviation; PASE = Physical Activity Scale for the Elderly

The unadjusted and adjusted associations between the vision function measures and functional status measures are shown in Table 5-2 and Table 5-3. In the age and gender adjusted analyses, there was a trend towards lower PASE scores in participants with greater severity of vision impairment, particularly reduced contrast sensitivity (r=0.30 to 0.36), depth perception (r=-0.31), motion perception (r=-0.33), RNFL thickness in better-eye (r=0.39) and visual field loss (VF24-2 better r=0.34; IVF-60 r=0.33; IVF-120 r=-0.28). Participants with greater inferior IVF-60 field loss also demonstrated slower TUGT scores (r=-0.23), weaker leg strength (r=0.26) and lower PASE scores (r=0.31). Similarly, greater inferior IVF-120 field loss was significantly associated with slower TUGT scores (r=0.23) and lower PASE scores (r=-0.27).

The overall functional status score was significantly associated with greater visual impairment, particularly CS better-eye (r=0.30) and visual field measures (24-2 better-eye r=0.27; IVF-60 r=0.28; IVF-120 r=-0.24). Greater inferior field loss was significantly associated with lower overall functional scores (IVF-60 r=0.34; IVF-120 r=-0.31). Scatterplots of the relationship between PASE scores and overall functional status scores with IVF-120 are presented in Figure 5-2 and Figure 5-3.

Table 5-2: Unadjusted Pearson's correlations between visual function and functional status measures†

	Six Min Walk Test	Timed Up and Go Test	Lower Limb Strength	PASE Score	Overal Functional Status
Visual Acuity (logMAR)					
better-eye	-0.13	0.18	-0.02	-0.15	-0.17
worse-eye	-0.15	0.18	-0.08	**-0.30** **	**-0.25** *
Contrast Sensitivity (logCS)					
better-eye	0.14	**-0.26** *	0.05	**0.28** *	**0.25** *
worse-eye	0.16	-0.19	0.05	**0.36** **	**0.27** *
Stereoacuity (present/absent)	-0.18	**0.32** **	0.04	**-0.31** **	-0.23
Motion sensitivity (log deg/sec)	-0.13	0.13	0.09	**-0.35** **	-0.18
Visual Field Sensitivity (dB)					
better-eye	-0.01	-0.16	-0.02	**0.27** *	0.14
worse-eye	0.02	-0.16	-0.03	**0.23** *	0.13
RNFL (μm)					
better-eye	-0.09	-0.13	-0.14	**0.31** *	0.07
worse-eye	0.03	-0.20	-0.10	0.11	0.08
IVF-60 (dB)					
overall field	0.00	-0.18	-0.01	**0.27** *	0.15
inferior field	0.12	**-0.26** *	0.09	**0.28** *	**0.26** *
superior field	-0.11	-0.08	-0.09	**0.24** *	0.04
IVF-120 (points missed)					
overall field	-0.04	0.19	-0.01	**-0.24** *	-0.17
inferior field	-0.16	**0.28** *	-0.12	**-0.26** *	**-0.29** *
superior field	0.08	0.09	0.09	-0.20	-0.03
VFQ-25 Composite Score	-0.05	0.18	-0.23	-0.17	-0.22

Notes: Bold values represent significant values; * $p<0.05$; ** $p<0.01$; † n=74, with the exception of RNFL (n=57) and VFQ-25 (n=72); RNFL = Retinal Nerve Fibre Layer; IVF = Integrated Visual Field; VFQ-25 = Visual Function Questionnaire (transformed scale); PASE = Physical Activity Scale for the Elderly

Table 5-3: Age and gender adjusted Pearson's correlations between visual function and functional status measures†

	Six Min Walk Test	Timed Up and Go Test	Lower Limb Strength	PASE Score	Overal Functional Status
Visual Acuity (logMAR)					
better-eye	-0.10	0.13	-0.04	-0.15	-0.15
worse-eye	-0.07	0.07	-0.12	**-0.29** *	-0.20
Contrast Sensitivity (logCS)					
better-eye	0.13	-0.19	0.19	**0.30** *	**0.30** *
worse-eye	0.11	-0.09	0.13	**0.36** **	**0.26** *
Stereoacuity (present/absent)	-0.10	0.20	-0.02	**-0.31** **	-0.21
Motion sensitivity (log deg/sec)	0.01	-0.04	0.14	**-0.33** **	-0.06
Visual Field Sensitivity (dB)					
better-eye	0.04	-0.14	0.20	**0.34** **	**0.27** *
worse-eye	0.06	-0.12	0.17	**0.29** *	**0.24** *
RNFL (μm)					
better-eye	-0.03	-0.12	0.05	**0.38** **	0.20
worse-eye	0.08	-0.20	0.06	0.15	0.18
IVF-60 (dB)					
overall field	0.06	-0.17	0.21	**0.33** **	**0.28** *
inferior field	0.14	**-0.23** *	**0.26** *	**0.31** **	**0.34** **
superior field	-0.03	-0.09	0.14	**0.32** **	0.19
IVF-120 (points missed)					
overall field	-0.06	0.17	-0.14	**-0.28** *	**-0.24** *
inferior field	-0.14	**0.23** *	-0.20	**-0.27** *	**-0.31** **
superior field	0.03	0.09	-0.06	**-0.25** *	-0.14
VFQ-25 Composite Score	-0.02	-0.10	0.13	0.17	0.16

Notes: Bold values represent significant values; * $p<0.05$; ** $p<0.01$; † n=74, with the exception of RNFL (n=57) and VFQ-25 (n=72); RNFL = Retinal Nerve Fibre Layer; IVF = Integrated Visual Field; VFQ-25 = Visual Function Questionnaire (transformed scale); PASE = Physical Activity Scale for the Elderly

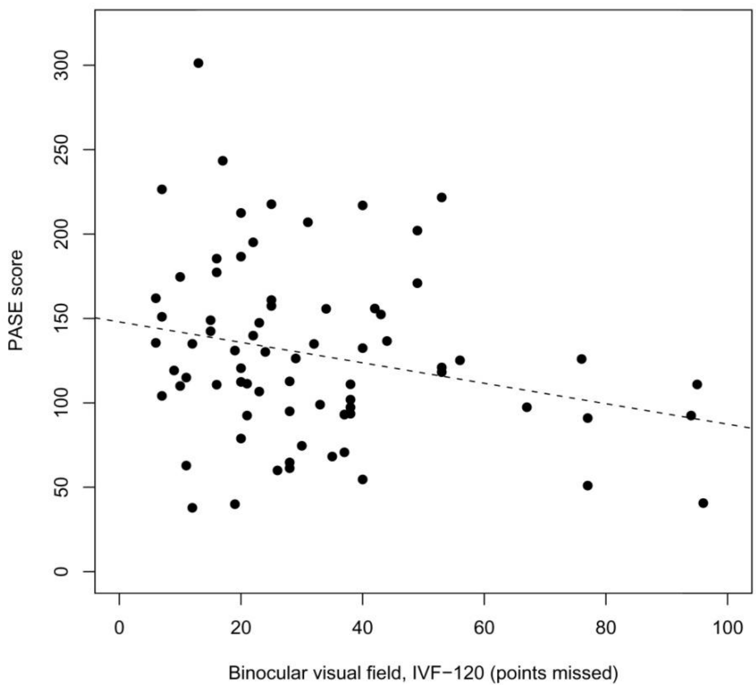

Figure 5-2: Integrated 120° visual field score (IVF-120) as a function of PASE scores (Age- and gender-adjusted Pearson's correlation r=-0.28, p=0.02).

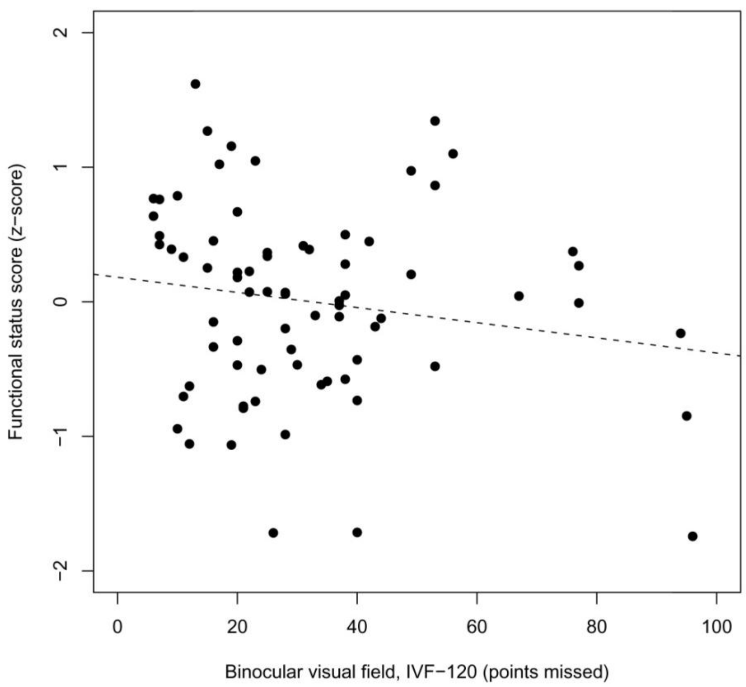

Figure 5-3: Integrated 120° visual field score (IVF-120) as a function of overall functional status score (z-score) (Age- and gender-adjusted Pearson's correlation r=-0.24, p=0.047).

Results from the linear regression models are presented in Table 5-4. After adjustment for age and gender, each decibel reduction in overall IVF-60 was associated with nearly 3 units decrease in PASE (model 13) and 0.03 unit decrease in overall functional status (model 17), while each 10 points missed on the IVF-120 was associated with around 7 units decrease in PASE score (model 15) and 0.07 unit decrease in overall functional status (model 19). When both the IVF-60 superior and inferior fields were considered together in a model, the inferior fields remained statistically significant with 6MW, TUGT and LLS, whereas the superior field estimates fell short of statistical significance.

In these models, each decibel reduction in IVF-60 inferior field was associated with a reduction in 6MW by 4 metres (model 2), TUGT by 0.1 seconds (model 6), leg strength by 0.4 kg (model 10) and summary score by 0.05 (model 18). Similar trends were noted for the IVF-120 models, where each 10 points missed on the IVF-120 inferior field was associated with a reduction in 6MW by 21 metres (model 4), TUGT by 0.6 seconds (model 8), LLS by 2.2 kg (model 12) and summary score by 0.27 (model 20). The superior and inferior fields were not independently associated with lower PASE scores (models 14 and 16).

The VIF values calculated in the linear regression models ranged from 2.48 to 2.93 suggesting some variance inflation due multicollinearity between the superior and inferior field variables. While the results should be interpreted with some care, none of the VIF values were greater than 10. An alternative analysis to support these findings is presented in Appendix 7.

Table 5-4: Visual field factors associated with functional status outcomes (linear regression models, adjusted for age and gender; n=74)

	Model	Vision Variables	B coefficient (95% CI)		Beta	p-value	VIF
Six-minute Walk Test	1	IVF-60 overall field (per dB)	0.56	(-1.77 to 2.89)	0.05	0.638	
	2	IVF-60 inferior field (per dB)	**4.10**	**(0.55 to 7.66)**	**0.37**	**0.027**	2.72
		IVF-60 supeior field (per dB)	-3.22	(-6.51 to 0.07)	-0.33	0.059	2.91
	3	IVF-120 overall field (per 10 points)	-1.72	(-8.43 to 4.99)	-0.05	0.618	
	4	IVF-120 inferior field (per 10 points)	**-21.17**	**(-40.64 to -1.7)**	**-0.33**	**0.037**	2.48
		IVF-120 superior field (per 10 points)	16.90	(-1.83 to 35.63)	0.28	0.081	2.57
Timed Up and Go Test	5	IVF-60 overall field (per dB)	-0.04	(-0.11 to 0.02)	-0.15	0.167	
	6	IVF-60 inferior field (per dB)	**-0.12**	**(-0.21 to -0.02)**	**-0.38**	**0.022**	2.76
		IVF-60 supeior field (per dB)	0.06	(-0.03 to 0.15)	0.23	0.171	2.93
	7	IVF-120 overall field (per 10 points)	0.13	(-0.05 to 0.31)	0.14	0.157	
	8	IVF-120 inferior field (per 10 points)	**0.60**	**(0.07 to 1.13)**	**0.34**	**0.030**	2.50
		IVF-120 superior field (per 10 points)	-0.32	(-0.83 to 0.2)	-0.19	0.231	2.57
Lower Limb Strength	9	IVF-60 overall field (per dB)	0.22	(-0.03 to 0.47)	0.18	0.084	
	10	IVF-60 inferior field (per dB)	**0.40**	**(0.02 to 0.79)**	**0.33**	**0.044**	2.72
		IVF-60 supeior field (per dB)	-0.16	(-0.51 to 0.2)	-0.14	0.392	2.91
	11	IVF-120 overall field (per 10 points)	-0.43	(-1.16 to 0.29)	-0.12	0.246	
	12	IVF-120 inferior field (per 10 points)	**-2.19**	**(-4.31 to -0.07)**	**-0.31**	**0.047**	2.48
		IVF-120 superior field (per 10 points)	1.25	(-0.79 to 3.29)	0.19	0.235	2.57
Physical Acitivity Score (PASE)	13	IVF-60 overall field (per dB)	**2.87**	**(0.97 to 4.76)**	**0.34**	**0.004**	
	14	IVF-60 inferior field (per dB)	1.28	(-1.72 to 4.28)	0.15	0.406	2.72
		IVF-60 supeior field (per dB)	1.57	(-1.2 to 4.35)	0.21	0.270	2.91
	15	IVF-120 overall field (per 10 points)	**-6.80**	**(-12.38 to -1.22)**	**-0.27**	**0.020**	
	16	IVF-120 inferior field (per 10 points)	-8.83	(-25.51 to 7.85)	-0.18	0.303	2.48
		IVF-120 superior field (per 10 points)	-4.86	(-20.9 to 11.18)	-0.11	0.555	2.57
Overall functional status (z-score)	17	IVF-60 overall field (per dB)	**0.03**	**(0.01 to 0.05)**	**0.25**	**0.017**	
	18	IVF-60 inferior field (per dB)	**0.05**	**(0.01 to 0.08)**	**0.43**	**0.007**	2.72
		IVF-60 supeior field (per dB)	-0.02	(-0.05 to 0.01)	-0.17	0.287	2.91
	19	IVF-120 overall field (per 10 points)	**-0.07**	**(-0.14 to 0)**	**-0.20**	**0.047**	
	20	IVF-120 inferior field (per 10 points)	**-0.27**	**(-0.46 to -0.08)**	**-0.41**	**0.008**	2.48
		IVF-120 superior field (per 10 points)	0.12	(-0.06 to 0.31)	0.20	0.202	2.57

Notes: Bold values represent significant values; IVF = Integrated Visual Field; VIF = Variance Inflation Factor; CI = confidence interval

5.7 Discussion

In this cross-sectional study, greater visual impairment was significantly associated with declines in functional status among older adults with glaucoma. Participants with greater binocular visual field loss reported lower physical activity levels and had lower overall functional status, independent of age and gender. Furthermore, greater inferior visual field loss was associated with declines in the six-minute walk test, timed-up and go test, lower limb strength and overall functional status score, independent of superior visual field loss. The mechanism of these relationships, albeit speculative, is that visual field loss may initiate restriction of activity due to mobility difficulties, and subsequent physical inactivity can lead to reductions in lower limb strength and functioning (Deshpande et al., 2008).

To the best of our knowledge, this is the first study to examine the impact of visual field loss on functional status among older adults with glaucoma. This is an important finding, as frailty or reduced functional status, is reported to increase the likelihood of serious adverse health outcomes among older adults, such as falls, fractures, institutionalisation and mortality (Fried et al., 2001; Ensrud et al., 2007; Rockwood et al., 2007; Cesari et al., 2009; Ensrud et al., 2009). Declines in physical function, functional limitations and frailty have been reported among older adults with central vision loss (Klein et al., 2003a; Laitinen et al., 2007), and our findings provide further evidence that peripheral visual function loss is linked to declines in functional status. The independent associations between functional status and the visual function measures could not be examined, due to their strong inter-correlations (and hence concerns regarding multicollinearity of the data); therefore, central visual function measures were also related to functional status in the present study.

The results of this study are supported by the findings from Study 1a, where greater visual field loss was associated with poorer self-reported physical function, according to the SF-36 physical component score. This is due to the significant correlations between the functional status measures and SF-

36 physical component scores (r=0.27 to 0.51, Appendix 9), which is consistent with previous studies that have reported strong links between physical function and self-reported functional limitations (McAuley et al., 2007).

Compared to other studies, the cohort in the present study demonstrated similar, if not higher, levels of physical functioning than previous studies. Chad (2005) reported average PASE scores among 351 community-dwelling older adults (aged 65 - 79 years) around 128 units, while average PASE score among glaucoma patients in a small case-control study was 117 units (Haymes et al., 2007). Studies of non-institutionalized older adults have found average six minute walk distances between 385 and 442 metres (Lord & Menz, 2002; Tiedemann et al., 2005), which is lower than that demonstrated in the current study. Our cohort also demonstrated slightly faster timed up and go scores, as compared to averaged in previous studies of between 11 to 13 seconds (Haymes et al., 2007; Liu-Ambrose et al., 2008). As our cohort was a relatively high functioning group, it is likely that the associations between visual field loss and functional status would be even stronger among frailer glaucoma populations.

Physical inactivity has been shown to precede reductions in physical functions (Keysor, 2003; Spirduso et al., 2005), which may explain the stronger associations found between physical activity levels and visual field loss, compared to the performance-based measures. It is possible that over time, reduction in physical activity levels would lead to physical de-conditioning and functional declines among older adults, but this cross-sectional study was unable to establish this. Additional research is required to examine whether visual field loss is a significant predictor of functional decline over time.

The results of our study also showed that inferior visual field loss was more strongly associated with the performance-based functional measures than superior visual field loss. This is the first study to explore this association. The inferior visual field plays an important role in mobility (Lovie-Kitchin et al., 1990; Turano et al., 2004; Marigold & Patla, 2008), and greater loss in this area may lead to physical activity restriction. While this is difficult to establish from our cross-sectional findings, physical activity restriction may lead to loss of physical function over time.

While physical activity and exercise holds great potential for improving and maintaining physical function among older adults (Pahor et al., 2006), this may be challenging among visually impaired populations. One study examined an exercise program among visually impaired older adults (Campbell et al., 2005), and found that the rate of falls was greater in those receiving the exercise programme, although not significantly so. Their findings suggest that physical activity programs among visually impaired populations may be problematic and even possibly harmful. Careful consideration of this is needed in future studies.

Clinically, it would be desirable to provide some guidance as to the point in disease progression at which glaucoma impacts on functional status. However, the cross-sectional nature of this study means that such estimates cannot be determined. This is an area that would benefit from further research using longitudinal methods to better understand the impact of glaucoma on functional status.

There are a number of strengths in the current study, which include the extensive assessment of visual function. While frailty is difficult to measure given the lack of accepted definition and protocols, the outcome measures selected for use in the study were well-validated and widely used functional status measures. However, some caution is required in generalising the results based on the overall functional score, as this measure was derived exclusively for this study and lacks prior validation. Chapter 8 provides additional discussion on strengths and limitations pertaining to all of the studies presented in this thesis, along with important implications arising from the findings.

5.8 Conclusion

In this cross-sectional study comprising of community-dwelling older adults with glaucoma, greater visual field loss was associated with poorer functional status. In addition, participants with greater inferior visual field loss performed worse in a number of functional outcome measures, including the six-minute walk test, timed-up and go test, lower limb strength and overall functional status, independent of superior field loss.

This research provides important insights into the association between vision impairment and functional status, and identifies potential challenges in the prevention of functional decline for this population. Understanding the relationship between vision impairment and functional status has important implications to guide future strategies to promote and maintain the independence, health and well-being in this population

Chapter 6: Visual Impairment and Postural Sway among Older Adults with Glaucoma [Study 1c][1]

6.1 Introduction

Postural stability is fundamental to human functioning, ensuring the body remains upright during standing and walking activities. The literature review outlined the impact of age on postural stability and the consequences of postural instability. In addition, the importance of vision as a sensory system in maintaining postural stability was discussed, with reference to studies which have demonstrated the negative impact of visual impairment on postural stability among older adults. However, our understanding of the impact of visual field loss or glaucoma on postural stability among older adults remains limited. This introduction presents a review of the current literature which has examined the influence of visual field loss or glaucoma on postural control.

6.2 Peripheral visual field and postural sway

The visual system is a key sensory contributor to postural control, and the body's ability to generate appropriate postural responses to maintain upright stance relies on accurate visual input, both from the central and peripheral visual field areas. Early research from Straube et al (1994) demonstrated that occlusion of the peripheral visual field areas resulted in greater postural sway among young participants with normal vision, compared to full field viewing conditions. More recent experimental studies lend further support to Straube's findings (Nougier et al., 1997; Berencsi et al., 2005; Piponnier et al., 2009). Not only does the peripheral visual system provide important spatial information relating to body position relative to the environment, but it

[1] This study was published in part: Black, AA, Wood, JM, Lovie-Kitchin, JE, & Newman, BM. (2008). Visual impairment and postural sway among older adults with glaucoma. Optom Vis Sci, 85(6), 489-497.

is also highly sensitive to motion. The ability to detect body movement relative to the environment is important in guiding compensatory postural movements of the body (Guerraz & Bronstein, 2008).

The relative importance of the peripheral visual field, compared to central vision, in regulating postural control remains contentious. In an experimental study comprised of normally-sighted adults while wearing LCD occluding goggles, Nougier et al (1997) reported that the central 10 degree visual area was responsible for the regulation of medio-lateral sway, while the peripheral field area (central occlusion of 20 degree diameter occlusion) regulated anterio-posterior sway. Berencsi et al (2005) showed a preferential contribution of the peripheral rather than central vision in maintaining stable stance. The normally sighted participants swayed less when viewing with only peripheral vision (occlusion of either the central 4 and 7 degrees radius) compared to viewing with central vision alone (either the central 4 and 7 degrees radius).

Recently, Piponnier et al (2009) reported that the central and peripheral visual field areas were equally important in postural control. The postural sway of the normally sighted participants was similar when viewing a static target, irrespective of the area (size and location) of visual field stimulated. However, when viewing an optic flow pattern, peripheral vision played a critical role in compensatory sway, which suggests that the peripheral visual field area is an important contributor to postural control during movement.

Ageing may also influence the efficiency of the peripheral visual system to contribute to postural control, most likely due to the age-related reduction in retinal nerve fibres (Sing et al., 2000). It is well known that artificially inducing retinal motion results in greater postural instability, as the body attempts to compensate for the perceived body motion (Kelly et al., 2005). A recent study examined the ability of the postural system to adapt and adjust to sudden changes in optic flow patterns among 25 healthy young and 24 older adults, all with normal vision (O'Connor et al., 2008). Older adults were able to adjust their postural system to repeated sudden changes in optic flow patterns; however, this habituation required a greater number of exposures compared to the young adults. This suggests that ageing impairs the ability to quickly detect, process and modify the postural responses for postural stabilisation.

Age-related eye diseases that result in visual field loss, including glaucoma, are likely to impair postural stability. In a population study of 1,505 older adults, aged between 65 and 84 years, Freeman et al (2008a) reported that more extensive visual field loss and impaired motion-sensitivity were the only visual functions associated with inability to perform various standing balance tests, independent of a range of visual function measures. Visual acuity and contrast sensitivity were not significant contributors to postural stability. Despite the limitations in their low-tech balance measures, the study highlights the importance of the peripheral visual field and motion sensitivity in the control of posture among older adults.

The effect of different types of spectacle lens corrections on postural stability has also been explored, as corrections such as multifocals (including bifocal or progressive lenses) blur and magnify the lower visual field area. These experimental studies, however, have shown that the use of multifocal corrections does not significantly affect postural stability among young adults (Paulus et al., 1989) or older adults (Johnson et al., 2009).

6.3 Visual field loss and adaptive gait

Gait adaptation is a strategy used by individuals to respond to challenges in dynamic postural stability during locomotion, and is an important link between postural instability and falls. These adaptations are used to preserve safe locomotion, and often present as more conservative or cautious walking patterns to avoid obstacles and maintain stability. The role of the visual field in controlling adaptive gait has been examined in a number of recent studies. These studies, however, have not specifically examined the gait characteristics of older adults with visual field loss, and may not reflect long-term gait adaptations which may develop over time to compensate for the loss of peripheral visual cues.

In a study of young normally sighted participants, Graci et al (2010) found that occlusion of the peripheral visual field (all but the central 20 degree of visual field) significantly affected a number of gait characteristics during obstacle crossing, particularly lead and trail foot horizontal distance and lead-limb toe clearance, compared to full field vision. An earlier study also showed that this level of peripheral occlusion resulted in more cautious gait strategies, as demonstrated by increased minimum-foot-clearance and decreased walking speed and step length (Graci et al., 2009). These gait changes can be interpreted as motor control strategies which aim to safely clear obstacles in the absence of peripheral visual cues.

Studies have also examined changes in gait with restriction of the inferior visual field, which removes visual information during lower limb placement and obstacle clearance. Experimental studies of young normally sighted individuals have demonstrated increased lead foot placement and toe clearance during obstacle crossing when the inferior visual field was restricted compared to full field vision (Rietdyk & Rhea, 2006; Rhea & Rietdyk, 2007). Furthermore, restriction of the inferior visual field among young normally sighted individuals, compared to full field vision, was shown to reduce gait speed and step length when negotiating irregular terrain (Marigold & Patla, 2008), and altered the mechanics of landing behaviour during step descent (Timmis et al., 2009).

6.4 Glaucoma and postural sway

To date, only one study has examined postural stability exclusively among individuals with glaucoma. Shabana et al (2005) assessed postural stability using force platform analysis in 35 open-angle glaucoma patients and 21 age-matched controls, aged 40 to 66 years. No significant differences in sway velocity were found between the two groups, nor was there any association between visual field loss and sway velocity in the glaucoma group. The visual contribution to postural stability was lower among the glaucoma patients, which correlated with the extent of visual field loss. The similarities in sway between the groups, however, was due to a greater somatosensory contribution to postural control in the glaucoma group compared to controls, which was determined by the somatosensory stabilisation ratio (sway on foam versus firm surface). These findings may be explained by the fact that the glaucoma patients included in their study were relatively young and demonstrated the capacity to compensate for the reduction in visual input to postural stability using their remaining sensory systems. As Shabana's cohort was relatively young, it remains unclear if visual field loss affects postural stability in older populations. Further research is vital, given that older age is associated with greater prevalence of glaucoma (Tuck & Crick, 1998; Weih et al., 2001; Rudnicka et al., 2006), increasing declines in the postural sensory systems (Manchester et al., 1989; Woollacott, 2000; Era et al., 2006) and higher rates of falling (Freeman et al., 2007).

Postural stability among adults with glaucoma may also be impaired due to motion sensitivity deficits. Glaucoma reportedly results in selective loss of the movement sensitive retinal nerve fibres, which may occur before standard perimetry defects are evident (Shabana et al., 2003; Falkenberg & Bex, 2007). Research has demonstrated that individuals with glaucoma show impairments in motion sensitivity compared to controls with normal vision (Bullimore et al., 1993; McKendrick et al., 2005; Falkenberg & Bex, 2007). Motion sensitivity impairment has been linked to reductions in postural stability, both in experimental research of young normally sighted individuals (Kelly et al., 2005) and population-based research among older adults (Freeman et al., 2008a). Therefore, greater severity of glaucoma and the subsequent reduction in motion sensitivity may reduce postural stability, yet this remains to be investigated.

6.5 Visual field loss, glaucoma and visuomotor control

As the visual system is an important sensory contributor to postural control, guiding appropriate motor postural responses, it is likely that the visuomotor pathway is an integral component in the control of posture. Visuomotor control, or visually guided movement, has been shown to be mediated by the dorsal stream of the visual pathway, which runs from the visual cortex to the posterior parietal cortex (Milner & Goodale, 2008); although this hypothesis remains controversial (Elliott et al., 2009).

Deficits in visuomotor control among glaucoma patients have been recently reported. In a laboratory study examining reaching and grasping hand movements, Kotecha et al (2009) demonstrated that planning and control of movement was significantly impaired among 16 glaucoma patients, compared to 16 normally sighted controls. The deficits in the glaucoma group correlated with both the severity of binocular visual field loss and stereoacuity.

It has also been reported that the inferior visual field provides a greater contribution to visuomotor control, demonstrated by better spatial accuracy relative to the superior visual field (Khan & Lawrence, 2005; Krigolson & Heath, 2006). Khan & Lawrence (2005) examined spatial accuracy of upper limb movements in the superior and inferior field areas (16 degrees from fixation) among young participants with normal vision. Compared to the superior field, the inferior field showed better performance in movement execution. Similarly, Krigolson & Heath (2006) showed that arm reaching movements in young participants with normal vision showed less variability when reaching for targets within the inferior field areas (12 degrees from fixation) compared to the superior field.

Studies of normally sighted individuals have also demonstrated differences in visual function and processing between the inferior and superior visual fields, which suggest higher levels of performance of the inferior visual field over the superior visual field. This asymmetry is likely to arise from the higher ganglion cell densities in the superior retina (inferior visual field) compared to the inferior retina (Curcio & Allen, 1990). Improved performance for the inferior visual field compared to the superior field has been shown for visual field sensitivity (Demirel & Robinson, 2003; Hermann et al., 2008), mid spatial frequency contrast sensitivity (Silva et al., 2010), flicker sensitivity (Casson et al., 1993) and focal ERG amplitudes (Miyake et al., 1989). There is also evidence of an inferior visual field advantage over the superior visual field for higher-level visual processing, such as visual feedback processing (Danckert & Goodale, 2001; Khan & Lawrence, 2005) and perceptual processing time (Carlsen et al., 2007). Research also has shown an inferior visual field advantage during visual search, particularly during attentionally demanding conditions (Lakha & Humphreys, 2005).

It is plausible, therefore, that the inferior visual field area may be a stronger contributor to postural control than the superior field area. However, no studies have explored the relative importance of these field areas in the control of posture in laboratory studies or among adults with visual impairment. It could be hypothesised that poor visuomotor control from inferior visual field impairment may be a contributing factor to the greater mobility difficulties found among visually impaired older adults (Lovie-Kitchin et al., 1990; Turano et al., 2004), and may even be linked to an increased propensity for falls (Coleman et al., 2007).

6.6 Rationale for the study

The visual system is an important contributor to postural stability, and visual field loss from glaucoma has been shown to reduce the visual contribution to postural stability. One study has examined the association between visual field loss from glaucoma and postural stability, however, the relationship was not significant, probably because of the relatively young adult cohort. As such, the association between glaucoma and postural stability among older adults with visual field loss remains unclear. In addition, the relative contribution of visual field areas in the control of posture has not been examined previously. The current study sought to examine the association between severity and location of visual field loss and postural stability in a cohort of older adults with glaucoma.

6.7 Aims and hypotheses

Using a cohort of community-dwelling older adults with glaucoma (n=74), the aim of the research was to examine the cross-sectional relationship between severity and location of visual field loss and postural stability, based on clinical postural sway measures.

The hypotheses of the research (expressed as alternate hypotheses) described in this chapter are that:

- Greater severity of visual field loss is associated with a reduction in the visual contribution to postural control, and is associated with greater amounts of postural sway;
- Inferior visual field loss is more strongly associated with postural sway than superior visual field loss.

6.8 Additional methods

6.8.1 Postural sway outcome measures

Postural sway was measured during quiet stance with a portable swaymeter (Prince of Wales Medical Research Institute, Sydney, Australia), which determines the amount of body displacement at waist height. The device consists of a rod attached to the participant's waist with a firm belt, as shown in Figure 6-1. The 40cm rod, which extends behind the subject, has a vertically-mounted pen at its end to record body movement directly onto graph paper fastened to the top of an adjustable height table. This method of posturography provides a simple, valid clinical measure of postural control, used frequently in falls risk assessment (Lord et al., 2003b). Lord et al (1991) demonstrated excellent test-retest reliability for this swaymeter procedure among older adults, showing reliability coefficients greater than 0.73.

Figure 6-1: Postural sway assessment standing on the firm surface [left image] and on the foam surface [right image]

Testing was performed with bare feet set comfortably apart, with arms relaxed by the side, while gazing directly ahead at the top letters of a visual acuity letter chart (6/60) mounted on a wall. The habitual refractive correction was worn for testing. Sway was measured for 30 s in each of four conditions: (i) eyes open, firm surface; (ii) eyes closed, firm surface; (iii) eyes open, foam surface; (iv) eyes closed, foam surface. The firm surface was a carpeted, level floor. The foam surface was a high-density foam rubber matt (70 x 60 x 15 cm thick), used to reduce the somatosensory contribution to postural stability. Prior to testing, the height of the table was adjusted so that the rod was horizontal and the tip of a pen could record body movements on the paper. The participants were not given specific feedback about performance during the task. The examiner remained close to the participant during testing to provide any assistance if necessary. The recording of postural sway commenced around 10-15 seconds following participants' familiarisation with the task.

Postural sway in each condition was calculated as the total sway area (mm^2), determined by the product of maximal amplitude of anterior-posterior and lateral sway. To normalise the distribution, a logarithmic transformation was applied. Larger values indicated a greater amount of postural sway.

The visual contribution to postural stability was calculated using a visual stability ratio (VSR). Previous studies have established that this ratio, compared with the Romberg quotient, has less variability and a normal distribution (Cornilleau-Peres et al., 2005; Shabana et al., 2005). The VSR, defined in Equation 2, was calculated for both the firm and foam surfaces (referred to as VSR_{FIRM} and VSR_{FOAM}, respectively). A VSR value of 0 or less indicates no visual contribution to postural stability. Values greater than 0 indicate a visual contribution, such that less postural sway occurred with eyes open as compared with eyes closed.

Equation 2:

$$\text{Visual Stability Ratio (VSR)} = 1 - \left(\frac{\text{Postural sway with eyes open}}{\text{Postural sway with eyes closed}} \right)$$

6.8.2 Statistical analysis

Pearson's correlations were used to examine the relationship between the continuous variables and sway and VSR outcomes; point biserial correlations were used to examine relations between the categorical variables and sway outcomes. Further analyses adjusted for age and gender. P-values were not adjusted for multiple comparisons, as reported in Section 3.7.2.

Linear regression models, adjusting for age and gender, examined the association between integrated visual field loss (IVF-60 and IVF-120) and postural sway with the eyes open on firm and foam and VSR on foam, given the significant associations at the bivariate level. RNFL thickness in the better-eye was also examined in linear regression models, due to its strong bivariate associations with postural sway.

To examine the independent association between postural sway and location of visual field loss, the superior and inferior field integrated field measures were considered together in a regression model, adjusted for age and gender. These models were examined separately for the IVF-60 and IVF-120 measures. Multicollinearity was assessed using the collinearity diagnostics in SPSS based on the variance inflation factors (VIF).

6.9 Results

The socio-demographic, medical and visual characteristics have of the cohort has been described in detail in Chapter 3.

The means and standard deviations of postural sway area are presented for each of the four testing conditions in Figure 6-2. Participants exhibited the least amount of postural sway on the firm surface with eyes open and the greatest amount of postural sway on the foam condition with eyes closed. Because two participants could not complete the sway testing with eyes closed on the foam condition unassisted, VSR_{FOAM} data were available for only 72 participants. The means and standard deviations of the VSR are presented for each of the two testing conditions in Figure 6-3. The VSR_{FIRM} showed little value in determining the amount of visual contribution in this condition, as a significant proportion of participants had a negative VSR value, i.e. greater amounts of postural sway with eyes open as compared to eyes closed. The VSR_{FOAM} demonstrated more consistent findings with less variability than VSR_{FIRM}. The majority of participants demonstrated positive VSR_{FOAM} values, such that less postural sway occurred with eyes open compared to eye closed.

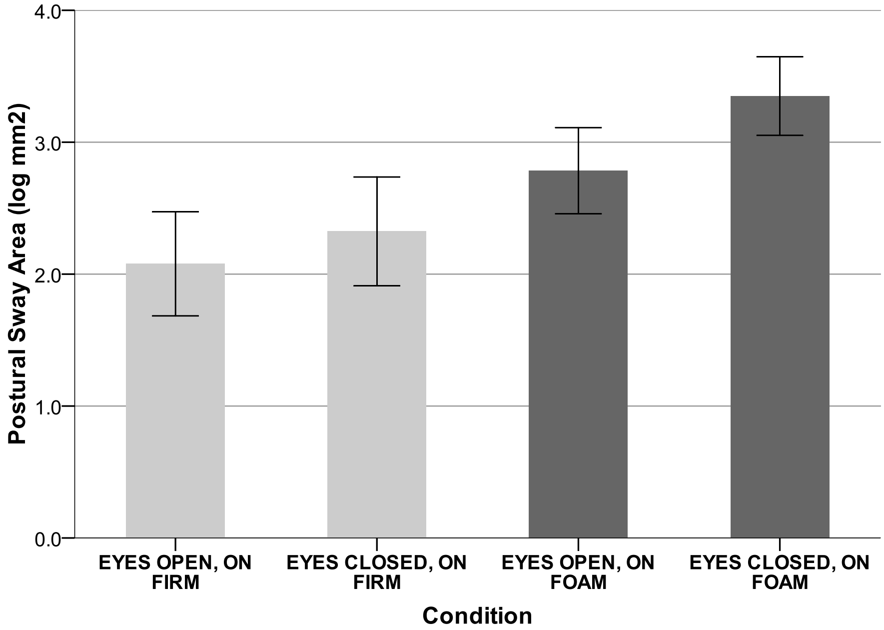

Figure 6-2: Mean postural sway area (log mm^2) across the four testing conditions. Error bars indicate the standard deviation of the means.

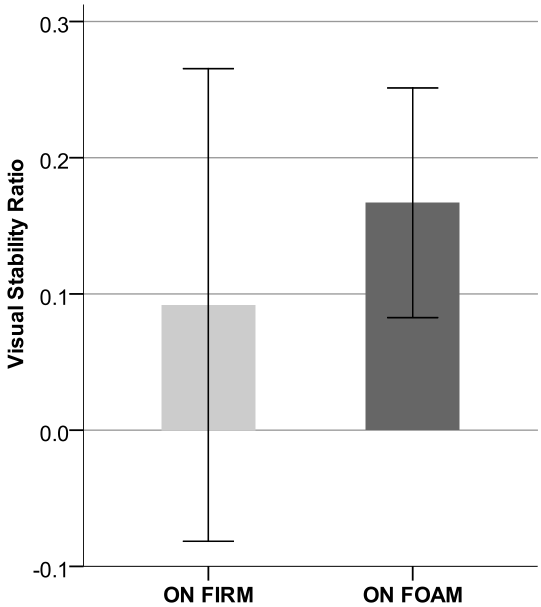

Figure 6-3: Mean visual stability ratio on firm and foam surface. Error bars indicate the standard deviations of the means. Values less than 0 correspond to a visual destabilising effect on postural control.

6.9.1 Severity of visual impairment and postural sway

The unadjusted associations between the vision factors and postural sway measures are shown in Table 6-1. Poor performance on most vision measures was associated with greater postural sway area on both surfaces and lower VSR_{FOAM} values. The strengths of association were markedly stronger in the eyes open conditions compared to the eyes closed conditions. Although some associations were found between postural sway with eyes closed and a number of vision measures, these associations were relatively weak (r=|0.24| to |0.31|) and showed little consistency on either the firm and foam surfaces. When comparing the eyes open on firm and foam surfaces, the strengths of association were consistently stronger across all vision measures on the foam surface compared to the firm surface. The associations were stronger between VSR_{FOAM} and the visual function measures, compared to VSR_{FIRM}. The strongest associations were noted for the RNFL in the better-eye (r=0.48) and IVF measures (IVF-60 total, r=0.36; IVF-120 total, r=-0.36), although caution is required when comparing correlation coefficient due to variations in sample sizes.

The correlations between sway outcomes (eyes open on the firm and foam surface, and VSR_{FOAM}) and the visual function measures with adjustment for age and gender are shown in Table 6-2. Greater sway on the firm surface with eyes open was associated with reduced visual function, particularly reduced contrast sensitivity in the worse-eye (r=-0.32), visual field sensitivity in the better-eye (r=-0.37), and IVF measures (r=|0.36|). Stronger associations were found on the foam with eyes open, particularly reduced visual acuity in the better-eye (r=0.37), contrast sensitivity in the worse-eye (r=-0.43), visual field sensitivity in the better-eye (r=-0.43) and IVF measures (IVF-60, r=-0.44; IVF-120, r=0.46). Scatterplots of the relationship between postural sway and IVF-120 and IVF-60 are presented in Figure 6-4 and Figure 6-5, respectively.

After adjusting for age and gender, reduced VSR_{FOAM} was associated with poorer visual function, particularly better-eye contrast sensitivity (r=0.27), visual field sensitivity in the better-eye (r=0.35) and IVF measures (IVF-60, r=0.36; IVF-120, r=-0.35). RNFL scores for the better and worse eye were also strongly correlated with VSR on foam (r=0.44 and 0.43, respectively). A scatterplot of the relationship between VSR on foam with RNFL thickness is presented in Figure 6-6.

Table 6-1: Pearson's correlations between visual function measures and postural sway measures†

	Firm surface		Foam surface		VSR	
	Eyes Open	Eyes Closed	Eyes Open	Eyes Closed	Firm surface	Foam surface
Visual Acuity (logMAR)						
better-eye	**0.25 ***	0.10	**0.39 ****	**0.31 ****	-0.14	-0.19
worse-eye	**0.32 ****	0.17	**0.39 ****	**0.31 ****	-0.12	-0.18
Contrast Sensitivity (logCS)						
better-eye	**-0.32 ****	**-0.27 ***	**-0.34 ****	-0.15	0.03	**0.27 ***
worse-eye	**-0.38 ****	**-0.30 ***	**-0.47 ****	**-0.24 ***	0.06	**0.31 ****
Stereoacuity (absent/present)	**0.31 ****	**0.28 ***	**0.31 ****	0.13	-0.02	**-0.24 ***
Motion sensitivity (log deg/sec)	**0.26 ***	0.09	**0.27 ***	0.12	-0.14	-0.20
Visual Field Sensitivity (dB)						
better-eye	**-0.40 ****	**-0.26 ***	**-0.43 ****	-0.14	0.12	**0.35 ****
worse-eye	**-0.38 ****	**-0.27 ***	**-0.38 ****	-0.13	0.12	**0.32 ****
RNFL (µm)						
better-eye	**-0.33 ***	-0.04	**-0.49 ****	-0.09	**0.27 ***	**0.48 ****
worse-eye	-0.20	0.04	**-0.36 ****	0.04	0.26	**0.44 ****
IVF-60 (dB)						
overall field	**-0.38 ****	**-0.26 ***	**-0.44 ****	-0.14	0.11	**0.36 ****
inferior field	**-0.43 ****	**-0.29 ***	**-0.46 ****	-0.17	0.12	**0.36 ****
superior field	**-0.30 ****	-0.20	**-0.37 ****	-0.11	0.09	**0.34 ****
IVF-120 (points missed)						
overall field	**0.38 ****	0.20	**0.47 ****	0.18	-0.17	**-0.36 ****
inferior field	**0.42 ****	**0.25 ***	**0.51 ****	0.22	-0.15	**-0.36 ****
superior field	**0.30 ***	0.12	**0.37 ****	0.13	-0.17	**-0.32 ****
VFQ-25 Composite Score	-0.03	0.00	**-0.31 ****	-0.09	0.10	**0.31 ***

Notes: Bold values indicate significant correlations; *p<0.05; **p<0.01; † n=74, with the exception of RNFL (n=57) and VFQ-25 (n=72); RNFL = Retinal Nerve Fibre Layer; IVF = Integrated Visual Field; VFQ-25 = Visual Function Questionnaire (transformed scale).

Table 6-2: Pearson's correlations between visual function and postural sway measures, adjusted for age and gender†

	Firm surface, eyes open	Foam surface, eyes open	VSR on foam surface
Visual Acuity (logMAR)			
better-eye	0.22	**0.37 ****	-0.20
worse-eye	0.25 *	0.34 **	-0.19
Contrast Sensitivity (logCS)			
better-eye	**-0.25 ***	**-0.30 ***	**0.27 ***
worse-eye	**-0.32 ****	**-0.43 ****	**0.33 ****
Stereoacuity (absent/present)	0.21	0.23	-0.26 *
Motion sensitivity (log deg/sec)	0.17	0.20	-0.22
Visual Field Sensitivity (dB)			
better-eye	**-0.37 ****	**-0.43 ****	**0.35 ****
worse-eye	**-0.34 ****	**-0.37 ****	**0.31 ****
RNFL (µm)			
better-eye	**-0.31 ***	**-0.45 ****	**0.44 ****
worse-eye	-0.15	**-0.35 ***	**0.43 ****
IVF-60 (dB)			
overall field	**-0.36 ****	**-0.44 ****	**0.36 ****
inferior field	**-0.40 ****	**-0.44 ****	**0.36 ****
superior field	**-0.28 ***	**-0.38 ****	**0.33 ****
IVF-120 (points missed)			
overall field	**0.36 ****	**0.46 ****	**-0.35 ****
inferior field	**0.39 ****	**0.49 ****	**-0.36 ****
superior field	**0.29 ***	**0.38 ****	**-0.31 ****
VFQ-25 Composite Score	0.07	**0.31 ****	**-0.31 ****

Notes: Bold values indicate significant correlations; *p<0.05; **p<0.01; † n=74, with the exception of RNFL (n=57) and VFQ-25 (n=72); VSR = Visual Stability Ratio; RNFL = Retinal Nerve Fibre Layer; IVF = Integrated Visual Field; VFQ-25 = Visual Function Questionnaire (transformed scale).

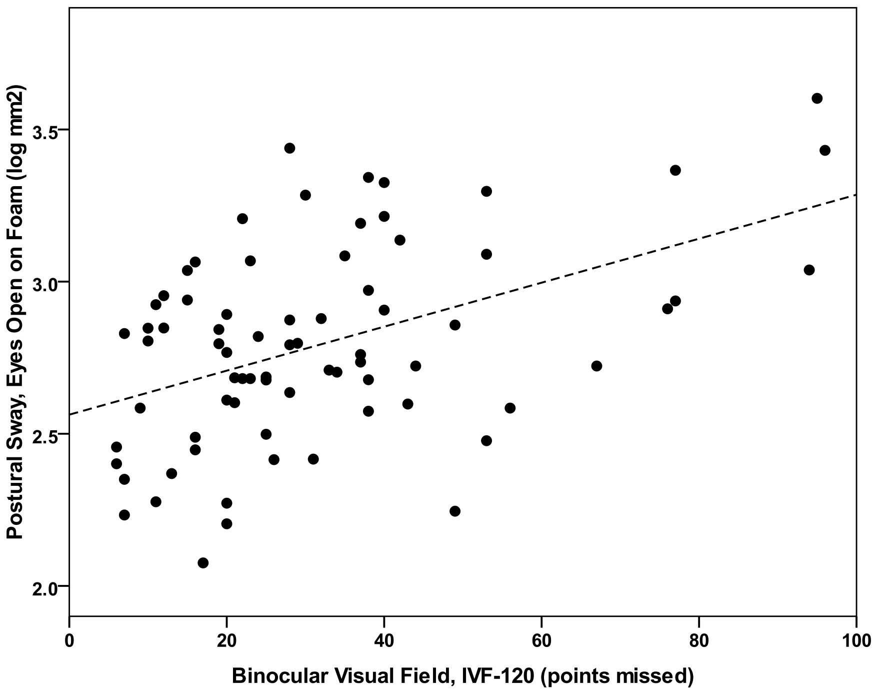

Figure 6-4: Integrated 120° visual field score (IVF-120) as a function of postural stability with eyes open on foam surface. Pearson's correlation r=0.47, P<0.001, adjusted for age and gender.

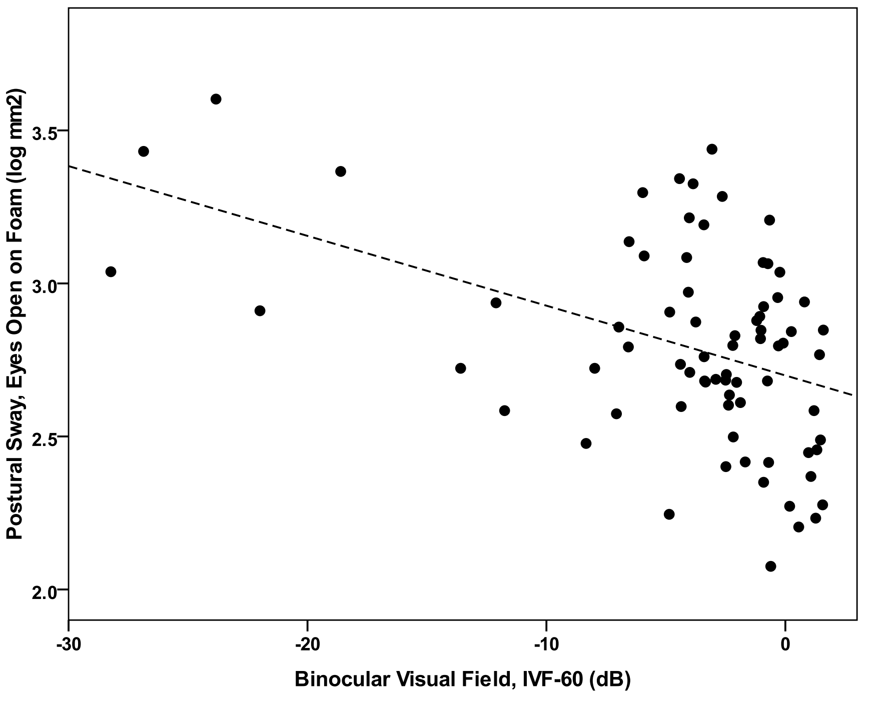

Figure 6-5: Integrated 60° visual field score (IVF-60) as a function of postural stability with eyes open on foam surface. Pearson's correlation r=-0.45, P<0.001, adjusted for age and gender.

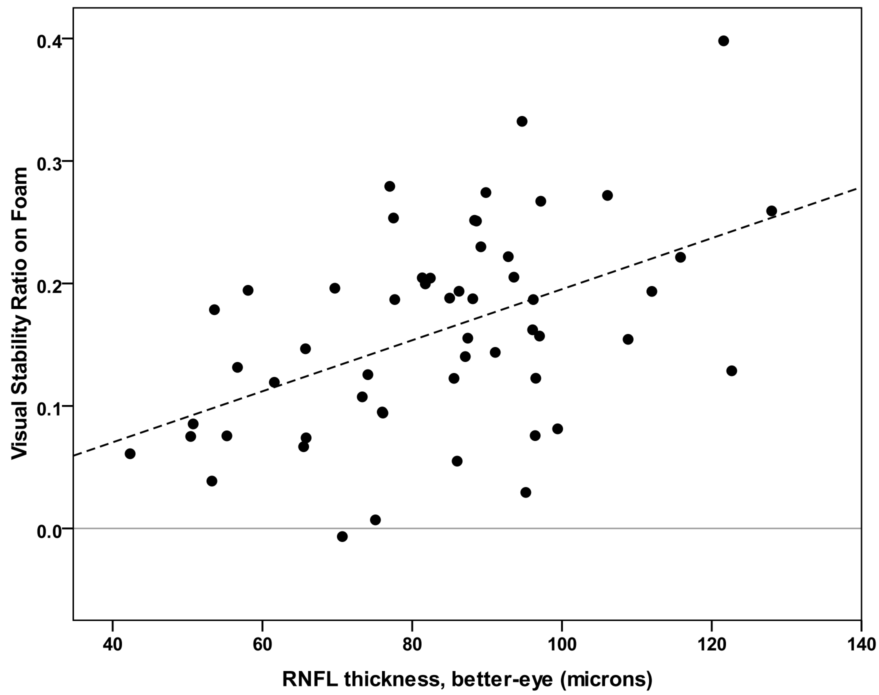

Figure 6-6: Retinal Nerve Fibre Layer (RNFL) thickness as a function of Visual Stability Ratio (VSR) on foam. VSR less than 0 correspond to a visual destabilising effect on postural control. Pearson's correlation r=0.38, P<0.001, adjusted for age and gender.

The results from the linear regression models are presented in Table 6-3. The association between IVF and RNFL measures and sway with eyes open on firm were similar (betas = |0.29| to |0.34|, Models 1, 3 and 5) and sway with eyes open on foam (betas = |0.43| to |0.50|, Models 6, 8 and 10). When both the IVF-60 superior and inferior fields were considered together in a model (Models 2 and 7), only the inferior fields remained statistically significant with postural sway on the firm and foam, whereas the superior field estimates fell short of statistical significance. Similarly, when both the IVF-120 superior and inferior fields were considered together in a model (Models 4 and 9), the inferior field was significantly associated with sway on the foam condition, whereas the superior field estimate fell short of statistical significance.

Table 6-3: Visual field factors associated with postural sway (linear regression models, adjusted for age and gender) †

Model		B coefficient (95% CI)		Beta	p-value	VIF
SWAY FIRM, EYES OPEN						
1	IVF-60 overall field (per 5dB)	**-0.11**	**(-0.04 to -0.18)**	**-0.34**	**0.002**	
2	IVF-60 inferior field (per 5dB)	**-0.14**	**(-0.03 to -0.24)**	**-0.43**	**0.013**	2.72
	IVF-60 superior field (per 5dB)	0.02	(0.12 to -0.08)	0.07	0.681	2.91
3	IVF-120 overall field (per 10 points)	**0.06**	**(0.02 to 0.10)**	**0.33**	**0.002**	
4	IVF-120 inferior field (per 10 points)	**0.14**	**(0.02 to 0.25)**	**0.38**	**0.020**	2.48
	IVF-120 superior field (per 10 points)	-0.01	(-0.12 to 0.1)	-0.02	0.882	2.57
5	RNFL better-eye (per 10um)	-0.06	**(-0.11 to -0.01)**	**-0.29**	**0.026**	
SWAY FOAM, EYES OPEN						
6	IVF-60 overall field (per 5dB)	**-0.11**	**(-0.06 to -0.17)**	**-0.43**	**0.000**	
7	IVF-60 inferior field (per 5dB)	**-0.09**	**(-0.01 to -0.18)**	**-0.36**	**0.036**	2.72
	IVF-60 superior field (per 5dB)	-0.02	(0.06 to -0.1)	-0.09	0.590	2.91
8	IVF-120 overall field (per 10 points)	**0.07**	**(0.04 to 0.1)**	**0.45**	**0.000**	
9	IVF-120 inferior field (per 10 points)	**0.14**	**(0.04 to 0.23)**	**0.46**	**0.005**	2.48
	IVF-120 superior field (per 10 points)	0.00	(-0.08 to 0.09)	0.02	0.927	2.57
10	RNFL better-eye (per 10um)	**-0.08**	**(-0.12 to -0.04)**	**-0.50**	**0.000**	
VSR, FOAM						
11	IVF-60 overall field (per 5dB)	**0.03**	**(0.04 to 0.01)**	**0.38**	**0.002**	
12	IVF-60 inferior field (per 5dB)	0.02	(0.04 to -0.01)	0.26	0.180	2.89
	IVF-60 superior field (per 5dB)	0.01	(0.03 to -0.01)	0.14	0.483	3.10
13	IVF-120 overall field (per 10 points)	**-0.01**	**(-0.02 to -0.01)**	**-0.36**	**0.003**	
14	IVF-120 inferior field (per 10 points)	-0.02	(-0.05 to 0.00)	-0.30	0.107	2.68
	IVF-120 superior field (per 10 points)	-0.01	(-0.03 to 0.02)	-0.08	0.690	2.79
15	RNFL better-eye (per 10um)	**0.02**	**(0.01 to 0.03)**	**0.49**	**0.000**	

Notes: Bold values indicate statistical significance; † n=74, with the exception of RNFL (n=57); IVF = Integrated Visual Field; RNFL = Retinal Nerve Fibre Layer; VSR = Visual Stability Ratio; VIF = Variance Inflation Factor

The association between VSR_{FOAM} and RNFL better-eye (beta = 0.49, Model 15) was stronger relative to the associations between VSR_{FOAM} and IVF measures (betas = |0.36| to |0.38|, Models 11 and 13), although caution is required when comparing coefficients due to variations in sample sizes for the various analyses. When the superior and inferior fields were considered together in a model, neither was independently associated with VSR_{FOAM} (Models 12 and 14).

The VIF values calculated in these models ranged from 2.64 to 3.14 suggesting some variance inflation due multicollinearity between the superior and inferior field variables. While the results should be interpreted with some care, none of the VIF values were greater than 10. An alternative analysis to support these findings is presented in Appendix 7.

6.10 Discussion

In this study, visual impairment was significantly associated with postural sway in a cohort of older community-dwelling adults with glaucoma. In particular, greater binocular visual field loss was associated with larger magnitudes of postural sway with eyes open, particularly on the foam surface, independent of age and gender. To our knowledge, this study is the first to report a significant link between severity of visual field loss and postural sway among older adults with glaucoma. Our study included high-functioning older adults, similar to general community-dwelling older populations in terms of their level of physical activity (Chad et al., 2005) and performance-based functional measures (Lord & Menz, 2002; Tiedemann et al., 2005). In a frailer population, the effect of glaucomatous visual impairment on postural stability is likely to be even greater.

Our results do not support those of Shabana et al (2005), who failed to demonstrate an association between glaucomatous visual field loss and postural sway, based on measures of force platform sway velocities. The glaucoma patients in Shabana's study, aged between 40 and 66 years, showed greater somatosensory contributions to postural stability to maintain steady stance, as compared to controls. While there are differences in the measures of sway and the degree of visual impairment between studies, it is likely that Shabana et al's failure to find an association between visual field loss and postural sway is due to their considerably younger sample (40 to 66 years) as compared to those tested in the current study (62 to 90 years). Ageing, particularly in those aged over 60, is associated with significant declines in the somatosensory and vestibular systems (Woollacott, 2000; Choy et al., 2003; Era et al., 2006) in addition to an increasing prevalence of glaucoma (Weih et al., 2001; Rudnicka et al., 2006). Our results suggest that adults with glaucomatous visual impairment aged over 60 years are less able to increase their somatosensory contribution to postural stability, resulting in greater amounts of postural sway.

In support of our findings, a population study by Freeman et al (2008a) showed that visual field loss among community-dwelling older adults was significantly associated with greater postural instability. Every 10 points missed in the binocular visual field, identical to the IVF-120 measure in the present study, was associated with around a 30 to 40 per cent increased likelihood of being unable to perform the most difficult standing balance tests (tandem and soleo stance), following adjustment for age, sex, race, body mass index, and number of comorbid conditions. Experimental studies also support our findings, as occlusion of the peripheral visual field areas results in greater postural sway among normally sighted individuals, compared to normal full field viewing (Straube et al., 1994; Nougier et al., 1997; Berencsi et al., 2005; Piponnier et al., 2009).

It would be useful to provide some clinical guidance as to the point in disease progression at which glaucoma begins to impact on postural sway. However, it is difficult to estimate this from the cross-sectional nature of this study. Such estimates would also be highly dependent on factors specific to an individual and their recreational balance requirements. Our findings indicate, however, that adults who are physically active and require greater balance reserves, and also suffer from greater visual field loss are more likely to experience difficulties in their postural control when undertaking demanding activities.

Although research suggests that glaucoma reduces motion sensitivity (Bullimore et al., 1993; McKendrick et al., 2005; Falkenberg & Bex, 2007), we did not find a significant association between motion sensitivity and postural stability. In contrast, Freeman et al (2008a) reported significant associations between postural instability and reduced motion sensitivity in a general population, measured within a 10 degree diameter retinal area. The limited findings in the present study may be due to the smaller motion sensitivity target, which subtended a 3 degree diameter retinal area. Furthermore, comparisons are difficult due to the differences in the balance measures used and cohort visual characteristics, which may explain inconsistencies in results.

As expected, we found stronger associations between the vision measures and postural sway on the foam surface, compared to on the firm. This is consistent with findings from previous studies (Lord & Menz, 2000; Anand et al., 2002; Anand et al., 2003a; Shabana et al., 2005), as the contribution of vision to postural control increases to maintain balance in compensation for the reduced somatosensory input on the foam surface. The findings on the foam surface emphasize the significant relationship between vision and balance and highlight the detrimental effect of glaucomatous visual field loss on postural control. Importantly, the findings have implications for postural stability in situations of reduced somatosensory input, such as uneven and unstable surfaces, for example walking on carpeted surfaces. There were few significant associations between the vision measures and postural sway with eyes closed on both surfaces, which was expected given the lack of visual input during these conditions.

Our results are the first to suggest that the inferior visual field may provide a stronger contribution to postural stability than the superior visual field. This finding was particularly evident on the foam condition with eyes open, for both of the binocular visual field measures. Previous studies with visually impaired individuals have indicated that greater loss in the central and inferior visual field areas are significantly associated with reduced mobility performance (Lovie-Kitchin et al., 1990; Turano et al., 2004). Moreover, there is some evidence that falls may occur more frequently in those with inferior visual field loss. Coleman et al. (2007) reported that the odds of falling among older women with severe inferior visual field loss, compared with no inferior loss, was 91% higher, whereas the odds of falling among those with severe superior visual field loss, when compared with no superior visual field loss, was 74% higher. Experimental studies have demonstrated the importance of the inferior visual area in mobility and navigation (Marigold & Patla, 2008), particularly for obstacle detection and avoidance.

It has been hypothesized that the inferior visual field provides a greater contribution to the dorsal visual pathway, a pathway which mediates visually guided movements (Khan & Lawrence, 2005; Krigolson & Heath, 2006). A number of laboratory-based studies have shown that the inferior visual field is more effective in visually guided reaching and aiming movements compared with the superior visual field among visually normal participants (Khan & Lawrence, 2005; Krigolson & Heath, 2006). Further support is provided by an experimental study by Kimura et al (1981) which found significantly slower latency times for visually evoked potentials by a moving stimulus in the superior field (15 degrees above fixation), compared to latencies in the central and inferior visual fields. Their findings suggest that the central and inferior field areas are more efficient at recognition of moving stimuli than the superior field.

The cortical control of postural stability may incorporate the visuomotor pathway, as greater inferior visual field loss was associated with larger amounts of postural sway, independent of superior field loss. It is possible that the visuomotor system relies more heavily on inferior visual field areas, since our visual environment tends to contain a greater proportion of visual cues in this area relative to the superior field. It is also possible that the greater inferior visual field contribution to the visuomotor system forms during early brain development. In any case, inferior visual field loss appears lead to less awareness of relative body position, resulting in greater postural instability. Although this was demonstrated in the current study, it was beyond the scope of the present study to determine the mechanisms underlying this finding.

The relative contribution of vision to postural control was shown to decline steadily with increased binocular visual loss in the present study, in agreement with previous studies (Turano et al., 1993; Shabana et al., 2005). Shabana et al (2005) demonstrated that individuals with glaucomatous visual field loss reduce their visual contribution to postural stability, by an amount that correlated with severity of field loss. Shabana et al (2005) found that the mean deviation visual field index in the worse-eye was the strongest correlate with the visual stabilization ratio (r=0.40, Spearman's). The present study found comparable bivariate relations between visual field measures and VSR on foam (r=|0.36|), despite considerable differences between the cohort characteristics, postural stability and visual field measures. In a study by Turano et al (1993), individuals with retinitis pigmentosa demonstrated a steady decrease in visual contribution to stability, correlating strongly with visual field loss (r = -0.59). In the same study, they further demonstrated that artificial field restriction in those with normal vision correlated with a reduction in the visual contribution to stability, although not to the same extent as in those with retinitis pigmentosa.

Interestingly in the current study RNFL thickness was strongly correlated with the visual contribution to postural stability. This association may be due to the fact that damage to the RNFL may precede visual field loss (Sihota et al., 2006), or that RNFL thickness may reflect declines in other visual functions that influence postural control, such as motion detection (Kelly et al., 2005).

The strengths of this study include extensive assessment of different vision components, including the use of binocular integrated visual fields, and the use of a an older cohort, which is an age group where glaucoma is more prevalent (Rochtchina & Mitchell, 2000; Weih et al., 2001) and falls are common events (Dolinis et al., 1997; Ivers et al., 2003).

There are a number of limitations to this study. Previous studies have included the use of force platform analysis, which can provide extensive quantitative data pertaining to velocity, area and displacement of the centre of pressure occurring at ground level. However, no one sway measure completely reflects the complex nature of postural stability, due to the many inherent factors that can contribute to the variability of these measures (Hageman et al., 1995). While the sway measure used in the current study is less detailed than data from force platforms, it does provide a basic representation of body trunk displacement, shown to be a valid measure of underlying balance impairment (Goldberg et al., 2005), and its reliability has been established in previous studies (Lord et al., 1991; Lord et al., 2003b). It does, however, limit our ability to examine the peripheral contribution to various components of sway, as Nougier (1997) reported that the peripheral field regulated sway in the anterio-posterior direction. Despite this, data generated from the swaymeter device are continuous measures and are less prone to significant floor or ceiling effects, which can occur with the use of standing balance tests, such as the semi-tandem and tandem stand (Era et al., 2006).

Chapter 8 provides additional discussion on a number of strengths and limitations pertaining to all of the studies presented in this thesis, along with important implications arising from the findings.

6.11 Conclusion

In summary, greater binocular visual field loss or thinner RNFL was associated with increased postural sway among older community-dwelling adults with glaucoma. Furthermore, the magnitude of postural sway was larger in those with greater inferior visual field loss, particularly on the foam surface, independent of superior visual field loss. Greater visual field loss or RNFL thickness was accompanied by a steady decrease of the visual contribution to postural control. These postural changes may be an important underlying factor in the increased risk of falls and fall-related injuries among older adults with glaucoma (Dolinis et al., 1997; Ivers et al., 2003; Haymes et al., 2007).

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Chapter 7: Visual Impairment and Falls among Older Adults with Glaucoma: A 12-Month Follow-Up Study [Study 2]

7.1 Introduction

Falls are an important and preventable health problem for adults aged 65 years and older. Approximately one in three community-dwelling older adults will experience a fall each year, with many experiencing multiple falls. There are serious consequences of falls, as they represent 4% of hospital admissions, 40% of injury-related deaths and 1% of total deaths in Australians aged over 65 years (Lord et al., 2007).

The literature review presented evidence demonstrating that visual impairment from various eye diseases increases the risk of falls among older adults. A likely explanation for this link is that the visual system is essential for safe and efficient navigation, guiding locomotion within the environment. Importantly, deficits in safe and efficient navigation can potentially lead to falls. Individuals with visual impairment from various eye diseases show reduced mobility performance compared with visually normal individuals (Black et al., 1997; Kuyk et al., 1998; Kuyk & Elliott, 1999; Hassan et al., 2002). Furthermore, greater severity of visual impairment is associated with further decrements in mobility performance, in studies in general populations (Turano et al., 2004), and in specific eye disease groups, such as macular degeneration (Hassan et al., 2002).

There is also strong supporting evidence of the link between visual impairment, from a range of eye diseases, and falls and fractures (Ivers et al., 1998; Ivers et al., 2003; Coleman et al., 2004; Coleman et al., 2007; Freeman et al., 2007; Coleman et al., 2009). As the aim of this thesis was to evaluate the relationship between visual impairment and falls among older adults with glaucoma, the remainder of this introduction reviews and discusses the available evidence in this area.

7.2 Visual field loss, glaucoma and mobility

Vision is essential for interacting with the environment when walking, particularly for obstacle avoidance, locomotion planning and foot placement. The peripheral visual field contributes to efficient navigation, through the creation of an accurate spatial relationship between self and object, which is constantly updated while travelling within the environment (Turano et al., 2005).

Recent research has demonstrated significant reductions in accurate encoding and memory of the visual environment among adults with visual field loss, compared to those with no vision loss, based on directional errors when walking within a virtual reality environment (Turano et al., 2005). These virtual spatial misrepresentations also increased with greater severity of visual field loss (Fortenbaugh et al., 2008).

In a study of adults with normal vision, Hassan et al (2007) estimated that the minimum field of view diameter required for safe navigation with simulated visual impairment when walking within a virtual environment was around 11 degrees under a high contrast environment, and around 32 degrees under a low contrast environment. This suggests that loss of visual field within the central 30 degrees can significantly impact on safe navigation under low contrast situations, which occur in the real-world. The findings of these studies, however, should be viewed with some caution, as they do not take into account that individuals with true, rather than simulated, visual impairment may develop coping strategies over time.

Visual field loss, from any cause, has been linked with reduced mobility. In a study comprising 1,504 community-dwelling older adults, slower completion of a mobility course was associated with greater binocular visual field loss, but not for reduced visual acuity or contrast sensitivity (Patel et al., 2006). From the same study, Turano et al (2004) also demonstrated that greater binocular visual field loss was associated with a 22% increase in collision with obstacles.

There is also good evidence that non-glaucomatous visual field loss reduces mobility performance. Most of this research has focused on retinitis pigmentosa (RP) which primarily results in mid-peripheral visual field loss. Individuals with RP have demonstrated poorer mobility performance compared to visually normal controls (Black et al., 1997), and mobility performance deteriorates according to severity of visual field loss (Haymes et al., 1996). Haymes et al (1996) reported that adults with RP maintain good mobility performance until visual field loss occurs within the central 20 degrees.

Individuals with glaucoma also report difficulties in mobility. In a study of 79 adults with glaucoma, over 25% of participants reported moderate to severe restriction in their mobility, more so than other activities of daily living, according to the Impact of Vision Impairment questionnaire (Noe et al., 2003). Greater visual field loss in these participants, measured using the Esterman test, was associated with greater self-reported mobility difficulties, even after adjustment for age and visual acuity. Recently, Geruschat et al (2007) quantified the mental effort required for walking among adults with glaucoma, measured by reaction times for a secondary task. Greater mental effort was required in complex environments, particularly approach-to-stairs and stairs. Moreover, individuals with greater visual field loss required extra mental effort to safely navigate these situations.

Research has demonstrated that greater visual field loss from glaucoma impairs mobility performance. Turano et al (1999) reported that reduced visual field sensitivity in the better-eye among 47 glaucoma participants was associated with slower walking speed in a mobility course, and correlations were stronger compared to visual acuity or contrast sensitivity. Recently, Friedman et al (2007) showed that older adults with bilateral glaucoma (n=74) walked more slowly and experienced more bumps in a mobility course compared to those with no signs of glaucoma or visual field loss (n=1064). Adults with unilateral glaucoma (n=76) showed no differences in their mobility performance, compared to controls, which suggest that mobility is not affected until glaucoma affects visual function in both eyes. The severity of binocular visual field loss in the bilateral glaucoma group was the primary visual function which contributed to poorer mobility performance, independent of visual acuity loss.

Safe and efficient navigation also relies on accurate inferior visual field information. When walking, individuals fixate approximately two steps ahead (Land, 2006), and central fixation is generally not re-directed to suddenly appearing obstacles in the travel path (Marigold et al., 2007). Thus, the inferior visual field is critical for successful obstacle avoidance during locomotion.

A study by Lovie-Kitchin et al (1990) was the first to examine the relative importance of visual field areas for safe navigation. Using an indoor course, mobility performance of 9 visually impaired adults, from various eye diseases, was compared to 9 age-matched controls. Associations were examined between mobility performance and visual field areas within the 90 degree radius, based on 15 subdivisions of the visual field. The central 37 degree field areas and the inferior field areas to 58 degrees were the strongest correlates with the number of obstacle contacts. These field areas were also strong correlates with walking speed, albeit weaker than with the obstacle contacts. In a more recent mobility study involving 1,504 community-dwelling older adults, Turano et al (2004) found that the central (40 degree diameter) and inferior visual field areas were independently associated with walking speed in the course, while the superior field area was not significant. Only the central visual field area, however, was significantly associated with the number of collisions.

Marigold & Patla (2008) recently examined the impact of inferior visual field occlusion (up to approximately 20 degree radius from fixation) on gait patterns among visually normal healthy adults when walking across an experimental walkway of varying terrains. Compared to viewing with full field, participants reduced their gait speed and step length when the inferior visual field area was occluded. Participants also demonstrated greater tilting of the head (pitch) to increase the area of inferior visual field, further highlighting the importance of this field area. There are, however, some limitations to the study, particularly the crude form of field occlusion attached to a spectacle frame, and the inability to control the extent of field occlusion, as participants were able to increase the area of visual field by tilting their heads. Despite these limitations, the study provides early experimental evidence that the inferior visual field is a significant contributor to safe navigation.

Limited visual scanning among adults with visual field loss may also be a contributing factor to their mobility difficulties. Vargas-Martin et al (2006) showed that adults with RP, with less than 20 degree of remaining field, showed similar magnitudes of scanning eye movements when walking compared to controls. It was thought that adults with RP would demonstrate greater scanning eye movements to compensate for missing peripheral vision information, but this was not the case. The authors suggested that the limited scanning may be due to lack of peripheral visual stimulation to prompt eye movements. Poor visual scanning may be an important underlying factor between visual field loss and falls, yet this remains to be explored.

7.3 Visual field loss and falls

Visual field loss had been linked to an increased falls risk among older adults, both in retrospective (Ivers et al., 1998; Klein et al., 1998; Klein et al., 2003b) and prospective population studies (Ramrattan et al., 2001; Coleman et al., 2007; Freeman et al., 2007). These associations are also supported by prospective hip fractures (Ivers et al., 2003; Coleman et al., 2009).

The Rotterdam Eye Study examined the prevalence and causes of visual field loss among older adults aged 55 years and older, as well as the number of falls and fractures in the following two years (Ramrattan et al., 2001). The likelihood of experiencing frequent falls (more than 4 falls) in the two years after the baseline eye examination was six times greater in those with unilateral and bilateral visual field loss, compared to those with no visual field loss. The association also remained significant after adjusting for visual acuity. In addition, the likelihood of experiencing a wrist fracture was around 3 times greater in those with unilateral visual field loss; however, the results are limited by small numbers of reported fractures. The study provides good evidence that visual field loss increases the risk of falls, although the results are somewhat limited by the retrospective nature of the falls outcome.

Several well-designed prospective falls studies provide strong evidence that visual field loss is an independent risk factor for falls (Coleman et al., 2007; Freeman et al., 2007). Freeman et al (2007) monitored falls prospectively, for an average of 17 months, comprising of 2,375 community-dwelling older adults, aged between 65 and 84. Binocular visual field loss (based on merged monocular field tests) was significantly associated with falling, more so than reductions in visual acuity, contrast sensitivity, or stereoacuity. The risk of falling was 8 per cent greater for every 10 points missed in a binocular visual field (odds ratio 1.08 [1.03–1.13]), even after adjustment for a number of confounding factors.

In a study by Coleman and colleagues (2007), binocular visual field loss (based on merged monocular field tests) was a significant predictor for multiple falls during a 12 month follow up, among 4,071 women aged over 70 years. Women with moderate visual field loss (10-19 points missed) were 37 per cent more likely to experience multiple falls (odds ratio 1.37 [1.01–1.84]), while those with severe visual field loss (20 points or more missed) were 50 per cent more likely to experience multiple falls (odds ratio 1.50 [1.11–2.02]). Neither visual acuity nor contrast sensitivity was associated with falls.

Significant associations have also been reported between visual field loss and prospective fracture rates. In a recent study comprising 4,773 older women, Coleman et al (2009) found that severe binocular visual field loss (20 or more points missed) increased the odds of a hip fracture by 66 per cent (odds ratio 1.66 [1.19–2.32]), and odds of a non-spine, non-hip fracture by 59 per cent (odds ratio 1.59 [1.24–2.03]), during the average 8 years of follow up. Reduced visual acuity and contrast sensitivity was associated with non-spine, non-hip fractures, but not hip fractures.

Similarly, Ivers et al (2003) found that the risk of a hip fracture was over five times higher in participants with more than five points missed in the better-eye monocular 76-point field screening (hazard ratio, 5.40 [1.30–22.2]), in a study of 3,654 community dwelling adults. An earlier study by the same research group also demonstrated that participants with visual field loss measured using the same strategy were nearly three times more likely to experience a prospective ankle fractures during the 5 year follow-up (relative risk, 2.7 [1.1–6.2]), but not for wrist or shoulder fractures (Ivers et al., 2002).

Several retrospective falls studies have identified significant links between visual field loss and falls, although their findings are limited by the retrospective nature of the falls outcomes. The Beaver Dam Eye Studies found that reduced visual field sensitivity, assessed on a Henson perimeter, almost doubled the risk of a fall or fracture (Klein et al., 1998; Klein et al., 2003b), while the Blue Mountains Eye Study showed that more than five points missed on a Humphrey screening test increased the risk of falls by 50 per cent (Ivers et al., 1998).

In contrast, a retrospective study of 489 patients of patients attending a glaucoma clinic, most of whom had glaucoma, found that those with 40% or more loss in visual field were more likely to report an injurious fall in the previous year, yet this failed to reach statistical significance (Glynn et al., 1991). The findings are limited by the use of an unconventional definition of visual field loss, as severity of visual field loss was estimated using the average sensitivity within the central 30 degree radius field, divided by the normal average for a 65 year old, then multiplied by 100 to convert to a percentage of normal. Friedman and co-workers (2002) found no association between the number of points missed on a visual field screening test (81-point screening field) and reported falls at a 12 month follow-up examination among 2,212 older adults. The findings, however, are limited by the inclusion of previous falls in the analyses, which is a factor likely to be in the causal pathway between vision loss and incident falls, thus reducing the association.

Evidence of the link between visual field loss and falls is also shown in a recent analysis of retrospective medical claims. Bramley et al (2008) examined the economic implications of glaucoma-specific vision loss, including falls, injury, fractures and nursing home placement in over 180,000 adults with glaucoma aged over 65. Patients with any vision loss, as compared to those with no vision loss, were 59 per cent more likely to experience falls and accidents, and 67 per cent more likely to experience femur fracture. Furthermore, the adjusted risk of nursing home placement more than doubles for glaucoma patients with vision loss compared to those with no vision loss. These findings, albeit limited by the crude visual field loss classification based on the medical records, confirm that visual field loss is associated with increased risk of adverse health outcomes, particularly falls and fractures.

An area of falls and vision research that has received limited attention is the effect of the location of the field loss on falls. Studies have shown that greater loss in the central and inferior visual field areas are significantly associated with reduced mobility performance among visually impaired individuals (Lovie-Kitchin et al., 1990; Turano et al., 2004). As outlined in Chapter 2, glaucomatous visual field defects can occur in either superior or inferior hemifield regions, and defects tend to correspond within the same hemifield between eyes (Hoffmann et al., 2006). As such, patients with glaucoma can present with bilateral defects in the superior or inferior hemifields.

Coleman et al (2007) reported that the odds of falling among older women with severe inferior visual field loss, when compared with no inferior loss, were 91% higher (odds ratio, 1.91 [1.05–1.56]), whereas the odds of falling among those with severe superior visual field loss, when compared with no superior visual field loss, were 74% higher (odds ratio, 1.74 [1.36–2.23]). The superior and inferior fields were calculated according to locations above and below the horizontal midline of the integrated visual field, respectively. Coleman's study, however, did not examine the independent contributions of these field areas to the risk of falls.

In contrast, Freeman and colleagues (2007) examined the independent contributions of the superior and inferior field areas to falls, yet failed to show any significant difference in falls risk in their community-dwelling cohort. Their analysis was based on 3 regions of visual field area within the integrated binocular field: the central 20 degree radius and the remaining inferior and superior field regions. The combined inferior and superior peripheral field regions were stronger predictor for falls than central field loss, yet neither the superior or inferior field locations were statistically significant when considered together in a model.

In summary, the literature confirms the importance of the peripheral visual field areas in mobility, and visual field loss is associated with an increased risk of falls and fractures. However, the relationship between the location of visual field loss and falls remains uncertain, although findings from mobility studies suggest that the inferior visual field region is essential for safe navigation.

7.4 Visual attention and falls

Safe navigation and falls of older adults may also be influenced by AFV performance. As outlined in the literature review, previous studies have used various AFV tests, based on either attentional processing speed within a fixed visual field area, or the extent of attentional visual field area using a fixed processing speed. AFV measures can vary in task complexity, from divided attention tests (a single central and peripheral target), to more cognitively demanding selective attention tests (the addition of peripheral distracting targets). AFV measures are influenced by visual functioning, as well as higher-order visual/cognitive processes (Clay et al., 2005).

Broman et al (2004) reported that a decrease of 50 ms in processing speed for a divided attention task was associated with a 4.9% increase in number of bumps made in a mobility course among 1,504 community-dwelling older adults, even after adjusting for visual field loss. In a mobility study comprising of 35 participants with a range of eye diseases, Leat & Lovie-Kitchin (2008) found that mobility errors and walking speed in the course was associated with number of points missed in the divided and selective AFV area. These associations were considerably weaker when adjusted for visual field loss, which was expected given that previous work by the authors showed that attentional field performance among visually impaired adults is strongly influenced by visual field loss (Leat & Lovie-Kitchin, 2006).

The link between AFV and falls, however, remains unclear. Reduced attention fields, using timed divided and selective AFV tests, were not associated with the number of previous falls in a study of 342 community-dwelling older adults aged 55 to 85 years (Owsley & McGwin, 2004). In a retrospective falls study, Haymes et al (2007) reported significant difference in AFV processing speeds in 48 participants with glaucoma, compared to 47 normally sighted controls, in both divided and selective tasks. While the glaucoma group were more likely to report previous falls than controls, the association between AFV performance and previous falls was not examined.

7.5 Glaucoma and falls

There is mixed evidence whether the presence of glaucoma increases falls risk among older adults. It is likely that the increased risk of falling is due to the loss of visual fields given the evidence from the population-based studies described earlier. There is also evidence that other factors may contribute to the risk of falls, including the use of particular topical anti-glaucoma medications. It is important to note that comparison between studies is difficult due to different methods of glaucoma diagnosis (self-report vs. eye examination), lack of glaucoma severity grading, different methods of falls or fracture ascertainment (retrospective vs. prospective) and variations in study cohorts.

Only one study investigated the association between glaucoma and falls in a predominantly glaucoma population (Glynn et al., 1991). This study comprised 489 older adults attending a glaucoma clinic, 70% of whom had a definite diagnosis of glaucoma and the remainder being glaucoma suspects. The findings are limited due to the variety of visual field tests included (Octopus, Humphrey and Goldmann tests) and the non-standardised method to grade visual field severity, as described earlier. Participants with 40% or more loss in visual field were three times more likely to report an injurious fall in the previous year, yet this failed to reach statistical significance.

Significant links between glaucoma and retrospective falls have been shown in population studies. In a study of over 1,900 community-dwelling adults aged over 70, participants with self-reported glaucoma were nearly twice as likely to report a previous fall, even after adjustment in a multivariate model (Dolinis et al., 1997). Ivers et al (1998) reported that glaucoma, confirmed by eye examination, was associated with an increased risk of falls, adjusted for age and gender. In a study of 3,266 adults aged over 40 years, participants with glaucoma (n=21), defined by eye examination, were 4 times more likely to report a fall in the previous 12 months (Lamoureux et al., 2008). Furthermore, a study examining hospital discharge records found that glaucoma was a significant risk factor associated with hospitalisation for an unintentional fall, based on over 15,000 medical records of adults aged 65 and older (Guse & Porinsky, 2003).

A population study by McCarty et al (2002), however, failed to show any significant association between glaucoma, confirmed by eye examination, and falls risk in the previous month. Their findings are limited, however, by the use of falls reported in the previous month, which is a time frame rarely used in falls research.

Findings from case-control falls studies are mixed. Turano et al (1999) reported that the rate of reported falls in the previous year was greater in subjects with glaucoma (18/47 participants; 38%) as compared to controls (14/47 participants; 30%), however the difference was not significant. More recently, Haymes et al (2007) found that the rate of reported falls in the previous year was greater in subjects with glaucoma (35%; 17/48 participants) as compared to age-matched controls (13%; 6/47 participants). Compared to controls, participants with glaucoma were over three times more likely to have had a fall, even after adjustment for age, gender, body mass index, number of systemic medications and better eye visual field loss. It is unclear, however, why the authors controlled for visual field loss in their multivariate analysis, given that visual field loss is likely to mediate the relationship between glaucoma and falls. Moreover, the rate of falling in their control group (mean age 67 years) was relatively low, compared to populations studies which report falls rates in the order of 30% (Tinetti et al., 1988; Graafmans et al., 1996; Freeman et al., 2007).

Two case-control studies have failed to show any relationship between self-reported glaucoma and hip fracture. Grisso et al (1991) examined various medical factors among 174 hip fracture patients aged between 55 and 103, and age-matched controls. Self-reported glaucoma was not a significant risk factor, which may be due to the limitations of self-reported data and unknown numbers in the cohort with glaucoma. A larger case-control study by Ivers et al (2000) examined 911 cases of hip fracture, with 910 age and sex-matched controls. Self-reported glaucoma was not significantly associated with hip fractures in this study. However, the results from Ivers' study are inconsistent, as the hip fracture group had a significantly lower prevalence of cataracts than the control group, which contradicts recent prospective research showing an increased risk of hip fracture among adults with cataracts (Harwood et al., 2005). These inconsistent findings may be due to limitations of retrospective case-control studies.

Research from prospective hip fractures studies are also conflicting. A two year prospective hip fracture study by Ivers et al (2003) found that glaucoma, confirmed by eye examination, was a significant risk factor for hip fractures in people aged 75 and older (hazard ratio 8.1). Felson et al (1989) reported that 18 per cent of hip fractures were attributable to visual impairment, yet failed to find significant associations with common eye diseases, including glaucoma. This may be due to the small number of glaucoma participants in their study, as approximately 1 per cent of their cohort were classified as having glaucoma which is considerable lower than the reported population prevalence rates (Weih et al., 2001).

In summary, it is difficult to draw conclusions from these studies, particularly due to limitations in the retrospective and case-control studies. Furthermore, there is a lack of data on the prospective falls among older adults with glaucoma. Importantly, glaucoma patients present with a wide spectrum of visual impairment, and many of studies have failed to consider the binocular functional impact of glaucoma in their analyses. Despite the limited prospective research, older adults with glaucomatous visual field loss are likely to have a greater propensity for falling, given that glaucoma is the primary cause of visual field loss (Ramrattan et al., 2001) and there is compelling evidence that visual field loss increases risk of falls in population studies (Coleman et al., 2007; Freeman et al., 2007).

7.6 Glaucoma medications and falls

The use of topical anti-glaucoma medications, particularly beta-blockers, has been linked to an increased likelihood of falls in retrospective studies (Glynn et al., 1991; Ivers et al., 1998), although prospective studies are yet to confirm this association. The systemic absorption of topical eye medications and the chronic nature of glaucoma results in significant systemic exposure to these active ingredients (Labetoulle et al., 2005). Topical beta-blockers absorbed systemically act on the beta receptors located in the heart and bronchial tissue, and may lead to side effects such as bradycardia, bronchospasm and lethargy (Gandolfi et al., 2005; Nieminen et al., 2005; Tattersall et al., 2006),

Glynn et al (1991) examined factors associated with injurious falls reported in the previous year among 489 patients attending a glaucoma clinic, 70% of whom were being treated for glaucoma. Compared to participants not using any topical medications (n=120), those using non-miotic glaucoma medications (n=181, 90% of which were beta-blockers) were over 5 times more likely to report a previous injurious fall, while those using glaucoma medications including miotics (n=188) were over 3 times more likely to report a previous injurious fall. Similarly, Ivers et al (1998) examined factors associated with multiple falls reported in the previous year among community dwelling 3,299 older adults aged over 49 years. Compared to participants not using any non-miotic medications (n=3,138), those using non-miotic medications (n=52, 94% of which were beta-blockers) were twice as likely to report multiple falls in the previous year.

There are, however, some important limitations to these two studies. The risk estimates were referenced against participants who were not using any topical glaucoma medications, and as such, were less likely to suffer glaucoma or have visual field loss. Their analyses failed to consider this possible confounding effect. Furthermore, the findings from Ivers et al (1998) were based on a small sample of patients using non-miotic medications (n=52).

More recent research casts doubt on the link between topical beta-blocker use and falls. Ramdas et al (2009) examined the association between long-term use of topical beta-blockers and previous falls among 148 older adults with glaucoma (mean age 73.7 years, range 61–91). The proportion of participants using a topical beta-blocker was around 57%, while the remainder were using topical prostaglandins. In comparison to those only using prostaglandins, the odds of reporting a previous fall was not significantly higher in those using topical beta-blockers, even with adjustment for age, gender and other falls risk systemic medications. In addition, beta-blocker use was not associated with an increased risk of dizziness or orthostatic hypotension compared to prostaglandin use.

Similarly, Turano et al (1999) found no relationship between the use of topical beta-blockers and previously reported falls among 47 glaucoma patients. Of the 18 (38%) participants reporting a previous fall, only 7 (39%) were using a topical beta-blockers. Furthermore, the use of oral beta-blockers, used to treat conditions such as hypertension and angina, has not been linked to falls in previous studies (Cumming et al., 1991; Leipzig et al., 1999; Lee et al., 2006). Until there are definitive studies assessing the risk associated with prospective falls or fractures among those using topical beta-blockers, it is unlikely that the current debate in this area will be resolved.

7.7 Mediating factors between visual field loss and falls

Understanding the factors that may influence the relationship between visual field loss and falls may help guide the development of effective falls prevention interventions. From an epidemiological standpoint, mediating factors are associated with the explanatory factors (such as visual field loss), and the outcome measures (such as falls), but also lie on the causal pathway between the two. There are likely to be many mediating factors between visual field loss and falls, the most important of which would be the impaired ability to avoid obstacles and trip hazards, increasing the risk of trips and falls.

Another possible mediating factor is postural stability. Visual loss has been associated with greater postural instability in our research (Study 1c) and others (Freeman et al., 2008a), and postural instability is a risk factor for falling (Freeman et al., 2007). However, this has not been explored in any previous research studies, and it remains unclear if postural stability mediates the relationship between visual field loss and falls. Interventions targeted towards improving postural stability among older adults may be beneficial in preventing falls in this population.

Frailty and physical function may also be factors in the causal link between visual field loss and falls, yet these also remain unexplored. It is plausible that visual impairment reduces physical function and increases frailty over time, although there is only cross-sectional evidence in the literature (Klein et al., 2003a; Klein et al., 2006). Given that frailty is a risk for falls and fractures (Ensrud et al., 2007), it is possible that physical function or frailty may be a mediating factor between visual field loss and falls. Interventions targeted towards improving the functional status among older adults may also assist in the prevention of falls in this population.

7.8 Rationale for the study

Although several studies have examined the relationship between visual field loss and prospective falls and fractures in population studies (Ramrattan et al., 2001; Coleman et al., 2007; Freeman et al., 2007; Coleman et al., 2009), we are not aware of any previous study that has assessed this association in a cohort of older adults with glaucoma. The evidence regarding the association between glaucoma and falls is inconsistent, and is based on findings from retrospective falls studies which have considerable limitations. Questions still remain as to whether the link between visual field loss and falls is consistent among specific eye disease populations, as the underlying mechanisms responsible for falling may differ.

In addition, little is known about the effect of the location of field loss on falls among older adults with glaucoma. Research also indicates that some glaucoma treatments may increase the risk of falling, particularly topical beta-blocker use, although there is no evidence to support this in any prospective falls studies.

This research extends on previous research, and addresses some of the shortfalls in the previous literature. Careful consideration was given to monitoring falls prospectively and incorporating standardised visual function. Furthermore, a number of additional factors, such as location of visual field loss and glaucoma medication use, were examined to evaluate their association with falls among older adults with glaucoma.

7.9 Aims and hypotheses

Using a cohort of community-dwelling older adults with glaucoma (n=71), the aim of the research was to examine the association between severity and location of visual field loss and prospective falls, collected during a 12-month follow-up.

The hypotheses of the research (expressed as alternate hypotheses) described in this chapter are that:

- Greater visual field loss is associated with a higher rate of falls;
- Greater visual field loss in the inferior field region is associated with a higher rate of falls;
- The use of topical beta-blocker medications is associated with a higher rate of falls.

7.10 Additional methods

7.10.1 Falls outcome measures

7.10.1.1 *Definition of a fall*

There is no standard definition of a fall (Hauer et al., 2006). The World Health Organization defines a fall as "an event which results in a person coming to rest inadvertently on the ground or floor or other lower level" (World Health Organization). Many studies expand on this definition to exclude falls caused by intrinsic events such as a stroke or syncope, or by external forces, such as being pushed over by a person or object (Kellog International Work Group, 1987; Lamb et al., 2005; Lord et al., 2005). The present study defined a fall based on the latter definition, being an event which results in a person coming to rest inadvertently on the ground or other lower level and other than a consequence of the following: sustaining a violent blow, loss of consciousness, sudden onset of paralysis (as in stroke) or epileptic seizure (Kellog International Work Group, 1987; Lamb et al., 2005).

7.10.1.2 *Monthly falls calendars*

Participants were monitored for 12-months following the baseline assessment using monthly falls calendars to determine the number of falls. This method has been used widely in longitudinal fall studies (Lord et al., 2005; Cumming et al., 2007). Fall calendars with daily recording of fall events are considered the gold standard, as recall bias is minimised (Hauer et al., 2006). Recall bias can result in significant under-reporting of falls, given around 13 to 32 per cent of falls are not be recalled by older adults (Cummings et al., 1988).

During the baseline assessment, participants were supplied with a set of 12, monthly falls calendars. An example of a monthly falls calendar is provided in Appendix 10. Participants were provided with clear instructions on how to complete and return the monthly calendars at the end of each month, using the supplied pre-addressed, pre-paid envelopes. The definition of a fall was discussed with participants, and instructions were provided on how to record each day if any falls were experienced. If a fall occurred, participants were asked to provide details of each fall, to ensure that the event met the definition of a fall. Circumstances of each fall was examined and assessed according to location, activity, reported cause and spectacle use at the time of the fall (Berg et al., 1997).

In those instances where the calendars were not returned promptly, participants were contacted by telephone to ascertain the occurrence of any falls for the corresponding month. Two participants reported difficulties completing the calendars due to their visual impairment and telephone interviews were conducted at the end of each month to gather the required information.

7.10.2 Statistical analyses

There are various statistical approaches to analysing count data, particularly for recurrent events such as falls. These approaches take into consideration that falls data are discrete count values which are limited to non-negative integer values and often do not assume a normal distribution. The negative binomial regression approach was selected in the present study as it accounts for recurrent events, and has been recommended and used in previous falls research (Lord et al., 2003a; Lamb et al., 2005; Robertson et al., 2005; Cumming et al., 2007; Gill et al., 2009; Kulmala et al., 2009).

Negative binomial regression is a generalization of the Poisson regression model. These models allow for the outcome measure to show significant overdispersion, where the variance is greater than the mean, and can account for the large number of zero falls recorded (Byers et al., 2003). Overdispersion was evident in the falls data collected in the present study (mean of 1.02 and a variance of 3.66).

Negative binomial modelling has reported advantages over the logistic regression models (Robertson et al., 2005), as it avoids the arbitrary dichotomization of the falls outcome and maintains the original continuous response which models the probability of falling based on the total number of falls during the follow-up. Although the power of the logistic regression models was likely to be low in this small sample size, analyses were performed using any falls (one or more fall versus none) and multiple falls (two or more falls versus one fall or none) outcomes. The findings are presented in Appendix 11, but are not discussed in this thesis.

7.10.2.1 *Regression models*

Generalized linear models with a log link and negative-binomial likelihood function were used to examine the bivariate association between the vision variables and the number of falls reported during the 12-month follow-up. Additional analyses adjusted for age and gender. From these models, incident rate ratios (IRRs) were obtained by exponentiation of the estimated regression coefficients (exp(beta)) and 95% confidence intervals were calculated. The rate ratios for the continuous vision variables were given per clinically relevant units, or per around 10% increment of the total range, to provide rate ratios that were clinically meaningful. The unit change required to double the IRR was also calculated, and this procedure is outlined in Appendix 12. P-values were not adjusted for multiple comparisons, as discussed in Section 3.7.2.

To examine the independent association between field loss location and falls, the superior and inferior integrated visual field measures, were considered together in a model, adjusting for age and gender. These models were examined separately for the IVF and AFV measures. Multicollinearity in the models was assessed using the collinearity diagnostics in SPSS and R.

Standardised deviance residual plots were examined for any sign of abnormal distribution of deviance residuals together with plots of fitted values. Model fit was assessed by examining the deviance statistics. The ratio of deviance divided by degrees of freedom provides a measure for assessing the adequacy of the model, with ratios close to 1 indicating a good fit (Byers et al., 2003). Plots of the residuals (Pearson and deviance) and leverage were examined to identify outlying or influential cases.

7.10.2.2 *Potential mediating factors*

Postural stability and functional status were considered to be potential mediators in the relationship between visual field loss and falls, given their association with glaucomatous visual field in earlier studies in this thesis. Study 1b found associations between visual field loss and functional status in this cohort, and poorer functional status has been linked with a greater likelihood of falling (Ensrud et al., 2007). Similarly, Study 1c reported associations between visual field loss and postural sway, and greater postural instability has been shown to increase the likelihood of falling (Campbell et al., 1989; Maki et al., 1994; Freeman et al., 2007).

The mediating effect of postural stability and functional status was examined separately, by including these factors together with IVF measures in the regression models. For a factor to be considered to play a mediating role, it should be significantly related to both visual field loss and falls, and its inclusion into a model should lower the strength of the association between visual field loss and falls (Baron & Kenny, 1986).

7.11 Results

7.11.1 Description of study cohort

Of the 74 participants enrolled at baseline, 71 participants completed the 12 months falls calendars. One participant died and 2 withdrew before completing all 12 months of follow-up. The group of 34 (48%) women and 37 (52%) men, for whom prospective falls data were collected, had a mean age of 73.9 ± 5.7 years (age range 62 to 90 years). There was little difference in age according to gender (female 73.7 years versus males 74.1 years, t=-0.26, p=0.79).

The baseline visual characteristics of the cohort who completed the falls calendars (n=71) are presented in Table 7-1. Several visual function measures contain missing data. This was due to some participants being unable to perform the tests (motion sensitivity), time limitations (AFV measures), poor quality scans (RNFL) and limited equipment availability (RNFL).

The cohort comprised a heterogeneous group regarding severity of glaucoma. The mean binocular visual field loss ranged was -4.21dB (range 1.59dB to -28.23dB) on the IVF-60, and 32 points missed (range 6 to 96 points) on the IVF-120. The treatment of glaucoma in all but one participant was by means of topical anti-glaucoma medications. Of these, 26 (37%) were using two or more topical preparations (ranging from 1 to 3 medications) and 21 (30%) were using a topical beta-blocker medication. In terms of the self-rated general health of the participants, 30 (39.4%) reported very good or excellent health, 35 (49.3%) reported good health and 8 (11.3%) reported poor health (data not shown). Twenty-four participants (33.8%) reported a fall in the previous year at baseline, and 16 (22.5%) reported fear of falling (data not shown).

Table 7-1: Baseline visual function characteristics of participants completing the 12-month falls follow up (n=71)

			Better-eye measures		Worse-eye measures		Binocular measures	
		N	**Mean ± SD**	**Range**	**Mean ± SD**	**Range**	**Mean ± SD**	**Range**
Visual Acuity (logMAR)		71	0.06 ± 0.13	(-0.26 to 0.52)	0.2 ± 0.25	(-0.10 to 1.40)		
Contrast Sensitivity (logCS)		71	1.54 ± 0.18	(0.65 to 1.70)	1.45 ± 0.26	(0.25 to 1.70)		
Stereoacuity ,n (%)	present	59					59	(83.1%)
	absent	12					12	(16.9%)
Motion Sensitivity (log deg/sec)		68					-1.38 ± 0.24	(-1.87 to -0.80)
Visual Field Sensitivity (dB)		71	-4.41 ± 6.49	(-28.01 to 1.29)	-8.75 ± 8.64	(-31.99 to 0.81)		
RNFL (um)		55	84.01 ± 19.36	(42.33 to 128)	73.28 ± 18.65	(38.92 to 116.17)		
IVF-60 (dB)	overall field	71					-4.21 ± 6.38	(-28.23 to 1.59)
	inferior field	71					-3.61 ± 6.38	(-28.36 to 2.75)
	superior field	71					-4.8 ± 7.13	(-28.96 to 3.25)
IVF-120 (points missed)	overall field	71					32.13 ± 21.54	(6 to 96)
	inferior field	71					15.31 ± 11.14	(1 to 50)
	superior field	71					16.82 ± 11.84	(2 to 46)
AVF_{DIV} (points missed)	overall field	58					7.4 ± 5.56	(0 to 24)
	inferior field	58					2.76 ± 2.5	(0 to 9)
	superior field	58					3.28 ± 2.52	(0 to 9)
AVF_{SEL} (points missed)	overall field	58					14.19 ± 4.84	(3 to 24)
	inferior field	58					6.4 ± 1.8	(2 to 9)
	superior field	58					5.03 ± 2.42	(0 to 9)

Notes: RNFL = Retinal Nerve Fibre Layer; IVF = Integrated Visual Field; AFV_{DIV} = Divided Attentional Visual Field; AFV_{SEL} = Selective Attentional Visual Field

7.11.2 Reported falls

During the 12 month follow-up, 31 (43.7%) participants reported one or more falls, with a total of 75 falls reported. Of the 31 participants, 17 (23.9%) fell only once while 14 (19.7%) fell two or more times (up to a maximum of 9 falls). Approximately 47% of falls (35 of 75 falls) resulted in some form of soft tissue injury, primarily bruises, abrasions, and sprains of the upper and lower limb. No serious falls-related injuries, such as any fractures or head injuries, were reported. Three participants reported more than five falls during 12 month follow-up. These participants were included in the analysis, as two of these suffered from advanced bilateral glaucoma.

Specific details on the reported falls are presented in Figure 7-1 to Figure 7-5. Most falls occurred around the home, either indoors (35.5%) or outdoors (28.9%), and mostly between 6 am and midday (60.5%). The most common activity in which fallers were engaged at the time of a fall was walking on a level surface (52.6%), following by walking involving stairs or steps (26.3%). The most commonly reported type of fall was a trip (47.4%), followed by misplaced step (18.4%), slip (15.8%) and loss of balance (14.5%).

Most falls occurred when wearing no spectacle correction (47.4%; 35 of 75 falls). When falls involving participants who did not use any distance correction are excluded (6 falls), around 42% (29 of 69) of the remaining falls occurred when participants did not wear their habitual spectacle correction. The remainder of the falls occurred when wearing either a multifocal correction (bifocal and progressive lenses, 44.7% and 6.6%, respectively) or single vision distance correction (1.3%).

Of the 31 participants who experienced at least one fall during the study:

- 55% (17 out of 31) experienced each fall when wearing their habitual correction (including those who did not use any distance correction);
- 19% (6 out of 31) experienced falls both with and without their habitual correction; and

- 26% (8 out of 31) experienced each fall when not wearing their habitual correction.

Regular use of any multifocal spectacle correction (bifocal and progressive lenses) was associated with an increased rate of falls, adjusted for age and gender, but did not reach statistical significance (IRR 1.814 [0.824-3.995], p=0.14).

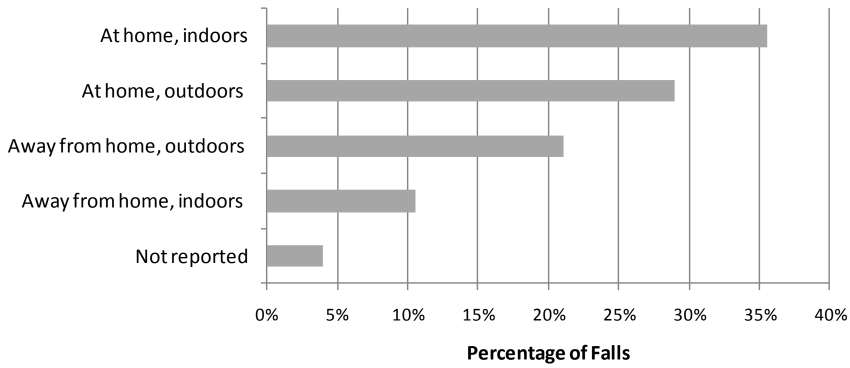

Figure 7-1: Location of falls

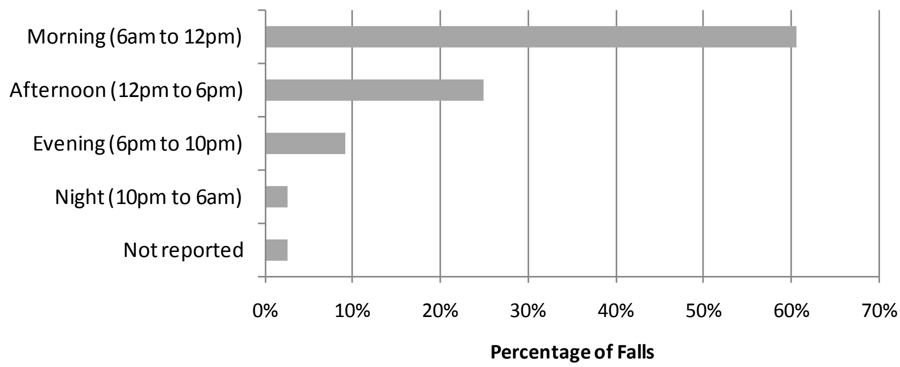

Figure 7-2: Time of day at which falls occurred

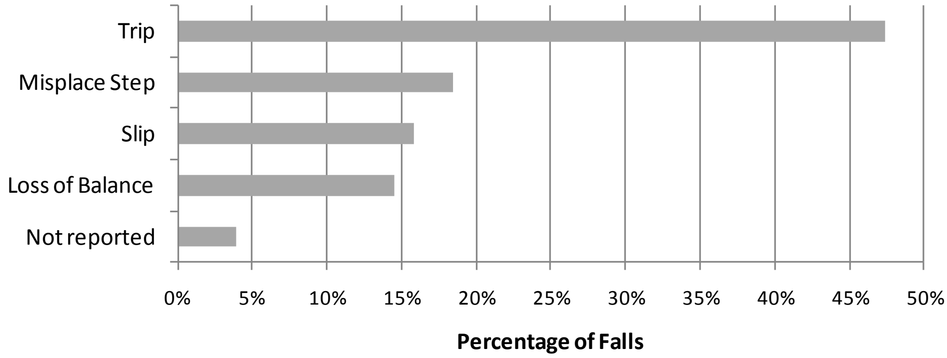

Figure 7-3: Type of falls

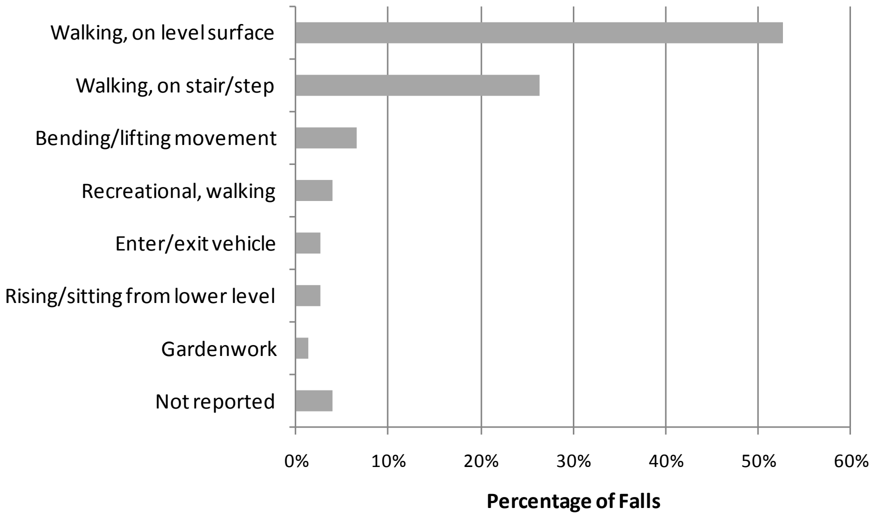

Figure 7-4: Activities in which fallers were engaged at the time of a fall

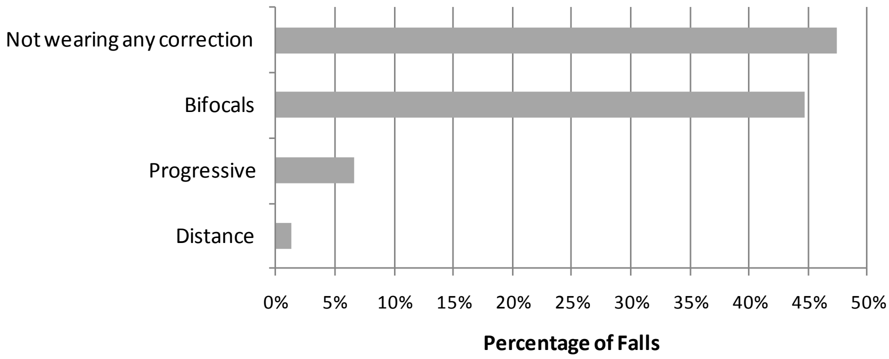

Figure 7-5: Type of spectacle correction worn at time of a fall

7.11.3 Relationship between falls and severity of visual field loss

The visual factors associated with falls are presented in Table 7-2. Of the central vision measures, reduced visual acuity and contrast sensitivity, particularly in the better-eye, was associated with an increased rate of falls. Visual field loss was associated with an increased rate of falls, particularly in the better-eye 24-2, IVF-60 and IVF-120. Similar levels of association with falls were noted between the 24-2 better-eye and IVF-60. Inferior visual field loss, in both the IVF-60 and IVF-120, were more strongly associated with falls compared to superior visual field loss or overall visual field loss.

In the regression models, adjusting for age and gender, each 5 dB reduction in IVF-60 sensitivity increased the rate of falling by around 47% (IRR 1.47 [1.16 - 1.87]), while 10 points missed on the IVF-120 increases the rate of falling by around 25% (IRR 1.25 [1.08-1.44]). The rate of falling was estimated to double for around a 10dB reduction in IVF-60 sensitivity and 30 points missed on the IVF-120.

Poor AVF performance was associated with increased risk of falling, although the levels of association with falls were similar between the divided and selective tasks. Falls were more strongly associated with performance in the inferior field in both tasks, as compared to the superior and total field. Retinal nerve fibre layer thickness, depth perception and motion sensitivity were not associated with falls.

Table 7-2: Association between visual function measures and falls using negative binomial regression models†

	Rate Ratio (95%CI)					
Variable	**Unadjusted**			**Age and gender adjusted**		
Visual Acuity, per line missed						
better-eye	**1.30**	**(1.06 - 1.59)**	*	**1.32**	**(1.07 - 1.64)**	**
worse-eye	**1.14**	**(1.03 - 1.26)**	*	**1.15**	**(1.03 - 1.28)**	*
Contrast Sensitivity, per triplet missed						
better-eye	**1.09**	**(1.02 - 1.17)**	**	**1.11**	**(1.03 - 1.20)**	**
worse-eye	**1.06**	**(1.01 - 1.12)**	*	**1.08**	**(1.02 - 1.13)**	**
Stereoacuity (reference: present)	2.12	(0.96 - 4.71)		2.32	(0.94 - 5.73)	
Motion sensitivity, per SD reduction	0.86	(0.58 - 1.25)		0.81	(0.54 - 1.23)	
24-2 Mean deviation, per 5dB reduction						
better-eye	**1.36**	**(1.10 - 1.67)**	**	**1.48**	**(1.17 - 1.88)**	**
worse-eye	**1.22**	**(1.04 - 1.44)**	*	**1.31**	**(1.08 - 1.59)**	**
RNFL, per 10µm reduction						
better-eye	1.10	(0.92 - 1.31)		1.12	(0.92 - 1.35)	
worse-eye	1.18	(0.96 - 1.45)		1.20	(0.96 - 1.51)	
IVF-60 , per 5dB reduction						
overall field	**1.35**	**(1.09 - 1.67)**	**	**1.47**	**(1.16 - 1.87)**	**
inferior field	**1.44**	**(1.16 - 1.79)**	**	**1.56**	**(1.22 - 1.99)**	**
superior field	**1.22**	**(1.01 - 1.48)**	*	**1.32**	**(1.06 - 1.65)**	*
IVF-120, per 10 points missed						
overall field	**1.21**	**(1.06 - 1.38)**	**	**1.25**	**(1.08 - 1.44)**	**
inferior field	**1.55**	**(1.20 - 2.00)**	**	**1.62**	**(1.23 - 2.14)**	**
superior field	**1.31**	**(1.02 - 1.67)**	*	**1.39**	**(1.06 - 1.81)**	*
VFQ-25 Composite, per transformed unit reduction	**1.64**	**(1.12 - 2.41)**	*	**1.69**	**(1.12 - 2.56)**	*
AVF_{DIV}, per point missed						
overall field	**1.11**	**(1.05 - 1.17)**	**	**1.15**	**(1.08 - 1.24)**	**
inferior field	**1.23**	**(1.08 - 1.40)**	**	**1.33**	**(1.14 - 1.56)**	**
superior field	**1.23**	**(1.08 - 1.40)**	**	**1.31**	**(1.13 - 1.53)**	**
AVF_{SEL}, per point missed						
overall field	**1.13**	**(1.05 - 1.22)**	**	**1.15**	**(1.06 - 1.25)**	**
inferior field	**1.36**	**(1.10 - 1.68)**	**	**1.38**	**(1.09 - 1.75)**	**
superior field	**1.16**	**(1.00 - 1.33)**	*	**1.19**	**(1.02 - 1.38)**	*

Notes: Bold values indicate significance; * $p<0.05$; ** $p<0.01$; † n=71, with the exception of RNFL (n=55), VFQ-25 (n=70) and AVF (n=58); RNFL = Retinal Nerve Fibre Layer; IVF = Integrated Visual Field; AFV_{DIV} = Divided Attentional Visual Field; AFV_{SEL} = Selective Attentional Visual Field

7.11.4 Relationship between falls and location of visual field loss

The results from the regression models are presented in Table 7-3. When both the IVF-60 superior and inferior fields were considered together in a model (Model 2), only the inferior fields remained statistically significant, whereas the superior field estimates fell short of statistical significance. Similarly, when both the IVF-120 superior and inferior fields were considered together in a model (Model 4), the inferior field was significantly associated with falling, whereas the superior field estimate fell short of statistical significance. Compared to their respective overall field models, the inferior field measures in both the IVF-60 and IVF-120 were stronger predictor of falls. It can be estimated that the rate of falling doubles for around a 5dB reduction in inferior field IVF-60 sensitivity (Model 2, IRR 2.20 [1.33 - 3.64]) and 10 points missed on the inferior IVF-120 (Model 4, IRR 2.04 [1.22-3.42]).

Similar findings were found according to the AFV measures. When both the inferior and superior AVF measures were considered together in a model (Models 6 and 8), the inferior field measures remained significantly associated with the rate of falls, while the superior field fell short of statistical significance.

The largest VIF in these models was 5.03, suggesting some variance inflation in the models. While the results should be interpreted with some care, none of the VIF is greater than 10. To corroborate these findings, an alternate approach using factor analysis was examined, and is presented in Appendix 7.

Table 7-3: Association between visual field factors and falls (negative binomial regression models, adjusted for age and gender) †

Model	Variables	Rate Ratio (95% CI)			VIF
1	IVF-60, overall field (per 5dB reduction)	**1.47**	**(1.16 - 1.87)**	**	
2	IVF-60 inferior field (per 5dB reduction)	**2.20**	**(1.33 - 3.64)**	**	4.97
	IVF-60 superior field (per 5dB reduction)	0.68	(0.42 - 1.09)		5.03
3	IVF-120, overall field (per 10 points missed)	**1.25**	**(1.08 - 1.44)**	**	
4	IVF-120, inferior field (per 10 points missed)	**2.04**	**(1.22 - 3.42)**	**	3.40
	IVF-120, superior field (per 10 points missed)	0.75	(0.44 - 1.28)		3.51
5	AVF_{DIV}, overall field (per point missed)	**1.15**	**(1.08 - 1.24)**	**	
6	AVF_{DIV}, inferior field (per point missed)	**1.22**	**(1.02 - 1.46)**	*	1.70
	AVF_{DIV}, superior field (per point missed)	1.19	(1.00 - 1.41)		1.57
7	AVF_{SEL}, overall field (per point missed)	**1.15**	**(1.06 - 1.25)**	**	
8	AVF_{SEL}, inferior field (per point missed)	**1.30**	**(1.00 - 1.68)**	*	1.23
	AVF_{SEL}, superior field (per point missed)	1.10	(0.92 - 1.30)		1.23

Notes: Bold values indicate significance; * p<0.05; ** p<0.01; † n=71, with the exception of AVF (n=58); CI = Confidence Interval; VIF = Variance Inflation Factor; IVF = Integrated Visual Field; AFV_{DIV} = Divided Attentional Visual Field; AFV_{SEL} = Selective Attentional Visual Field

7.11.5 Mediating factors

The findings from the mediation models are presented in Table 7-4. When postural sway with eyes open on the foam was included in these models, the association between visual field loss and falls was reduced, by around 8.6 to 12.3%, and was no longer significant. The reduction in rate ratio in the IVF-60 (IRR 1.47 to 1.29) and IVF-120 (IRR 1.25 to 1.14) suggest that postural stability may partially mediate the causal pathway between visual impairment and falls. Adjusting for functional status resulted in a slight attenuation in the association between visual field loss and falls (around 6.2 to 9.6%), but the magnitude of reduction was lower than the models adjusting for postural stability.

Table 7-4: Association between visual field factors and falls (negative binomial regression models, adjusted for potential mediating factors, age and gender; n=71)

	Rate Ratio (95% CI)		
Variables in Model	**Separate Models**	**Combined Models**	**Change in Estimate (%)**
IVF-60, overall field (per dB reduction)	**1.47 (1.16 - 1.87) ****	1.29 (0.96 - 1.73)	-12.34%
Sway on foam surface, eyes open (per unit reduction)	**5.33 (1.88 - 15.07) ****	2.68 (0.74 - 9.70)	
IVF-120, overall field (per 10 points missed)	**1.25 (1.08 - 1.44) ****	1.14 (0.95 - 1.37)	-8.64%
Sway on foam surface, eyes open (per unit reduction)	**5.33 (1.88 - 15.07) ****	2.93 (0.79 - 10.84)	
IVF-60, overall field (per dB reduction)	**1.47 (1.16 - 1.87) ****	**1.33 (1.02 - 1.73) ***	-9.61%
Overall functional status (per 1SD decline)	**2.34 (1.36 - 4.02) ****	1.80 (0.99 - 3.28)	
IVF-120, overall field (per 10 points missed)	**1.25 (1.08 - 1.44) ****	**1.17 (1.00 - 1.37) ***	-6.24%
Overall functional status (per 1SD decline)	**2.34 (1.36 - 4.02) ****	**1.87 (1.03 - 3.38) ***	

Notes: Bold values indicate significance; * p<0.05; ** p<0.01; IVF = Integrated Visual Field; CI = Confidence Interval

7.12 Discussion

7.12.1 Severity of visual field loss and falls

This study of community-dwelling older adults with glaucoma demonstrated that greater visual impairment, particularly binocular visual field loss, was associated with an increased risk of prospective falls. This finding is consistent with previous research among population-based cohorts (Coleman et al., 2007; Freeman et al., 2007), and suggests that the reduction in mobility arising from glaucomatous visual field loss (Turano et al., 1999; Turano et al., 2004; Friedman et al., 2007) increases the risk of falls in this population. To our knowledge, this study is the first to report a significant link between visual field loss and prospective falls exclusively among older adults with glaucoma.

The rate of falls among older adults with glaucoma is not well known. The prospective monitoring of falls in the present study provided a detailed description of falls in this population, where around 44% of participants reported one or more falls and around 20% reported two or more falls during the 12-month follow-up. The overall rate of falls is consistent with previous studies, although it is difficult to make direct comparisons to previous studies because of the variations in cohorts, falls outcomes and study designs. Prospective community-based studies have reported annual falls rates in the order of 30% (Freeman et al., 2007), and annual rates of multiple falls in the order of 16% (Coleman et al., 2007). Around 35% to 38% of participants with glaucoma reported one or more falls in the previous year in retrospective case-control studies (Haymes et al., 1996; Turano et al., 1999), while around 10% of participants attending a glaucoma clinic, of whom 70% were being treated for glaucoma, reported a previous injurious fall which required medical attention (Glynn et al., 1991).

Several studies have reported significant associations between visual field loss and prospective falls risk (Coleman et al., 2007; Freeman et al., 2007), which is consistent with our findings. Comparisons to these previous studies are made difficult, however, due to differences in the visual field assessments, fall outcomes, statistical analyses and study populations. Freeman (2007) reported that every 10 point loss of binocular visual field (identical to the IVF-120 in the present study) increased the risk of falling by 8% (odds ratio 1.08), after adjustment for potential confounding factors in their population-based study. Coleman et al (2007) found that the risk of falling among older women was 50% greater (odds ratio 1.50) in those with severe visual field loss, defined as 20 or more points missed in a binocular visual field from a 76-point field screening strategy, compared with those with no visual field loss. In the present study, every 10 points missed on IVF-120 increased the rate of falls by 25%, while every five dB reduction in IVF-60 sensitivity increased the rate of falls by 47%.

The present study, however, was unable to examine the contribution of visual field loss on falls, independent of the central vision measures. This is due to the cohort being a single disease group where the peripheral and central visual function measures were strongly inter-correlated. This was anticipated a priori, as increasing severity of glaucoma affects both peripheral and central visual function. As such, visual acuity and contrast sensitivity were also identified as significant predictors of falls, and we cannot rule out that these factors may have a substantial influence on falls in this cohort. There is, however, compelling evidence that visual field loss is a stronger predictor of falls, more so than visual acuity and contrast sensitivity loss (Coleman et al., 2007; Freeman et al., 2007). These studies were able to examine the independent associations between a number of visual functions and falls, due to their heterogeneous cohorts and large sample sizes.

An important point of difference was the use of threshold visual field measures in the present study, used widely to detect and monitor the progression of glaucoma, compared to the screening visual field measures used in previous studies (Coleman et al., 2007; Freeman et al., 2007). Our analyses found that every five dB loss in binocular IVF-60 sensitivity or monocular 24-2 sensitivity in the better-eye increased the rate of falling by around 47%. Our findings provide clinically meaningful estimates for risk of falls, and enable eye-care practitioners to better understand and interpret the falls risk of patients based on the assessment of visual fields routinely performed in clinical practice.

In the present study, monocular 24-2 better-eye measures were shown to be equally good predictors of falls compared to the binocular IVF-60, given their similar strengths of association (rate ratios 1.48 and 1.47, respectively). Although our findings do not indicate that the binocular field measures are better predictors of falls than monocular field measures, analysing the independent contributions of the superior and inferior field areas was facilitated by the use of the integrated field measures, as it provides a more accurate representation of the extent of binocular visual loss (Owen et al., 2008). The integrated binocular field approach has been used widely in mobility and falls research (Turano et al., 2004; Coleman et al., 2007; Freeman et al., 2007; Friedman et al., 2007), and has been shown to be a better predictor of driving crash incidents among older drivers than monocular field loss (Rubin et al., 2007).

Retinal nerve fibre loss was not a significant predictor of falls in the present study, indicating that functional field loss, rather than structural nerve loss, is more strongly related to falls. Motion sensitivity was also not a significant predictor of falls, although reductions in motion sensitivity has been linked to impaired balance control in population studies (Freeman et al., 2008a). It is possible that our findings are limited by the small retinal area assessed in the present study (central 3 degree diameter of visual field), and thus requires further investigation.

Impaired depth perception has been linked to an increased risk of falls or fractures in some studies (Nevitt et al., 1989; Ivers et al., 2000; Lord & Dayhew, 2001), although our study and other recent population studies do not support this association (Friedman et al., 2002; Klein et al., 2003b; Freeman et al., 2007). However, stereoacuity tests are usually measured at near, and may not necessarily relate to depth perception at distances required for mobility and walking. Impaired depth perception at the critical distances required for walking may increase risk of falls due to impaired obstacle judgement (Lord et al., 2002), but this area of research requires further research using appropriate and well-validated tests.

Our findings indicate that attentional visual field measures may be useful predictors of falls in the absence of any standard visual field measures. In support of this, poor attentional field performance has been associated with poor mobility performance in previous studies (Broman et al., 2004; Owsley & McGwin, 2004; Leat & Lovie-Kitchin, 2008). This finding was expected, given that poor attentional visual fields among visually impaired adults has been shown to be strongly influenced by visual field sensitivity (Leat & Lovie-Kitchin, 2006). To date, there are no other studies that have examined the association between attentional field performance and falls. Additional research is required to establish if attentional visual field measures, independent of visual field sensitivity, is a risk factor for falls among older adults with glaucoma.

Self-reported visual disability, measured using the VFQ-25 composite score, was also a significant predictor of falls. These vision-related QOL measures, which were shown to correlate highly with clinical measures of visual impairment, may assist in identifying high-risk fallers, either in the absence of or in conjunction with clinical vision measures. This finding supports a small retrospective falls study by Kamel et al (2000), which demonstrated that scores on the Activities of Daily Vision Scale were useful in identifying fallers.

An interesting finding in the present study was that 42% of the falls reported during the 12 month follow-up occurred while participants were not wearing their habitual spectacle correction, excluding those who did not use any distance correction. It is possible that visual impairment due to uncorrected refractive blur may have contributed to some of these falls. This could explain why baseline visual function measures which are robust to the effects of refractive blur, such as visual fields and contrast sensitivity, were more strongly associated with falls given the significant rate of uncorrected refractive error at the time of the fall. Conversely, it is also possible that the use of multifocal spectacle corrections may increase the risk of falls among older adults (Lord et al., 2002), possibly even more so than uncorrected refractive error. However, the impact of either uncorrected refractive error or use of multifocal corrections on falls among older adults with visual impairment remains unclear, and is an important area for future research.

The use of topical beta-blockers was not associated with prospective falls in the present study. Our findings are consistent with a recent retrospective falls study which found that older adults with glaucoma using topical beta-blockers were no more likely to report a fall in the previous year than those using topical prostaglandins (Ramdas et al., 2009). In support of these findings, studies have not reported significant links between oral beta-blocker use and falls (Cumming et al., 1991; Leipzig et al., 1999; Lee et al., 2006).

Our findings, however, do not support those of Glynn (1991) and Ivers (1998), who found that individuals using non-miotic medications, mainly topical beta-blockers, were more likely to report previous falls, as compared to those not using any glaucoma medications. Importantly, these studies failed to consider the confounding effect of vision loss in their analyses, given that participants not using any glaucoma medications are less likely to suffer glaucoma or visual field loss. As the use of topical beta-blockers remains widespread, our results indicate that these topical medications pose no additional risk for falls among older adults compared to other topical glaucoma medications.

7.12.2 Location of visual field loss and falls

The inferior field area was shown to be an important predictor of prospective falls in the present study, more so than superior field loss. To our knowledge, this study is the first to demonstrate this important link. Previous work by Coleman et al (2007) suggested that falls may occur more frequently in those with inferior visual field loss from any cause. The study reported that the odds of falling among older women with severe inferior visual field loss, when compared with no inferior loss, were 91% higher, whereas the odds of falling among those with severe superior visual field loss, when compared with no superior visual field loss, were 74% higher. Although the risk of falls appears higher among those with inferior field loss, the study did not statistically assess the independent contributions of these field areas to the risk of falls.

Freeman and colleagues (2007) did examine the independent contributions of field loss location on prospective falls, but neither the superior nor inferior field areas were significant predictors when both were considered together in a model. The same binocular field measure was used as in the present study (IVF-120), although Freeman's study calculated the superior and inferior field scores from 20 degree radius from fixation and beyond. The significant findings found in the present study indicate that the inferior central 20 degree area is an important area for safe navigation.

The role of the inferior visual field is critical when negotiating real-world complex environments, as was demonstrated in this study. When walking, people fixate approximately two steps ahead (Land, 2006), and the inferior visual field contributes a major proportion of visual information used in lower limb movements, foot placement and obstacle detection (Marigold & Patla, 2008). Studies comprising adults with visual impairment also report that greater loss in the central and inferior visual field areas results in reduction mobility performance (Lovie-Kitchin et al. 1990; Turano et al. 2004). Furthermore, studies have demonstrated that visual guidance on foot placement is significantly affected by blur (Buckley et al., 2008) and blurring of the inferior field of vision in multi-focal spectacles (bifocal, trifocal, or progressive) has been implicated in the increased risk of falling when wearing these corrections (Lord et al., 2002). In our study, however, regular use of multifocal spectacles was not significantly associated with increased rate of falls, nor were differences noted in the type of spectacle correction worn at the time of a fall (47% no correction vs. 51% multifocal correction). This is an area of research that would benefit from further research, as the small sample size in the present study limited the extent to which this could be analysed.

Our findings provide important insights into the relative importance of the various visual field areas in falls risk. Future research using larger cohorts is needed to confirm and expand on these findings, so that falls prevention assessments and interventions can target high-risk fallers based on the well-established risk factors. Investigation is also required into the eye movement patterns of adults with inferior visual field impairment when walking, as deficits in scanning patterns may contribute to their risk of falls. These are important areas of future research which may assist in designing effective interventions to minimise the risk of future falls among older adults with visual field loss.

7.12.3 Mediating factors

Postural stability was found to be a significant predictor for falls in the present study, consistent with previous studies (Campbell et al., 1989; Maki et al., 1994; Freeman et al., 2007). Our analyses suggest that postural stability may be a potential mediating factor in the pathway between visual field loss and falls. This finding is plausible, as visual field loss is associated with greater postural instability, which may lead to the inability to maintain equilibrium in instances where obstacle contact may occur, particularly tripping, or during situations of reduced somatosensory input, such as walking on uneven or compliant surfaces.

Reduced functional status was a significant predictor for falls in the present study, consistent with other investigations (Tromp et al., 2001; Moreland et al., 2004; Tiedemann et al., 2008). It was hypothesised that functional status would be a potential mediating factor, as Study 1b found significant associations between visual field loss and physical function measures. Functional status, however, was not a strong mediating factor between visual field loss and falls compared to postural stability.

Future research is needed to better understand the link between visual impairment and frailty, and whether improving functional status among older adults with visual impairment reduces the risk of falling. A study by Campbell (2005) examined whether a strength and balance retraining programme was beneficial in reducing falls among 391 community dwelling adults (aged ≥ 75 years) with visual acuity of 6/24 or worse. However, the exercise programme, which the authors had previously shown to be of benefit among general community dwelling groups, was not successful in this population. The rate of falls was in fact greater in those receiving the exercise programme, although not significantly so. This study indicates that careful consideration is required regarding the promotion of physical activity among visually impaired populations, given that it may be problematic or even harmful.

To our knowledge, no previous studies have examined potential mediating factors between visual field loss and falls. Some caution, however, needs to be placed in interpreting our findings, given the small sample size, the cross-sectional nature of the mediating factors and crude statistical modelling. Further large-scale studies are required to more accurately explore the potential causal pathways between visual field loss and falls using advanced statistical techniques, such as structural equation modelling (Christ et al., 2008; Karpa et al., 2009).

7.12.4 Study strengths and limitations

This study has several strengths, including the extensive assessment of different vision components and the use of binocular integrated visual fields in a well-defined cohort of older adults with glaucoma. In addition, this was a prospective study that measured falls using a method which allowed for daily recording of falls to minimise the risk of recall bias (Hauer et al., 2006).

A considerable limitation, however, is the small sample size. Additional research in a larger cohort is required to refine the estimates of the association between visual field loss and falls. Furthermore, visual function was not reassessed at the end of the study, nor was any data collected on factors which might alter visual function during the follow-up period, such as updating of spectacle correction. It would be useful for future longitudinal studies to examine these factors. However, any potential measurement or misclassification bias which may have occurred as a result of changes in visual function is likely to have affected all groups equally, i.e. a non-differential measurement bias. Hence, the consequence of this type of bias is a weakening of the strength of association towards accepting the null hypothesis.

Chapter 8 provides additional discussion on a number of strengths and limitations pertaining to all of the studies presented in this thesis, as well as important implications arising from the research.

7.13 Conclusion

In conclusion, this investigation adds to the evidence pointing to the increased falls risk with greater visual field loss among older adults. Falls were a common occurrence in this cohort of community-dwelling older adults with glaucoma, as around 44 per cent experienced at least one fall during the 12 month study. Greater visual field loss was associated with a higher rate of falls, particularly among participants with inferior field loss, more so than superior field loss. Postural stability appeared to be a factor which may underlie the relationship between visual field loss and falls. In addition, the use of topical beta-blocker medications was not associated with falls.

This study is the first to report on prospectively measured falls among older adults with glaucoma. Falls have serious consequences, both through immediate effects of injury, as well as longer term effects on disability, fear of falling and loss of independence. The prevention of falls is a vital component to promote and maintain the independence, health and well-being of older adults. The findings of the present study will help guide future research and strategies to reduce the incidence of falls among older adults with glaucoma.

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Chapter 8: Summary and Conclusions

8.1 Overview

The association between visual impairment, disability and falls among older adults has been examined in previous studies. These studies, however, have predominantly involved general populations of older adults, or cohorts of individuals with a range of eye diseases. Furthermore, most of these associations have been based on central visual function loss, and much less is known about the association between peripheral visual function loss and disability and falls. In addition, there are few studies in this area involving older adults with glaucoma, which is the leading cause of peripheral visual field loss in this population (Ramrattan et al., 2001).

Glaucoma is a major cause of irreversible visual impairment worldwide and constitutes increasingly significant global health problem (Quigley & Broman, 2006; Leske, 2007). It is a chronic, progressive eye disease, of which primary open-angle glaucoma is the most common form (Gupta, 2005), affecting around 3 per cent of the Australian population aged 60 years or older (Rochtchina & Mitchell, 2000; Weih et al., 2001). Estimates indicate that the number of adults with glaucoma in the United States will increase by 50 per cent by the year 2020, due to the growth of the ageing population (Friedman et al., 2004). A major concern is that the rate of undiagnosed glaucoma remains high, as around half of those in the community with glaucoma remain undiagnosed (Weih et al., 2001; Friedman et al., 2004).

Glaucoma leads to irreversible loss of peripheral visual function in its early stages, and loss of central visual function loss when the disease is more advanced. Medical and surgical treatments for glaucoma focus on lowering IOP, to slow the progression of the disease (Heijl et al., 2002), although disease progression still occurs in up to 20% of patients (Chen, 2003; Zahari et al., 2006; Musch et al., 2009).

The purpose of this thesis was to examine the association between visual impairment, disability and falls among older adults with glaucoma. The first component (Studies 1a, 1b and 1c) examined the association between glaucoma and health-related QOL, functional status and postural sway among older adults. The second component (Study 2) examined the association between glaucomatous visual impairment and falls, which can lead to further disability due to the physical and psychological consequences of falls. Ultimately, falls among older adults with glaucomatous visual impairment has the potential to significantly impact on health and well-being, increasing the risk of injury and mortality, and placing heavy demands on the healthcare system.

It is unclear, however, whether glaucomatous visual impairment is associated with poorer health-related QOL among older adults. Adults with glaucoma self-report lower health-related QOL compared to visually normal adults, both in population studies (McKean-Cowdin et al., 2008) and clinical studies (Sherwood et al., 1998; Wilson et al., 1998). There is inconsistent evidence though, whether the severity of visual field loss is related to declines in health-related QOL. One population study demonstrated significant correlations between severity of visual field loss, from any cause, and health-related QOL scores (McKean-Cowdin et al., 2007), but the findings were not confirmed in a follow-up study restricted to glaucoma participants (McKean-Cowdin et al., 2008). A number of clinical studies have reported associations between severity of field loss and health-related QOL (Parrish et al., 1997; Iester & Zingirian, 2002), although others have failed to find such assosciations (Wilson et al., 1998; Jampel et al., 2002a; Jampel et al., 2002b; Muir et al., 2008). The wide age range of participants included in these studies limits the generalisability of these findings to older age groups, who are likely to experience greater levels of disability than younger age groups.

Despite the evidence that visual field loss may affect health-related QOL, there is limited research into the association between peripheral vision loss and functional status or frailty among older adults. Central visual impairment has been linked to greater functional declines among older adults, both in cross-sectional (Klein et al., 2003a; Klein et al., 2006) and longitudinal research (Lin et al., 2004). It is unknown whether visual field loss is associated with functional declines among older adults, and this research sought to examine this possible link.

Vision is also an important contributor to postural control among older adults, particularly due to the age-related declines in the somatosensory and vestibular systems (Woollacott, 2000; Choy et al., 2003; Era et al., 2006). While central vision loss has been linked with reduced postural stability among older adults, it is uncertain if postural control is affected by visual field loss. Shabana et al (2005) did not demonstrate differences in postural stability between participants with glaucoma and age-matched controls, nor any association with severity of visual field loss. Shabana's findings were, however, limited by the relatively young cohort, aged 40 to 66 years. It thus remains unclear whether glaucomatous visual field loss affects postural stability in older populations.

Visual impairment is also an important contributor to falls among older adults. Recent studies report that visual field loss is the strongest visual predictor of prospective falls (Coleman et al., 2007; Freeman et al., 2007) and prospective fractures (Coleman et al., 2009) among general population cohorts, more so than central vision loss. This may explain findings from population studies which have reported significant associations between glaucoma and retrospective falls (Dolinis et al., 1997; Lamoureux et al., 2008). To date, however, no previous studies have examined the impact of visual field loss on prospective falls exclusively among older adults with glaucoma. Furthermore, the effect of the location of the field loss on falls has received little attention, which is surprising given the importance that the inferior visual field region has been shown to have in safe and efficient navigation (Lovie-Kitchin et al., 1990; Turano et al., 2004; Marigold & Patla, 2008).

The remainder of this chapter provides a summary of the major findings arising from the thesis, followed by a discussion on the strengths and limitations of the research. The clinical and public health implications of the research are discussed, along with directions for future studies arising from the research.

8.2 Summary of major findings

8.2.1 Studies 1a, 1b, 1c

Is there an association between the severity and location of visual field loss and health-related quality of life among older adults with glaucoma?

In Study 1a, greater severity of binocular visual field loss was significantly associated with lower self-reported health-related QOL in the physical domain, based on the SF-36 survey, even after adjusting for age and gender. These weak but significant findings are consistent with previous population studies (McKean-Cowdin et al., 2007). Greater inferior visual field loss on the IVF-120 was more strongly associated with lower SF-36 physical component scores, independent of superior visual field loss. No significant associations were found between visual field loss and SF-36 mental health component scores, which is in support of previous research (Wilson et al., 2002; Jampel et al., 2007; Skalicky & Goldberg, 2008).

The findings of this study, albeit cross-sectional in nature, suggest that glaucomatous visual field loss may significantly contribute to the reduction in self-reported physical well-being among older adults. Visual field loss may initiate restriction of activity and participation due to mobility difficulties, which in turn may lead to functional limitations and disability which is reflected in the SF-36 scores in the physical domain. Further research, however, is required to confirm this hypothesis in longitudinal studies.

Is there an association between severity and location of visual field loss and functional status among older adults with glaucoma?

Study 1b found significant associations between binocular visual field loss and performance on a number of functional status measures. After adjustment for age and gender, greater binocular visual field loss was associated with lower self-reported levels of physical activity and poorer results on the tests of overall functional status. In linear regression models, greater binocular inferior visual field loss, independent of superior visual field loss, was associated with poorer results on all of the performance-based tests. These findings, based on objective measures of functional status, support those found using self-reported physical function in Study 1a, using the SF-36 survey.

The cross-sectional nature of our study does not permit us to infer whether visual field loss decreases functional status; however, it is likely that visual field loss leads to reductions in functional status rather than the reverse. Visual field loss may initiate restriction of activity and participation due to mobility difficulties, and lead to functional limitations and disability over time. This may also explain the associations between functional status and inferior visual field area, as this region is an important contributor to safe and efficient navigation (Lovie-Kitchin et al., 1990; Marigold & Patla, 2008). This hypothesis, however, requires additional longitudinal research to determine whether it is a true explanation of the findings reported in this thesis.

Is there an association between severity and location of visual field loss and postural sway among older adults with glaucoma?

In Study 1c, greater binocular visual field loss was significantly associated with increased postural sway, both on firm and foam surfaces, independent of age and gender. The findings are in contrast to Shabana et al (2005), who found no association between postural sway and severity of visual field loss. Our findings are likely to be due to the relatively older cohort than Shabana's, since older adults are less likely to compensate for the reduction in visual contribution due to age-related declines in their remaining postural control systems (Woollacott, 2000; Choy et al., 2003; Era et al., 2006).

In linear regression models, inferior visual field was more strongly associated with postural stability, independent of the superior visual field, particularly on the foam condition with eyes open. This supports studies which suggest that the inferior visual field provides a greater contribution to the visual pathway which mediates visually guided movements (Khan & Lawrence, 2005; Krigolson & Heath, 2006).

The visual contribution to postural control was also found to decline steadily with increasing binocular visual loss, in agreement with previous studies (Turano et al., 1993; Shabana et al., 2005), and confirms the important contribution of peripheral visual field to postural sway. Interestingly, RNFL thickness was the strongest predictor of the visual contribution to postural stability, explaining nearly twice that of the binocular visual field measures. This finding may reflect declines in other visual functions which influence postural control, such as motion detection (Kelly et al., 2005), however further research is needed to confirm this relationship.

There are important consequences of impaired postural stability, the most serious of which is an increased falls risk. Insights gained from this research improve our understanding of the association between visual field loss and postural stability among older adults with glaucoma. It also guides further research into developing strategies for improving postural stability in this population with the aim of reducing the risk of future falls.

8.2.2 Study 2

Does severity and location of visual field loss predict falls among older adults with glaucoma?

This longitudinal study comprised of 71 older adults with glaucoma who successfully completed the 12 month follow up (mean age 73.9 years). During this follow-up, 44% reported one or more falls, and around 20% reported two or more falls. Greater binocular visual field loss was found to be a significant predictor of falls, in support of findings from general population studies (Coleman et al., 2007; Freeman et al., 2007). After adjusting for age and gender, every 10 points missed on the IVF-120 increased the rate of falls by 25%, or every 5dB reduction in IVF-60 increased the rate of falls by 47%. It was estimated that the rate of falling doubles for every 10dB reduction in IVF-60 sensitivity or 30 points missed on the IVF-120.

Inferior binocular visual field loss was a significant predictor of falls, more so than superior field loss. It was estimated that the rate of falling doubles for around 5dB reduction in inferior field IVF-60 sensitivity and 10 points missed on the inferior IVF-120. These findings highlight the importance of the inferior visual field area in safe and efficient navigation as shown in previous mobility (Lovie-Kitchin et al., 1990) and experimental studies (Marigold & Patla, 2008).

Do factors, such as postural stability or functional status, mediate in the relationship between visual field loss and falls?

Study 2 also examined the role of postural stability and functional status as potential mediating factors in the relationship between visual field loss and falls. Of these, postural stability appeared to be a stronger mediating factor, as a considerable reduction in the association between visual field loss and falls was shown with its inclusion in the regression models.

This finding is plausible, as visual field loss reduces the visual contribution to postural control and reduces postural stability, leading to a greater propensity for falls during situations where postural stability is challenged. These challenging situations are more likely to occur among adults with visual field loss, due to the increased likelihood of obstacle contact due to mobility difficulties (Turano et al., 2004). These findings, however, are only preliminary, and further research is required to confirm these findings in a larger cohort.

Does the use of topical beta-blockers increase the risk of falls?

Topical beta-blocker use was not significantly associated with an increased rate of falls compared to the use of other topical glaucoma preparations. This study is the first to report such findings based on prospective falls, and supports recent retrospective falls research (Ramdas et al., 2009). Two studies have reported cross-sectional associations between topical beta-blocker use and falls (Glynn et al., 1991; Ivers et al., 1998); however, their findings are limited by the use of retrospective falls and inappropriate control groups.

8.3 Implications for clinical practice

There are several important clinical implications arising from this research, as greater visual field loss, particularly in the inferior visual field region, was significantly associated with poorer health-related quality of life, reduced functional status, greater postural instability and a higher rate of falls. Therefore, older adults with moderate to severe levels of visual field loss, particularly in the inferior visual field regions, should be regarded as a high risk group for falls or further disability.

Greater efforts are needed to increase the awareness of the association between visual field loss, disability and falls among eye care practitioners. Practitioners are in a key position to provide appropriate advice to patients, given their detailed knowledge of their patient's visual status. They are also in a position to provide prompt and appropriate referrals to other health care services, including general practitioners, physiotherapists and occupational therapists, for evaluation and remediation of potential disabilities. Eye-care practitioners are in contact with a considerable proportion of the older population, and it is important that they contribute to the overall management of their patient's health and well-being by being aware of the association between visual field loss and falls.

The findings of this research also provide guidance for practitioners on the impact of visual field loss and falls, based on visual fields which are routinely measured for detection and diagnosis of eye diseases, such as HFA 24-2 monocular fields. Practitioners need to consider their patient's binocular visual fields, which can be derived from standard monocular fields using software such as Progressor (Medisoft Ophthalmology, UK), which is available with current visual field technology. A reduction of approximately 10dB in overall binocular visual field sensitivity (integrated 24-2 fields), or 5dB in inferior binocular visual field sensitivity, was estimated to double the rate of falls. In the absence of integrated binocular visual fields, practitioners may need to rely on their clinical judgement to estimate the extent of binocular visual field loss.

Eye care practitioners should also be mindful when prescribing particular spectacle lens corrections, such as multifocal or bifocal lenses, which blur the inferior field areas required for walking. Multifocals have been reported to increase the risk of falls (Lord et al., 2002), and increase obstacle contact while walking during divided attention tasks (Menant et al., 2009). It is possible that the use of multifocals may be potentially even more harmful when prescribed to patients with inferior binocular visual field loss, by exacerbating the risk of obstacle contacts, trips and falls. This is an area that requires further research, as this was not explored in the present thesis.

Greater efforts are also required to promote and increase awareness of the association between visual field loss and falls among older adults with glaucoma. Education and awareness campaigns should be developed specifically for this population, to draw attention to the association between vision and falls and to promote behavioural change, primarily through reduction in risk-taking behaviours to minimise exposure to high-risk situations. It is hoped that future research will also provide evidence to develop appropriate physical activity and exercise programs for older adults with visual field loss, taking into consideration their visual and balance requirements. Awareness campaigns should also address the poor adherence to prescribed glaucoma medication in this population (Deokule et al., 2004; Nordstrom et al., 2005; Shaw, 2005). Poor adherence has been linked to a range of factors, some of which include low patient education, cost of medications and side effects (Friedman et al., 2008). The preservation of remaining visual function is important, to minimise further disability and risk of falls.

There are also aspects of this research that can inform public health policy. The findings support the need to improve the early detection and treatment of glaucoma, to minimise visual impairment among older adults. Early detection and treatment will minimise the loss of visual function, as well as delay the onset of disability and minimise the likelihood of falls. This is crucial because around half of those in the community with glaucoma remain undiagnosed (Weih et al., 2001; Friedman et al., 2004), and treatment is vital to prevent further vision loss.

Falls programs are an essential public health component in the prevention of falls within the community setting, yet they need to be mindful of the challenges faced by older adults with visual impairment. Research has reported that the promotion of physical activity among visually impaired populations can be problematic and even possibly harmful (Campbell et al., 2005). The research findings from this thesis provide important insights into potential underlying risk factors associated with falls among older adults with glaucoma, such as postural stability. While intervention programs should target these factors, as improvements in these areas are likely to minimise or reduce the rate of falls, further research is required to establish the most effective manner in which to achieve this.

Finally, the findings of the present study and that of other recent studies (Coleman et al., 2007; Freeman et al., 2007; Coleman et al., 2009) highlight the importance of screening for visual field loss as an integral component in fall risk assessments. Visual field loss is a strong risk factor for falls, more so than central vision loss; however, perimetric screening for visual field loss can be difficult for non-eye care practitioners, due to the specialised equipment required and expertise in both administering and interpreting the tests.

Newer visual field technology, such as the Matrix Frequency Doubling Perimeter (Carl Zeiss Meditec, Dublin, CA, USA), provide sensitivity similar to that of standard automated perimetry in the detection of glaucoma (Medeiros et al., 2004) and provide greater usability and portability than older technology. This newer technology will enhance the ability of health care practitioners to screen for visual field loss among older adults, with abnormal findings prompting a more detailed assessment of visual fields with eye-care practitioners. Visual field screening will assist in identifying older adults at high risk of falls and fractures, and improve the detection of visual impairment in older populations. It is also vital that eye-care practitioners contribute to the education and awareness of these issues to other health care providers, to improve the visual and overall health in the older population.

8.4 Overall study strengths and limitations

There are several strengths and limitations that should be considered in relation to the experimental approach of the research described in this thesis.

An important strength was the inclusion of extensive visual function assessment, based on standardised central and peripheral measures of visual function, rather than self-reported assessment. It was also important to include integrated visual field measures into the analyses, to provide an accurate representation of the extent of binocular visual loss. These assessments were carried out by a single investigator, a qualified optometrist, minimising the potential for inter-tester variability. Furthermore, participants' glaucoma was well diagnosed by their treating ophthalmologists, rather than self-reported, and the baseline eye examination screened for any ocular diseases other than glaucoma.

Another important strength was the use of prospective assessment of falls, which is considered the gold-standard, as it reduces the potential risk of recall bias that occurs in retrospective falls data (Cummings et al., 1988; Hauer et al., 2006). The longitudinal design also enabled assessment of possible mediating factors in the pathway between visual field loss and falls, since baseline risk factors were examined prior to the fall events.

The cross-sectional design of the first three studies, however, precludes inferences about causality in the relationship between visual field loss and health-related QOL, functional status and postural stability. Further investigation using a longitudinal design is required to establish whether visual field loss results in further declines in these outcomes.

The study population comprised community-dwelling older volunteers with glaucoma. This means that the results may not be generalisable to other populations, such as those with other eye diseases, poorer health or residing in alternate settings. It is also possible that the underlying mechanisms responsible for these outcomes may vary among different eye disease populations, or among those with co-existing eye disease. Furthermore, these was potential for recruitment bias towards more highly functioning participants, which may have resulted in conservative estimates of the associations between visual field loss and the outcomes. Indeed, as even physically active independent older people were found to experience falls, the association are likely to be even stronger in frailer populations.

A notable limitation in this study was the small sample size in the falls study and an uneven distribution of the severity of visual field loss within the cohort. This was due to a combination of the strict inclusion and exclusion criteria and difficulties in enrolling the intended number of participants within the study period. Despite the relatively small cohort, significant and clinically meaningful findings were demonstrated. However, the small sample limited the extent to which additional aspects in the dataset could be reliably examined, such as whether there was an interaction between multifocal spectacle lens use, visual field loss and rate of falls. In addition, the estimates obtained in the regression models need to be interpreted with caution, owing to the small numbers.

8.5 Recommendations for further research

Based on the findings of this thesis, the following recommendations are suggested for further research to examine the relationship between visual field loss and falls among older adults.

Firstly, the findings from this study need to be validated in a larger sample of older adults with glaucoma before definitive recommendations can be made for clinical practice. Future research should also examine environmental and personal factors which may influence disability and falls among adults with glaucoma, according to the ICF framework (see Figure 1-1), as these factors were not examined in this thesis. For example, the use of multifocal lens correction has been implicated in increasing the risk of falls among older adults (Lord et al., 2002), and it is possible that the risk of falls may be exacerbated by the use of these spectacle corrections among older adults with inferior visual field loss.

The influence of the physical environment contributing to falls among older adults with visual field loss should also be examined, particularly the influence of environmental lighting. The risk of falls is likely to greater under low lighting, particularly due to reduced postural stability and the increased likelihood to tripping. Low lighting has been shown to be associated with reductions in postural stability among older adults (Brooke-Wavell et al., 2002), and its impact among those with visual impairment is likely to be even greater. Low lighting has been shown to reduce obstacle and hazard detection among visually impaired older adults (Kuyk et al., 1996; Kuyk et al., 1998), although there is limited evidence in this area.

Further longitudinal research is also required to provide a clearer picture of the impact of visual field loss on these outcomes over time. Although Studies 1a, 1b and1c reported significant associations between visual field loss and health-related QOL, functional status and postural stability, these relationships are correlative rather than causal. It is likely that longitudinal studies of at least two years duration would be required, given the slow rate of glaucomatous visual field progression among treated adults, estimated around 1 to 2dB per year (Broman et al., 2008).

The specific components of postural sway associated with visual field loss among older adults with glaucoma were not been explored in this research, and requires further investigation. Although Study 1c employed a clinical and validated measure of postural stability, the swaymeter (Lord et al., 1991; Lord et al., 2003b), this device lacks the precision of electronic force plates which can provide outcomes such as path length and sway velocity. Experimental studies have shown that various regions of the visual field regulate different components of postural sway (Nougier et al., 1997; Piponnier et al., 2009). Studies have also reported that simulated visual impairment among older adults affects specific components of postural stability, particularly in the anterior-posterior direction (Anand et al., 2003a).

In order to develop effective falls prevention strategies among older adults with visual field loss, further research is required into the underlying factors which contribute to falls. Possible factors include deficiencies in eye movement control, such as rate and extent of scanning eye movements. This may be an important factor among older adults with inferior visual field loss, as this was a significant predictor of falls in Study 2.

Future research should also examine the impact of visual field loss on gait and stepping patterns among older adults, particularly during challenging situations such as stair negotiation (Startzell et al., 2000). Previous studies have highlighted the importance of vision in the control of stepping accuracy, particularly in studies of simulated blurred vision (Buckley et al., 2005), simulated visual field restriction (Graci et al., 2009) and among those wearing multifocal lenses (Johnson et al., 2007). Additional research is required among older adults with visual field loss, as it remains unclear if unsafe stepping or gait patterns are significant contributing factors in falls.

Even though visual field loss from glaucoma cannot be reversed, there are some potential intervention strategies which may prove useful in reducing the risk of falls in this population. Possible interventions include:

- Strategies to improve eye movement scanning when walking, if shown to be a significant factor in safe mobility.

- Modification of non-vision falls risk factors, such as balance, strength and exercise training to improve lower limb strength, increase postural stability and minimise frailty. This strategy, however, would need to be carefully designed, implemented, and evaluated, as previous studies among older adults with central visual impairment have found that exercise programs may do more harm than good (Campbell et al., 2005).

- Home hazard management to reduce trip hazards. This intervention has been successful among older adults with central visual impairment (Campbell et al., 2005). It is also likely to be effective among older adults with visual field loss, although further research is required to establish this.

- Education and awareness strategies to improve knowledge of visual limitations and promote behavioural change. Adults with glaucoma are often unaware of the extent and location of their visual field loss. Eye care practitioners can play an important role, by communicating this knowledge to patients, and encouraging reductions in risk-taking behaviour, which may help prevent future falls.

8.6 Conclusion

In reference to the ICF framework (Figure 1-1), this research has demonstrated that glaucoma is associated with significant disability among older adults, and is an important predictor of falls, a condition which may lead to further disability.

Based on the results of the first component of the thesis, greater visual field loss was associated with greater impairment in body functions, including postural stability, muscle strength and endurance. Greater visual field loss was also associated with increasing functional limitation and restriction, including functional mobility, self-reported physical function and physical activity levels. Moreover, visual field loss in the inferior field area was more strongly associated with these outcomes than superior visual field loss. Although the nature of this cross-sectional research cannot verify the causal processes which underlie these disabilities, a possible pathway could be hypothesised. Greater visual field loss may lead to activity restriction due to increasing mobility difficulties and postural instability, which may result in subsequent physical de-conditioning and functional limitations. Additional research is needed to better understand this complex process.

The findings from the second component of the thesis showed that fall events were common in this population, as 44% of participants reported at least one fall during the 12 month follow-up. Greater binocular visual field loss was found to be a significant predictor of falls. Importantly, inferior visual field loss was a significant predictor of falls, more so than superior visual field loss, which highlights the important contribution of this visual field area to safe and efficient navigation in the real-world environment. Postural instability was identified as a possible factor in the causal pathway between visual field loss and falls. Prevention of falls is vital to avert further physical and psychological disability among older adults, particularly among those with visual impairment.

The clinical implications of this research include the need to raise awareness of these findings to eye care practitioners and adults with glaucoma and to include visual field screening in falls risk assessments among older adults. The findings also highlight the vital need to improve early identification and treatment of glaucoma among older adults, to prevent vision loss and the onset of disability and falls.

Glaucoma is responsible for a significant proportion of visual impairment among older adults, and will become even more prevalent with the ageing of the population. The onset of disability and occurrence of falls pose a serious threat to the health, quality of life and independence of this population, increasing the burden on the healthcare system. The research described in this thesis provides important insights into the association between visual field loss, disability and falls among older adults with glaucoma. Further research, however, is needed to better understand the mechanisms which underlie these relationships. This will provide an evidence base for interventions aimed at preventing declines in the health and well-being of older adults with glaucoma, as well as promote and maintain their quality of life and independence.

Chapter 9: References

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Appendix 1: Telephone screening questionnaire

Prior to invitation to participate in the study, potential participants were screened over the telephone using the following questions to establish suitability for participation in the study.

Are you over 65?	[ ] yes / pass	[ ] no / fail
Are you being treated for glaucoma?	[ ] yes / pass	[ ] no / fail
Do you have any other eye conditions?	[ ] no / pass	[ ] yes / fail
Are you living independently?	[ ] yes / pass	[ ] no / fail
Do you use a walking aid?	[ ] no / pass	[ ] yes / fail
Do you suffer from vestibular conditions that affect your balance?	[ ] no / pass	[ ] yes / fail
Do you suffer from Parkinson's Disease?	[ ] no / pass	[ ] yes / fail

Appendix 2: Socio-demographic, health and medical questionnaire

Name: Last	First	Initial
Address:		
Phone: Home	Mobile	Other
Email:		

What is your date of birth:

What is your gender: [ ] Male [ ] Female

What is your country of birth?

What type of accommodation do you live in?

[ ] House [ ] Unit [ ] Other (please specify):

Who else lives with at home with you?

[ ] Spouse [ ] Alone [ ] Relatives [ ] Other (please specify):

What is the highest level of education you have completed?

[ ] University or College degree
[ ] Trade or technical certificate
[ ] Secondary High School
[ ] Primary School
[ ] Other. Please specify:

Which of the following best describes your current employment status?

[ ] Retired
[ ] Employed full-time
[ ] Employed part-time or casual
[ ] Home Duties
[ ] Disabled/Unable to work
[ ] Other. Please specify:

What is the main source of your household income?

[ ] Salary or wage

[ ] Superannuation, investments or other private income

[ ] Pension (aged, disability, carer, or other government pensions)

[ ] Other. Please specify:

Apart from Medicare, are you currently covered by private health insurance?

[ ] Yes [ ] No

Do you currently drive? [ ] Yes [ ] No

Have you ever smoked?

[ ] Yes [ ] No, please skip the following smoking questions

Have you ever smoked at least 100 cigarettes (or the equivalent amount of tobacco) in your lifetime?

[ ] Yes [ ] No

Have you ever smoked daily?

[ ] Yes [ ] No

How old were you when you first began smoking on a regular basis? ___ years

Do you now:

[ ] smoke daily [ ] occasionally [ ] not at all

How old were you when you completely stopped smoking? ___ years

On average, what number of the following items do/did you smoke per day?

___ manufactured cigarettes

___ hand-rolled cigarettes

___ bidis

___ pipefuls of tobacco

___ cigars/cheroots/cigarillos

___ goza/hookah

Keeping in mind that you may have stopped and started several times, overall how many years have/did you smoke(d) regularly?

___ years

On average, how often do you have an alcoholic drink of any kind?

[ ] daily (6-7 days per week)

[ ] several times a week (2-5 days per week)

[ ] once a week (1 per week)

[ ] monthly (1-3 per month)

[ ] less often (less than 1 per month)

[ ] never

On a day when you do drink alcohol, how many do you usually have?

[ ] more than 12 drinks

[ ] 7-12 drinks

[ ] 5-6 drinks

[ ] 3-4 drinks

[ ] 1-2 drinks

What medications are you currently taking?

Please include all medications prescribed by your doctor, as well as any bought from the chemist or shop without prescription. Please list all tablets, capsules, mixtures, powders, injections, eye drops, vitamins etc.

If you are not taking any medications at all, tick this box [ ]

Medication Name	Frequency
1.	
2.	
3.	
4.	
5.	
6.	
7.	

Please attach an extra page if needed.

Do you suffer/have you ever suffered any of the following conditions?

Arthritis	[ ] Yes [ ] No
Parkinson's Disease	[ ] Yes [ ] No
Stroke	[ ] Yes [ ] No
Hearing Impairment	[ ] Yes [ ] No
Diabetes	[ ] Yes [ ] No
Heart Disease	[ ] Yes [ ] No
High Blood Pressure	[ ] Yes [ ] No
Incontinence	[ ] Yes [ ] No
Hip Fracture	[ ] Yes [ ] No
Foot Disorders	[ ] Yes [ ] No
Any form of cancer	[ ] Yes [ ] No
Other	[ ] Yes [ ] No

Please specify:

In the last month, have you suffered from any of the following:

Vertigo/dizziness

[ ] Yes [ ] No

Light headedness when standing up from seat/bed

[ ] Yes [ ] No

Body Pain

[ ] Yes [ ] No

If so, what part of the body?

Which eye/s are being treated for glaucoma?	[ ] Right	[ ] Left
Who is your current eye specialist?		
When was your last visit to your eye specialist?		
How frequently do you see your eye specialist?		
In which year were you first diagnosed with glaucoma?		
Were you noticing visual problems at the time?	[ ] Yes	[ ] No
What glaucoma medications (and dosage) are you using currently:		
Medication Name	Dosage	Frequency
1.		
2.		
3.		

Have you had any surgery for your glaucoma? [ ] Yes [ ] No

If yes, please provide details:

How many falls have you had in the past 12 months? __________

As a result of these falls, did you suffer any injuries that affect your mobility now?

[ ] Yes, please provide details:

[ ] No

Apart from being in a high place, in the past 12 months, have you been worried or afraid that you might fall?

[ ] Yes [ ] No

Do you ever limit your activities, for example, what you do or where you go, because you are afraid of falling?

[ ] Yes [ ] No

Appendix 3: Medication coding

All prescription medications were coded into the following therapeutic classifications, according to MIMS Online (www.mims.com.au), which is a comprehensive web-based pharmaceutical database of medications available in Australia.

(1) Alimentary System; (2) Cardiovascular System; (3) Central Nervous System; (4) Analgesia; (5) Musculoskeletal System; (6) Endocrine and Metabolic Disorders; (7) Genitourinary System; (8) Infections and Infestations; (9) Neoplastic Disorders; (10) Immunology; (11) Respiratory System; (12) Allergic Disorders; (13) Ear, Nose and Oropharynx; (14) Eye; (15) Skin; (16) Surgical Preparations; (17) Diagnostic Agents; (18) Contraceptive Agents; (19) Nutrition; (20) Poisoning, Toxicity and Drug Dependence; (21) Vitamins and Minerals; and (22) Herbal and other complementary medicines.

Appendix 4: Confounding analyses

Systematic assessment of potential confounding factors was performed.

The bivariate Pearson's correlations (and p-values) between the potential confounding factors and the binocular visual field and outcomes measures are presented in Table A. 4-1.

The change-in-estimate calculations are presented in Table A. 4-2 using the negative binomial models as described in Chapter 7. This table presents the percentage change in the rate ratios between visual field loss and falls, according to the unadjusted and adjusted estimates for each potential confounder assessed separately.

Table A. 4-1: Pearson's correlations (and p-values) between potential confounding factors, explanatory and outcomes measures

	Bincolar Visual Field Measures		SF-36 Outcome Measures		Functional Status Measures					Postural Sway Measures	
Potential Confounding variable	**IVF-60**	**IVF-120**	**Physical Component Score**	**Mental Component Score**	**6-Min Walk Test**	**Timed-Up and Go Test**	**Leg Strength**	**PASE score**	**Functional Summary Z-score**	**Sway Firm Eyes Open**	**Sway Foam Eyes Open**
Socio-demographic Variables											
Age	0.06 (0.59)	0.00 (0.99)	**-0.17 (0.14)**	-0.15 (0.20)	**-0.51 (<0.01)**	**0.49 (<0.01)**	**-0.26 (0.03)**	**-0.19 (0.10)**	**-0.51 (<0.01)**	**0.28 (0.01)**	**0.25 (0.03)**
Gender	**0.30 (0.01)**	**-0.21 (0.08)**	-0.07 (0.58)	0.05 (0.70)	-0.05 (0.68)	**-0.25 (0.03)**	**-0.5 (<0.01)**	-0.09 (0.44)	-0.14 (0.23)	**-0.30 (0.01)**	**-0.20 (0.09)**
Smoking Status	-0.11 (0.37)	0.04 (0.76)	-0.08 (0.48)	0.07 (0.53)	-0.07 (0.55)	0.15 (0.20)	**0.23 (0.05)**	-0.03 (0.80)	0.00 (0.99)	0.14 (0.24)	0.03 (0.78)
Alcohol Consupmtion	0.00 (0.97)	0.01 (0.93)	-0.07 (0.56)	**0.15 (0.19)**	-0.04 (0.76)	-0.08 (0.51)	0.08 (0.51)	-0.01 (0.96)	0.03 (0.78)	-0.06 (0.63)	-0.07 (0.55)
Self-reported Medical Conditions											
Diabetes	0.10 (0.40)	-0.13 (0.28)	-0.1 (0.41)	0.01 (0.97)	-0.06 (0.60)	**0.17 (0.16)**	0.08 (0.51)	0.03 (0.82)	-0.03 (0.81)	-0.10 (0.39)	-0.12 (0.29)
Hearing Impairment	-0.07 (0.53)	0.08 (0.49)	-0.12 (0.32)	0.02 (0.85)	-0.05 (0.68)	-0.03 (0.78)	-0.13 (0.28)	-0.01 (0.90)	-0.05 (0.68)	0.11 (0.35)	**0.27 (0.02)**
Heart Disease	-0.12 (0.31)	0.08 (0.51)	-0.13 (0.28)	-0.03 (0.83)	0.05 (0.64)	0.03 (0.79)	0.00 (0.99)	0.09 (0.45)	0.04 (0.76)	-0.14 (0.23)	0.03 (0.81)
Hypertension	-0.06 (0.58)	0.08 (0.49)	-0.1 (0.39)	0.05 (0.69)	-0.12 (0.31)	0.04 (0.72)	-0.11 (0.37)	**-0.21 (0.08)**	**-0.16 (0.17)**	0.14 (0.25)	0.10 (0.40)
Comorbidity Index	0.02 (0.90)	0.00 (0.97)	**-0.21 (0.07)**	0.07 (0.57)	**-0.21 (0.07)**	**0.18 (0.12)**	-0.08 (0.51)	-0.11 (0.34)	**-0.20 (0.09)**	0.10 (0.41)	**0.17 (0.14)**
Medication Use											
Central Nervous System	0.00 (0.99)	0.02 (0.86)	-0.08 (0.5)	**-0.39 (<0.01)**	-0.13 (0.28)	0.11 (0.37)	**-0.23 (0.05)**	**-0.18 (0.13)**	**-0.23 (0.05)**	0.14 (0.23)	0.12 (0.29)
Hyponotics/Sedatives	0.09 (0.45)	-0.05 (0.65)	-0.01 (0.94)	**-0.46 (<0.01)**	-0.09 (0.43)	0.03 (0.77)	**-0.21 (0.07)**	-0.12 (0.29)	**-0.16 (0.17)**	0.04 (0.73)	0.01 (0.95)
Antidepressants	-0.08 (0.47)	0.11 (0.35)	**-0.17 (0.15)**	-0.15 (0.21)	-0.13 (0.25)	0.13 (0.29)	**-0.25 (0.03)**	-0.14 (0.23)	**-0.23 (0.05)**	**0.17 (0.16)**	**0.16 (0.18)**
Cardiac	-0.04 (0.72)	0.10 (0.40)	-0.13 (0.27)	**-0.17 (0.14)**	**-0.21 (0.08)**	0.12 (0.31)	**-0.20 (0.09)**	**-0.20 (0.10)**	**-0.25 (0.03)**	0.07 (0.54)	**0.17 (0.14)**
Beta-blockers (Oral)	**-0.21 (0.07)**	0.12 (0.33)	-0.05 (0.7)	**-0.16 (0.17)**	0.07 (0.57)	0.10 (0.42)	-0.07 (0.58)	-0.10 (0.41)	-0.07 (0.56)	-0.08 (0.49)	0.00 (0.98)
Endocrine	0.14 (0.25)	-0.07 (0.56)	**-0.31 (0.01)**	-0.11 (0.33)	**-0.26 (0.02)**	0.14 (0.25)	**-0.32 (0.01)**	-0.14 (0.23)	**-0.29 (0.01)**	-0.12 (0.29)	-0.03 (0.78)
Respiratory	-0.13 (0.27)	0.14 (0.22)	**-0.19 (0.11)**	0.14 (0.23)	-0.14 (0.24)	0.04 (0.75)	-0.12 (0.32)	-0.05 (0.66)	-0.12 (0.30)	0.05 (0.69)	0.13 (0.26)
Number of Medications	**-0.17 (0.14)**	**0.18 (0.13)**	**-0.31 (0.01)**	**-0.23 (0.05)**	**-0.22 (0.07)**	**0.27 (0.02)**	**-0.19 (0.11)**	-0.11 (0.37)	**-0.27 (0.02)**	0.07 (0.57)	**0.16 (0.18)**
Polypharmacy	0.00 (0.97)	-0.02 (0.86)	-0.15 (0.22)	**-0.22 (0.05)**	-0.12 (0.29)	0.10 (0.42)	**-0.23 (0.05)**	**-0.18 (0.12)**	**-0.22 (0.06)**	0.01 (0.90)	**0.16 (0.17)**

Notes: Bold values indicate p-values < 0.20; IVF = integrated visual field; SF-36 = Short-form 36 survey; PASE = Physical Activity Scale for the Elderly;

Table A. 4-2: Incident rate ratios between visual field loss and falls, adjusted for potential confounding factors

Potential Confounding variable	IVF-60 (per 5dB reduction)			IVF-120 (per 10 points missed)		
	IVF-60 IRR (95% CI)	Potential Confounder IRR (95%CI)	Change in IRR (%)	IVF-120 IRR (95% CI)	Potential Confounder IRR (95%CI)	Change in IRR (%)
No adjustment	1.350 (1.095 - 1.666)			1.213 (1.064 - 1.382)	-	-
Socio-demographic Variables						
Age	1.333 (1.647 - 1.079)	1.060 (1.001 - 1.121)	-1.28%	1.198 (1.050 - 1.367)	1.056 (0.998 - 1.118)	-1.23%
Gender	1.467 (1.858 - 1.158)	1.838 (0.859 - 3.932)	8.62%	1.257 (1.091 - 1.448)	1.637 (0.783 - 3.422)	3.62%
Smoking Status	1.395 (1.733 - 1.122)	0.558 (0.264 - 1.180)	3.27%	1.231 (1.077 - 1.406)	0.583 (0.277 - 1.226)	1.47%
Alcohol Consupmtion	1.299 (1.615 - 1.046)	1.514 (0.796 - 2.878)	-3.79%	1.186 (1.035 - 1.359)	1.511 (0.795 - 2.871)	-2.24%
Self-reported Medical Conditions						
Hearing Impairment	1.361 (1.701 - 1.090)	0.923 (0.444 - 1.916)	0.81%	1.217 (1.061 - 1.395)	0.949 (0.460 - 1.957)	0.30%
Heart Disease	1.369 (1.702 - 1.102)	0.800 (0.370 - 1.734)	1.40%	1.222 (1.069 - 1.397)	0.807 (0.373 - 1.746)	0.75%
Hypertension	1.331 (1.654 - 1.071)	1.210 (0.600 - 2.440)	-1.45%	1.202 (1.051 - 1.376)	1.227 (0.611 - 2.467)	-0.89%
Comorbidity Index	1.361 (1.690 - 1.096)	0.963 (0.751 - 1.235)	0.78%	1.218 (1.066 - 1.393)	0.963 (0.751 - 1.235)	0.45%
Medication Use						
Central Nervous System	1.324 (1.643 - 1.067)	1.619 (0.636 - 4.120)	-1.95%	1.198 (1.048 - 1.369)	1.642 (0.648 - 4.165)	-1.24%
Hyponotics/Sedatives	1.344 (1.660 - 1.088)	0.720 (0.163 - 3.179)	-0.47%	1.210 (1.061 - 1.379)	0.693 (0.155 - 3.096)	-0.26%
Antidepressants	1.293 (1.613 - 1.036)	2.372 (0.763 - 7.374)	-4.26%	1.179 (1.029 - 1.352)	2.363 (0.762 - 7.328)	-2.78%
Cardiac	1.323 (1.633 - 1.071)	2.890 (1.094 - 7.637)	-2.06%	1.191 (1.043 - 1.359)	2.708 (1.025 - 7.155)	-1.85%
Beta-blockers (Oral)	1.377 (1.722 - 1.101)	0.775 (0.289 - 2.075)	1.95%	1.218 (1.064 - 1.395)	0.886 (0.343 - 2.289)	0.44%
Endocrine	1.351 (1.667 - 1.094)	1.070 (0.526 - 2.178)	0.02%	1.213 (1.064 - 1.382)	1.036 (0.509 - 2.107)	-0.02%
Respiratory	1.304 (1.621 - 1.049)	1.911 (0.598 - 6.102)	-3.47%	1.187 (1.035 - 1.362)	1.820 (0.566 - 5.849)	-2.14%
Number of Medications	1.348 (1.698 - 1.071)	1.002 (0.887 - 1.131)	-0.15%	1.212 (1.051 - 1.399)	1.001 (0.887 - 1.130)	-0.04%
Polypharmacy	1.366 (1.691 - 1.104)	0.799 (0.396 - 1.612)	1.18%	1.220 (1.069 - 1.392)	0.817 (0.406 - 1.646)	0.57%

Notes: IVF = integrated visual field; IRR = incident rate ratio;

Appendix 5: Data quality control

The following procedures were undertaken to enhance the quality of data collected:

- Data were entered directly into a Microsoft Access Database. Field parameters were set to ensure accurate entry. Database forms were created to facilitate the visual review of the data to check for completeness and errors or problems.
- Database queries were created to automatically extract computed data to minimise error of human calculation.
- Data were exported using in-built database export functions.
- Data were checked for invalid entries by plotting histograms and examining frequency distributions for variables in SPSS.
- Where required, SPSS was used to recode continuous data into categorical values.
- Random data checks were carried out to ensure the accuracy of the dataset.

Appendix 6: Inter-correlations between integrated visual field measures

The bivariate Pearson's correlations between the integrated visual field measures are presented in Table A. 6-1.

Table A. 6-1: Pearson's correlations between the integrated visual field measures

	IVF-60 overall field	IVF-60 lower field	IVF-60 upper field	IVF-120 overall field	IVF-120 lower field	IVF-120 upper field
IVF-60 overall field	1					
IVF-60 lower field	0.94 **	1				
IVF-60 upper field	0.95 **	0.79 **	1			
IVF-120 overall field	-0.93 **	-0.86 **	-0.89 **	1		
IVF-120 lower field	-0.88 **	-0.72 **	-0.93 **	0.94 **	1	
IVF-120 upper field	-0.87 **	-0.91 **	-0.74 **	0.93 **	0.75 **	1

Notes: ** $p<0.01$; IVF = integrated visual field

Appendix 7: Location of visual field loss: a factor analysis

Factor analysis was used as a complementary statistical approach to examine the association between the location of visual field loss and the outcome measures. This approach was chosen as the inferior and superior visual field areas were highly correlated, and there was evidence of some multicollinearity in the models.

The four visual field variables (inferior and superior field regions for the IVF-60 and IVF-120) were submitted to principal components analysis using varimax rotation to derive two orthogonal statistically independent factors. These factors and the variable loadings are outlined in Table A. 7-1. The first factor loaded heavily on the superior visual field variables, and was termed the “superior” factor. The second factor loaded heavily on the inferior visual field variables, and was termed the “inferior” factor. These two factors accounted for 95.8% variance.

Table A. 7-1: Factor loading of four visual field variables on two independent visual field factors rotated and extracted by factor analysis*

	Superior Factor	Inferior Factor
IVF-120 superior	**0.896**	0.404
IVF-60 superior	**-0.871**	-0.450
IVF-120 inferior	0.420	**0.880**
IVF-60 inferior	-0.425	**-0.880**
Variance explained (%)	47.9	47.8

Notes: * Higher factor scores denote greater visual field loss; IVF = integrated visual field

Both the inferior and superior factors were included together in linear regression models to examine their independent association with SF-36 physical component scores, overall functional status scores, and postural sway measures (eyes open on firm and foam surface), adjusting for age and gender. To examine the independent association with falls, these factors were included together in negative binomial regression models, adjusting for age and gender. The incidence rate ratios (IRR) were calculated for every one standard deviation increase in factor scores.

The results are presented in Table A. 7-2. Greater inferior visual field loss, as indicated by higher inferior factor scores, was significantly associated with lower SF-36 physical component scores, lower overall function status and greater postural sway, both on the firm and foam surfaces. Furthermore, each standard deviation increase in inferior factor scores was associated with an 87% increase in the rate of falls (IRR 1.87). These associations were independent of the superior visual field factor scores, which showed no or little association with the outcome measures.

Table A. 7-2: Regression models results, adjusted for age and gender

Outcome variable	Predictor variable†	B coefficient	Standard Error	Beta	p-value
SF-36 Physical Component Score	Inferior factor	**-2.849**	**0.949**	**-0.337**	**0.004**
	Superior factor	-1.281	0.991	-0.151	0.200
Overall functional status	Inferior factor	**-0.225**	**0.069**	**-0.315**	**0.002**
	Superior factor	-0.001	0.072	-0.002	0.988
Sway , eyes open on firm	Inferior factor	**0.142**	**0.041**	**0.352**	**0.001**
	Superior factor	0.05	0.043	0.125	0.246
Sway , eyes open on foam	Inferior factor	**0.133**	**0.034**	**0.406**	**<0.001**
	Superior factor	**0.072**	**0.035**	**0.220**	**0.043**
		IRR	**Lower CI**	**Upper CI**	**p-value**
Number of falls (per 1 SD increase)	Inferior factor	**1.870**	**1.349**	**2.592**	**<0.001**
	Superior factor	0.946	0.635	1.407	0.782

Notes: Bold values represent significant associations; † Inferior and superior factors included together in each model; CI = confidence interval; SF-36 = Short-form 36 questionnaire; PASE = Physical Activity Scale for the Elderly

Appendix 8: Physical Activity Scale for the Elderly (PASE) Questionnaire

LEISURE TIME ACTIVITY

Q1.
Over the past 7 days, how often did you participate in **sitting** activities such as reading, watching TV, or doing handcrafts?

☐ NEVER Go to Q2. ☐ SELDOM (1-2 days) ☐ SOMETIMES (3-4 days) ☐ OFTEN (5-7 days)

What were these activities?

On average, how many hours per day did you engage in these sitting activities?

☐ LESS THAN 1 HOUR ☐ 1 BUT LESS THAN 2 HOURS ☐ 2-4 HOURS ☐ MORE THAN 4 HOURS

Q2.
Over the past 7 days, how often did you take a **walk** outside your home or yard for any reason? For example, for fun or exercise, walking to work, walking the dog, etc.?

☐ NEVER Go to Q3. ☐ SELDOM (1-2 days) ☐ SOMETIMES (3-4 days) ☐ OFTEN (5-7 days)

On average, how many hours per day did you spend walking?

☐ LESS THAN 1 HOUR ☐ 1 BUT LESS THAN 2 HOURS ☐ 2-4 HOURS ☐ MORE THAN 4 HOURS

Q3.
Over the past 7 days, how often did you engage in **light sport or recreational activities** such as bowling, golf with cart, fishing, swimming (no laps), etc.?

☐ NEVER Go to Q4. ☐ SELDOM (1-2 days) ☐ SOMETIMES (3-4 days) ☐ OFTEN (5-7 days)

What were these activities?

On average, how many hours per day did you engage in these light sport and recreational activities?

☐ LESS THAN 1 HOUR ☐ 1 BUT LESS THAN 2 HOURS ☐ 2-4 HOURS ☐ MORE THAN 4 HOURS

Q4.
Over the past 7 days, how often did you engage in **moderate sport and recreational activities** such as doubles tennis, golf without a cart, ballroom dancing, softball, etc.?

☐ NEVER Go to Q5. ☐ SELDOM (1-2 days) ☐ SOMETIMES (3-4 days) ☐ OFTEN (5-7 days)

What were these activities?

....

On average, how many hours per day did you engage in these moderate sport and recreational activities?

☐ LESS THAN 1 HOUR ☐ 1 BUT LESS THAN 2 HOURS ☐ 2-4 HOURS ☐ MORE THAN 4 HOURS

Q5.
Over the past 7 days, how often did you engage in **strenuous sport and recreational activities** such as jogging, cycling, singles tennis, aerobic dance, swimming laps, etc.?

☐ NEVER Go to Q6. ☐ SELDOM (1-2 days) ☐ SOMETIMES (3-4 days) ☐ OFTEN (5-7 days)

What were these activities?

....

On average, how many hours per day did you engage in these strenuous sport and recreational activities?

☐ LESS THAN 1 HOUR ☐ 1 BUT LESS THAN 2 HOURS ☐ 2-4 HOURS ☐ MORE THAN 4 HOURS

Q6.
Over the past 7 days, how often did you do any exercises specifically to increase **muscle strength and endurance**, such as lifting weights, push-ups, hand weights, etc.?

☐ NEVER Go to Q7. ☐ SELDOM (1-2 days) ☐ SOMETIMES (3-4 days) ☐ OFTEN (5-7 days)

What were these activities?

....

On average, how many hours per day did you engage in exercises to increase muscle strength and endurance?

☐ LESS THAN 1 HOUR ☐ 1 BUT LESS THAN 2 HOURS ☐ 2-4 HOURS ☐ MORE THAN 4 HOURS

HOUSEHOLD ACTIVITY

Q7.
During the past 7 days, have you done any light housework, such as dusting, washing dishes, ironing, laundry, meal preparation, etc.?

☐ No ☐ Yes

Q8.
During the past 7 days, have you done any heavy housework, such as vacuuming, scrubbing floors, washing windows, washing cars, etc.?

☐ No ☐ Yes

Q9.
During the past 7 days, did you engage in any of the following activities?

a. Home repairs like painting, wallpapering, electrical work, etc. ☐ No ☐ Yes

b. Lawn work or yard care, such as moving lawn, wood chopping, etc. ☐ No ☐ Yes

c. Outdoor gardening ☐ No ☐ Yes

d. Caring for an other person, such as children, dependent spouse, or an other adult. ☐ No ☐ Yes

Q10.
During the past 7 days, did you work for pay or as a volunteer?
☐ No ☐ Yes

If YES,

a. How many hours per week did you work for pay and/or as a volunteer? _______Hours

b. Which of the following categories best describes the amount of physical activity required on your job and/or volunteer work?

☐ Mainly sitting with slight arm movements. *Example*: office worker, bus driver.

☐ Sitting or standing with some walking. *Example*: cashier, general office worker, light tool worker.

☐ Walking, with some handling of materials generally weighing less than 50 pounds (23kg). *Example*: mailman, waiter, construction worker, heavy tool worker.

☐ Walking and heavy manual work often requiring handling of materials weighing over 50 pounds (23kg). *Example*: lumberjack, farm or general labourer.

Thank you for completing this questionnaire!

Appendix 9: Inter-correlations between functional status measures

The bivariate Pearson's correlations between the functional status measures are presented in Table A. 9-1.

Table A. 9-1: Pearson's correlations between the functional status and SF-36 PCS measures

	Six minute walk test	Timed up and go test	Lower limb strength	PASE score	Overall Functional Status	SF-36 PCS score
Six minute walk test	1					
Timed up and go test	-0.70 **	1				
Lower limb strength	0.36 **	-0.20	1			
PASE score	0.32 **	-0.17	0.30 **	1		
Overall Functional Status	0.83 **	-0.73 **	0.66 **	0.63 **	1	
SF-36 PCS score	0.44 **	-0.44 **	0.27 *	0.29 *	0.51 **	1

Notes: * $p<0.05$; ** $p<0.01$; PASE = Physical Activity Scale for the Elderly; SF-36 = Short-form 36 Survey; PCS = Physical component score

Appendix 10: Monthly falls calendar: example

Glaucoma and Falls Study

ID Code: _________

July 2008						
Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

Q1. Did you experience any falls this month?

[ ] No

[ ] Yes → Please tick on the calendar when the fall/s occurred, and provide details on the falls on the following page.

Q2. Have you had any changes in your glaucoma treatment or medications this month?

[ ] No

[ ] Yes → Please provide details of changes below:

....

....

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Fall 1:

Date:
Time of day:
Where did you fall?
Do you know what caused the fall?
Did you suffer any injuries as a result of the fall (even if minor)? [ ] No [ ] Yes: What injuries did you suffer? .... Did you seek medical attention? [ ] No [ ] Yes
What glasses were you wearing at the time of the fall? [ ] I was not wearing any glasses [ ] Distance glasses [ ] Reading glasses [ ] Bifocals [ ] Multifocals [ ] Contact Lenses

Fall 2:

Date:
Time of day:
Where did you fall?
Do you know what caused the fall?
Did you suffer any injuries as a result of the fall (even if minor)? [ ] No [ ] Yes: What injuries did you suffer? .... Did you seek medical attention? [ ] No [ ] Yes
What glasses were you wearing at the time of the fall? [ ] I was not wearing any glasses [ ] Distance glasses [ ] Reading glasses [ ] Bifocals [ ] Multifocals [ ] Contact Lenses

Please attach additional pages if further falls occurred.

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Appendix 11: Logistic regression models

Table A. 11-1: Association between vision factors and falls using logistic regression models, adjusted for age and gender

Variable	Odds Ratio (95%CI) Any Falls		Multiple Falls		
Visual Acuity, per line missed					
better-eye	1.36	(0.92 - 2.01)	1.15	(0.72 - 1.82)	
worse-eye	1.17	(0.94 - 1.45)	1.10	(0.86 - 1.40)	
Contrast Sensitivity, per triplet missed					
better-eye	1.11	(0.96 - 1.30)	1.09	(0.92 - 1.29)	
worse-eye	1.07	(0.97 - 1.19)	1.04	(0.93 - 1.17)	
Stereoacuity (reference: present)	1.54	(0.38 - 6.20)	0.83	(0.14 - 5.01)	
Motion sensitivity, per SD reduction	0.94	(0.55 - 1.60)	0.56	(0.26 - 1.21)	
Visual Field Sensitivity, per dB reduction					
better-eye	1.07	(0.98 - 1.16)	1.07	(0.97 - 1.18)	
worse-eye	1.01	(0.95 - 1.08)	1.03	(0.95 - 1.11)	
RNFL, per 10μm					
better-eye	1.09	(0.81 - 1.46)	0.91	(0.62 - 1.34)	
worse-eye	1.10	(0.80 - 1.50)	0.95	(0.65 - 1.39)	
IVF-60 , per dB reduction					
overall field	1.06	(0.97 - 1.15)	1.07	(0.97 - 1.18)	
inferior field	1.07	(0.98 - 1.16)	1.09	(0.99 - 1.20)	
superior field	1.03	(0.96 - 1.11)	1.03	(0.94 - 1.14)	
IVF-120, per 10 points missed					
overall field	1.15	(0.91 - 1.45)	1.16	(0.86 - 1.56)	
inferior field	1.37	(0.87 - 2.16)	1.47	(0.85 - 2.54)	
superior field	1.19	(0.77 - 1.84)	1.14	(0.65 - 2.01)	
AVF_{DIV}, per point missed					
overall field	1.11	(0.99 - 1.24)	**1.24**	**(1.06 - 1.44)**	**
inferior field	1.26	(0.99 - 1.60)	1.35	(0.98 - 1.86)	
superior field	1.15	(0.92 - 1.45)	**1.49**	**(1.07 - 2.06)**	*
AVF_{SEL}, per point missed					
overall field	1.11	(0.99 - 1.25)	1.16	(0.99 - 1.37)	
inferior field	1.12	(0.82 - 1.52)	**1.78**	**(1.08 - 2.95)**	*
superior field	1.09	(0.87 - 1.37)	1.08	(0.80 - 1.46)	

Notes: Bold values indicate significant associations; * $p<0.05$; ** $p<0.01$; Any Falls (no falls vs. 1 or more falls); Multiple Falls (none or 1 fall vs. 2 or more falls); OR = odds ratio; RNFL = Retinal Nerve Fibre Layer; IVF = Integrated Visual Field; AVF_{DIV} = Divided Attentional Visual Field; AVF_{SEL} = Selective Attentional Visual Field

Appendix 12: Incident Rate Ratio Calculations

The unit change required to double the IRR was calculated by using the following Microsoft Excel formula:

$UNIT_{[double]}$ = LOG(2, $IRR_{[per\ original\ unit\ change]}$), where $IRR_{[per\ original\ unit\ change]}$ represents the IRR calculated using the original unit change, and $UNIT_{[double]}$ represents the unit change which equates to an IRR of 2.

For example, in the unadjusted models presented in Chapter 7, every 10 points missed on the IVF-120 increased the rate of falls by 1.21 times (IRR = 1.21). Using the above formula, every 36 points missed on the IVF-120 would increase the rate of falls by 2 times (IRR = 2.00). To further illustrate this calculation, Table A. 12-1 presents the equivalent IRR for various unit change estimates (in 10 steps).

Table A. 12-1: Incident Rate Ratios for falls according to different unit change in IVF-120.

	Incident Rate Ratio
IVF-120 (per 10 points missed)	1.213
IVF-120 (per 20 points missed)	1.471
IVF-120 (per 30 points missed)	1.785
IVF-120 (per 40 points missed)	2.165
IVF-120 (per 50 points missed)	2.626