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Long-Term Incidence of Visual Impairment in Older Persons: Associated Factors, Burden and Impacts

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Preface

This thesis describes the candidate's work on the Blue Mountains Eye study 15-year follow-up data. The Blue Mountains Eye study is a population-based cohort study of vision and common eye diseases in a suburban Australian population 49+ years residing in the Blue Mountains area, west of Sydney. The baseline examination examined 3654 participants between 1992 and 1994. Surviving baseline participants were invited to participate in the 5-, 10- and 15-year follow-up examinations. Professor Paul Mitchell (candidate's co- supervisor) is the Principal Investigator. Professors Jie Jin Wang (candidate's primary supervisor), Robert Cumming, Wayne Smith and Stephen Leeder were co-investigators of this cohort study.

This thesis examines the long-term incidence of visual impairment and blindness among older people and the associated impacts over the short-term and long-term. Aims of this thesis include the following: firstly to describe the changes in visual acuity among the Blue Mountains Eye study population over a 15-year period; Secondly, to investigate the associated impacts following the onset of visual impairment on the affected individuals and their family and community over time.

Abstract

Purpose: To assess the long-term incidence of visual impairment (VI) in an older Australian population over a 15-year period, the association between diet quality and the incidence of VI, and associations between VI and the subsequent use of support services, subsequent events of falls, fractures, depressive symptoms, and cognitive decline over the short- (5 years) and long-terms (10+ years).

Methods: The Blue Mountains Eye Study (BMES) is a population-based cohort study of vision and common eye diseases in a sample of Australians aged 49+ years, residing in the Blue Mountains area, west of Sydney. Surviving participants were invited to return 5-, 10- and 15-years after the baseline examination.

VI was defined as best corrected visual acuity (VA) <6/12 (less than 39 letters read) with the exception of chapters 4 and 7 only, where presenting VA was used to defined different levels of VI. The incidence of bilateral VI was defined as the development of VI in the better eye at follow-up examinations when at least one eye was at risk of developing VI (VA≥6/12 at baseline). The incidence of unilateral VI was defined as the development of VI in the first eye at follow-up examinations when both eyes were at risk of developing VI at baseline. The incidence of any VI was defined as the development of bilateral or unilateral VI at the follow-up examinations.

Participants who had incident VI detected at the 5- and 10-year follow-up examinations were assessed for outcome events at the 10-year and 15-year follow-up examinations respectively, and a duration of 5 years or less between detecting VI and measures of outcome events was defined as “short-term”. Participants who had VI at baseline or incident VI detected at the 5-

year follow-up examination were assessed for outcome events at the 10- and 15-year follow-up examinations respectively, and a duration of 10+ years between VI diagnoses and outcome event measures was defined as “long-term”.

Face-to-face interviews and questionnaires were used to assess new use of community support services (formal support services), as well as the incidence of self-reported falls, fractures and depressive symptoms. We used a semi-quantitative food frequency questionnaire to calculate a total diet score (TDS) to assess diet quality. Participants in the highest TDS quartile were compared to people in the lowest TDS quartile. Mini Mental State Examination (MMSE) was performed at each of the three follow-up visits. A modified version of MMSE (after removing vision-related tasks, termed MMSE blind scores) was used and a reduction of ≥3 scores between the previous and subsequent visits was indicative of cognitive decline.

All longitudinal associations were assessed after adjusting for baseline age, sex, education, presence of a walking disability (use of walking aids or a wheelchair), living arrangements, smoking status, alcohol consumption, self-rated health, chronic co-morbidities (self-reported histories of diabetes, hypertension, hyperlipidaemia, stroke, myocardial infarct, angina and arthritis) and having had a hospital admission in the 12 months prior to the baseline examination. Hazard ratios (HR) or odds ratios (OR) and 95% confidence intervals (95% CI) were estimated using discrete logistic regression or logistic regression models with time-dependent variables when appropriate.

Results: The 15-year cumulative incidence of unilateral and bilateral VI was 12.3% and 5.2%, respectively. Approximately 40% of participants with mild VI (VA <6/12 but ≥6/24) improved to normal vision, while only approximately 10% of older participants with

moderate/severe VI (VA <6/24) improved to no visual impairment over the course of 15 years. Participants aged 65+ years who consumed a high quality diet (in the highest TDS quartile), were found to have a reduced risk of developing any VI compared to participants who consumed a low quality diet (in the lowest TDS quartile) (adjusted HR 0.63, 95% CI 0.38-0.98).

Compared to participants with normal vision, participants with incident bilateral VI were more likely to subsequently need community support services (adjusted OR 3.32, CI 1.96-5.59), to report experiencing ≥2 falls in the 12 months prior to the next follow-up visit (adjusted OR 1.46, 95% CI 1.04-2.04) and report subsequently the presence of depressive symptoms at the next follow-up visit (adjusted OR 3.06, 95% CI 1.72-5.44) over the short-term since the detection of VI. Participants with incident bilateral VI, however, were not more likely to experience a fracture (adjusted OR 1.07, 95% CI 0.77-1.50) over the short-term. Participants with any VI were also not more likely to have a decline (≥3 points) in MMSE scores (adjusted OR 0.74, 95% CI 0.26-2.17) over the short-term.

In contrast, compared to participants with normal vision, participants with incident bilateral VI were no longer more likely to subsequently use community support services (adjusted OR 0.19, 95% CI 0.03-1.30), to report experiencing ≥2 falls (adjusted OR 0.36, 95% CI 0.04-3.19) or report subsequently the presence of depressive symptoms (OR 1.29, 95% CI 0.84-1.98) over the long-term. Similar to the findings over the short-term, there were no associations found between VI and subsequently self-reported fracture (OR 1.12, 95% CI 0.22-5.74) or between VI and a decline in MMSE scores (OR 0.67, 95% CI 0.26-1.98) over the long-term.

Conclusions: We found similar incidence rates of VI as that were documented in other longitudinal studies. A healthy diet was associated with a reduced risk of developing VI in this older Australian sample.

Within the first 5 years since VI was diagnosed, the demand for community support services, and adverse event rates such as falls and self-reported depressive symptoms, were higher among older participants with VI than those without. However, these associations diminished over the long-term (10+ years), suggesting possible adaptation of the impairment with aids and support, treatment and rehabilitation. The possibilities of reduced study power and healthy survival bias associated with older cohort samples may also partly explain the disappearance in these associations over the long-term. These findings highlight the importance of prevention, early detection and early treatment of VI to maintain the aging population in a healthy state for as long as possible.

Brief Summary

Rationale of the Research Projects

Though cross-sectional associations and short–term (≤ 5 years) longitudinal associations between visual impairment (VI) and increased risks of falls, fractures, depression and other adverse events in older persons have been reported previously[1-10], there have been only few long-term follow-up (10+years) studies reporting the associations between VI and systemic health outcomes, and the findings have been inconsistent[11-13]. Limitations of previous studies include ambiguous information about definitions of VI (mostly self-reported) and duration of VI, relatively small sample sizes, and adjustment for limited numbers of confounding variables in statistical models. There has been no study conducted to assess the longitudinal associations of visual impairment with the subsequent use of community support services, the incidence of depression and cognitive decline.

Objectives of the Thesis Projects

The **objectives** were to:

- Report the long term incidence of visual impairment, blindness and the dynamic changes in visual impairment states among an older Australian population.
- Describe the effect of diet quality on the long-term (10+ year) incidence of visual impairment.
- Assess the impact of visual impairment on subsequent use of community support services over the short (5 years) and long-terms (10+ years).
- Assess the associations of visual impairment with subsequent falls and fractures over the short and long-terms.
- Assess the short and long-term associations of visual impairment with depressive symptoms at subsequent follow-up visits.
- Assess the associations of sensory impairment (visual impairment and hearing loss) with the decline in Mini Mental State Examination Scores over short- and long-terms.

Key Findings

Long Term Incidence of Visual Impairment in an Older Population

The 15-year cumulative incidence of unilateral and bilateral VI (VA<6/12) was 12.3% and 5.2%, respectively, while unilateral and bilateral blindness (VA<6/60), was 3.7% and 0.9%, respectively. There were no significant differences in the incidence rates of VI or blindness between men and women after adjusting for age. Deterioration of vision (a loss of ≥15 letters read) occurred in 6.9%, and an improvement in vision (a gain of ≥15 or more letters read) occurred in 1.6% of participants between baseline and the 15-year follow-up examination.

Cataract was responsible for a majority (48.5%) of unilateral and bilateral incident VI, followed by age-related macular degeneration (26.9%). Age related macular degeneration was responsible for a majority of unilateral and bilateral incident blindness (56.9%), followed by cataract (20.7%). Cataract surgery was the cause for visual improvements in the majority of persons.

Cumulative incidence rates of VI and blindness increased significantly with age. The incidence rates observed in this older cohort, and were comparable to that of other longitudinal studies.

Transition Rates of Visual Impairment States in Older Persons Over 5, 10 and 15 Years

Multi-state Markov models were used to estimate the transitional probabilities between VI states while adjusting for age and sex. We found a low probability of worsening vision between baseline and the 5-, 10- and 15-year follow-up examinations (2-7%). There was a 2-7% probability of improving vision from moderate/severe VI (VI<6/24) to mild VI (VA <6/12 but ≥6/24) between baseline and the 5-, 10- and 15-year follow-up examinations (7%,

3% and 2% respectively). There was approximately a 10% probability of improving vision from moderate/severe VI (VI<6/24) to no VI (≥6/12) between baseline and the 5-, 10- and 15-year follow-up examinations (8%, 10% and 10% respectively). There was approximately a 40% probability of improving vision from mild VI to no VI between baseline and the 5-, 10- and 15-year follow-up examinations (43%, 44% and 39% respectively).

Adherence to Australian Dietary Guidelines and the 10-year Incidence of Visual Impairment

A semi-quantitative food frequency questionnaire was used to calculate a total diet score (TDS) based on the Australian diet quality index. The risk of developing VI (VA <6/12 in one or both eyes) was lower among participants in the highest compared to the lowest TDS quartile (Hazard ratio (HR) 0.71, 95% confidence intervals (CI) 0.47-1.05) after adjusting for smoking, education and diabetes. This association was significant among participants aged 65+years at baseline (HR 0.63, 95% CI 0.38-0.98) but not among those aged <65 years (HR 0.95, 95% CI 0.46-1.97). The risk of VI reduced with each unit increase (e.g. improvement from 1 to 2) in the TDS (HR 0.94, 95% CI 0.88-1.00). A higher quality of diet and lifestyle, indicated by adherence to dietary guidelines, was associated with a decreased 10-year risk of VI in this older Australian cohort.

Visual Impairment and the Use of Community Support Services among Older People

Older participants who had incident VI were had a greater likelihood of subsequent use of community support services in 5 years, compared to those with normal vision during the entire follow-up period (OR 3.32, 95% CI 1.96-5.59 for incident bilateral VI and OR 1.77 95% CI 1.21-2.60 for incident unilateral VI), after adjusting for age, sex, home ownership,

self-rated health, living arrangements, receiving a pension, had a walking disability, had a hospital admission in the last 12 months prior to baseline examination, and had 2+ co-morbidities at baseline. Compared to people with no VI, participants with incident VI were not significantly more likely to rely on support from family or friends (informal supports) during the same follow-up period (OR 1.79, 95% CI 0.70-4.55 for incident bilateral VI and OR 1.60 95% CI 0.92-2.80 for incident unilateral VI).

Compared to participants with normal vision, those with incident VI were no longer more likely to subsequently use community support services (OR 0.19, 95% CI 0.03-1.30 for bilateral VI and OR 0.93, 95% CI 0.49-1.74 for unilateral VI) in 10 or more years. Similarly, there were no associations between incident VI and subsequent use of informal supports (OR 1.64, 95% CI 0.31-8.66 for bilateral and OR 1.11 95% CI 0.65-2.02 for unilateral VI) in 10 or more years.

Visual Impairment and the Incidence of Falls and Fractures among Older People

Older participants with incident VI were more likely to report having ≥2 falls in the 12 months prior to the next 5-year follow-up visit, compared to participants with normal vision over the same follow-up period (OR 1.46, 95% CI 1.04-2.04 for bilateral and OR 1.22, 95% CI 0.98-1.51 for unilateral VI), after adjusting for age, sex, the presence of a walking disability and having 3 or more co-morbidities. Compared to participants with normal vision, those with incident unilateral VI had a higher incidence of fractures in 5 years (OR 1.27, 95% CI 1.04-1.55), however, no similar associations were observed among those with incident bilateral VI (OR 1.07, 95% CI 0.77-1.50).

Compared to participants with normal vision, those with incident VI were not more likely to report ≥2 falls (OR 1.10, 95% CI 0.45-2.69 for bilateral VI and OR 1.26, 95% CI 0.79-2.01

for unilateral VI) or a fracture in 10 or more years (OR 1.27, 95% CI 0.53-3.06 for bilateral VI and OR 1.51, 95% CI 0.96-2.37 for unilateral VI).

Visual Impairment and Subsequently Self-reported Depressive Symptoms among Older People

Compared to participants with normal vision, participants with incident VI were more likely to report depressive symptoms in 5 years, after adjusting for age, sex, walking disability living arrangements, and hospital admission within 12 months of baseline (OR 4.60, 95% CI 1.67-12.69 for bilateral and OR 4.06, 95% CI 2.06-7.99 for unilateral VI), but were not more likely to report depressive symptoms in 10 or more years (OR 0.63, 95% CI 0.17-2.34 for bilateral VI and OR 1.47, 95% CI 0.90-2.20 for unilateral VI).

Sensory Impairment and Cognitive Function Decline among Older People

Compared to participants with no sensory impairment, participants with the presence of any VI (VA<6/12 in the worse eye), hearing loss (>40 decibels in the worse ear), or both (dual sensory impairment) were not more likely to have a decline (reduction of ≥3 points) in mini-mental state exam (MMSE) blind scores over 5 years, after excluding participants who had a history of stroke, and adjusting for age and sex (OR 0.74, 95% CI 0.26-2.17 for VI only, OR 1.30, 95% CI 0.83-2.01 for hearing loss only, and OR 1.46, 95% CI 0.67-3.17 for dual sensory impairment).

Compared to participants with no sensory impairment, participants with any VI, hearing impairment or both were not more likely to have a decline in MMSE blind scores over 10 or more years (OR 1.09, 95% CI 0.52-2.30, OR 1.09, 95% CI 0.65-1.82 and 1.15, 95% CI 0.28-4.73 for those with VI only, hearing loss only and dual sensory impairment, respectively).

Older baseline age was found to be significantly associated with a decline in MMSE blind scores over 5 and 10+ years (OR 1.07, 95% CI 1.04-1.10 and OR 1.07, 95% CI 1.04-1.10 respectively, for each year increase in age).

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Abbreviations

ABS	Australian Bureau of Statistics
ADL	Activities of Daily Living
AHFS	Auckland Hip Fracture Study
AMD	Age-related Macular Degeneration
BDES	Beaver Dam Eye Study
BES	Beijing Eye Study
BMES	Blue Mountains Eye Study
BMI	Body Mass Index
BMES	Blue Mountains Eye Study
CI	Confidence Interval
CCES	Copenhagen City Eye Study
ETDRS	Early Treatment of Diabetic Retinopathy Study
FFQ	Food Frequency Questionnaire
HACC	Home and Community Care
HR	Hazard Ratio
HR-QoL	Health-Related Quality of Life
LALES	Los Angeles Latino Eye Study
LogMar	Logarithm of the minimum angle of resolution
MCS	Mental Component Score of the SF-36
MHI	Mental Health Index
MMSE	Mini Mental State Exam
MVIP	Melbourne Visual Impairment Project
NDI	National Death Index
NHMRC	National Health and Medical Research Council
OR	Odds Ratio
PCO	Posterior Capsular Opacity
PCS	Physical Component Score of the SF-36
QoL	Quality of Life
RR	Relative Risk
SD	Standard Deviation
SEE	Salisbury Eye Evaluation Study

SEEDS	Salisbury Eye Evaluation Driving Study
SF-36	Short Form 36 Questionnaire
TDS	Total Diet Score
USA	United States of America
VA	Visual Acuity
VF	Visual Function
VF-14	Visual Function 14 Questionnaire
VI	Visual Impairment
WHO	World Health Organisation
95% CI	95% Confidence Intervals

Publications Relating to this Thesis

First-Authored Publications

1. **Hong T**, Mitchell P, Rochtchina E, Fong CS, Chia EM, Wang JJ. *Long Term Changes in Visual Acuity in an Older Population over a 15-Year Period: the Blue Mountains Eye Study.* Ophthalmology. 2013 Oct;120(10):2091-9.

2. **Hong T**, Flood V, Rochtchina E, Mitchell P, Russell J, Wang JJ. *Adherence to dietary guidelines and the 10-year cumulative incidence of visual impairment: the Blue Mountains eye study.* American Journal of Ophthalmology. 2014 Aug;158(2):302-8.

3. **Hong T**, Mitchell P, Burlutsky G, Fong CS, Rochtchina E, Wang JJ. *Visual impairment and subsequent use of support services among older people: longitudinal findings from the Blue Mountains Eye Study.* American Journal of Ophthalmology. 2013 Aug;156(2):393-399.

4. **Hong T**, Xie J, Rochtchina E, Mitchell P, Wang JJ. *Longitudinal transition rates of Visual impairment states in older people: Observations from the Blue Mountains Eye Study.* Under preparation.

5. **Hong T**, Mitchell P, Burlutsky G, Samarawickrama C, Wang JJ. *Visual impairment and the incidence of Falls and Fractures among older people: longitudinal findings from the Blue Mountains Eye Study.* Investigative Ophthalmology & Visual Science. 2014 Nov: 55(11):7589-93.

6. **Hong T**, Mitchell P, Burlutsky G, Gopinath B, Liew G, Wang JJ. *Visual impairment and development of Depressive Symptoms in among older Australian cohort: the Blue Mountains Eye Study.* British Journal of Ophthalmology. 2015 Feb (Epub ahead of print).

7. **Hong T**, Mitchell P, Burlutsky G, Liew G, Wang JJ. *Visual impairment and Cognitive Function in an older population: longitudinal findings from the Blue Mountains Eye Study.* Journal of the American Geriatrics Society (Under review of second revised version).

Other publications completed during the candidature

1. **Hong T,** Tan AG, Mitchell P, Wang JJ. *A Review and Meta-analysis of the Association between C-Reactive Protein and Age-related Macular Degeneration.* Survey of Ophthalmology. 2011 May-June: 56:184-194.

2. **Hong T**, Mitchell P, Fong CS, Rochtchina E, de Loryn T, Wang JJ. *Patients' Short-Term Satisfaction with Cataract Surgery and Sustainability of Improved Visual-Related Quality of Life after Cataract Surgery: Findings from a 3-year follow-up of a cataract surgical cohort.* Asia Pacific Journal of Ophthalmology, 2014: 3(2):83

3. **Hong T,** Broadhead GK, Chang AA. *Response of Pigment Epithelial Detachments to Intravitreal Aflibercept among Patients with Treatment-Resistant Neovascular Age-Related Macular Degeneration.* Retina, 2015 Jan (Epub ahead of print).

Co-Authored Publications relating to this thesis

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2. Fong CS, Mitchell P, de Loryn T, Rochtchina E, **Hong T**, Cugati S, Wang JJ. *Long-term outcomes of phacoemulsification cataract surgery performed by trainees and consultants in an Australian cohort.* Clinical and Experimental Ophthalmology. 2012 Aug; 40(6):597-603.
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3. Chang AA, Li H, Broadhead GK, **Hong T**, Schlub TE, Wijeyakumar W, Zhu M. *Intravitreal aflibercept for treatment-resistant neovascular age-related macular degeneration.* Ophthalmology. 2014 Jan;121(1):188-92.
4. Broadhead GK, **Hong T**, Chang AA. *Treating the untreatable patient: current options for the management of treatment-resistant neovascular age-related macular degeneration.* Acta Ophthalmology. 2014 Dec:92(8):713-23.
5. Zhu M, Chew J, Broadhead GK, Luo K, Joachim N, **Hong T**, Syed A, Chang AA. *Intravitreal Ranibizumab for Neovascular Age-related Macular Degeneration in Clinical Practice: 5 Year Treatment Outcomes.* Graefe's Archive for Clinical and Experimental Ophthalmology, 2014 Sep (Epub ahead of print).

Presentations

Paper Presentations

1. **Hong T**, Mitchell P, Burlutsky G, Fong CS, Rochtchina E, Wang JJ. *Visual Impairment and Subsequent Use of Support Services Among Older People: Longitudinal Findings from the Blue Mountains Eye Study,* **ARVO (Association for Research in Vision and Ophthalmology) 2011,** Ft Lauderdale, FL, USA.

2. **Hong T**, Burlutsky G, Rochtchina E, Mitchell P, Wang JJ. *Visual Impairment and the Incidence of Falls in Five Years among Older People: Longitudinal observation from the Blue Mountains Eye Study cohort,* **ARVO 2012,** Ft Lauderdale, FL, USA

3. **Hong T**, Broadhead GK, Li, H, Zhu M, Wijeyakumar W, Chang A. *Response of Pigment Epithelial Detachments following Intravitreal Aflibercept for Age-related Macular Degeneration.* **RANZCO (Royal Australian and New Zealand College of Ophthalmologists) 2013**, Hobart, TAS, AUS.

Poster Presentations

1. **Hong T**, Tan AG, Mitchell P, Wang JJ. *Systematic Review of the Association Between C-Reactive Protein and Age-Related Macular Degeneration,* **ARVO 2010,** Ft Lauderdale, FL, USA.

2. Hong T, Tan AG, Mitchell P, Wang JJ. *Systematic Review of the Association between C-Reactive Protein and Age-Related Macular Degeneration,* **Hospital Week 2010, Westmead Hospital.**

3. **Hong T**, Mitchell P, Fong CS, Rochtchina E, Wang JJ. *Long-Term Changes in Visual Acuity in an Older Population over a 15-Year Period,* **ASIA ARVO 2011**, Singapore.

4. **Hong T**, Mitchell P, Burlutsky G, Gopinath B, Wang JJ. *Impact of Un-correctable Visual Impairment on Depressive Symptoms among Older People: the Blue Mountains Eye Study,* **APAO (Asia-Pacific Academy of Ophthalmology) 2011**, Sydney, Australia.

5. **Hong T**, Broadhead GK, Li, H, Zhu M, Wijeyakumar W, Chang A. *Response of Pigment Epithelial Detachments following Intravitreal Aflibercept for Age-related Macular Degeneration.* **ARVO 2014**. Orlando, FL, USA.

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Candidate's contributions

Thomas Hong

With the guidance and assistance of Professor Jie Jin Wang and Professor Paul Mitchell, the candidate conceived some of the primary hypotheses for the thesis. With assistance from Professor Jie Jin Wang, the candidate developed the scientific questions, and wrote up the first drafts of all manuscripts for which he is listed as the lead author. These manuscripts form the majority of the chapters in this thesis. The candidate provided intellectual input into the other manuscripts for which the candidate is listed as a co-author. The candidate proposed some statistical analysis plans that were refined by Professor Jie Jin Wang, Mrs Elena Rochtchina or Mr George Burlutsky. The candidate performed statistical analysis for the article included in Chapter 7 with guidance from Mr George Burlutsky.

The candidate collected data for the Blue Mountains Eye Study 15-year follow-up examination which included assessment of visual acuity, visual field testing, biometry, retinal tomography and retinal fundus photography. The candidate acknowledges the efforts of others who collected data at the baseline, 5- and 10-year follow-up Blue Mountains Eye Study examinations.

The candidate gave oral presentations at the Association for Research in Vision and Ophthalmology (ARVO), Ft Lauderdale, Florida, USA, in 2011 and 2012, and at the Annual Scientific Congress of the Royal Australian and New Zealand College of Ophthalmologists (RANZCO), Hobart, Tasmania, Australia, in 2013. The candidate also gave five poster presentations at local and international conferences between 2010 and 2014.

Section I

Brief Literature Review

Section I

Brief Literature Review

Chapter 1: The Incidence and Impact of Long-term Visual Impairment in Older People

Introduction

Visual impairment (VI) affects up to 27% of people worldwide [14-24]. A large majority of VI data in the literature were cross-sectional findings pertaining to the prevalence of VI in different populations[19;20;25-36].

The cross-sectional associations between VI and physical, mental and social functioning have been extensively studied, often with conflicting results. Several cross-sectional studies have also found associations between VI and the prevalence of falls and fractures [38;45-62]. The prevalence of VI has consistently been found to be associated with the use of formal support services and help from family and friends[37-40]. A meta-analysis found a higher prevalence of depression among persons with VI (pooled Odds Ratio, OR 1.94 95% CI 1.68-2.25)[41], however a study by Evans et al[42] did not find any difference in the prevalence of depression between those with and those without VI after adjusting for age, sex and activities of daily living (ADL). Persons with VI have been reported to be more likely to have cognitive impairment than those without VI in some studies [43;44], however others have not found any associations after adjusting age, sex and history of cerebrovascular disease[45;46].

Limited longitudinal data regarding the incidence of VI and associated factors have been reported. This review aims to summarise the available data on the incidence of VI and blindness and the subsequent impacts of VI on both the affected individuals and their families and community.

Method of Literature Search

We searched Medline and Pubmed for articles during August 2014 with the following search words: visual impairment, incidence, incident, longitudinal, eye study, impact, visual function, quality of life, QOL, cognitive function, cognition, depression, depressive symptoms, driving, falls, fractures, mortality, death, support, hospitalisation, institutionalisation, eye care. The search was limited to publications written in English, and covered the years 1980 to 2014. We also hand searched bibliographies of identified studies for additional references.

1.1 Definitions of Visual Impairment and Blindness

The term VI usually refers to a reduced visual acuity (VA), however visual field loss and a reduced contrast sensitivity have also been included in some reports[18;63;64]. For the purposes of the following summary, only VA measures of VI are considered.

Various cut offs in the level of reduced VA have been used to define VI worldwide. The World Health Organisation (WHO) defines VI as best-corrected VA <6/18[65]. In the United States of America (USA)[14] VI is usually defined as ≤6/12. In Australia VI is defined as VA <6/12, which is the minimum VA requirement to obtain and maintain an Australian drivers license[66].

Similar to VI, differing definitions of blindness are used worldwide. The WHO defines blindness as best-corrected VA <6/120[65], whereas blindness is defined as ≤6/60 in the USA[24;67] and <6/60 in Australia[68;69]. The incidence of VI and blindness refers to VI that is present in an eye at a follow-up examination, but it was not present at the previous examination. An eye is at risk of incident VI when the VA in that eye is better than the

defined VA cut off for VI in the corresponding report, e.g. according to the Australian definition of VI (VA<6/12), an eye is at risk of developing VI when VA≥6/12 at the previous examination[67;68].

1.2 Incidence of Visual Impairment and Blindness in Older Persons

Australian Studies

The Blue Mountains Eye Study (BMES) baseline examinations were conducted between 1992 and 1994 in the Blue Mountains area, west of Sydney[70]. Permanent residents aged 49+ years were eligible to participate. Out of 4433 eligible residents identified using a private, door-to-door census, 3654 persons (82.4% participation rate) took part in the study at baseline. Between 1997 and 1999, 75.1% (n=2335) of survivors returned for re-examination after 5-years. Foran et al[68] reported that the 5-year incidence of bilateral VI (VA<6/12) was 1.7% (n=37) and incident bilateral blindness (VA<6/60) was 0.1% (n=3) in this population-based sample of older Australians aged 49+ years who had normal vision at baseline.

The Melbourne Visual Impairment Project (MVIP) was a population-based study of age-related eye diseases conducted in 9 adjacent pairs of urban districts randomly selected from the Melbourne statistical division. Among 3941 eligible participants who resided at their current address for 6 months or longer, identified using a door-step approach and household census[71], 3271 (83% participation rate) aged 40 years and over took part in the baseline examination between 1992 and 1994. Between 1997 and 1999, 2594 (85% of survivors) participants were subsequently re-examined. After 5 years, the reported incidence of bilateral VI (VA <6/12) was 4.2% (n=105), and bilateral blindness (VA<6/60) was found in 0.43% (n=11)[72].

The Central Australian Ocular Health Study examined the 30 largest remote communities within the statistical local area of central Australia[73]. Of the 5173 persons aged 20 years and older within the target area, 1884 (36.4%) attended the remote clinics for examination and identified themselves as indigenous Australians between 2005 and 2008. Between 6 months and 3 years later (a median follow-up period of 2 years), 608 (32%) were subsequently re-examined. Incident bilateral VI (VA<6/12) occurred in 11.4% (n=51) and blindness (VA<6/60) occurred in 0.84% (n=5) participants[74].

International Studies

Studies with follow-up period 5 or less years

The Los Angeles Latino Eye Study *(LALES)* was a population-based cohort study of participants of Latino background aged 40 years and over[75]. Of the 7789 eligible residents in 6 census districts invited to participate in La Puente, California, USA, 6357 (82%) completed an in-home questionnaire and clinical examination between 2000 and 2003. Four years later, 4658 participants were re-examined (76% of survivors). The 4-year incidence of bilateral VI (VA<6/12) was 1.2% (n=55) and blindness (VA≤6/60) was 0.3% (n=12)[24].

The Reykjavik Eye Study was a population-based cohort of Icelanders aged 50 years and over, during 1996[76]. Participants were randomly selected from inhabitants of Reykjavik using the national population consensus. Of the 1379 persons randomly selected, 1045 persons (75.8%) were examined and 846 participants were subsequently re-examined (88.2% of survivors) during 2001. The 5-year incidence of bilateral VI (VA<6/12) was 3.49% (n=29) and bilateral blindness (VA≤6/60) was 0.95% (n=8)[77].

The Beijing Eye Study was a population-based cohort of the greater Beijing area including both rural and urban areas during 2001. Of the 5324 eligible participants aged 40 years and over identified from local mayor registries, 4439 (83.4%) were examined in either school houses or community houses throughout the 7 communities[78]. After 5-years, 3251 participants were re-examined (73.2% of survivors). The 5-year incidence of bilateral VI (VA<6/12) was 1.1% (n=35) and blindness (VA<6/60) was 0.1% (n=2)[79].

The Liwan Eye Study was a population-based study of participants aged 50 years and over during 2003 within urban southern China[80]. Of the 1864 eligible subjects who lived in the Liwan district for ≥6 months, 1405 (75.4%) were examined at baseline. During 2009 all participants were invited to take part in the follow-up examination, with 924 participants subsequently re-examined (75% of survivors). The 5-year incidence of bilateral VI (VA<6/12) was 9.85% (n=86) and blindness (VA≤6/60) was 1.42% (n=13)[81].

Studies with follow-up period greater than 5 years

The Priverno Eye Study examined a cohort of 860 participants between the ages of 45 and 69 years within the town of Priverno, Italy in 1987. This study sample was drawn from participants currently enrolled in another study of cardio-vascular risk factors[18]. After 7-years, 619 participants (81.4%) were re-examined and the incidence of bilateral VI (VA<6/24) was found in 1.3% (n=8) of participants. The incidence of bilateral blindness (VA<6/120) was found in 0.2% (n=12) of participants[82].

The Barbados Eye Study (BES) was a population–based study between 1987 and 1992 to determine prevalence and risk factors for VI and major eye disease among predominately African American Barbadian-born citizens aged 40 to 84 years[19]. Of the 4631 participants examined at baseline, 3427 (85% of survivors) participants were re-examined between 1992

and 2003. The 9-year incidence of bilateral VI (VA≤6/12) was 6.4% (n=195) and bilateral blindness (VA≤6/60) 2.1% (n=69)[83].

The Ponza Eye Study examined residents of the island of Ponza, Italy, between 1986 and 1988. Of the 3292 persons within the municipality, 1226 were eligible (aged 40 years and over) and invited to participate with 1028 (83.8%) participants completing the baseline examination[18]. After 12 years, 441 participants returned for re-examination (70.7% of survivors). Nucci et al[84] reported the 12-year cumulative incidence of bilateral VI (VA<6/18) to be 3.9% (n=16), and bilateral blindness (VA<6/120) was 0.7% (n=3)[84].

The Copenhagen City Eye Study (CCES) was a population-based survey of vision and eye disease in persons aged 60 to 80 years as part of the wider *Copenhagen City Heart Study*. Of a randomly selected sample of 976 eligible participants between 1986 and 1988, 946 (96.9%) participants were examined at baseline[26] and 359 participants (97.3% of survivors) were-re-examined between 2000 and 2002. The 14-year cumulative incidence of bilateral VI (VA<6/12) was 16.7% (n=56) and of bilateral blindness (VA<6/60) was 5.1% (n=18)[85].

Beaver Dam Eye Study (BDES) is the only study reporting 5-, 10-, 15- and 20-year longitudinal data on vision changes among older persons. The baseline study was conducted between 1987 and 1988. Of the 5924 eligible residents of the city of Beaver Dam aged 43 to 84 years, 4926 (83.2%) completed the baseline examination[86]. Participants were invited to attend follow-up examinations 5-, 10-, 15- and 20-years after the baseline examination. The 5-, 10- and 15-year cumulative incidence of VI was 2.9% 5.9% and 8.0 % respectively. The corresponding cumulative incidence of blindness was 0.3%, 0.8% and 0.8% respectively[14;15;67]. The 20-year follow-up examinations were conducted between 2008 and 2010, with 1758 participants (89.4% of survivors) being re-examined. The estimated 20-year

cumulative incidence of bilateral VI (VA<6/12) varied from 0.6% among persons aged 50 years of age to 30.3% in persons aged 75 years. The corresponding cumulative incidence of bilateral blindness (VA≤6/60) varied from 0.3% to 2.7%[87].

The incidence of VI and blindness in the reported studies have been summarised in **Table 1.1**.

Table 1.1: Summary of major population-based studies of the incidence of visual impairment among older people

Years of baseline examinations	Name/location	Population size at baseline	Years of follow-up	Age at baseline (years)	Incidence of visual impairment (%) definition by visual acuity level				Incidence of blindness (%) definition by visual acuity level		
					<6/12	≤6/12	<6/18	<6/24	<6/60	≤6/60	<6/120
Australian											
2005-2008	CAOHS*	1884	2	20+	11.4				0.84		
1992-1994	BMES†	3654	5	49-97	1.7	1.9			0.1	0.1	
1992-1994	MVIP‡	3271	5	40-84	4.2				0.43		
International											
2000-2003	LALES§	4439	4	50+	1.2		0.8			0.3	
1996	Reykjavik	1045	5	50+	3.49		1.07			0.95	0.35
2001	Beijing	6357	5	40+	1.1				0.1		
2003	Liwan	1045	5	60+	9.85		5.38			1.42	0.33
1987	Priverno	860	7	45-69				1.3			0.3
1987-1992	Barbados	4631	9	40-84		6.4	4.5			2.1	1.0
1986-1988	Ponza	1028	12	40+			3.9				0.7
1986-1988	Copenhagen	946	14	60-80	16.7				5.1		
1987-1988	BDES**	4926	20	43-84	0.6-30.3					0.3-2.7	0.2

* Central Australian Ocular Health Study
† Blue Mountains Eye Study
‡ Melbourne Visual Impairment Study
§ Los Angeles Latino Eye Study
** Beaver Dam Eye Study

1.3 Impact of Visual Impairment on the Affected Older Individuals

Visual function

Visual function encompasses many aspects of vision including; VA, visual field and contrast sensitivity [88;89]. VA is the most widely used measure of visual function; however, recently, questionnaires assessing vision-related quality of life have also been used in research and clinical practice to assess changes in patient perceptions of visual function associated with progression and treatment of ocular diseases[49;90-92].

A reduction in VA associated with progression of cataract and AMD has previously been found to be correlated with a reduced visual function measured with visual function questionnaires[93-95]. Many studies have found short-term improvements in visual function following cataract surgery [96;97]. Some studies have assessed the long-term improvements in visual function following cataract surgery and found that short-term gains in visual function gradually decrease over a period of up to 10 years. The sample sizes of these studies were relatively small (n<550)[98;99].

Physical function

Mobility, Falls and Fractures

Mobility is an important aspect of daily function, and requires the co-ordination of a number of different physiological processes, including vision. The ***BDES*** found that persons with bilateral VI were more likely to use walking aids after 5 years compared to persons without VI, although the risk estimate was not statistically significant after adjusting for age, gender, diabetes and self-rated health (OR 2.4, 95% CI 0.9-6.7)[87]. The ***Salisbury Eye Evaluation Study*** found a correlation between a reduction in VA and an increase in difficulties of ADL over 8 years[100].

Falls are common among older people and can lead to permanent physical and psychological disability[101]. The multi-factorial nature of falls among older people has been well documented, and vision is an inconsistent risk factor[102;103] . The ***BMES*** reported no apparent associations between baseline VI status (VA<6/12) and risk of hip fracture after 5 years (age and sex adjusted Hazard Ratio, HR 1.1 95% CI 0.3-4.4)[6]. The ***Auckland Hip Fracture Study*** (AHFS)[7] showed an increased risk of hip fractures within 2.5 years of VI detection (age and sex adjusted OR 1.5 95% CI 1.1-2.0) among persons with VI (VA<6/18) at baseline. However, the exact duration of VI cases at baseline was unclear in both the ***BMES*** and ***AHFS***. ***The Framingham Eye Study***[12] examined 2675 participants at baseline between 1973 and 1975, and found an increased risk of subsequent fractures over a 10-year period among persons with moderate VI in at least 1 eye (VA 6/9-6/24) detected at baseline after adjusting for age, sex, weight and alcohol use (Risk Ratio, RR 1.5, 95% CI 0.95-2.5), although this was marginally non-significant. A study by Javitt et al[1] found that progressive visual loss was associated with an increased risk of non-specific injury over a 4 year follow-up period. The

BDES found that persons with bilateral VI were more like to experience two or more falls after adjusting for age, sex, self-rated health, diabetes and arthritis (OR 1.6, 95% CI 0.8-3.1) and fractures (OR 2.0, 95% CI 1.1-3.6, adjusted for age, sex and diabetes) in the subsequent 5 years following detection of VI[3].

Although there have been several studies assessing the longitudinal associations between VI and falls and fractures, the exact duration of VI have been unclear in some studies [6;7;12]. The longitudinal associations found between VI with falls and fractures have been consistent over the short-term[1;3;7], however as time progresses, these associations appear to be weaken or to disappear.[12]

Driving

There are various criteria for the required VA level, with or without visual field measurement, to obtain a driver's licence around the world. The presence of VI deprives the sufferer of the privilege of a licence, and the loss of independence due to cessation of driving could be associated with psychological stress of the affected individuals[104;105]. However, persons who wilfully stop driving due to visual problems may have come to terms with their impairment over time, and cope better compared to those who have their license taken away for the same reason[106].

Some studies have reported that even though persons with VI do worse on driving simulators, this did not translate into higher risk of road accidents[107]. Visually impaired persons were found to be cautious of their visual limitations, and less likely to take risks whilst driving leading to actions which may reduce accidents such as driving slowly and locally only, and limiting driving at night or under low light conditions such as rainy days[108-110].

However, the ***BDES*** did not find that persons with bilateral VI were more likely to stop driving at night in the following 5 years since VI was detected (OR 0.8, 95% CI 0.2-3.4)[111]. Conversely, the ***Salisbury Eye Evaluation Driving Study*** (SEEDS) investigators examined 1452 licensed drivers aged between 67 and 87 years of age, and found that a decrease in contrast sensitivity was associated with cessation of driving over the following 12 months after adjusting for age and sex (OR 1.2, 95% CI 1.0-1.2)[112].

Mental and cognitive function

Depression

Both VI and depression have increasingly been recognised as major issues affecting the overall well-being of older people[113-117]. Depression has been reported to be associated with detrimental effects on physical, mental and social functioning[16;118;119]. Depressive symptoms have been found to be more prevalent among persons with specific vision-impairing eye diseases such as AMD and diabetic retinopathy compared to persons without these conditions[51;120].

There have been a few longitudinal studies assessing the associations between VI and depression, and conflicting results have been reported[2;5;8]. A retrospective study by Tournier et al[5] found that VI was associated with a greater incidence of depression in an older Canadian population (65+ years) over a 3 year period after adjusting for age, sex, chronic diseases and a history of depression (HR 1.35, 95% CI 1.09-1.69 for moderate VI). Harris et al[2] found that persons with poor vision at baseline were associated with incident depression detected at the 2-year follow-up visit after adjusting for age, sex, location and baseline depression (OR 2.9, 95% CI 1.3-6.3). However, a study by Prince et al[8] followed a cohort of

889 residents of London aged 65+ years over a 1 year period, and found that self-reported eyesight problems were not associated with development of depression in 1 year (adjusted OR 0.8, 95% CI 0.3-2.1). Similarly, a study by Forsell et al[4] did not find any associations between VI and the onset of depression after 3 years in a Swedish population aged 75+ years. The duration and definitions of VI or poor vision have been unclearly reported from these above studies, making comparisons across studies difficult.

Cognitive function

Longitudinal studies have reported an association between VI and cognitive function decline in older persons[9;11;13]. Lin et al examined 6112 women aged 69 years and older in the ***Study of Osteoporotic Fractures***[9] and found a greater risk of subsequent cognitive decline among persons with VI after an average of 4.4 years compared to persons without VI. After adjusting for age, education, smoking, vertebral fracture, body mass index (BMI), grip strength, social network and baseline cognitive status, persons with bilateral VI (VA<6/12) at baseline were more likely to experience cognitive decline (OR 1.78 95% CI 1.21-2.61)[9]. The ***Maastricht Aging Study***[11] investigators examined 418 Dutch adults aged 55 years and older, and found that a deterioration in VA over a 6-year period was associated with a decline in cognitive function at the 6 year follow-up examination. Reyes-Ortiz et al[13] examined 2140 Mexican Americans aged 65 years and older at the baseline examination between 1998 and 1999, participants were subsequently re-examined 2-, 5- and 7-years later. Persons with near VI (<7-point type size) at baseline had an average decline of 0.13 more MMSE blind scores per year than the average decline in persons with normal near vision over the 7 year period (p=0.045). They found, however, no difference in the change in MMSE blind scores per year between persons with distance VI and those with normal distant vision at baseline (p=0.14)[13].

Although a decline in VA was associated with a subsequent decline in cognitive function over time among older persons in these studies, age and other factors may have contributed to the decline of both visual and cognitive functions. In the above mentioned studies, the duration of VI was not clearly defined.

Mortality

Several population-based studies have found that VI was associated with an increased risk of death among older people, compared to their aged peers without VI[10;121-126]. The ***BMES*** found an increased 5-year risk of death among people with VI (VA<6/12) at baseline, adjusted for age, sex, home ownership, self-rated health, BMI, history of co-morbidities, smoking status and alcohol consumption (RR 1.7, 95% CI 1.2-2.3)[121]. The ***BDES***[123] found an increased risk of death after 14 years among persons with VI (VA≤6/12) at baseline, after adjusting for age, sex, proteinuria, history of cancer, BMI, education, smoking status and history of other co-morbidities (HR 1.16, 95% CI 1.03-1.32). The ***MVIP*** found an increased 5-year risk of death among persons with VI (VA<6/12) at baseline, after adjusting for age, sex, smoking status, hypertension, arthritis (OR 2.34 95% CI 1.03-5.32) [122]. Thiagarajam et al found an increased risk of death among elderly persons (75+ year) with VI (VA<6/18) in the United Kingdom after adjusting for age, sex, BMI, ADLs, and co-morbidities (rate ratio 1.17, 95% CI 1.07-1.27)[124]. ***The Jerusalem Longitudinal Study***[10] examined 261 persons aged 70+years and found an increased risk of death after 7 years among persons with VI (VA≤6/12), after adjusting for sex, self-rated health, ADLs, smoking status, financial difficulties and co-morbidities (OR 2.84, 95% CI 1.48-5.46).

As to specific eye diseases and mortality, the ***Beijing Eye study*** found that cataract, retinopathy and glaucoma were associated with an increased risk of death compared to

persons with no major eye diseases, after adjusting for age, sex, rural or urban region, education and smoking status ($p<0.01$ for all)[125]. The ***CCES***[126] followed 946 people for 14 years and reported women but not men with any AMD (early or late) had an increased risk of death compared to persons without AMD, after adjusting for age, sex, smoking status, hypertension, diabetes, and cardiovascular disease (HR 1.59, 95% CI 1.23-2.07). The association between VI and mortality among older persons could have been due to the effect of other underlying co-morbidities, and therefore the VI-mortality association is likely to be indirect.

Other studies have assessed the underlying factors responsible for the association between VI and mortality, or factors that may coexist with VI and are known to be associated with mortality, including diabetes, cardiovascular disease, injuries and depression. Walking disability, indicative of frailty, was consistently found to be a possible factor partially explaining the increased risk of death among older persons with VI[127;128]. The ***SEE*** study[129] persons with VI at baseline were indirectly at an increased risk of death by way of decreasing instrumental ADL over time (HR 1.16, 95% CI 1.04-1.28) using structural equation modelling adjusted for age, sex, race, smoking status, alcohol consumption, BMI, depression and co-morbidities. In addition, older age and other co-existing age-related co-morbidities are highly likely the reasons explaining the association between VI and poor survival. Whilst most studies reporting this association had controlled for co-factors associated with mortality, the co-factors that were adjusted for were inconsistent across studies and unlikely to be inclusive of all confounding factors.

Although it would not be possible to adjust for all residual confounding effects, evidence supporting a reverse association, i.e. the association between correction of VI and improved survival, would have important implications to eye health care provision to older persons

with VI. The ***SEE*** study[130] found that persons who gained 2+ lines over 2 years were less likely to die in the next 10 years after adjusting for age, sex, race, smoking history, BMI, diabetes and other co morbidities (HR 0.47, 95% CI 0.23-0.95). Blundell et al[131] found that correcting cataract-related VI via cataract surgery was associated with a significantly decreased risk of mortality after adjusting for age and sex (standardised mortality rates 0.88, 95% CI 0.79-0.99)[131]. Compared to persons with persistent VI due to cataract who did not have cataract surgery, the ***BMES*** found a 45% reduction in the 15-year risk of death among 354 participants who had had cataract surgery to correct VI, after adjusting for age, sex, smoking status, BMI, home ownership, qualifications, poor self-rated health, poor mobility and co-morbidities (HR 0.55, 95% CI 0.35-0.86)[132]. In addition, the same group of authors, Fong et al[133], also found that cataract surgical patients who no longer had VI one month post cataract surgery were 30% less likely to die in the next 5 years, compared to cataract surgical patients who had persistent moderate-sever VI post-operatively. This protective association was after adjusting for age, sex, smoking status, BMI and co-morbidities (HR 0.71, 95% CI 0.51-0.99)[133]. Evidence supporting a reverse association between correction of VI and improved survival among older persons suggests the benefit of eye health care to older people with VI is beyond the eye, vision and visual functions.

1.4 Impact of Visual Impairment on the Community

Support use

Though some studies have reported the associations between VI and loss of independence, findings were largely from cross-sectional studies[38;57;58]. There has been few longitudinal data to support the sustained or incident use of support services subsequent to development of VI. The ***Jerusalem Longitudinal Study*** found that baseline VI (VA≤6/12) among participants aged 70+ year was associated with a subsequent greater dependence in ADLs over an 8-year period[10].

Hospitalisation and institutionalisation

A study by Evans et al[134] conducted among 14394 persons aged 75+ years, found a slightly increased likelihood of hospital admission in persons with VI (<6/18) over a 2 year period, after adjusting for age, sex, housing tenure, financial difficulties, smoking, diabetes, major illness and MMSE score (RR 1.19, 95% CI 1.06-1.34). Persons with VI were also found to have longer durations of hospital stay compared to persons without VI, although this could be due to the increased co-morbidities associated with VI[134;135]. The ***BMES*** found that baseline bilateral VI (≤6/12) was associated with an increased risk of nursing home placement over 6 years following baseline examinations, after adjusting for age, home ownership, self-rated health walking disability and smoking status (RR 1.8, 95% CI 1.1-2.9)[37]. The ***BDES*** found that persons with binocular incident VI (≤6/12) were more likely to be newly admitted to a nursing home within the next 5 years, after adjusting for age, sex, self-rated health and arthritis (OR 4.2, 95% CI 2.3-7.6)[111].

Eye care and economic burden

A study by Sloan et al found that persons having regular eye exams were less likely to experience visual decline[136]. Screening programs have been implemented worldwide with the focus on early detection and management of VI [137;138] A retrospective study by Maclennan et al found that among persons diagnosed with an eye problem, eye care use was found in 33.2% of the cohort within 1 year and 45% within 2 years[139]. Many factors could affect the use of eye care services by those who need these services. In general, the main reasons for not using eye care services were economic and cultural factors[140-146].

A systematic review on the economic burden of VI and blindness of 22 studies by Koberlein et al[147] found that there is a considerable impact of VI and blindness on direct and indirect costs to the individual and the community. Costs to the individual include a loss of independence and productivity. VI also adversely impacts on the ability of individuals to participate in social and community activities[55;148;149]. There is also an increased use of formal and informal support services[37-40].

Overall, Wittenborn et al[145] found that in the US, indirect cost of VI were $13 billion and the direct cost of VI were $14.5 billion. In Australia, a study by Taylor et al[113] estimated direct and indirect cost of VI in 2004 to be $1.8 billion and $3.2 billion AUD respectively.

1.5 Summary

In summary, many longitudinal population-based studies have reported the incidence of visual impairment and blindness among older people. Many studies have also reported the impact of visual impairment on the affected individual and their community. However, findings have mainly been short-term associations[5;6;10;11;37;87;111;121;122;125], and a limited number of studies have reported the associations over 10 or more years.

While the short–term associations between VI and the increased risk of falls, fractures and depression has been consistent, the long-term associations have not been consistent[2;3;5;8;87;100]. This could have resulted from limitations of previous studies, including poorly defined VI and unclear duration of VI, relatively small sample sizes, and different confounding variables included in statistical models. In addition, little data exist for the long-term associations between VI and the subsequent use of support services, and between VI and incidence of depression or cognitive decline. Longitudinal studies with clearly defined VI and information of temporal relation may help better understanding the impacts of VI, and better planning of eye health and aged care for the aging population.

Section II

Study Sample and Methods

Section II

Study Sample and Methods

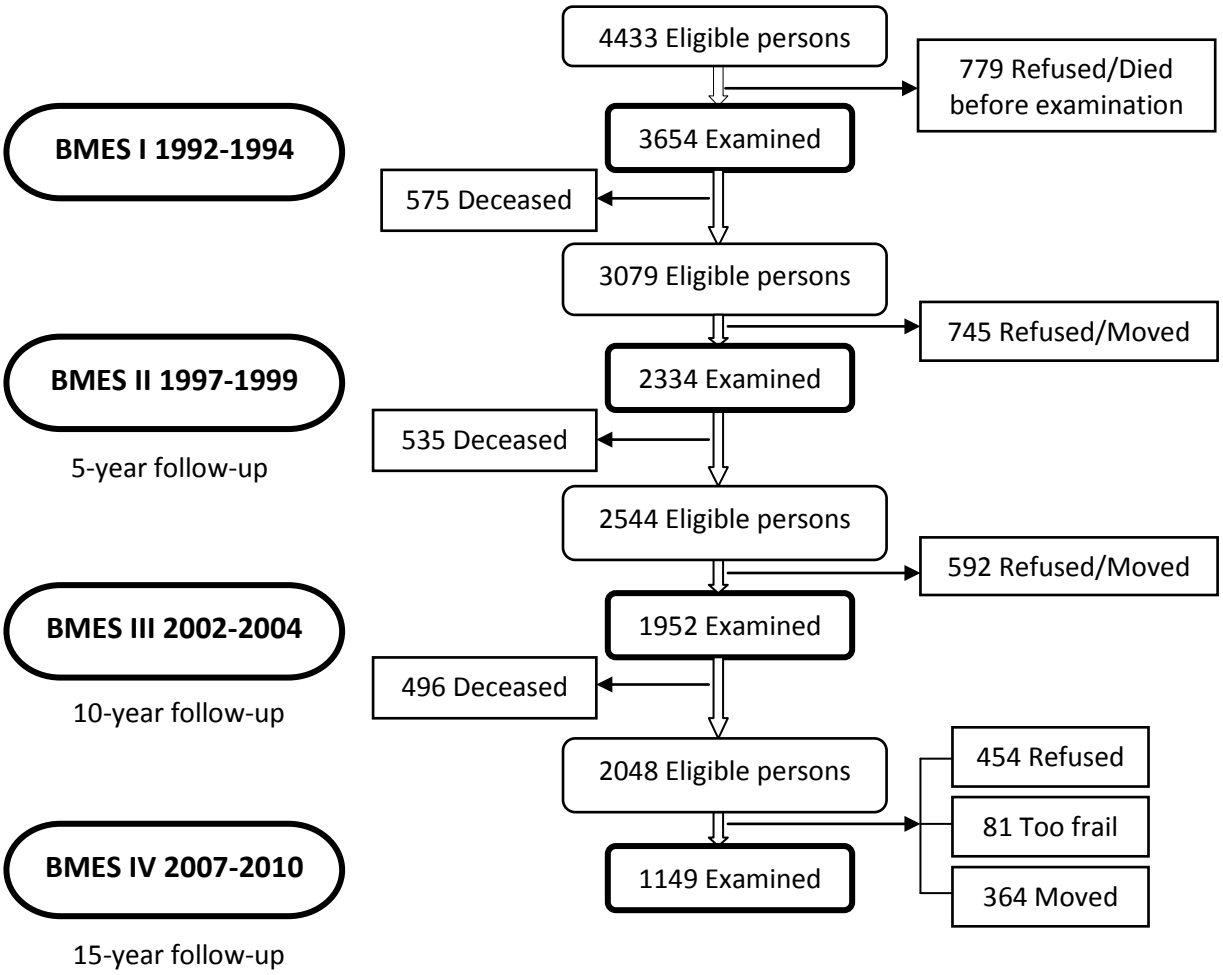
Chapter 2: Characteristics and Follow-up of the Blue Mountains Eye Study population, Data Collection Methods, Definitions, Statistical Methods

2.1 Characteristics and Follow-up of the Blue Mountains Eye Study population

The Blue Mountains Eye study (BMES) is a population-based cohort study of vision and common eye diseases in a suburban Australian population 49+ years residing in the Blue Mountains area, west of Sydney. Detailed methods of the baseline survey were reported previously[70]. In summary, at baseline we recruited and examined 3654 participants between 1992 and 1994. Surviving baseline participants were invited to participate in the 5-, 10- and 15-year follow-up examinations. Of these, 2334 returned after 5 years (75.8% of survivors), 1952 after 10 years (76.7% of survivors) and 1149 after 15 years (56.1% of survivors). Over the period between the 10- and 15-year visits, 364 had moved, 81 were admitted to a nursing home and were too frail to participate, 454 refused re-examination, and 496 had died (**Figure 2.1).**

All baseline and follow-up examinations of the BMES were approved by the Human Research Ethics Committees of the University of Sydney and the Western Sydney Area Health Service, and were conducted adhering to the tenets of the Declaration of Helsinki. Signed informed consent was obtained from all participants at each examination visit.

Figure 2.1: Participation Flow Chart of the Blue Mountains Eye study (BMES) cohort: 3654 participants were examined at baseline (BMES I), 2334 (75.8% of 3079 surviving participants) returned after 5 years (BMES II), 1952 (76.7% of 2544 surviving participants) after 10 years (BMES III) and 1149 (56.1% of 2048 surviving participants) after 15 years (BMES IV).



A comparison of some differences in demographic and socio-economic characteristics between participants of the baseline BMES population and the Australian population are presented in **Table 2.1.** The baseline BMES population was slightly older compared to the Australian population, and a higher proportion of BMES participants reported owning their own home and were born outside of Australia.

Table 2.1: Comparison of demographic and socio-economic characteristics between the baseline Blue Mountains Eye study (BMES) population (1992-1993) and the Australian population (1991 census data) aged 50 years or older[38].

	BMES		**Australian**	
	Women	**Men**	**Women**	**Men**
Age (years)	**%**	**%**	**%**	**%**
49	0.6	0.7	3.8	4.5
50-59	27.2	27.4	32.8	38.0
60-69	26.9	25.5	21.8	18.6
70-79	26.9	25.5	21.8	18.6
80*	10.6	9.2	11.0	6.2
Marital status				
Never married	8.0	7.0	5.3	7.3
Now married	51.8	77.1	58.4	77.0
Separated/divorced	13.6	8.3	8.0	8.5
Widowed	26.5	7.6	28.3	7.2
Country of birth				
Outside Australia	38.0	42.0	30.4	35.1
Home ownership	87.3	90.1	79.3	79.9

Table 2.2 presents selected characteristics of participants of the Blue Mountains Eye study baseline population. Approximately 63% of participants were married, 89% owned a home and 28% lived alone.

Table 2.2: Selected characteristics of participant of the Blue Mountains Eye study baseline population (n=3654)[70;150].

Characteristic	n	%
Female	2072	56.7
Age		
<60	1019	27.9
60-69	1309	35.8
70-79	960	26.3
80-89	330	9.0
90+	36	1.0
Married	2289	62.8
Lives alone	991	27.5
Owns home	3153	88.6
Current smoker	491	13.4
History of		
Cataract	603	16.5
Glaucoma	219	6.0
AMD*	88	2.4
Hypertension	1480	40.5
Diabetes	218	6.0
Stroke	194	5.3
Heart disease	587	16.2

*Age-related Macular Degeneration

2.2 Data Collection Methods

Examination procedures

The details of the examination procedures for the Blue Mountains Eye Study baseline examination have been described previously[70], the 5- and 10-year follow-up examinations used similar procedures **(Appendix 1).** Details of the 15-year follow-up examination procedures used in this study are briefly described below.

Study Questionnaire

A comprehensive interview-administered questionnaire was conducted detailing socio-demographic characteristics, driving, dependency, mobility, self-rated health, family history of eye disease. Past surgical and medical histories of angina, acute myocardial infarct, stroke, arthritis, hypertension, diabetes, the presence of a walking disability (the use of a cane, crutch, walking frame or wheelchair) and any hospital admissions (at least overnight) in the 12 months prior to each visit, smoking, alcohol intake, past and current medication use **(Appendix 2).**

Use of Community and Informal Support Services

Participants were asked the following questions to determine the use of community and informal support services;

- Do you get regular help from Meals on Wheels?
- Do you get regular home visits from a community nurse?
- Do you get regular visits from Home Care?
- Who usually cleans your house?
- Who usually does your shopping?
- Are you able to go out alone?

Assessment of Falls and Fractures

Participants were asked the following question to determine the occurrence of falls over a 12-month period prior to the study examination; “During the past 12 months, have there been any falls where you have landed on the ground or floor?” If the response was yes, additional questions were asked including how many falls they had suffered.

Participants were asked the following question to determine the incidence of fractures over a 5-year period between the visit when visual impairment was detected and the subsequent visit after visual impairment was detected; “Have you broken or fractured a bone since the last examination?”

Assessment of Depressive Symptom

Depressive symptoms were assessed using the Mental Health Index (MHI) component of the Short-Form-36 (SF-36). The SF-36 self-rated health questionnaire addresses a wide range of health issues consisting of eight separate domains including; Physical Function, Role Function Physical, Role Function Emotional, Social Function, General Health, Mental Health, Vitality and Pain. The Mental Health Index (MHI) component of the SF-36 has previously been validated as a screening instrument to detect depressive symptoms among elderly participants[151;152]. The MHI consists of five questions relating to the prior 4 weeks "Have you been very nervous? Have you felt so down in the dumps that nothing could cheer you up? Have you felt calm and peaceful? Have you felt down? Have you been happy?". The responses to these questions were limited to; "All of the time, most of the time, a good bit of the time, a little of the time, none of the time" and were allocated a score between 1 and 6. An overall score was calculated by adding the scores of the five responses, subtracting 5 and multiplying by 4. This results in a score between 0 and 100, with 100 indicating the best mental health. A score of <59 is indicative of having depressive symptoms[152]. Self-reported use of anti-depressant medication was considered as severe manifestation of depressive symptoms requiring treatment.

Assessment of Cognitive Function

Cognitive function was assessed using a modified version of min-mental state exam (MMSE), termed MMSE blind, excluding vision-related items with remaining items conserving the purpose of assessing memory, calculation and orientation[60;153;154]. Tasks of MMSE blind are added up to a maximum score of 22 (indicating the best level of cognitive function).

Dietary Assessment

Diet was assessed with a semi-quantitative food frequency questionnaire which included 145 items adapted for the Australian diet from a Willett food frequency questionnaire [155]. Participants used a frequency scale ranging from never to four times a day to indicate typical consumption of particular food items throughout the past year. Participants were excluded if their food frequency questionnaires had more than 12 food frequency questionnaire items missing; had energy intakes <2500kJ or >18000kJ. Finally, nutrient data were screened for extreme values, inspecting values in the upper and lower 2% of the distribution to locate and correct any data entry errors and to check for plausibility, by an accredited practising dietician (VF). Validity of the food frequency questionnaire was assessed in a subsample (n=78) at baseline comparing nutrient intakes from the food frequency questionnaire to the weighed food records over twelve days [155;156], energy adjusted Spearman correlations above 0.5 were found for most nutrients. Australian Tables of Food Composition were used to estimate dietary nutrient intakes, using the electronic database NUTTAB90 [157] for the food frequency questionnaires collected at baseline and a purpose built software analysis system to generate average daily nutrient intake.

Visual Acuity Assessment

VA was measured prior to pupil dilation using a retro-illuminated logarithm of minimum angle of resolution (LogMAR) chart (Vectorvision CSV-100TM, Vectorvision, Inc, Daytona, OH). Distance VA was measured at 244 cm for each eye with current spectacles if worn, followed by pinhole acuity. Either a previous spectacle prescription or an auto-refraction (Humphrey automatic refractor, model 597, Humphrey-Zeiss, Germany) provided the baseline for a subjective refraction.

Subjective refraction was performed using the Early Treatment Diabetic Retinopathy Study protocol[158]. VA was recorded as the number of letters read correctly in each eye (from 0-70). **Table 2.3** shows the equivalent scores. If no letters could be read from the chart at 244cm, VA was further assessed at 61cm, and recorded as count fingers, hand movements, light perception, or no light perception.

Table 2.3: Equivalent letter scores for reading logMAR chart at 244 cm and 61 cm

Letter Score 2.44m	Snellen VA 244 cm	LogMAR VA 244 cm	Snellen VA 61 cm	LogMAR VA 61 cm
5	6/60	1.0	6/150	1.4
10	6/48	0.9	6/120	1.3
15	6/38	0.8	6/95	1.2
20	6/30	0.7	6/75	1.1
25	6/24	0.6	6/60	1.0
30	6/19	0.5	6/48	0.9
35	6/15	0.4	6/38	0.8
40	6/12	0.3	6/30	0.7
45	6/9.5	0.2	6/24	0.6
50	6/7.5	0.1	6/19	0.5
55	6/6	0.0	6/15	0.4
60	6/4.8	-0.1	6/12	0.3
65	6/3.8	-0.2	6/9.5	0.2
70	6/3	-0.3	6/7.5	0.1

Hearing Assessment

Hearing was assessed at the 5-, 10- and 15-year follow-up examinations by means of pure-tone audiometry (PTA), performed by an audiologist in sound-proof booths using THD-39 (total dynamic distortion-39) earphones and Madsen OB822 audiometers (Madsen Electronics, Denmark).

Measurement of other variables

Peripheral visual fields were assessed via automated perimetry in both eyes using Humphrey 24-2 Sita Standard tests (Humphrey-Zeiss, Model 530, Germany). After pupil dilation with tropicamide 1% and phenylephrine 10%, eye examinations were performed including a slit lamp (Haag Streit) and retro-illumination (Neitz) camera to assess the lens. Retinal photographs were taken using a Canon fundus camera with digital back (CF-60DSi, EOS 1Ds Mk III, Japan).

Diagnosis of the causes of Visual Impairment

Cataract was diagnosed during the dilated slit lamp examinations and also recorded during lens photographic grading. AMD was diagnosed at the time the dilated fundus examination was conducted and confirmed by retinal photographic grading. Glaucoma was diagnosed when glaucomatous field loss was detected, based on repeated visual field tests where the visual field defect corresponded to optic disc changes, consistent with typical glaucomatous cupping [159].

2.3 Definitions of Visual Impairment

A number of different definitions of VI have been used worldwide, which have been described earlier. The definition of VI may vary between chapters to allow for comparison between Australian and international reports. Visual acuity was based on the number of letters read correctly on a LogMar chart, and usually refers to best-corrected VA (defined as VA after subjective refraction) throughout this thesis unless specified. We used best-corrected VA for a majority of the analysis to assess the associations between true VI and the outcome variables. Presenting or habitual VA (defined as VA measured before subjective refraction) was used in Chapters 4 and 7 only **(Table 2.4)**. As falls usually occur when the subject is wearing their current spectacles or no spectacles at all, we used presenting VA in the primary analysis of VI and falls and fractures. A supplementary analysis using best-corrected VA was also performed in this chapter. We used presenting VA in Chapter 4 to increase the number of cases for the analysis; we also assessed VI according to best-corrected VA in Chapter 4 but the number of cases was too small. VI was defined as VA <6/12 (39 letters or less letters read), and blindness as VA <6/60 (4 letters or less read) unless specified. The definition for VI is in keeping with the definitions used in previous BMES reports, and it is the minimum VA requirement to obtain and maintain an Australian Driver's license.

An eye was considered to be at risk of developing VI if VA was 6/12 or better and at risk of developing blindness if VA was 6/60 or better at baseline. Incident ***unilateral*** VI was defined as development of VI in only one eye (the worse eye) at follow-up visits where both eyes were at risk of VI at baseline. Similarly, incident ***bilateral*** VI was defined as development of VI in both eyes when at least one eye was at risk of developing VI at baseline, and was defined based on VA in the better eye at follow-up. In addition, incident ***any*** VI was defined

as having at least one eye at risk of developing VI at baseline where the at-risk eye was found to have VI at the follow-up examination.

Incidence of ***any blindness*** was defined as having at least one eye at risk of developing blindness at baseline and that the at-risk eye was found to develop blindness at the follow-up examination.

Table 2.4: Definitions of visual impairment in each chapter by eye and visual acuity measurement.

Chapter	Topic	Eye	Best-corrected or presenting Visual Acuity
3	Cumulative Incidence of VI	Better and Worse or either	BCVA
4	Dynamic Changes in Vision	Better	Presenting
5	Total Diet Score and incidence of VI	Better and Worse	BCVA
6	Support Use	Better and Worse or either	BCVA
7	Falls and Fractures	Better and Worse	Presenting
8	Depressive symptoms	Better and Worse or either	BCVA
9	Cognitive Decline	Better or Worse	BCVA

VI - visual impairment

BCVA – best-corrected visual acuity

2.4 Statistical Analysis

SAS (Version 9, SAS Institute Inc, Cary, NC) was used for all analyses, with the exception of Chapter 4. Age was defined as age at baseline for all analysis.

Cumulative 15-year incidence of VI was calculated while considering the competing risk of death[160]. The competing risk regression model is an adaptation of the Kaplan-Meier method that takes into account two competing events; in this case the events would be either development of VI or death.

Analyses adjusted for co-variables or potential confounders were performed using logistic regression (PROC LOGISTIC) and discrete logistic regression (PROC PHREG), with the use of time-dependent study (VI) and outcome variables (support service use, falls, fractures, depressive symptoms and cognitive decline), to compute odds ratios for participants with and without visual impairment.

Multi State Markov (MSM) package in R version 2.13.0[161] (R Foundation for Statistical Computing, Vienna, Austria) was used for analysis for Chapter 4 to estimate the probability of transition from one VI state to another within a specific time period. This model uses data which is usually right censored in tradition analyses of longitudinal data. As many diseases such as visual impairment can improve or worsen over the course of a disease, this model can describe dynamic changes over time. All models were adjusted for age and sex. The model was represented by a four state system: no VI (State 1), mild VI (State 2), moderate/severe VI (State 3), and death (State 4). The estimated transition probability matrix P(t) within a given time (5-, 10- and 15-years) was extracted using the function “pmatrix.msm”.

Association estimates are presented together with 95% confidence intervals (CIs).

Section III

Research Findings

Section III

Part 1: Long-Term Incidence of Visual Impairment and Associated Factors

Chapter 3: Long Term Changes in Visual Acuity in an Older Population

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Material in this Chapter has been published in

Hong T, Mitchell P, Rochtchina E, Fong CS, Chia EM, Wang JJ. *Long Term Changes in Visual Acuity in an Older Population over a 15-Year Period: the Blue Mountains Eye Study.*

Ophthalmology. 2013 Oct;120(10):2091-9.

ABSTRACT

Purpose: To describe the change in visual acuity and incidence of visual impairment (VI) in an older population over a 15-year period.

Methods: Of the 3654 participants of the Blue Mountains Eye Study (BMES) baseline examination during 1992-1994, 1149 were re-examined during the 15-year follow-up between 2007 and 2010. Best-corrected visual acuity (VA) by means of subjective refraction was measured with a logarithm of the minimum angle of resolution (LogMAR) chart using Early Treatment Diabetic Retinopathy Study (ETDRS) methods at each examination. Unilateral VI was defined as VA <6/12 and blindness as VA <6/60 in the worse eye. Incident bilateral VI and blindness was determined according to VA in the better eye at the 15-year visits. Doubling of the visual angle was defined as a loss of 15+ letters from baseline to the 15-year visit. Halving of the visual angle was defined as a VA improvement of 15+ letters over the same period. Causes of VI were determined at examination, by photographic grading and from medical records.

Results: Cumulative 15-year incidence of unilateral and bilateral VI was 12.3% and 5.2%, respectively, and for unilateral and bilateral blindness, was 3.7% and 0.9%, respectively. These incidence rates increased significantly with increasing age ($p < 0.01$). Doubling and halving of the visual angle occurred in 6.9% and 1.6% of participants, respectively.

Cataract accounted for the majority (48.5%) of unilateral and bilateral incident VI, followed by age-related macular degeneration (AMD) (26.9%). AMD accounted for the majority of unilateral and bilateral incident blindness (56.9%), followed by cataract (20.7%).

Conclusions: These data provide population-based estimates of the cumulative 15-year incidence of visual changes in an older population. The cumulative incidence of blindness accounting for competing risk of death in our population was similar to that of the Beaver Dam Eye Study (BDES) after age standardization. However, the cumulative incidence of VI was higher in the BDES compared to our population. This may partially be explained by a higher mortality rate among our population.

Background

Previous population-based studies have provided important data on the prevalence and causes of visual impairment (VI) in older persons[14-24]. The prevalence of VI is known to increase with age[14;128;162]. It has been shown to be associated with a loss of independence and an increased likelihood of reliance on community support services among affected older individuals[38]. VI has also been documented consistently to be associated with an increased risk of death[14;122;128;130;163] in multiple older population samples. VI among the older population is thus a major condition demanding not only eye health care but also increases need for aged care services by affected individuals[38].

A number of studies have examined the long-term changes in vision and long-term incidence of VI among older persons in the USA[14;24] and Europe[82;84]. The purpose of this report is to describe the 15-year change in visual acuity (VA) and the incidence of VI in the sample of older Australians attending the Blue Mountains Eye Study (BMES). This information may aid in the effective allocation of resources towards vision-related treatment, rehabilitation and prevention.

Specific Methods

Visual impairment definitions have been described previously in **chapter 2**, page 67. VA used in this chapter refers to the best-corrected acuity after subjective refraction.

A change in the number of letters read correctly was defined as the difference in the numbers of letters read between the 15-year and baseline examinations. Deterioration or doubling of the visual angle was defined as a loss of 15+ letters read correctly in the better eye from baseline to the 15-year visits. Improvement in vision (halving of the visual angle) was

defined if there was an improvement of 15+ letters read correctly over the same period. Eyes were at risk of deteriorating or improving VA (doubling or halving the visual angle) if their baseline VA was light perception or better, or if the baseline VA was 55 or less letters, respectively.

Causes of Visual Impairment

Cataract was diagnosed during the dilated slit lamp examinations and also recorded during lens photographic grading. AMD was diagnosed at the time the dilated fundus examination was conducted and confirmed by retinal photographic grading. Glaucoma was diagnosed when glaucomatous field loss was detected, based on repeated visual field tests where the visual field defect corresponded to optic disc changes, consistent with typical glaucomatous cupping [159].

The primary cause of VI was defined as the condition which explained at least 50% of the vision loss. This was confirmed by review of the participant's photographs and medical records. Cases where there was no obvious cause or where multiple causes were present were reviewed by an Ophthalmologist (PM) to determine the primary cause.

Statistical Analysis

SAS (Version 9, SAS Institute Inc, Cary, NC) was used for all analyses, and age was defined as age at baseline. Cumulative 15-year incidence was calculated while considering the competing risk of death[160]. The competing risk regression model is an adaptation of the Kaplan-Meier method that takes into account two competing events; in this case the events would be either development of VI or death. Persons eligible for inclusion in analyses contributed information up to the time when either of these two events occurred. Persons

were considered as censored when reasons other than death prevented them from participation in the follow-up examinations. Multivariable-adjusted analyses were performed with the following co-variables in the model: age, sex, employment status, marital status, education, previous medical history, smoking status and alcohol consumption.

The incidence rates of VI and blindness reported by the Beaver Dam Eye Study (BDES) were age-standardized to the BMES population for comparison. For this comparison, we used modified definitions of VI (VA $\leq$ 6/12) and blindness (VA $\leq$ 6/60) following the definitions used in the BDES.

Results

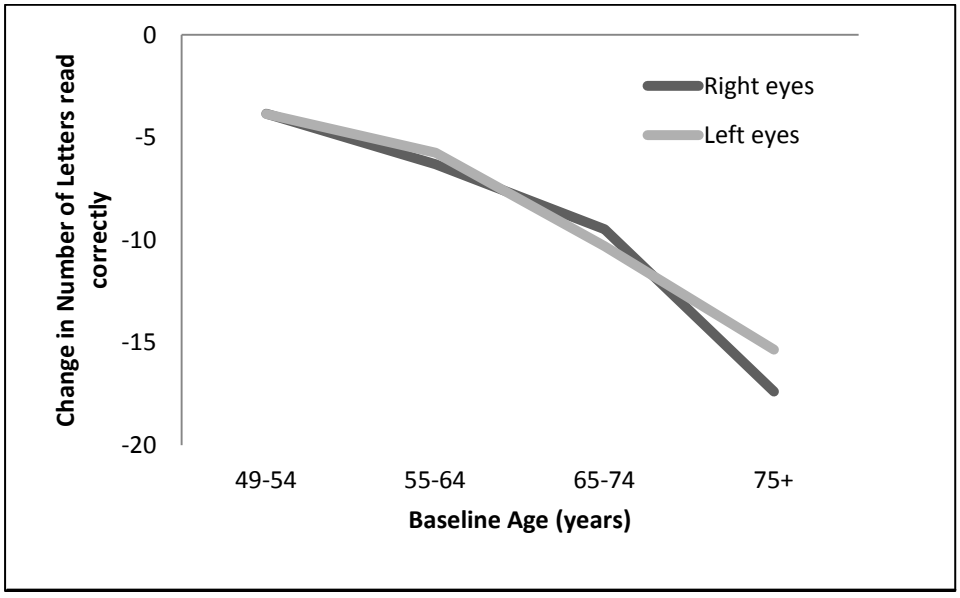
The mean age of participants at baseline was 64.5 years, and 57.9% were female. **Table 3.1** shows the baseline characteristics of the 2572 participants who attended at least one follow-up examination after the baseline.

Table 3.1: Baseline Characteristics of Participants in the Blue Mountains Eye Study: 15-year Follow-up Examinations

	Participants with follow-up information				**Non-participants**			
	Attended the 15-year follow-up examinations		***Attended at least 1 follow-up examination (5, 10 or 15 years)***		***Alive***		***Dead***	
Characteristics	*Crude %*	*n*	*Crude %*	*n*	*Crude %*	*n*	*Crude %*	*n*
Total (BMES I, n = 3654)	*31.4*	*1149*	*70.4*	*2572*	*22.3*	*815*	*7.3*	*267*
Age (years) at baseline								
<55	22.2	237	14.7	368	*27.5*	*84*	3.9	33
55-64	48.45	517	37.1	928	42.2	129	13.6	115
65-74	26.34	281	34.5	862	24.84	76	32	271
75+	3	32	13.7	343	5.6	17	50.5	428
Sex, female	57.9	618	42.2	1056	62.8	192	51.4	435
Education *(trade certificate or higher)*	66.0	682	60.6	1445	55.1	157	51.3	384
Employment								
High prestige *(Daniel's Prestige Scale <5)*	65.6	691	63.5	1558	63.8	190	57.6	465
Receiving pension	38.1	397	53.4	1295	42.8	125	80.7	653
Home ownership	93.3	986	90.9	2224	83.9	250	83.7	679
Currently married	71.8	766	65.9	1648	62.4	191	53.1	450
Visual impairment in worse eye								
Any *(VA 6/12 or worse)*	2.8	30	5.9	147	6.2	19	19.2	161
Severe *(VA 6/60 or worse)*	0.8	9	1.8	45	3.3	10	9.2	77
History of								
Stroke	1.9	20	3.3	83	7.8	24	24.1	204
Heart Disease *(AMI or angina)*	10.2	109	14.3	358	3.0	9	12.1	102
Hypertension	35.2	375	42.5	1063	41.8	128	53.6	454
Diabetes	5.2	55	6.4	160	8.5	26	11.6	98
Cancer	6.3	67	7.4	186	6.2	19	12.4	105
Smoking status								
Non-smoker	54.8	572	51.24	1239	42.5	124	43.4	335
Previous smoker	32.9	343	13.2	319	34.6	101	38.5	297
Current smoker	12.3	128	35.6	860	23.0	67	18.1	140
Heavy Drinker (>4 drinks per day)	3.3	34	3.8	91	3.8	11	3.4	26

The overall mean decrease in number of letters read correctly over the 15 years was similar in right and left eyes (-6.9 and -6.8 letters respectively); there was an inverse relationship between reduction in mean numbers of letters read correctly from baseline to the 15-year examinations and age, shown in **Figure 3.1**. There was no significant sex difference in the changes in numbers of letters read correctly in either right or left eyes ($p = 0.97$ and $p = 0.25$ respectively).

Figure 3.1: Mean Change in Number of Letters Read Correctly in Right and Left Eyes by Age between Baseline and 15-year Follow-up



The 15-year cumulative incidence of bilateral VI was 5.2% (119 participants), and varied from 0.4% in those aged <55 years to 10.5% in those aged ≥75 years at baseline. The incidence of bilateral blindness was 0.9% (21 participants), and varied from 0% in those aged <55 years to 1.7% in those aged ≥75 years at baseline. Women were more likely than men to have bilateral VI (6.8% vs. 3.4%, age-adjusted p=0.02) and bilateral blindness (1.2% vs. 0.5%, age-adjusted p=0.09). The incidences of VI and blindness were strongly age-related in both men and women (p values <0.001) (**Table 3.2**).

Table 3.2: Incidence of Bilateral Visual Changes by Age at Baseline and Sex in the Blue Mountains Eye Study

	Doubling of the Visual Angle [*]			***Visual Impairment*** [†]			***Blindness*** [‡]			***Halving of the Visual Angle*** [§]		
Age (years)	*At risk*	*%*	*P for trend*	*At risk*	*%*	*P for trend*	*At risk*	*%*	*P for trend*	*At risk*	*%*	*P for trend*
Female												
<55	217	2.6		212	0.7		217	0.0		118	2.7	
55-64	564	3.6		541	2.1		559	0.3		365	1.0	
65-74	579	11.8		534	11.5		567	2.0		475	1.5	
75+	375	12.3		238	13.6		338	2.4		365	1.4	
Total	1735	8.0	<0.001	1525	6.8	<0.001	1681	1.2	<0.001	1323	1.4	0.43
Male												
<55	170	1.4		165	0.0		167	0.0		66	0.0	
55-64	441	5.2		427	2.9		434	0.3		231	2.2	
65-74	464	6.0		413	3.7		447	0.5		340	2.1	
75+	294	8.1		195	7.0		264	0.8		279	1.9	
Total	1369	5.6	<0.001	1200	3.4	<0.001	1312	0.5	0.008	916	1.9	0.032
All												
<55	387	2.0		377	0.4		384	0.0		184	1.7	
55-64	1005	4.3		968	2.5		993	0.3		596	1.4	
65-74	1043	9.0		947	7.7		1014	1.3		815	1.8	
75+	669	10.4		433	10.5		602	1.7		644	1.6	
Total	3104	6.9	<0.001	2725	5.2	<0.001	2993	0.9	<0.001	2239	1.6	0.038

[*] Doubling of the visual angle was defined as a loss of 15 letters or more in the better eye at follow-up visits
[†] Incidence of visual impairment was defined a visual acuity < 6/12 at follow-up in the better eye when both eyes were ≥ 6/12 at baseline examination
[‡] Incidence of severe visual impairment was defined as visual acuity < 6/60 at follow-up in the better eye when both eyes were ≥ 6/60 at baseline examination
[§] Halving of the visual angle was defined as a gain of 15 letters or more in the worse eye at the follow-up visit

The 15-year cumulative incidence of unilateral VI was 12.3% (293 participants), and varied from 3.4% in those aged <55 years to 15.4% in those aged ≥75 years at baseline. The incidence of unilateral blindness was 3.7% (95 participants), and varied from 1% in those aged <55 years to 6.9% in those aged ≥75 years at baseline. Women were more likely than men to develop unilateral VI (13.3% vs. 10.8%) and blindness (4.7% vs. 2.6%), however these differences were not statistically significant after adjusting for age ($p = 0.5$ and $p = 0.1$) (**Table 3.3**).

The cumulative incidence of any VI was 17.3% (412 participants), and incidence of blindness in any eye 4.6% (116 participants). As expected, women had a higher incidence of any VI (19.7% vs. 14.2%, age-adjusted $p = 0.06$) and blindness (5.9% vs. 3.1%, age-adjusted 0.03) compared to men (**Table 3.3**).

Table 3.3: Incidence of Unilateral and Any Visual Impairment by Age at Baseline and Sex in the Blue Mountains Eye Study

	Unilateral						Any					
	Visual Impairment*			***Blindness**†*			***Visual Impairment**‡*			***Blindness**§*		
Age (years)	*At risk*	*%*	*P for trend*	*At risk*	*%*	*P for trend*	*At risk*	*%*	*P for trend*	*At risk*	*%*	*P for trend*
Female												
<55	212	2.6		217	1.2		212	3.3		217	1.2	
55-64	541	10.6		559	2.3		541	12.5		559	2.5	
65-74	534	18.7		567	6.5		534	29.2		567	8.5	
75+	238	17.4		338	8.4		238	30.6		338	8.7	
Total	1525	13.3	<0.001	1681	4.7	<0.001	1525	19.7	<0.001	1681	5.9	<0.001
Male												
<55	165	4.4		167	0.8		165	4.4		167	0.8	
55-64	427	10.1		434	1.9		427	12.9		434	2.2	
65-74	413	13.3		447	2.6		413	16.9		447	3.1	
75+	195	12.7		264	5.1		195	19.4		264	5.9	
Total	1200	10.8	<0.001	1312	2.6	<0.001	1200	14.2	<0.001	1312	3.1	<0.001
All												
<55	377	3.4		384	1.0		377	3.8		384	1.0	
55-64	968	10.4		993	2.1		968	12.7		993	2.4	
65-74	947	16.3		1014	4.6		947	23.5		1014	5.9	
75+	433	15.4		602	6.9		433	25.5		602	8.6	
Total	2725	12.3	<0.001	2993	3.7	<0.001	2725	17.3	<0.001	2993	4.6	<0.001

* Incidence of **unilateral visual impairment** was defined as visual acuity < 6/12 at follow-up in only one eye (worse eye) when both eyes were ≥ 6/12 at baseline examination

† Incidence of **unilateral blindness** was defined as visual acuity < 6/60 at follow-up in only one eye (worse eye) when both eyes were ≥ 6/60 at baseline examination

‡ Incidence of **any visual impairment** was defined as having at least one eye at risk of developing visual impairment (visual acuity < 6/12) at baseline and the at risk eye developing visual impairment at the follow-up examination

§ Incidence of **any blindness** was defined as having at least one eye at risk of developing blindness (visual acuity < 6/60) at baseline and the at risk eye developing blindness at the follow-up examination

Doubling of the visual angle occurred in 183 participants (6.9%) based on the better eye, which was significantly associated with age in both men and women ($p < 0.001$). Halving of the visual angle occurred in 34 participants (1.6%) based on worse eye VA, and there was no significant association of halving the visual angle with age in either sex. Of these 34 participants, 20 (59%) had undergone cataract surgery during the follow-up period.

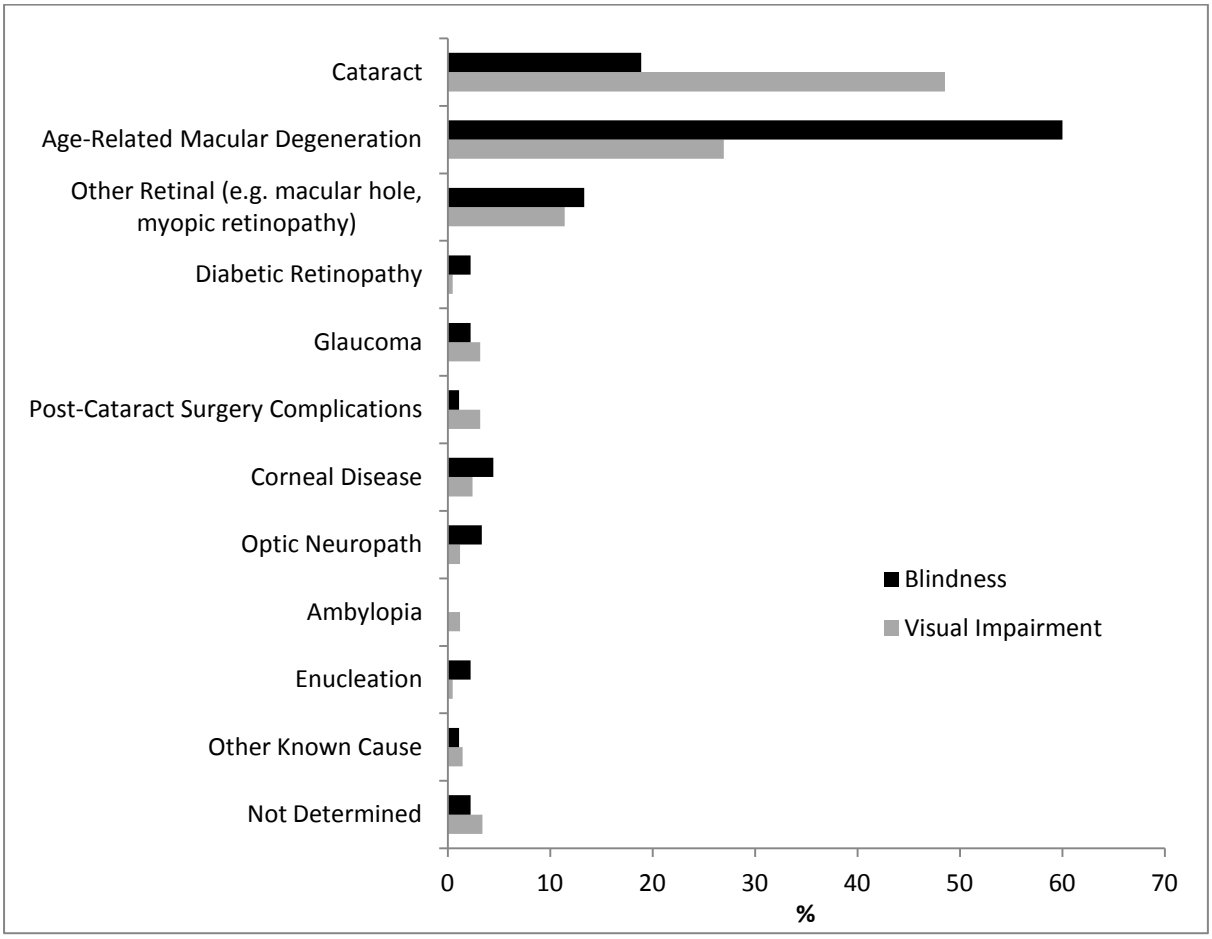
Table 3.4 shows a comparison of the incidence of VI between our study and BDES[14] findings using the modified definition of VI and blindness, after direct standardization to the age distribution of the BMES population. Incidences of VI were higher in the BDES population (11.1%) compared to our population (6.4%), after adjusting for competing risk of death. However, the incidences of blindness were similar among the BDES population (1.2%) and our population (1.1%) Similar sex differences and age-related trends in incidences were also observed in the BDES population.

Table 3.4: 15–year Incidence of Visual Impairment and Blindness accounting for the competing risk of death by Age and Sex in the Blue Mountains Eye Study Compared to the Beaver Dam Eye Study

	Visual Impairment						Blindness					
	Blue Mountains Eye Study			***Beaver Dam Eye Study***		***Standardized to Blue Mountains Eye Study***	***Blue Mountains Eye Study***			***Beaver Dam Eye Study***		***Standardized to Blue Mountains Eye Study***
Age at baseline (Years)	At Risk	Crude %	95% Confidence Interval	At Risk	Crude %	% (95% Confidence Interval)	At Risk	Crude %	95% Confidence Interval	At Risk	Crude %	% (95% Confidence Interval)
Female												
<55	211	0.7		661	1.5		217	0.0		667	0.2	
55-64	536	3.1		574	5.6		559	0.5		578	0.2	
65-74	523	12.6		569	18.4		565	2.3		598	0.9	
75+	226	15.7		270	29.7		335	3.5		327	5.0	
Total	1496	7.8	6.3-9.3	2074	10.2	13.1 (11.6-14.6)	1676	1.3	0.9-2.3	2170	1.0	1.4 (0.9-3.4)
Male												
<55	165	0.0		586	1.4		167	0.0		588	0.2	
55-64	424	4.3		507	2.8		433	0.3		510	0.0	
65-74	405	4.8		436	12.6		446	0.5		447	1.6	
75+	182	10.4		185	18.5		263	1.2		211	1.8	
Total	1176	4.8	3.5-6.1	1714	6.0	8.4 (7.1-9.7)	1309	0.5	0.2-1.0	1756	0.6	0.9 (0.2-0.9)
All												
<55	376	0.4		1247	1.4		384	0.0		1255	0.2	
55-64	960	3.6		1081	4.3		992	0.4		1088	0.1	
65-74	928	8.9		1005	15.9		1011	1.5		1045	1.2	
75+	408	13.3		455	25.1		598	2.5		538	3.7	
Total	2672	6.4	5.4-7.4	3788	8.3	11.1 (10.1-12.1)	2985	1.1	0.7-1.5	3926	0.8	1.2 (0.7-2.4)

Figure 3.2 presents the proportions of incident cases by primary attributable causes for any VI and blindness in any eye (either first or second eye). Cataract accounted for the majority (48.5%) of any VI, followed by age-related macular degeneration (AMD) (26.9%). However, AMD was responsible for the majority of any blindness cases (56.9%) followed by cataract (20.7%). Bilateral AMD was responsible for 71.4% of bilateral blindness.

Figure 3.2: Causes of Any (Unilateral or Bilateral) Visual Impairment and Blindness



Discussion

In our study the overall cumulative incidence of VI and blindness over the 15-year period was 5.2% and 0.9%, respectively. Women had approximately twice the incidence of any impairment when compared to men. The age-related increasing trend in incident VI was consistent in both sexes. Cataract and AMD were predominantly the primary causes of VI and blindness in this population.

Our report from the BMES cohort complements previously findings from the BDES[14], which is the only other study reporting 15-year longitudinal data on vision changes among older participants. Both studies included similar samples drawn from older, predominately white populations. The overall mean numbers of letters read correctly were similar between the two study populations. The BDES reported a mean decrease of -5.4 (SD=12.5) and -7.1 (SD=13.7) in right and left eyes respectively over 15 years, compared to the corresponding mean decreases of -6.9 (SD=13.6) and -6.8 (SD=13.3) letters for the two eyes, respectively, in our study. However, the cumulative incidence of VI accounting for the competing risk of death was substantially higher in the BDES than the BMES across all age groups (**Table 3.4)**.

The overall mortality rate was substantially higher in our study sample (43.6%) compared to the BDES (29.8%). Competing risk of death may partially explain the discrepancies in VI incidences between the two studies as the BDES had a younger population at baseline. Without adjusting for the competing risk of death in the analysis, the cumulative incidence of VI in our population changed from 6.4% to 9.6%, which is similar to the estimates from the BDES population (11.1%).

Overall doubling and halving of the visual angles were also similar between the two studies: doubling of the visual angle occurred in 6.9% and 7.2%, and halving of the visual angle occurred in 1.6% and 1.9%in the BMES and the BDES, respectively.

A number of longitudinal studies have examined long-term changes in vision in older persons. The Barbados Eye Study (BES)[83] reported 9-year incidence data from a predominately African American population aged 40 to 84 years at baseline, using the same VI definitions as the BDES[14]. The BES found a slightly higher incidence rate of VI, but double the incidence of blindness (6.4% and 2.1%, respectively) compared to our study estimates, albeit over a shorter follow-up period than our study follow-up period. Using World Health Organisation definitions (VA <6/21 in the better eye for VI, and VA <6/120 for blindness), two population-based longitudinal studies in Italy reported VI incidence data among adults. The Ponza Eye Study[84] reported that12-year incidence of bilateral VI was 3.9%, and bilateral blindness was 0.7% in participants aged 40+ years at baseline. The Priverno Eye Study[82] reported that7-year incidence of bilateral VI was 1.3% and bilateral blindness was 0.2% in participants aged between 45 and 69 years at baseline. Both studies had acceptable follow-up rates of 70.7%[84] and 81.4%[82], respectively.

Our data confirm an inverse relationship between increasing age and worsening VA over the 15-year period. The higher incidence of VI and blindness in the oldest age group is consistent with higher prevalence rates of macular degeneration and cataract[164;165] in this age group. Consistent with previous reports that women were more likely to have VI, both by prevalence[16;21;23] and incidence[14;82], we observed the same sex difference in the long-term incidence of VI and blindness. This is likely due to women having greater longevity than men, the latter having mortality as a competing risk that could have occurred before VI/ blindness developed or was detected at the study follow-up visits[166;167].

The estimated VI and blindness incidences could have been underestimated in our population. Participants who did not return to any of the follow-up visits were almost twice as likely to be current smokers at baseline, compared to participants who attended the 15-year follow-up examinations. Smoking has consistently been documented to be associated with an increased risk of AMD[150;168], the leading cause of blindness in our and other study populations. Participants who did not attend any follow-up examinations (including those who died) after the baseline examination had higher prevalence of VI and blindness at baseline. This could have led to an underestimated incidence of blindness, but should not have affected the estimation of incidence of VI, as these prevalent VI cases were no longer at risk of VI**.**

Of eyes that developed blindness over the 15-year period, late AMD was found to be the primary cause of incident blindness in both the BMES (56.9%) and the BDES (52%). Cataract was found to be the primary cause of blindness in 20.7% of eyes in the BMES and 12% of eyes in the BDES[14].

Vision screening may help detect vision threatening conditions earlier. However, several trials reported that vision screening in older participants (>75 years) did not lead to improvement in vision or vision-related quality of life[138;169].

In summary, our estimated cumulative incidences of VI were lower than those reported from the BDES and BES, while our study samples had a higher mortality rate, a competing risk to VI development. Our study showed that age was strongly associated with the development of VI in this older population, likely due to the increasing prevalence of many common ocular diseases associated with aging. Women were twice as likely as men to develop VI and

blindness, even after adjusting for age, which is likely a result of different age-specific mortality rates between men and women.

Based on the population estimates from the Australian Bureau of Statistics[170] (2006), the U.S. Census Bureau[171] (2000) and the VI incident rates from our data, we estimate the number of older persons aged 50+ years with VI will increase from 480,000 to 1 million in Australia and from 3 million to 18 million in the USA. This translates to an estimated demand for additional 23,000 and 180,000 cataract surgical procedures in the next 15 years in the two countries, respectively, in order to treat unilateral and bilateral new cases of blindness due to cataract.

Section III

Part 1: Long-Term Incidence of Visual Impairment and Associated Factors

Chapter 4: Longitudinal transition rates of Visual Impairment States among Older People

Abstract

Purpose: To estimate transitional probabilities of visual impairment (VI) states in an older Australian cohort.

Methods: Of 3654 baseline participants of the Blue Mountains Eye study, 2334, 1952 and 1149 were re-examined after 5-, 10- and 15-years. VI was defined as presenting visual acuity (VA) in the better eye and was categorised into three states; State 1 (VA ≥ 6/12), State 2 (VA <6/12 but ≥6/24), and State 3 (VA <6/24). Deaths (State 4) were confirmed via data linkage to the Australian National Death Index. Multi-state hidden Markov models were used to estimate the transitional probabilities and average life expectancy associated with each VI state, adjusting for age and sex.

Results: The probability of improving vision from State 2 to State 1 was 0.43, 0.44 and 0.39 at the 5-, 10- and 15-year time points, respectively. The probability of improving vision from State 3 to State 1 was 0.08 at the 5-, and was 0.10 at both 10- and 15-year. The probability of worsening vision from State 1 to 2 and from State 2 to 3 was relatively low, with 0.07 and 0.06 at 5-, 0.07 and 0.03 at 10-, and 0.06 and 0.02 at 15-year, respectively.

Conclusions: In this older Australian cohort aged 50+ years, we found that approximately 40% of those with mild VI improved to normal, and 10% of those with moderate/severe VI improved to normal, reflecting successful outcomes of eye healthcare services for older people.

Background

Traditionally, risk factors associated with vision impairment (VI) are determined with the use of association estimates such as odds ratios or relative risks[10;121;123]. However, the dynamic changes in VI states and the time associated with each state cannot be assessed using traditional regression models.

Multi-State Markov (MSM) model estimates the probability of disease state transitions using information which is usually right censored over the course of the disease. As vision can improve or worsen, it is informative to describe dynamic changes of disease states over time, particularly for conditions that are treatable such as VI.

The purpose of this paper is to illustrate the longitudinal dynamic changes in VI states in an older population-based sample, and estimate the probability of improvement, deterioration and death from each VI state. A better picture of the dynamic changes in VI levels among older persons may also be useful to health policy planning for prevention and services provision.

Specific Methods

Visual Impairment

VI was defined as presenting VA in the better eye and categorised into three states; State 1: No VI, defined as VA ≥ 6/12 (≥39 letters read correctly), State 2: Mild VI, defined as VA <6/12 and ≥6/24 (24-38 letters read correctly), and State 3: Moderate to Severe VI, defined as VA <6/24 (<23 letters read correctly).

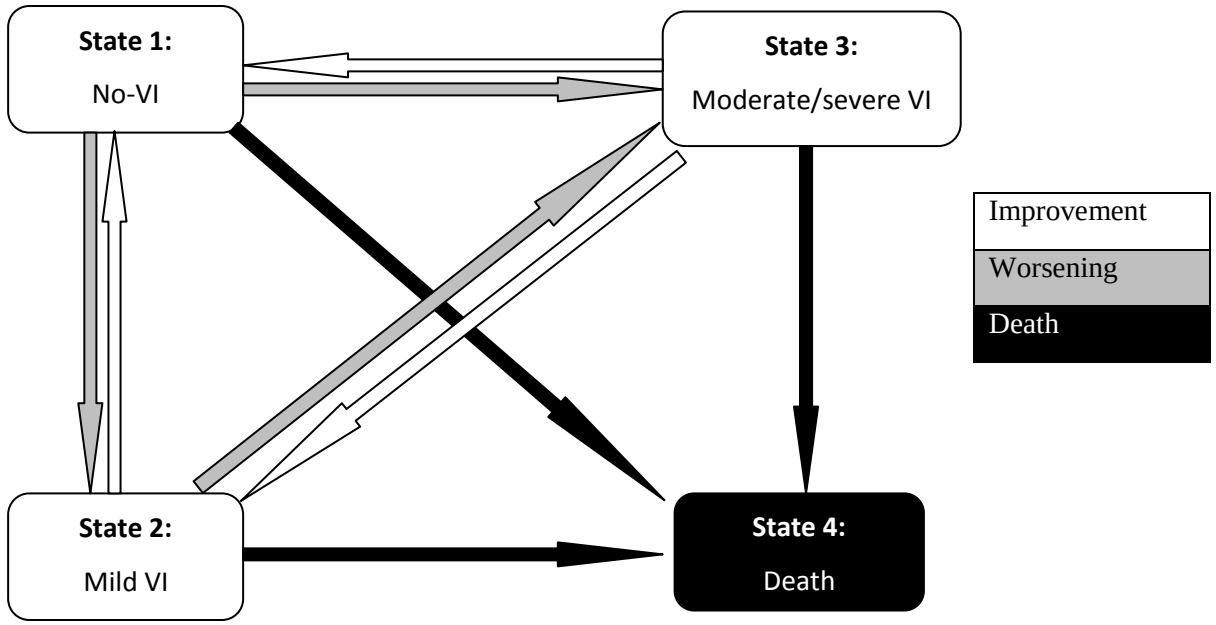
To identify and confirm participants who died (State 4) after the baseline examination, demographic information of the participants were cross-matched with Australian National Death Index (NDI) data for deaths to the end of 2007. Information provided by family members during the follow-up period about any deaths was also included. Date of death and causes of death were also provided by the NDI.

Statistical Analysis

MSM package in R version 2.13.0[161] (R Foundation for Statistical Computing, Vienna, Austria) was used to estimate the probability of transition from one state to another within a specific time period. All models were adjusted for age and sex. Participants were censored if no VA data was available at a follow-up examination. The model was represented by a four state system: no VI (State 1), mild VI (State 2), moderate/severe VI (State 3), and death (State 4). All possible transitions are shown in **Figure 4.1**. Participants in the middle two states could transition to either a better or a worse state. The estimated transition probability matrix P(t) within a given time (5-, 10- and 15-years) was extracted using the function "pmatrix.msm".

Simple statistics included chi-squared (χ^2) test to compare proportions of categorical variables, and a p value of less than 0.05 was considered statistically significant.

Figure 4.1: A matrix of Multi-state Markov model depicting possible transitions between different states of vision impairment (VI) and death.



Rectangular boxes represent the four states and the arrows represent transitional directions between different states. Transitions could occur in both directions for states of mild VI and moderate/severe VI. The three colours (white, grey and black) for arrows and oval boxes represent transition to better, worse VI state or death, respectively.

Results

Of the 3654 baseline participants, 1606 had died by the 15-year follow-up examination. At baseline, 334 of the 3654 (9.2%) had mild VI and 69 (1.9%) had moderate/severe VI. Of the 2334 and 1952 participants who attended the 5- and 10-year follow-up visits, 194 (8.4%) and 175 (9.8%) had mild VI, and 40 (1.7%) and 41 (2.3%) had moderate/severe VI in their better eyes, respectively, at the 5- and 10-year follow-up time points. Of the 1149 participants who attended the 15-year follow-up examination, 86 (8.1%) had mild VI and 36 (3.4%) had moderate/severe VI at the 15-year follow-up time point. The mean follow-up time of this cohort was 15.6±0.6 years. **Table 4.1** presents the distributions of participants by VI state and by sex at baseline and each follow-up examination time point. Women were consistently found to have a higher prevalence of moderate to severe VI compared to men at all examination time points.

Table 4.1: Distribution of visual impairment (VI) level by gender at each examination time point

Visual Impairment level	All n (%)	Women n (%)	Men n (%)	P value
Baseline				
None	3246 (89.0)	1824 (88.2)	1422 (90.0)	0.08
Mild	334 (9.2)	198 (9.6)	136 (8.6)	0.32
Moderate/severe	69 (1.9)	47 (2.3)	22 (1.4)	0.05
5-year follow-up				
None	2085 (89.9)	1182 (88.5)	903 (91.9)	<0.01
Mild	194 (8.4)	125 (9.4)	69 (7.0)	0.04
Moderate/severe	40 (1.7)	29 (2.2)	11 (1.1)	0.05
10-year follow-up				
None	1570 (87.9)	910 (86.3)	660 (90.2)	0.01
Mild	175 (9.8)	111 (10.5)	64 (8.7)	0.21
Moderate/severe	41 (2.3)	33 (3.1)	8 (1.1)	<0.01
15-year follow-up				
None	940 (88.5)	535 (87.1)	405 (90.4)	0.10
Mild	86 (8.1)	52 (8.5)	34 (7.6)	0.60
Moderate/severe	36 (3.4)	27 (4.4)	9 (2.0)	0.03

Table 4.2 presents the age and sex adjusted projected probability of possible transitions between states at 5-, 10- and 15-years using data from observed states at prior and a specific follow-up visit. After age- and sex-adjustment, the probability of a participant with mild VI at baseline improving to no VI was approximately 40% (43%, 44%, and 39% at 5-, 10- and 15-year time points, respectively). The probability of a participant with moderate/severe VI at baseline improving to no VI was approximately 10% (8%, 10%, and 10% at 5-, 10- and 15-year time points, respectively).

The probability of a participant with no VI at baseline worsening to mild VI was about 7% (7%, 7% and 6%, respectively, at 5-, 10- and 15-year time points, respectively). Similarly, there was a low probability of a participant with mild VI at baseline worsening vision to moderate/severe VI (6%, 3% and 2%, respectively, at 5-, 10- and 15-year time points, respectively).

The probability of death among participants with moderate/severe VI at baseline was between 64-87% (64%, 81%, and 87% at 5-, 10- and 15-year time points, respectively). The probability of death among participants with no VI at baseline was between 13-36% (13%, 25%, and 36%, at 5-, 10- and 15-year time points, respectively), after adjusting for age and sex (**Table 4.2)**. **Figure 4.2** presents the goodness of fit of the MSM models by comparing the observed and expected proportions in each state after adjusting for age and gender. The predicted number of participants who died is under-estimated by the model after about 10 years. Similarly, the number of participants without VI is over-estimated after approximately 10 years.

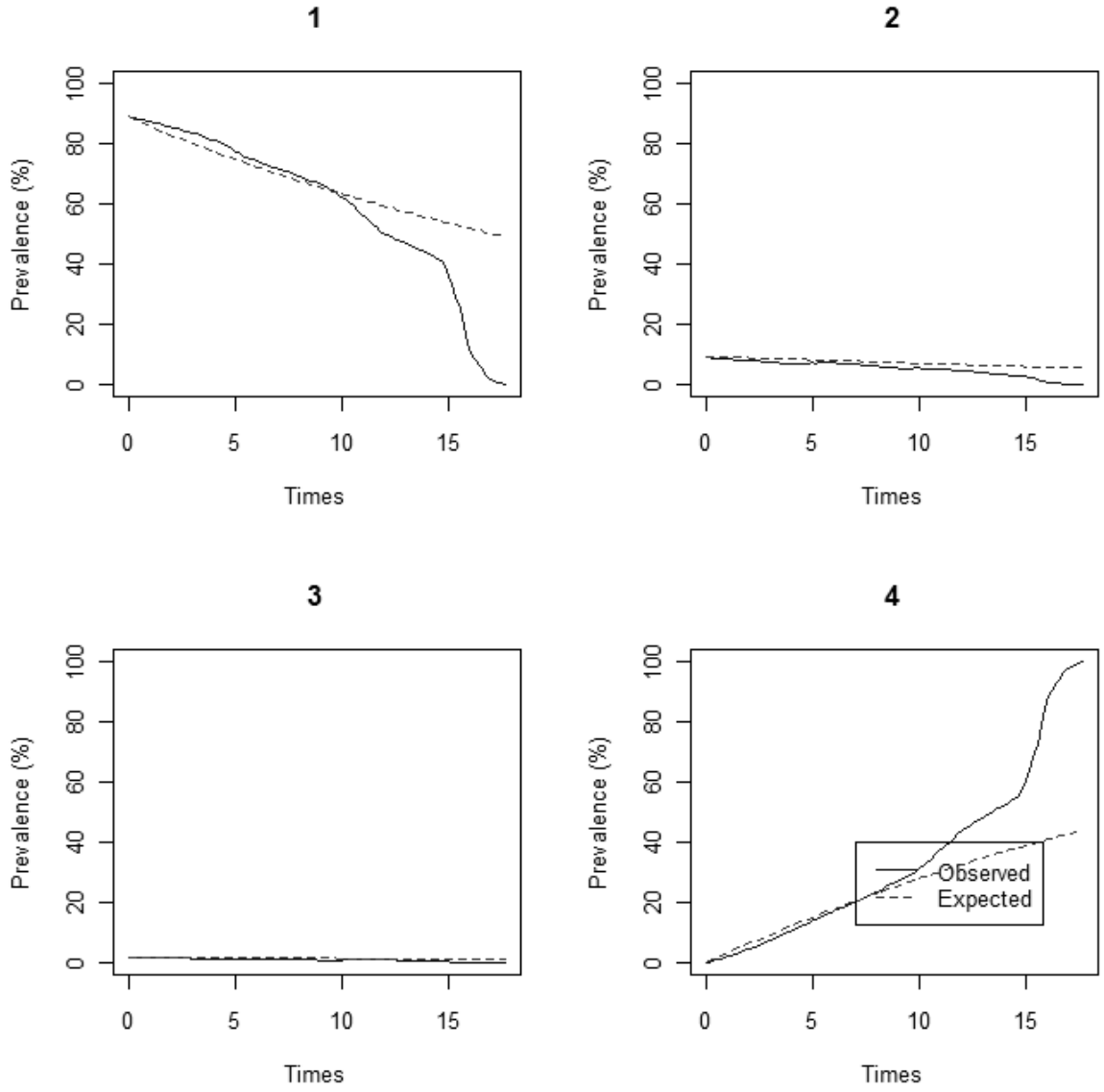
Table 4.2: Age and sex adjusted projected probabilities[*] of possible transitions between visual impairment states and death (at 5-year, 10-year and 15-year time points) shown in separated panels.

Estimated transitional probabilities at 5 year time point				
	Status at BMES[†] II			
VI status at baseline	**No VI**	**Mild VI**	**Moderate/ severe VI**	**Death**
No VI	0.80	0.07	0.01	0.13
Mild VI	0.43	0.22	0.06	0.29
Moderate/severe VI	0.08	0.07	0.22	0.64
Estimated transitional probabilities at 10 year time point				
	Status at BMES[†] III			
VI status at baseline	**No VI**	**Mild VI**	**Moderate/ severe VI**	**Death**
No VI	0.67	0.07	0.01	0.25
Mild VI	0.44	0.08	0.03	0.45
Moderate/severe VI	0.10	0.03	0.05	0.81
Estimated transitional probabilities at 15 year time point				
	Status at BMES[†] IV			
VI status at baseline	**No VI**	**Mild VI**	**Moderate/ severe VI**	**Death**
No VI	0.56	0.06	0.01	0.36
Mild VI	0.39	0.05	0.02	0.55
Moderate/severe VI	0.10	0.02	0.02	0.87

[*]Maximum likelihood estimates used data from observed states (e.g. the projected probability of transitions at 10-years used data from observed states at the 5- and 10-year follow-up visits).

[†]Blue Mountains Eye Study

Figure 4.2: Estimated goodness of fit of a multi-state model. Observed numbers of individuals occupying a state at a series of time plotted against forecasts from the fitted model for each state.



State 1 = no visual impairment

State 2 = mild visual impairment

State 3 = moderate/severe visual impairment

State 4 = Death

Discussion

The MSM model provides perspective estimates for changes in VI states of this older Australian cohort. We found a low probability of worsening vision (approximately 7%) over a 15-year period, and a moderate probability of improving vision from mild VI to no VI (around 40%), reflecting the outcome of eye health care interventions among older people with VI. We also found a relatively high probability of death (64-87%) among participants with moderate to severe VI compared to those with no VI (13%-36%) over the 15-year period.

Previously, other large population studies have reported between 1 and 16% incidence of worsening vision (<6/12) up to a period of 20 years [14;24;68;72;79;84;87;162]. Our findings of approximately 7% probability of worsening vision from either no VI or mild VI after controlling for the effect of age and sex are in keeping with these previous findings.

The moderate (40%) probability of an improvement in vision from mild VI to no VI is likely the results of multiple reasons. The most likely explanations are cataract surgery, posterior sub-capsular opacity laser treatment and correction of refractive errors. This finding suggests that earlier interventions and rehabilitation of mild VI is in place and effective in Australia. The probability of improvement from moderate/severe VI to no VI was about 10%, which could partly be due to the fact that treatments for causes of moderate/severe VI other than cataract and refractive errors may not be effective in vision restoration at the time of this study, due to the nature of the underlying disease (e.g. late stage AMD and diabetic retinopathy). This reinforces the benefit of earlier interventions and prevention of VI among older persons40626, 45612].

Previous reports have found that the more severe the level of VI, the higher the risk of death after adjusting for other known risk factors associated with mortality[172;173]. We found a high probability (up to 87%) of death among participants with moderate/severe VI over the 15-year period, after adjusting for age and sex. Other co morbidities associated with moderate/severe VI might contribute to this observation, including low self-rated health, frailty, falls, depression and dementia[174-177]. Many causes of VI are also associated with other systemic conditions that are associated with increased mortality, including diabetes, cardiovascular disease, and inflammatory conditions such as arthritis[178-186].

Previous studies using pathway analysis (structural equation modelling) found that VI was both directly and indirectly associated with mortality after adjusting for other co-morbidities[128;187]. Due to small numbers of participants with moderate/severe VI in our cohort sample, we could not adjust for more co-variables in the MSM model. Therefore the probabilities of death derived from our age-and sex-adjusted MSM model could be confounded by other co-morbidities, and should be interpreted with caution.

In summary, among older persons with mild visual impairment, there was approximately 40% probability of improving to no VI, and among those with moderate/severe VI, 10% probability of improving to no VI, over the course of 15 years. The estimated projected probabilities of transitions between VI states were relatively stable over the three time points. These data provide a picture of dynamic changes in terms of visual impairment states among older people. Regular eye health care services to detect and treat causes of visual impairment may help prevent further deterioration of visual disorders and maximize the probability of having good vision and good quality of life at older ages.

Section III

Part 1: Long-Term Incidence of Visual Impairment and Associated Factors

Chapter 5: Adherence to Australian Dietary Guidelines and the 10-year Cumulative Incidence of Visual Impairment

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Material in this Chapter has been published in

Hong T, Flood V, Rochtchina E, Mitchell P, Russell J, Wang JJ. *Adherence to dietary guidelines and the 10-year cumulative incidence of visual impairment: the Blue Mountains eye study.*

American Journal of Ophthalmology. 2014 Aug;158(2):302-8.

Abstract

Purpose: To assess whether adherence to dietary guidelines at baseline is associated with the incidence of visual impairment among older persons after 10 years.

Methods: A population-based cohort of 3654 participants of the Blue Mountains Eye Study were examined at baseline, and re-examined after 5- and 10-years. The incidence of visual impairment (VI) was defined as best corrected visual acuity (VA) <6/12 at follow-up in one or both eyes. Dietary information was obtained at baseline using a validated food frequency questionnaire (FFQ). Total Diet Scores (TDS) were calculated based on the Australian diet quality index. TDS includes components of diet quality; poor dietary habits; and energy balance. Discrete logistic regression models with time-dependent outcome variables were used to calculate hazard risk ratios (HR) and 95% confidence intervals (CI) associated with incidence of VI for each unit/quartile increase in TDS, adjusting for potential confounders.

Results: Of the 3654 baseline participants, 1963 had up to 10 years follow-up with completed FFQs. With each unit increase in TDS, the risk of VI decreased (HR 0.94, 95%CI 0.88-1.00). The risk of developing VI was lower among participants in the highest compared to the lowest TDS quartile (HR 0.71, 95%CI 0.47-1.05). This association was significant among participants aged 65+years (HR 0.63, 95%CI 0.38-0.98) but not those aged <65 years (HR 0.95, 95%CI 0.46-1.97).

Conclusions: Compliance to dietary guidelines was associated with a decreased long-term risk of VI in this sample of Australians aged 65+years.

Background

Different dietary guidelines and diet quality indices exist worldwide and vary according to different populations and diseases. The two most frequently used diet quality assessment tools are the Healthy Eating index [188] and the Diet Quality Index[189]. An unhealthy diet and lifestyle that includes a high consumption of fat, sugar, salt, alcohol and smoking can accelerate aging and degenerative processes via increased oxidative stress, which may contribute to the development of cataract and age-related macular degeneration (AMD), the two main causes of VI and blindness in older people worldwide [190-194]. However, to our knowledge, the association between overall diet quality and all cause VI has not been reported previously.

This study aimed to investigate longitudinal associations between baseline diet quality, indicated by adherence to the Dietary Guidelines for Australian Adults [195], and the 10-year incidence of VI in the Blue Mountains Eye Study cohort.

Specific Methods

Visual impairment definitions have been described previously in **chapter 2**, page 67. VA used in this chapter refers to the best-corrected acuity after subjective refraction.

Dietary assessment

The Total Diet Score (TDS) was developed based on a modified version of the Australian diet quality index [196] **(Table 5.1)**, to assess adherence to the Dietary Guidelines for Australian Adults[195], and the Australian Guide to Healthy Eating[197]. Development details of the total diet score have been published previously [198]. Briefly, the total diet score is divided into 10 components with a possible score of 0 to 2 per component. For example, a person who consumed fruit and vegetables more frequently, including a moderate variety of vegetables, scored a maximum score of 2 for this component. The dietary components of the total diet score considered intakes from the core food groups (vegetables, legumes and fruit; cereals; meat, and meat alternatives; milk, yogurt and cheese) and optimal food choices as recommended by the Australian Guide to Healthy Eating (whole grain cereals, lean red meat, low or reduced fat milk, low saturated fat intake, fish consumption as well as lower intakes of sodium, alcohol, sugar and extra foods that do not provide essential nutrients the body needs, e.g. energy dense nutrient poor foods (foods with high levels of fat, salt and sugar)). The recommended serves for each food group were taken from the Australian Guide to Healthy Eating[197] with some exceptions, for example, 2 serves of fruit per day were replaced with 3 serves per day and 5 serves of vegetables per day replaced with 7 serves per day to adjust for self-reported overestimation, as suggested by a previous study [155].

The non-dietary Australian Guide to Healthy Eating recommendation for preventing weight gain was also included as 1 of the 10 total diet score components. Half of this component was assigned to energy balance (the ratio of energy intake to energy expenditure) and the remaining half to leisure time physical activity. Physical activity levels were self-reported using questions from the Australian National Heart Foundation Risk Factor Prevalence Surveys (Risk Factor Prevalence Study Management Committee 1989)[199]. Walking, moderate

or vigorous activities were scored as Metabolic Equivalents as described by Craig et al [200]and divided into tertiles.

The sum of scores from the ten components was calculated for each person, with a maximum score of 20. Higher scores indicated greater adherence to the dietary guidelines.

Table 5.1: Total Diet scoring system based on the Australian Healthy Eating Guide.

Dietary guideline/ component	Score	Component subscore		Total score
1. Eat plenty of vegetables, legumes and fruit	Total vegetable serves/day	7 serves	0.5	2
		5·6 serves	0·4	
		4·2 serves	0·3	
		2·8 serves	0·2	
		1·4 serves	0·1	
	Vegetable variety score/day	≥1 serve green	0·1	
		≥1 serve orange	0·1	
		≥1 serve of cruciferous	0·1	
		≥1 serve of tuber or bulb	0·1	
		≥0·5 serves of legumes	0·1	
	Total fruit serves/day	3 serves	1	
		2 serves	0·5	
2. Eat plenty of cereals, preferably whole grain/meal	Total cereals serves/day			2
	Women	4 serves	1	
		3 serves	0·75	
		2 serves	0·5	
		1 serve	0·25	
	Men	6 serves	1	
		5 serves	0·83	
		4 serves	0·66	
		3 serves	0·5	
		2 serves	0·33	
		1 serve		
	Whole-grain cereal serves/day	0·166		
	Women	4 serves	1	
		3 serves	0·75	
		2 serves	0·5	
		1 serve		
	Men	0·25		
		6 serves	1	
		5 serves	0·83	
		4 serves	0·66	
		3 serves	0·5	
		2 serves	0·33	
		1 serve		
		0·166		
3. Include lean meats, fish, poultry and/or alternatives	Meat/alternative/day	≥1 serve	1·5	2
	Lean red meat/week (i.e. > 0·428/day)	≥3 serves	0·5	
4. Include milk, yoghurts, cheese and/or alternatives	Total dairy serves/day	≥2–3 serves	1·5	2
		≥3–4 serves	1·0	
		1–<2 serves	1·0	
		>4 serves	0·5	
		0–<1 serves	0	
	Ratio of skimmed/low fat (S/LF) intake: whole milk intake	S/LF>whole milk	0·5	
		S/LF=whole milk		
		0·25		
		Whole milk>S/LF	0	
5. Limit saturated fat and Moderate total fat intake	Percentage of energy from saturated fat	<10% energy	1	2
		10–12% energy	0·5	
		>12% energy	0	
	Fish serves/week	≥ 2 serves	1	
		1–<2 serves	0·5	
		<1 serve	0	

6. Choose foods low in salt	Na intake/day	≤ 40 mmol (920 mg) 2 > 40–≤100 mmol (920–2300 mg) 1 >100 mmol (2300 mg) 0	2
7. Limit alcohol intake if you choose to drink	Alcohol intake/day Women Men	 ≥0 g–<10 g 2 ≥10 g–<20 g 1 ≥20 g 0 ≥0g–<20 g 2 20 0	2
8. Consume only moderate amounts of sugars and foods with added sugars	Percentage of energy from sugar	<15% total energy 2 ≥15–<20% total energy 1 ≥20% energy 0	2
9. Extra foods, not essential to provide nutrients and maybe high in salt, fat or sugar	Extra food serves/day Women Men	 <2·5 serves 2 2·5–<4 serves 1 >4 serves 0 <3 serves/day 2 3–<5 serves 1 ≥5 serves 0	2
10. Prevent weight gain: be physically active and eat according to energy needs	Ratio of energy intake to energy expenditure Physical activity (METs)	0·76–1·24 1 <0·76 or >1·24 0 Lowest tertile 0 Middle tertile 0·5 Highest tertile 1	2

S/LF: skimmed/low fat, MET: metabolic equivalents

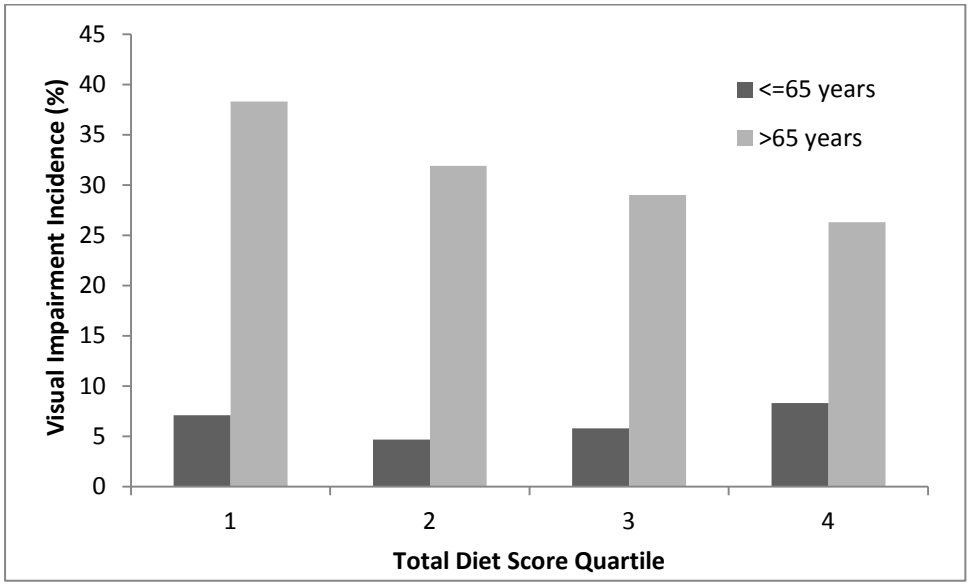
Statistical analysis

SAS 9.2 software (SAS Institute, Cary, NC) was used for statistical analyses. PROC LIFETEST was used to estimate the incidence rate of VI. Both continuous score data (per unit increase) and quartiles of TDS were used as independent variables and incidence of VI or blindness as dependent variables in analyses. Discrete logistic regression models (PROC PHREG) with a time-dependent outcome variable (VI) were used to estimate associations of incident VI or blindness with baseline TDS or TDS quartiles where quartile 1 (the group with the least adherence) of the TDS was the reference level. This model discrete logistic regression) allows the use of time information when VI was detected among participants who had attended one or both follow-up examination (5-year, 10-year follow-up visits).

The detrimental effect of smoking on visual impairing eye diseases such as AMD has been previously been well documented. Participants who smoked were excluded in a supplementary analysis to eliminate the effect of this potential confounder on the association under investigation.

VI has previously been found to be more frequent among participants older than 65 years compared to participants 65 years or younger in this cohort [201]; hence we performed analyses stratified by age group to assess the association between TDS and VI in the two age groups separately **(Figure 5.1)**. Analyses were adjusted for age, sex, history of diabetes or cardiovascular disease, smoking status, education and home ownership. The associations are presented as hazard risk ratios (HR) with 95% confidence intervals (CI).

Figure 5.1: 10-year incidence of visual impairment by quartiles of total diet score and age group



Incidence rates were calculated by Kaplan-Meier estimates

Results

Of the 3654 baseline participants, the food frequency questionnaire was attempted and returned by 3267 participants (89.4% response); of these 2897 were suitable for analysis (79.3% of participants). Among these participants, 1963 (67.8%) had been followed at the 10-year follow-up examination and thus were included in this report.

The baseline characteristics of participants who attended the 10-year follow-up examination compared to those who did not present to follow-up examinations are presented in **Table 5.2**. Participants who attended the 10-year follow-up examination were more likely to be female, and to have a younger age and a higher total diet score compared to participants who did not attend any follow-up visits.

Table 5.2: Baseline characteristics of participants and non-participants of the 10-year follow-up examination of the Blue Mountains Eye Study

	Participants	**Non-participants**	**P value**
Total numbers	1963	934	
Mean total diet score (range)	9.4 (9.3-9.5)	9.0 (8.9-9.1)	<0.001
Mean age in years (SD[*])	63.4 (63.1-63.8)	69.4 (68.7-70.1)	<0.001
Female (%)	57.1	53.5	0.07
Current Smoker (%)	12.6	17.3	<0.001
Tertiary Education (%)	61.8	54.9	<0.001
Married or de facto (%)	69.2	60.2	<0.001
Mean Body Mass Index (SD[a])	26.4 (26.2-26.6)	25.7 (25.4-26.0)	<0.001

[*] *SD=Standard deviation*

Baseline characteristics by quartile of TDS are presented in **Table 5.3.** Baseline total diet score ranged from a minimum score of 3.17 to a maximum of 15.40, out of a possible total score of 20**.** Women, non-smoking participants, and those reporting tertiary education had a higher mean total diet score.

Cross-sectional analysis of baseline data showed that each unit increase in baseline total diet score was non-significantly associated with a lower prevalence of VI (adjusted HR 0.96, 95% CI 0.90-1.02). Participants in the highest TDS quartile had a non-significant lower prevalence of VI compared to those in the lowest TDS quartile (adjusted HR 0.78, 95% CI 0.53-1.15).

Of the 1963 participants re-examined at the 10-year follow-up, we observed a 6% decrease in the 10-year risk of VI associated with per unit increase in baseline TDS (HR 0.94, 95% CI: 0.88-1.00). Participants in the highest total diet score quartile at baseline had a 29% decreased risk of developing VI compared to those in the lowest quartile, although this difference was not statistically significant (adjusted HR 0.71, 95% CI 0.47-1.05) **(Table 5.3)**. When participants who were current smokers were removed from the analysis, the association remained the same (adjusted HR 0.71, 95% CI 0.44-1.05).

Table 5.3: Baseline characteristics of participants who attended the 10-year follow-up examination of the Blue Mountains Eye Study (2002-2004) by baseline Total Diet Score quartiles

	Quartile 1	**Quartile 2**	**Quartile 3**	**Quartile 4**
Total Number	488	493	495	487
Mean total diet score (range)	6.6 (3.2-7.8)	8.6 (7.8-9.3)	10.1 (9.3-11.0)	12.2 (11.0-15.4)
Mean age, years (SD[*])	62.5 (8.1)	63.8 (8.2)	62.9 (8.1)	64.6 (7.7)
Female (%)	41.4	57.4	59.8	69.8
Any Visual impairment (%)	12.4	11.2	9.0	9.2
Smoking Status (%)				
Current	21.3	13.2	10.3	5.7
Past	41.78	38.1	33.6	32.6
Never	36.9	48.7	56.1	61.8
Tertiary Education (%)	59.2	61.7	62.6	63.8
Marital Status (%)				
Married or de facto	67.2	70.0	72.9	66.9
Divorced or Separated	13.8	10.1	11.7	11.9
Widowed	10.5	13.0	9.1	13.8
Never Married	8.6	6.9	6.3	7.4
Mean BMI[†] mean (SD[a])	26.4 (4.4)	26.7 (5.6)	26.6 (4.3)	25.9 (4.2)

[*] Standard deviation
[†] BMI = body mass index

When analyses were conducted in subgroups of participants stratified by age ≤65 and >65 years, we found that the reduced risk of VI associated with the highest TDS quartile, compared to the lowest quartile, was significant among participants aged >65 years (HR 0.61 95% CI 0.38-0.98) but not among those aged ≤65 years (HR 0.97, 95% CI 0.41-1.97) **(Table 5.4)**. When total diet score data were analysed continuously, the same association pattern was evident in the older aged group only (HR 0.92, 95% CI 0.85-0.99 per unit increase) but not in the younger group (HR 0.98, 95% CI 0.86-1.12 per unit increase). When participants who were current smokers were excluded, the association estimates were HR 0.93, 95% CI 0.86-1.01 per unit increase in the older age group and HR 0.97, 95% CI 0.84-1.11 per unit increase in the younger age group. We did not observe any significant associations between TDS and the incidence of blindness, either as a continuous (HR 0.97, 95% CI 0.83-1.14 per unit increase) or categorical variable (HR 0.71, 95% CI 0.27-1.83, highest versus lowest quartile).

Table 5.4: Associations between total diet score and the 10-year cumulative incidence of visual impairment

	n	Hazard Ratio*	95% CI	P value
All				
Quartile 1	88	1.0	-	-
Quartile 2	82	0.73	0.49-1.08	0.11
Quartile 3	78	0.69	0.46-1.03	0.07
Quartile 4	86	0.71	0.47-1.05	0.09
Per unit increase in TDS†		0.94	0.88-1.00	0.05
≤65 years				
Quartile 1	33	1.0	-	-
Quartile 2	24	0.60	0.27-1.35	0.21
Quartile 3	26	0.79	0.38-1.66	0.53
Quartile 4	32	0.95	0.46-1.97	0.89
Per unit increase in TDS[b]		0.98	0.86-1.12	0.79
>65 years				
Quartile 1	55	1.0	-	-
Quartile 2	58	0.75	0.47-1.19	0.22
Quartile 3	52	0.65	0.4-1.06	0.08
Quartile 4	54	0.61	0.38-0.98	0.04
Per unit increase in TDS[b]		0.92	0.85-0.99	0.03

Quartile 1 (TDS 3.2-7.8), Quartile 2 (TDS 7.8-9.3), Quartile 3 (TDS 9.3-11.0), Quartile 4 (TDS 11.0-15.4).

* Adjusted for age, sex, education, home ownership, smoking status, cardiovascular disease and diabetes

† TDS – Total Diet Score

Discussion

In an older Australian cohort followed over a decade, we documented that higher levels of adherence to dietary guidelines, indicating higher scores of diet quality and a healthy lifestyle, was associated with a nearly 40% reduction (95% CI 2%-62%) in the long-term risk of VI among participants aged 65+ years, independent of known VI risk factors including smoking, education and diabetes. These findings suggest the long-term benefits of higher diet quality to vision and the eye.

The associations between overall diet quality and specific eye conditions have been previously reported with different dietary scores; however it has not been assessed for association with incidence of VI. Mares et al [202;203] found that a higher Healthy Eating Index score (highest vs. lowest quintile) had a 40% reduced risk of cataract and up to a 70% reduced risk of AMD over a follow-up period of 6-7 years in a cohort of women aged 50 to 79 years of age. Both cataract and AMD are the leading causes of VI in older people, including participants of the Blue Mountains Eye Study cohort [34;159;162;204;205].

The associations between specific nutrients and specific eye conditions have also been widely reported. Several studies have found conflicting evidence that the consumption of supplements and foods rich in Vitamin C, Vitamin E, zinc, beta-carotene may lower the risk of incidence and progression of cataract and AMD [206-215]. Both the lens and retina are exposed to high levels of light, oxidative stress and metabolic activity. Lutein and xeazanthin are carotenoids which are highly concentrated in the macular area of the retina. Their roles have been suggested to be beneficial to the eye as they can filter blue light and have antioxidant properties and have been also been found to be associated with lower risk of cataract and AMD [216].

The long-term detrimental effects of low diet quality and unhealthy lifestyle may not manifest till later in life, when chronic conditions such as cardiovascular disease and diabetes are frequent, so that VI can be an additional burden to the quality of life of the affected individuals [217]. The associations between diabetes and cardiovascular disease with frequent age-related eye diseases such as macular degeneration and cataract [218-220] may partially explain some of the long-term associations we found between diet quality incident VI.

An overall diet quality score rather than a specific food or nutrient focused approach allows for the effects of both beneficial and detrimental foods to be considered together, including nutrient interactions with other nutrients, drugs and environment [221-225]. A review by Lien and Hammond [226] highlighted the importance of these complex interactions and the vulnerability of the visual system. If the benefits of nutritional intervention were shown to reduce risk of VI and eye disease, it is plausible that by maintaining a healthier lifestyle, including adherence to recommended dietary guidelines earlier in life, could incur greater benefit later in life reducing the incidence of VI.

Consistent with the design of the total diet score, people who had higher diet quality scores, consumed more vegetables (excluding potatoes), fresh fruit, wholegrain cereals, fish, lean red meat and low fat dairy products [198], confirming that the consumption of a variety of healthy foods that provide good sources of a range of nutrients, contribute to an overall healthy diet, consistent with dietary guidelines for Australians. The total diet score has been used previously to report associations between diet and reduced risk of incident kidney disease, pre-diabetes and all cause mortality [198;227;228]. It has also been reported that a higher diet quality assessed with the TDS was associated with a better quality of life and functional ability [229].

Strengths of our study include its large population-based sample with reasonable follow-up rates and standardized methods to assess VA. We have specified incidence duration and a clear temporal relationship with the use of longitudinal data. Limitations include the inability to adjust for all confounding variables that may influence diet quality. Many factors may affect diet quality including age, education, stress, familial and financial status [230]. Keller et al [231] found that the most important non-biological factor to affected diet quality was income. Participants with healthier diets may also be more likely to be health conscious and exercise more regularly to benefit the heart and other organs of the body in general. The use of the FFQ may under- or over-estimate certain nutrient or food groups [155]. Another limitation is survival bias; participants who were unable or refused to attend the follow-up visits, or who had died, could more likely have had co-morbid conditions including VI and also more likely to have poorer diet quality. Such bias could have reduced the magnitude of the association observed. Last, the total diet score or dietary behaviour could have changed over the 10-year period, in particular, it could have been influenced by the disease (including VI) diagnosis [232], we therefore decided to use only baseline TDS to avoid such indication bias.

In conclusion, in an older population-based cohort of Australians, we documented a possible long-term benefit on vision from higher diet quality, indicated by adherence to published dietary guidelines. Further research on diet and health outcomes including vision and ocular diseases is merited; given that dietary consumption is the most frequent, lifetime, but modifiable environmental exposure that affects health directly in the longer term.

Section III

Part 2: The Impact and Burdens of Visual Impairment

Chapter 6: Visual Impairment and Subsequent use of Support Services among Older People

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Material in this Chapter has been published in

Hong T, Mitchell P, Burlutsky G, Fong CS, Rochtchina E, Wang JJ. *Visual impairment and subsequent use of support services among older people: longitudinal findings from the Blue Mountains Eye Study.*

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Abstract

Purpose: To assess the impact of visual impairment and blindness on the incident use of community support services in the Blue Mountains Eye Study.

Methods: Of 3654 baseline participants (1992-94), 2334, 1952 and 1149 were re-examined after 5, 10 and 15 years, respectively. Incident VI was defined as subsequent development of VI (VA <6/12) in the better eye of subjects with best-corrected VA ≥6/12 at baseline. Community support service use included regular use of Meals on Wheels, Home Care or community nurse services. Informal support included assistance from family or friends. Discrete logistic regression models with time-dependent study and outcome variables were used to assess associations between VI and subsequent use of support, adjusted for potential confounders.

Results: Among participants with bilateral VI at baseline, incident use of community services over 5-15 years was 41.7% compared to 19.4% in those without VI at baseline (odds ratio, OR, 1.39, 95% confidence interval, CI, 0.54-3.60). Participants with incident bilateral VI were more likely to subsequently need community support (OR 3.32, CI 1.96-5.59) in 5 years, compared to participants without VI during the entire follow-up period. Baseline older age, walking disability, receiving pension and having 2+ hospital admissions within 12 months, were also significantly associated with incident use of support services.

Conclusions: Development of bilateral VI in this cohort was associated with greater likelihood of subsequent use of community or informal support services in five years, independent of physical co-morbidities.

Background

Government-funded community support services such as the Home and Community Care program [233] in Australia and the Home and Community-Based Services in the United States[234] are designed to assist older people with disabilities living at home. These programs support and preserve these older people's ability to live independently, maintain their quality of life and minimize the number of people being admitted to long-term residential care. Some of the services provided under the Home and Community Care program include; Home Care (personal care, domestic assistance, home maintenance), nursing care, meal delivery (Meals on Wheels) and transport. This is becoming increasingly important given the aging population.

Previously documented significant associations between the presence of visual impairment and the use of community support services have principally been observed in cross-sectional studies[38;57;58]. There has been no evidence from longitudinal data supporting such associations. In this report, we aimed to determine the impact of visual impairment (including its severity and duration) on the subsequent use of community support services over a period of 15 years in a population-based cohort of older Australians, the Blue Mountains Eye Study (BMES).

Specific Methods

Visual impairment

Visual impairment definitions have been described previously in **chapter 2**, page 67. VA used in this chapter refers to the best-corrected acuity after subjective refraction.

Use of Community and Informal Support Services

The use of community support services (formal support services) was defined as the regular use of one or more of the three services: Meals on Wheels, Home Care or regular home visits by a community nurse[235]. The use of informal support was defined as receiving assistance from either family members or friends for house cleaning or shopping. Participants using community support services and those using informal support were mutually excluded from the other category. The ability to go out alone was assessed separately. Incidence of the use of these support services was defined as occurring in participants who did not report using such services in the previous examination but did so at a later follow-up visit.

Statistical analysis

SAS 9.2 software (SAS Institute, Cary, NC) was used for statistical analyses. Discrete logistic regression models (PROC PHREG) with time-dependent study (VI) and outcome (formal or informal support use) variables were used to assess associations between VI and subsequent use of support services. Participants with incident VI detected at the 5- and 10-year follow-up visits were assessed for subsequent uptake of support services at the next follow-up visit with a 5-year interval.

Logistic regression models (PROC LOGISTIC) were used to assess the associations between incident VI detected at the 5-year follow-up and subsequent uptake of support services after 10 years (at the 15-year follow-up). All reported longitudinal associations were adjusted for baseline age and sex. These associations were also adjusted for the presence of a walking disability, home ownership, living arrangements, holding a pension, self-rated health, having ≥2 co-morbidities (angina, acute myocardial infarct, stroke, arthritis, hypertension and/or diabetes) at the time when VI was detected, and having hospital admissions in the 12 month period prior to the visit when VI was detected. Odds ratios (OR) and 95% confidence intervals (CI) are presented.

Results

Incidence of taking up formal and informal support services in the Blue Mountains Eye Study cohort

Of 3022 participants not already using formal support services at baseline the incidence of new community support service use over the 5-15 year period was 12.8%. Of 2239 participants not already using informal support at baseline the incidence of new reliance on support from family members and friends over the 5-15 year period was 53.6%. Older participants were more likely to use any support service regardless of VI status. Overall, the incidence of reporting inability to go out alone over the 5-15 year period was 6.9%.

Baseline visual impairment and subsequent use of support services

Of 3654 participants at baseline, 131 (4%) were found to have bilateral VI at baseline. Among participants with bilateral VI who had not used support services at baseline (n=85), the incidence of new use of community support services over the 5-15 year period was

41.7%, compared to 19.4% in those without VI at baseline (adjusted OR 1.39, 95% CI 0.54-3.60). Among participants with bilateral VI who did not rely on informal support at baseline, (n=59) the incidence of new use of informal support over the 5-15 year period was 61.9% in participants with bilateral VI compared to 31.6% in those without VI at baseline (adjusted OR 2.96, 95% CI 1.16-7.59). However, the new use of formal or informal support services was not significantly associated with unilateral visual impairment, any VI or any blindness (data not shown).

Incident visual impairment and subsequent use of support services

Of the 3523 participants without VI at baseline, 73 developed bilateral VI and 294 developed unilateral VI at any follow-up visit (after 5-, 10- or 15-years). Due to the small number of participants with incident bilateral blindness at follow-up visits, bilateral and unilateral blindness were grouped together as any blindness, and occurred in 69 participants over the 15-year period. **Table 6.1** shows baseline characteristics of participants with incident unilateral and bilateral VI detected at any follow-up visit and participants without VI over the entire follow-up period. Participants with any incident VI were more likely to be older, to receive a pension, to live alone, have a walking disability, have 2+ chronic conditions at baseline, and also to have had 2+ hospital admissions in the 12 month period prior to the baseline examination.

Table 6.1: Baseline characteristics of participants without visual impairment and participants with incident unilateral and bilateral visual impairment at any follow-up examination among older participants in the Blue Mountains Eye Study

Characteristic	No Visual Impairment (%) N=3179	Unilateral Visual Impairment (%) N=328	Adjusted P value*	Bilateral Visual Impairment (%) N=131	Adjusted P value*
Age at baseline (years) ± SD	64.8 ± 9.0	73.7 ± 9.4	<0.01	80.8 ± 9.1	<0.01
Male	43.7	44.2	0.87	29.8	<0.01
Home ownership	89.1	86.6	0.18	82.4	0.02
Receiving pension	55.1	80.9	<0.01	89.8	<0.01
Living alone	25.8	36.1	<0.01	47.3	<0.01
Walking disability	5.3	15.6	<0.01	33.9	<0.01
Chronic conditions (≥2)	16.3	25.6	<0.01	30.0	<0.01
Hospital admissions (≥2)‡	21.3	30.5	<0.01	38.2	<0.01

* Adjusted for age, sex, home ownership, pension, living status, walking disability, chronic conditions (diabetes, hypertension, arthritis, history of stroke or heart disease) and hospital admissions
‡ Within 12 months prior to baseline examination

SD = standard deviation

Of 442 participants who became new (incident) regular users of community support services over the follow-up period, bilateral VI was present in 5.7%. Of 1303 participants who became newly reliant on informal support over the follow-up period, bilateral VI was present in 2.4%. These proportions compare to 1.3% and 1.4%, among those who did not use any formal or informal support, respectively.

Of 73 participants with incident bilateral visual impairment, 46.0% became new regular users of community support services and 25.9% became reliant on informal support. These compare to 9.1% and 29.2% for formal and informal support, respectively, among subjects who did not have any VI over the follow-up period. Participants with incident bilateral (OR 3.32, 95% CI 1.96-5.59) or unilateral (OR 1.77 95% CI 1.21-2.60) VI during the follow-up period were subsequently more likely to become regular users of community support services within 5 years, compared to people without any VI over the entire follow-up period, after adjustment for age, sex, home ownership, and whether they lived alone, received a pension, had a walking disability, self-rated health, had a hospital admission in the last 12 months, or had 2 or more co-morbidities (diabetes, hypertension, arthritis, history of stroke or heart disease). However, those with incident VI were not significantly more likely to rely on family or friends for informal help in daily tasks within 5 years (OR 1.79 95% CI 0.70-4.55 for bilateral and OR 1.60 95% CI 0.92-2.80 for unilateral incident visual impairment). Incidence of any (bilateral or unilateral) blindness was significantly associated with an increased risk of subsequently taking up community support services (OR 2.68, 95% CI 1.48-4.87) and informal support (OR 2.46, 95% CI 0.97-6.27) within 5 years **(Table 6.2)**.

Table 6.2: Associations between incident visual impairment and the incident use of support services after 5 years among older people from the Blue Mountains Eye Study

	Support Service											
	Community				Informal				Community or Informal			
	n (%)	OR*	95% CI	P value	n (%)	OR*	95% CI	P value	n (%)	OR*	95% CI	P value
Visual Impairment												
Bilateral	73 (46.0)	3.32	1.96-5.59	<0.01	27 (25.9)	1.79	0.70-4.55	0.22	50 (60.0)	3.10	1.67-5.78	<0.01
Unilateral	194 (25.8)	1.77	1.21-2.60	<0.01	97 (21.7)	1.60	0.92-2.80	0.10	133 (42.9)	1.92	1.30-2.83	<0.01
Any (bilateral or unilateral)	228 (32.5)	2.39	1.70-3.35	<0.01	105 (25.7)	1.78	1.07-2.97	0.03	158 (50.6)	2.35	1.64-3.37	<0.01
Blindness												
Any (bilateral or unilateral)	59 (39.0)	2.68	1.48-4.87	<0.01	23 (34.8)	2.46	0.97-6.27	0.06	41(63.4)	3.71	1.88-7.31	<0.01

* Adjusted for age, sex, home ownership, pension, living status, walking disability, self-rated health, chronic conditions (diabetes, hypertension, arthritis, history of stroke or heart disease) and hospital admissions in the comparison of proportion of support service use between participants with visual impairment and those with no visual impairment.

However, participants with incident bilateral visual impairment, unilateral VI or blindness detected at the 5-year follow-up visit were not more likely to become regular users of community support after 10 years, at the 15-year follow-up visit (OR 0.19, 95% CI 0.03-1.30; OR 0.93, 95% CI 0.49-1.74 and OR 1.01, 95% CI 0.26-3.86, respectively). These participants were also not more likely to rely on informal support from family or friends either, after 10 years (OR 1.64 95% CI 0.31-8.66 for incident bilateral visual impairment; OR 1.11 95% CI 0.65-2.02 for unilateral VI and OR 2.45 95% CI 0.73-8.17 for any blindness) (**Table 6.3)**.

Table 6.3: Associations between incident visual impairment and the incident use of support services after 10 years among older people from the Blue Mountains Eye Study

	Support Service											
	Community				Informal				Community or Informal			
	%	OR*	95% CI	P value	%	OR*	95% CI	P value	%	OR*	95% CI	P value
Visual Impairment												
Bilateral (N=7)	28.57	0.19	0.03-1.30	0.09	57.14	1.64	0.31-8.66	0.56	57.14	0.65	1.12-3.50	0.61
Unilateral (N=58)	31.03	0.93	0.49-1.74	0.81	39.66	1.11	0.61-2.02	0.73	50.00	1.00	0.56-1.77	0.99
Any (bilateral or unilateral) (N=65)	30.77	0.79	0.43-1.46	0.45	41.54	1.15	0.65-2.02	0.64	50.77	0.95	0.55-1.65	0.86
Blindness												
Any (bilateral or unilateral) (N=13)	38.46	1.01	0.26-3.86	0.99	61.54	2.45	0.73-8.17	0.15	69.23	1.99	0.56-7.00	0.29

* Adjusted for age, sex, home ownership, pension, living status, walking disability, self-rated health, chronic conditions (diabetes, hypertension, arthritis, history of stroke or heart disease) and hospital admissions in the comparison of proportion of support service use between participants with visual impairment and those with no visual impairment.

Among participants with incident bilateral visual impairment, women were more likely to use community support services within 5 years, compared to men with the same condition (OR 1.56, 95% CI 1.24-1.96). However, women were less likely to rely on informal support by family and friends compared with men (OR 0.51, 95% CI 0.42-0.63). A similar sex difference was evident among participants with incident unilateral visual impairment, any VI or any blindness (data not shown).

Longitudinal association of visual impairment and inability to go out alone

Incident bilateral VI was significantly associated with subsequent reduced ability to go out alone (OR 6.14, 95% CI 2.72-13.85) after 5 to 10 years. However, incident unilateral VI was not significantly associated with subsequent reduced ability to go out alone (OR 1.78 95% CI 0.89-3.56), after adjusting for past history of angina, acute myocardial infarct, stroke, arthritis, hypertension and diabetes. Self-reported past histories of these systemic conditions at baseline, but not self-rated health, were significantly associated with subsequently becoming not able to go out alone (OR 2.41, 95% CI 1.62-3.58).

Discussion

In our sample we found that older participants who developed incident bilateral VI and blindness were significantly more likely to take up community support services within the following 5 years than participants who remained free of VI over the entire follow-up period. However this association diminished by the time the 10-year follow-up visit was conducted. This finding could suggest that older people with bilateral VI need community support over 5 years or so. After a period of time they may have received treatment (e.g. cataract surgery), adapted to the impairment, died, or moved to residential age care institutions[236], resulting in a reduced long-term need for community support services among these people.

Our longitudinal findings support previous cross-sectional findings from the BMES baseline examination[235], which also reported an increased likelihood of using community support services (OR 3.1), reliance on family and friends (OR 2.5), and a reduced ability to go out alone (OR 6.2) among visually impaired participants. These findings are also consistent with findings from a previous hospital-based cross-sectional study by Ke et al[57], which found that a higher proportion of participants with moderate VI compared to participants without VI received assistance from formal (52% vs. 35%) and informal (70% vs. 37%) support. The proportions of those using support services rose with increasing age and the severity of impairment[57].

We found that for the same levels of visual impairment, women were more likely to rely on community support services and were less likely to rely on informal support than men. In our study, women had a greater 15-year survival than men, which could imply that some older women could not rely on their spouse for support, as their spouses could have already died or been more frail than their wife. Women have previously been found to rely more on multiple

sources of support compared to men[237]. Other cross-sectional studies[238;239] found that visually impaired participants receiving support from both family and friends had better adaptation to their visual impairment, and the more social ties they had, the better their adaptation. Conversely to our findings, this adaptive effect appeared to be stronger among men compared to women [239].

Among older populations, the proportion of participants relying on informal support was relatively high regardless of visual status. Our findings suggested an increased use of formal support only over the following few years after the onset of bilateral visual impairment. As these people become older, chronic conditions and disabilities associated with aging likely offset the burden caused by VI and therefore over the longer term, the impact of bilateral VI on the use of formal support services becomes no longer apparent. It is important to note that these findings may only apply to developed countries, as support services may differ among developing countries[240;241].

Strengths of our study include its large population-based sample with reasonable follow-up rates and standardized methods to assess VA. We have specified a clear temporal relationship with the use of longitudinal data. Limitations include the inability to adjust for all potential confounding variables that may influence the uptake of both formal and informal support services such as cognitive factors. Furthermore, we did not adjust for factors which may improve vision such as cataract surgery or correction of refractive errors during the periods between follow-up visits which may have reduced the associations between VI and support use after 10 years. We had a relatively small number of participants with bilateral VI who were followed-up, which may limit our study power. Participants with bilateral VI may have been more likely to have been older and have more co-morbidity, and require more support which would have increased the association we found between VI and support use. Another

limitation is survival bias; participants who were unable or refused to attend the follow-up visits, or who had died, would likely have had more co-morbid conditions and have been more likely to rely on support services if they were alive, and thus selective survival would have reduced the study power to detect the association between VI and support use. Of person who had incident bilateral visual impairment, 63.9% had died by the 15-year follow-up. We have used death as a competing event for the study outcomes of incidence use of formal or informal support services. Finally, the use of formal and informal support was self-reported, which could have led to over or under-reporting of the use of these services.

This longitudinal study complements our previous finding of a cross-sectional association between VI and the use of community support in a developed country, and confirms the impact of VI on the community aged care burden. The latest report of the World Health Organization[242] estimates that about 285 million people have VI globally, 82% of whom are 50 years and older. These people are approximately 3 times more likely to need some form of community support. These findings emphasize the burden of VI among older participants, and the need for regular eye health care service provision to older people. Early detection of VI may permit timely interventions to help older people with visual disabilities and their families, and to maintain their relatively independent ability to live at home as long as possible to reduce the aged residential care burden associated with VI[37;39].

Section III

Part 2: The Impact and Burdens of Visual Impairment

Chapter 7: Long-Term Visual Impairment and the Incidence of Falls and Fractures among Older People

Material in this Chapter has been published in

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Investigative Ophthalmology and Visual Science. 2014 Nov: 55(11): 7589-93

Abstract

Purpose: To assess the impact of visual impairment (VI) on the incidence of falls and fractures in older persons.

Methods: Of 3654 baseline participants, 2334, 1952 and 1149 were re-examined after 5, 10 and 15-years. Presenting visual acuity (VA) was measured at each examination. Bilateral and unilateral VI was defined as VA worse than 6/12 in the better and worse eye, respectively. Incident VI was defined in eyes with VA 6/12 or better at baseline which subsequently developed VI. Incidence of falls was assessed over the 12-months prior to each visit; whereas incidence of fractures was assessed over the 5-years between two visits. Discrete logistic-regression models with time-dependent variables were used to assess associations between VI and subsequent falls and fractures after adjusting for potential confounding variables.

Results: The proportions of participants reporting ≥2 falls ranged between 10%-14%, and proportions reporting fractures ranged between12%-21%, across the three follow-up visits. Participants with incident VI were more likely to report ≥2 falls in 5-years, OR 1.46, 95% CI 1.04-2.04 (bilateral) and OR 1.22, 95% CI 0.98-1.51 (unilateral). Compared to participants with normal vision, those with incident unilateral VI had a higher incidence of fractures over 5-years (OR 1.27, 95%CI 0.98-1.51). No increased incidence of falls or fractures was evident after 5+ years among participants with VI.

Conclusions: In this older cohort, recent development of visual impairment was associated with increased likelihood of subsequent falls and fractures in the next 5 years, independent of other confounding variables.

Background

Approximately 1 in 3 persons aged 65+ years experiences a fall each year[243-245], with around one half occurring at home and one third resulting in a fracture in the hip or thigh[177;244;246]. Known risk factors for falls and fractures include older age, female gender, past history of cardio-vascular disease, stroke, diabetes, arthritis, walking disabilities, depression, use of medications (e.g. sedatives, tranquilizers) and visual problems[69;247-249].

Previously documented significant associations between the presence of VI and an increased likelihood of falls and fractures were largely observed from cross-sectional studies[25,26]. Longitudinal studies with follow-up periods up to 10 years also documented an increased risk of subsequent falls and fractures, however the duration of VI was unclear[1;12;48;111;248;250;251]. In this report we aimed to assess the impact of bilateral and unilateral VI, and the duration a person lived with VI, on subsequent falls and fractures over 5- and 10-year periods in a population-based cohort of older Australians, the Blue Mountains Eye Study (BMES).

Specific Methods

Visual Impairment

Visual impairment definitions have been described previously in **chapter 2**, page 67. VA used in this chapter refers to the presenting visual acuity before subjective refraction.

Incidence of Falls and Fractures

We determined the incidence of falls over a 12-month period prior to each visit among all participants who were examined at the visit. The incidence of falls was categorized into 2 groups; participants who reported 2 or more falls versus participants who reported one or no falls. The incidence of fractures was also categorized into 2 groups; any fractures versus no fracture.

Statistical Analysis

SAS 9.2 software (SAS Institute, Cary, NC) was used for statistical analyses. Discrete logistic models (PROC PHREG) with time-dependent study (VI) and outcome (any falls and fractures) variables were used to assess associations between VI and subsequent falls and fractures.

Participants with incident VI detected at each visit were assessed for falls and fractures at subsequent visits with a 5-year interval. This analysis used discrete logistic regression model and time-dependent variables to include VI detected at 5-year follow-up and outcome events reported at 10-year follow-up; and VI detected at 10-year follow-up and outcome events reported at 15-year follow-up visits. Participants with bilateral and unilateral VI were compared to participants without VI in either eye over the 15-year follow-up period.

Logistic regression models (PROC LOGISTIC) were used to assess the associations between incident bilateral or unilateral VI detected at the 5-year follow-up and subsequent falls and fractures at the 15-year follow-up visit (a 10-year interval). As falls were self-reported events, the exact time when each event occurred was not known, and events that occurred during the follow-up period but outside the 12-month period prior to the follow-up visit could have been omitted, we therefore used dichotomous variables (had or did not have) for both fall and fracture outcomes and logistic regression models to assess the longitudinal associations.

All models were adjusted for potential confounding variables known to be associated with having a fall or fracture including the presence of a walking disability, home ownership, living arrangements, cataract surgery within the follow-up period, having 3 or more co-morbidities (angina, acute myocardial infarct, stroke, arthritis, hypertension and diabetes), use of medications which could result in falls or fractures (tranquilizer, sedatives and anti-depressants), bifocal/multifocal spectacle correction and having any hospital admissions over the 12 months prior to the visit when VI was detected[252]. We used a p value <0.05 as the selection criterion for variables to be included in the final parsimonious, multi-variable models, unless variables needing to be adjusted for based on content knowledge. We cross-checked all variables excluded from the final models and confirmed that each of these variables did not change the association between VI and the outcome variables by more than 10% [253]. Supplementary analysis using best-corrected VA measured after subjective refraction in place of presenting VA was also performed. Odds ratios (OR) and 95% confidence intervals (CI) are presented.

Results

Baseline characteristics by the presence or absence of self-reported ≥2 incident falls or self-reported fractures at any follow-up visit (5-, 10- and 15-year) are presented in **Table 7.1**. Compared to participants without subsequent events of ≥2 falls or fractures, those with ≥2 falls were more likely to be women, to have had a hospital admission within the last 12 months prior to baseline visit, to live alone and have a walking disability at baseline. Participants with subsequent factures were more likely to be women and to have had a hospital admission within the last 12 months prior to baseline. The proportion of participants reporting ≥2 falls at the 5-, 10- and 15-year follow-up examinations was 10.4%, 13.9% and 10.4% respectively, and the corresponding proportion of participants reporting a fracture was 20.9%, 13.2% and 11.6% respectively.

Table 7.1: Baseline characteristics of participants reporting falls (≥2) and fractures at any follow-up visit (5-, 10- or 15-year)

Characteristic	No or <2 Falls n=832 (%)	≥ 2 Falls n=297 (%)	Adjusted P values*	No Fractures n=778 (%)	Fractures n=348 (%)	Adjusted P values*
Age (years) ± SD	60.0 ±6.6	62.6 ± 7.3	<0.01	60.1 ± 6.8	62.1 ± 6.7	0.06
Sex (Female)	55.1	66.7	<0.01	53.2	69.3	<0.01
Walking disability	0.7	3.7	<0.01	1.4	1.7	0.68
Living alone	17.6	24.8	<0.01	19.0	20.8	0.49
Chronic conditions (3+)	3.9	6.4	0.07	4.4	4.9	0.70
Hospital admissions (within last 12 months)	14.3	19.2	0.05	14.0	19.0	0.03

* Adjusted for age, sex, presence of a walking disability, 3 or more co-morbidities

Baseline visual impairment and subsequent falls and fractures reported at the 5-year follow-up visit

At baseline, bilateral VI was detected in 397 participants (10.9%) and unilateral VI was detected in 1073 participants (29.4%), of which 150 and 535 had complete data at the 5-year follow-up. Two or more falls in the year prior to the 5-year follow-up visit were reported by 16.0% and 14.2% of participants with bilateral and unilateral VI at baseline, respectively, compared to 9.72% of those without VI in either eye at baseline; adjusted OR 1.46, 95% CI 0.86-2.47 and 1.37, 95% CI 0.59-1.44 for participants presented with bilateral and unilateral VI at baseline, respectively. History of fractures in the past 5 years was reported at the 5-year follow-up by 26.0% and 27.1% of baseline participants with bilateral and unilateral VI, respectively, compared to 19.8% of participants who had no VI in either eye at baseline: adjusted OR 0.94, 95% CI 0.61-1.44 and OR 1.29, 95% CI 1.00-1.67 for participants with bilateral and unilateral VI at baseline, respectively **(Table 7.2).**

Table 7.2: Associations between baseline bilateral or unilateral visual impairment and subsequent falls (≥2) and fractures reported at the 5-year follow-up examination, shown as odds ratios (OR) with 95% confidence intervals (95% CI)

Baseline Visual impairment status	n (%) subjects reporting ≥2 falls at the 5-year follow-up	OR* (95% CI)	p value	n (%) subjects reporting a fracture at the 5-year follow-up	OR* (95% CI)	p value
Bilateral (N= 150)	24 (16.0)	1.46 (0.86-2.47)	0.16	39 (26.0)	0.94 (0.61-1.44)	0.77
Unilateral (N=535)	76 (14.2)	1.37 (0.98-1.90)	0.07	145 (27.1)	1.29 (1.00-1.67)	0.05
Male (N=982)	89 (9.1)	1.03 (0.63-1.75)	0.12	149 (15.2)	0.51 (0.41-0.64)	<0.01
Walking disability (N=74)	24 (32.4)	0.58 (0.34-2.44)	0.45	24 (32.4)	1.29 (0.77-2.17)	0.33
3+ Co-morbidities (N= 154)	19 (12.3)	3.32 (1.97-5.59)	<0.01	34 (22.1)	0.95 (0.64-1.43)	0.81

* Adjusted for age, sex, presence of a walking disability, 3 or more co-morbidities

Incident visual impairment and subsequent falls and fractures within 5-year intervals

Of the 2799 participants without VI at baseline, 81 developed bilateral VI at any follow-up visit (5-, 10- or 15-years). Due to small numbers of incident bilateral blindness at all follow-up visits, incidence of bilateral and unilateral blindness was grouped together as incidence of any blindness, and was found in 69 participants over the 15-year follow-up period.

Participants with incident bilateral VI during the follow-up period were more likely to report ≥2 subsequent falls in 5 years (adjusted OR 1.46, 95% CI 1.04-2.04), but were not more likely to report a subsequent fracture (adjusted OR 1.07, 95% CI 0.77-1.50, **Table 7.3)**.

Table 7.3: Associations between incident bilateral and unilateral visual impairment with subsequent falls and fractures in the next 5 or 10 years by duration of visual impairment, shown as odds ratios (OR) with 95% confidence intervals (95% CI)

	Subsequent falls		**Subsequent fractures**	
Incident bilateral VI				
Duration of VI	**OR* (95% CI)**	**p value**	**OR* (95% CI)**	**p value**
0 to 5 Years[#]	1.46 (1.04-2.04)	0.03	1.07 (0.77-1.50)	0.68
>5 to 10 Years[†]	1.10 (0.45-2.69)	0.84	1.27 (0.53-3.06)	0.59
Incident unilateral VI				
Duration of VI				
0 to 5 Years[#]	1.22 (0.98-1.51)	0.08	1.27 (1.04-1.55)	0.02
>5 to 10 Years[†]	1.26 (0.79-2.01)	0.33	1.51 (0.96-2.37)	0.08

*Adjusted for age, sex, presence of a walking disability, 3 or more co-morbidities
[#]Proc PHREG
[†]Proc LOGISTIC

Participants with incident unilateral VI during the follow-up period were also more likely to report ≥2 subsequent falls in 5 years (adjusted OR 1.22, 95% CI 0.98-1.51), although this association was marginally non-significant. In addition, they were significantly more likely to report a subsequent fracture in 5 years (adjusted OR 1.27, 95% CI 1.04-1.55).

Supplementary analyses using best-corrected VA measured after subjective refraction in place of presenting VA did not significantly change the associations between incident bilateral and unilateral VI and subsequent report of ≥2 falls or fractures in 5 or less years (data not shown).

Participants with incident blindness (unilateral or bilateral) during the follow-up period were not more likely to report ≥2 falls or a fracture in 5 years (adjusted OR 0.99, 95% CI 0.35-2.77 and OR 0.71, 95% CI 0.25-1.98, respectively).

Incident visual impairment and subsequent falls and fractures in more than 5 years

Participants with incident bilateral VI detected at the 5-year follow-up visit were not more likely to report ≥2 subsequent falls or a fracture in 10 years, i.e. at the 15-year follow-up visit (OR 1.10 95% CI 0.45-2.69 and OR 1.27 95% CI 0.53-3.06 for long-term incident falls and fracture, respectively, **Table 7.3)**. There were only 2 persons with incident blindness at the 5-year follow-up (n=2), and therefore the association between incident blindness and incident falls or fractures over 10 years was not assessed.

Discussion

We found that older persons who developed bilateral or unilateral VI during the follow-up period (had experienced VI recently) were more likely to report ≥2 falls within 5 years of visual impairment being detected, compared to participants who remained free of VI over the same follow-up period. However, this association diminished after 5 or more years. While incident bilateral visual impairment was not associated with subsequent self-reported fracture at any point in time, incident unilateral VI was associated increased likelihood of subsequent self-reported fractures in 5-years, after adjusting for potential confounders.

The lack of positive association between incident bilateral VI and subsequent fractures could have been a result of insufficient study power due to relatively small numbers.

Our finding of longitudinal association between VI and subsequent falls complement previous cross-sectional findings from the baseline examination of the same population[254], which also reported an increased likelihood of reporting ≥2 falls during the 12-month period prior to the study baseline (PR 1.4, 95% CI 1.1-2.0) among participants with mild VI (VA 6/12 to 6/18 at baseline. The non-significance of the longitudinal association between baseline VI and self-reported falls at the 5-year follow-up examination found in this current study may be due to the fact that some of these baseline participants had been living with VI for a long duration, as we do not have information about when VI developed prior to the baseline examinations for these participants.

Similar observations were reported by other population-based, cross-sectional studies of older people, including the Shihpai Eye Study[48] (OR 2.0, 95% CI 1.0-4.3) and the Singapore Malay Eye Study[50] (OR 1.3, 95% CI 1.0-1.6). However, a clinic-based study by Lamoureux et al.[49] did not find significant cross-sectional associations between falls and VI, contrast sensitivity, stereopsis or visual field loss. A review by Ambrose et al[252]. on risk factors of falls among

older participants reported that older participants at high risk of falls were more frail, more likely to have other co-morbidities and mobility problems, all that could have reduced their physical activities and therefore might also reduce the chance of falls[252].

Previous longitudinal reports from the Auckland Hip Fracture Study[7] showed an increased risk of hip fractures in 2.5 years (OR 1.3 95% CI 1.0-1.8) among persons with VA<6/9 in at least one eye. A study by Javitt et al [1] found that progressive vision loss in the better eye was associated with an increased risk of injury over a 4-year follow-up period. These previous findings support our observations of a short- to mid-term association between unilateral VI and fractures, i.e. persons with baseline and incident unilateral VI had approximately a 30% increased risk of fractures in subsequent 5 years but not 10 years. The significant associations found between unilateral but not bilateral VI and risk of fractures in this report may be due to the deficiency in stereo-acuity among unilateral VI cases that affects depth perception needed for navigating[7;245].

The Framingham Study[12] reported a non-significantly increased risk of fractures over a 10-year period retrospectively (adjusted RR 1.5, 95% CI 0.95-2.5) among persons with moderate VI in at least one eye (VA 6/9-6/24). In contrast, we found weakening or no associations between VI and falls and fractures over the long-term. There are many potential reasons that may explain a diminishing risk of falls and fractures associated with VI over the long-term. Individualized rehabilitation programs may have been implemented that addressed the potential risk of further falls[255]. Admission to aged-care facilities, when older people became frail and had developed other co-morbidities and disabilities, could have led to a selection bias in this surviving cohort sample. This may also explain our failing to detect the associations over the long-term.

Strengths of our study include its large population-based sample with reasonable follow-up rates and the use of standardized methods to assess VA. We have specified incidence, duration and a clear temporal relationship. Limitations include the inability to adjust for all confounding variables that may influence the risk of falls or fractures. Relatively small number of participants with bilateral VI at each follow-up visit may have limited the power of our study to detect the association between VI and the risk of falls or fractures. A major limitation is survival bias. Participants who did not attend follow-up visits could have been frailer, have had more co-morbid conditions including VI, and thus would have had more falls or fractures than participants who did attend, resulting in an under-reporting event rate of falls and fractures and potential underestimation of the associations. Additionally, falls and fractures were self-reported and could have been subject to recall bias[256]. The causes of fractures were not confirmed by radiology reports or hospital discharge summaries.

Previous studies have consistently shown that visual field loss is associated with an increased risk of falls [257-259]. Visual field, however, was not consistently measured at each follow-up examination in our cohort study. At baseline visit, we measured visual fields on over 80% of the participants. There was no single blindness case that was due to the criterion of visual field defect (visual field of less than 20 degrees from the point of fixation)[260].

In Australia, it was estimated that the average cost was $3906 per injury resulting from falls[261]. Over the one-year period from 2010 to 2011, the number of hospitalized injury cases due to falls in participants aged 65+ years was over 92,000[262]. Findings from previous and our current studies indicate that a period with a high risk of falls is within the first 5 years after the onset of visual impairment. Measures to minimize risk of falls should be taken soon after visual impairment develops[255]. Our findings also reinforce the need for regular eye examinations to detect and intervene visual impairment early among older persons, to avoid

adverse events such as falls and fractures and maintain their independent living status as long as possible.

Section III

Part 2: The Impact and Burdens of Visual Impairment

Chapter 8: Visual Impairment and Depressive Symptom among Older People

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Material in this Chapter has been published in

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British Journal of Ophthalmology: 2015 Feb: (Epub ahead of print)

Abstract

Purpose: To assess the association between visual impairment (VI) and subsequent presence of depressive symptoms among older persons.

Methods: Of the 3654 baseline participants (aged 49+years) of the Blue Mountains Eye Study, 2334, 1952 and 1149 were re-examined after 5-, 10- and 15-years. VI was defined as best-corrected visual acuity <6/12 in either or both eyes. Presence of depressive symptoms was defined if Mental Health Index (MHI) scores were <59 or incident use of anti-depressant medications. Persons with VI detected at the 5- or 10-year follow-up visits were assessed for subsequent development of depressive symptoms in 5-years. Persons with VI detected at baseline or the 5-year follow-up were assessed for depressive symptoms over 10+years. Controls were persons without VI over the corresponding period. Discrete logistic regression models with time-dependent study and outcome variables were used, adjusting for potential confounders.

Results: Of 1568 participants who had the MHI assessed at 2 consecutive visits, 226 had bilateral or unilateral VI detected 5 5ears earlier and 120 had VI 10 or more years earlier. Depressive symptoms were reported in 27% and 31.6% of cases with VI detected 5 and 10+years earlier, respectively, compared to 10.8 to 11.5% of controls. There was a significantly greater odds of presenting depressive symptoms among VI cases detected 5-years earlier (odds ratio, OR, 3.06, 95% confidence interval, CI 1.72-5.44), but this was non-significant for cases detected 10+years earlier (OR 1.29, 95% CI 0.84-1.98).

Conclusions: Visual impairment was associated with subsequently presenting depressive symptoms over 5 years among older persons.

Background

Depression has been associated with increased the risk of suicide and mortality, as well as having detrimental effects on physical, mental and social functioning[16;118;119]. Both VI and depression have increasingly been recognised as major issues affecting overall well-being of older people[113-117].

Cross-sectional associations between VI and depression have previously been reported among both general populations and institutionalised residents [42;51;263], with studies showing a greater proportion with depression among persons with VI compared to their age-peers with normal vision. Few studies have reported longitudinal associations between VI and subsequent depressive symptoms[264-266].

In this report we aimed to assess the longitudinal association between prior diagnoses of VI and subsequent self-reported depressive symptoms after 5 (short-term) and 10+ years (long-term) in a population-based cohort of older Australians, the Blue Mountains Eye Study (BMES).

Specific Methods

Visual Impairment

Visual impairment definitions have been described previously in **chapter 2**, page 67. VA used in this chapter refers to the best-corrected acuity after subjective refraction. Participants with VI detected at the previous visit 5 years earlier (e.g. from baseline to the 5-year follow-up visit or from the 5- to 10-year follow-up visit) were included to assess short-term incidence of depressive symptoms. Participants with known VI detected ≥10 years earlier (e.g. from baseline to the 10-year follow-up visit or from the 5-year to 15-year follow-up visit) were included to assess long-term incidence of depressive symptoms.

Depressive Symptoms

We defined the presence of depressive symptoms as either self-reported mental health index (MHI) score <59 or incident use of anti-depressant medications by participants with no previous history of using such medications, at later visits after VI was detected. Participants with MHI <59, or who were using anti-depressant medications at the preceding visit prior to VI was detected, or at the same visit when VI was detect, were excluded from those at risk of developing depressive symptoms.

Statistical Analysis

SAS 9.2 software (SAS Institute, Cary, NC) was used for statistical analyses. For subsequent presence of depressive symptoms over the short-term, persons with any incident VI detected at the 5- or 10-year follow-up visits were assessed for self-reported depressive symptoms at the end of each 5-year interval following the detection of VI (i.e. at the 10- or 15-year follow-

up visit). For subsequent presence of depressive symptoms over the long-term, persons with any prevalent VI at baseline or any incident VI detected at the 5- year follow-up visits were assessed for depressive symptoms at the follow-up visits with a 10-year interval (i.e. 10- or 15-year follow-up visit). For persons with normal vision (controls), depressive symptoms were assessed at the corresponding time-point when the VI cases were assessed.

Discrete logistic regression models (PROC PHREG) with time-dependent study (visual impairment) and outcome (self-reported depressive symptoms including incident use of anti-depressive medications) variables were used to assess associations between visual impairment and subsequently self-reported depressive symptoms.

All reported longitudinal associations were after adjusted for covariates known to be associated with depression[116;267;268] including; age, sex, presence of walking disability, living arrangements, having ≥3 co-morbidities (angina, acute myocardial infarct, stroke, arthritis, hypertension and diabetes) measured at the time when visual impairment was detected, and having hospital admissions in the 12-month period prior to the visit when visual impairment was detected. Odds ratios (OR) and 95% confidence intervals (CI) are presented.

Results

Of the 3654 baseline participants, 1568 had completed the MHI questionnaires on at least 2 consecutive visits and were included to assess the presence of depressive symptoms. **Table 8.1** shows baseline characteristics of persons with incident depressive symptoms versus those without depressive symptoms at the 5-year follow-up examination. Compared to participants without self-reported depressive symptoms, those with depressive symptoms were more likely to be women, to have walking disability or arthritis and were less likely to own their home.

Table 8.1: Baseline characteristics of Blue Mountains Eye Study participants by the presence of depressive symptoms at the 5-year follow-up examination

Baseline characteristics	**5-year follow-up With depressive symptoms*** **n (%)**	**5-year follow-up Without depressive symptoms n (%)**	**P Value**
Age (years) mean ± standard deviation	64.4 ± 8.9	64.4 ± 8.5	0.95
Gender (Female)	205 (65.7)	1038 (56.7)	<0.01
Any Visual Impairment (VA <6/12)	17 (5.5)	140 (7.7)	0.17
Any Blindness (VA<6/60)	5 (1.6)	31 (1.7)	0.91
Lives alone	86 (27.8)	454 (25.1)	0.30
Walking disability	18 (5.8)	48 (2.6)	<0.01
Married	195 (62.7)	1223 (66.9)	0.14
Home owner	270 (88.8)	1660 (92.5)	0.03
History of			
Stroke	15 (4.8)	57 (3.1)	0.31
Diabetes	23 (7.4)	116 (6.3)	0.49
Arthritis	182 (58.7)	827 (45.4)	<0.01
Hypertension	234 (75.2)	1271 (69.6)	0.04

* Defined as mental health index of <59 or the use of antidepressants

Incident bilateral or unilateral VI was recorded in 226 participants at either the 5- or 10-year follow-up visit, of which 27.0% (n=61) had subsequently reported depressive symptoms over the short-term, compared to 11.5% (n=66) of persons without VI over the same 5-year period. There were 120 participants with VI at either the baseline or 5-year follow-up visit, of which 31.7% (n=38) had subsequently reported depressive symptoms at either the 10- or 15-year follow-up visit, compared to 10.8% (n=133) of those without VI over the same period.

Participants with incident VI detected 5 years earlier were significantly more likely to report depressive symptoms at their first subsequent visit after VI detection, compared to those without VI (adjusted OR 3.06, 95% CI 1.72-5.44). Conversely, participants with VI detected 10+ years earlier were non-significantly more likely to report depressive symptoms compared to persons without VI over the same period (OR 1.29, 95% CI 0.84-1.98, **Table 8.2**).

Of the 226 participants who had incident VI diagnosed at the 5-year or 10-year follow-up visit, 22 had persistent VI over the entire 5-year follow-up duration. Analysis confined only to those with persistent VI showed a similar direction of association, but the association became non-significant (OR 1.57, 95% CI 0.88-2.81).

The greater odds over the short-term of reporting depressive symptoms among participants with VI detected 5 years earlier was similar between those with incident bilateral VI (OR 4.60, 95% CI 1.67-12.69) and those with incident unilateral VI (OR 4.06, 95% CI 2.06-7.99). The non-significant increased odds over the long-term for reporting depressive symptoms in participants with VI detected 10+ years earlier was also similar between unilateral and ‘any VI’ cases (**Table 8.2**).

When we stratified depressive symptoms into two separate outcomes (MHI <59, and the incident use of anti-depressant medication), we found similar associations. There was significantly increased short-term, but non-significantly increased long-term likelihood of

having either outcomes among cases with any VI or unilateral VI. There was no increased risk of having either of the two outcomes, or the combined outcome, among persons with bilateral VI detected 10+ years earlier **(Table 8.2)**.

Table 8.2: Longitudinal association between visual impairment and subsequent presence of depressive symptoms assessed by the mental health index (MHI) and the incident use of anti-depressive medication, presented as odds ratio (OR) and 95% confidence interval (CI)

	n	**Subsequent presence of Depressive symptoms** (MHI <60)		**Incidence of Anti-depressive medication use**		**Subsequent presence of Depressive symptoms** (MHI<59 or the incident use of anti-depressants)	
Period when Visual impairment was detected		OR*	95% CI	OR*	95% CI	OR*	95% CI
Bilateral							
5 years earlier	73	2.81	0.85-9.32	1.37	0.68-2.78	4.60	1.67-12.69
10+ years earlier	15	0.72	0.15-3.39	0.72	0.15-3.37	0.63	0.17-2.34
Unilateral							
5 years earlier	153	2.56	1.31-5.02	1.84	1.13-3.02	4.06	2.06-7.99
10+ years earlier	105	1.36	0.80-2.31	1.25	0.74-2.12	1.47	0.90-2.20
Any (Bilateral or Unilateral)							
5 years earlier	226	2.31	1.20-4.44	1.88	1.17-3.03	3.06	1.72-5.44
10+ years earlier	120	1.27	0.76-2.12	1.18	0.71-1.97	1.29	0.84-1.98

* Adjusted for age, sex, walking disability, hospital admissions in the past 12 months, living arrangements, having 3+ co-morbidities (arthritis, diabetes, stroke and cardiovascular disease, hypertension).

Discussion

In this population, we found that older participants with any or unilateral VI were more likely to subsequently report having depressive symptoms in the short-term (5 years), but not in the long-term (10+ years), compared to participants without VI. These longitudinal findings support earlier cross-sectional data.

A meta-analysis of 12 studies by Huang et al[41], reported a higher prevalence of depression among persons with low vision compared to those with normal vision (pooled OR 1.94, 95% CI 1.68-2.25). A study by Evans et al[42], found that older persons (75+ years) with bilateral VI had a higher prevalence of depression (OR 2.69, 95% CI 2.03-3.56, adjusted for age and gender). However, this association did not persist after further adjustment for other potential confounders including activities of daily living (ADL) (OR 1.26, 95% CI 0.94-1.70), possibly partly due to over-adjustment in addition to removal of confounding effects.

Noran et al[269] found that depression was more frequent in persons with bilateral VI (VA <20/60) and blindness (VA <20/400) (adjusted OR 2.64, 95% CI 1.27-5.5 and OR 4.99, 95% CI 1.90-12.95, respectively) among 430 elderly Malays (60+ years). They also assessed the associations between depression and the reported duration of VI, and found that depression was more frequent found among persons with VI for less than one month compared to those without VI (unadjusted OR 21.8, 95% CI 10.35-45.90).

Longitudinal studies assessing the association between VI and depression have reported conflicting results. Tournier et al[5] found that VI was independently associated with a greater incidence of depression among an older population (65+ years) after adjusting for potential confounding factors, and that the association was similar across different severity levels of VI, hazard ratio (HR) 1.54, 95% CI 1.40-1.69 for moderate and HR 1.56, 95% CI 1.43-1.71

for severe VI. A study by Harris et al[2] reported that persons with poor vision over a 2-year period were more likely to develop new onset of depression (adjusted OR 2.9, 95% CI 1.3-6.3). In addition, worsening vision between baseline and the 2–year follow-up visit was associated with new onset of depression (adjusted OR 3.4, 95% CI 1.6-7.1). In contrast, a study by Prince et al[8] examined 889 residents (65+ years) over a 1-year period and reported that self-reported eyesight problems were not associated with development of depression over 1 year (adjusted OR 0.8, 95% CI 0.3-2.1). A study by Forsell et al[4] did not find an association between VI and the onset of depression after 3 years in a Swedish population aged 75+ years. None of these reports has provided any definitions for poor or worsening vision, eyesight problems or VI, to enable useful comparison between studies.

Nevertheless, our study findings support the associations between VI and the subsequently self-reported depressive symptoms over the short-term (≤ 5 years). The weaker association between VI and self-reported depressive symptoms over the long-term may be partly explained by reduced numbers and therefore reduced study power, and/ or a progressive adaptation to VI. Factors such as support from family, friends, formal support services and the use of visual aids may play also role[270;271].

Strengths of our study include its large population-based sample with reasonable follow-up and standardised methods to assess VA. We have specified a clear temporal relationship with the use of longitudinal data. Limitations include the inability to adjust for all potential confounding variables that could have influenced the risk of developing depressive symptoms. We did not adjust for factors which may improve vision such as cataract surgery or refractive correction which may have reduced the associations between VI and depressive symptoms. The multi-factorial nature of depression could have been due to many other conditions that we could not adequately adjust for, such as cerebrovascular disease, hearing loss, low economic status, neurological abnormalities, cataract surgery, a past history of or a

family history of depressive symptoms[8]. We had a relatively small number of participants with VI and depressive symptoms who were followed-up over 10+ years, limiting our study power in the assessment of subsequently self-reported depressive symptoms over the long-term. Another limitation is survival bias of the cohort, such that persons who were unable or refused to attend the follow-up visits, or who had died, could have had more co-morbid conditions including depression while alive.

In summary, findings from this older cohort support previous cross-sectional associations found between VI and depression over the short-term. Persons with VI were 3-fold more likely to report depressive symptoms within a 5-year period after the development of VI. The magnitude of this association declined over the period of 10+ years. Our findings emphasise the importance of early detection of visual problems and rehabilitation to reduce the burden and negative impact of visual impairment in older people.

Section III

Part 2: The Impact and Burdens of Visual Impairment

Chapter 9: Sensory Impairment and Possible Cognitive Function Decline among Older People

Material in this Chapter has been submitted and under review of a revised version

Hong T, Mitchell P, Burlutsky G, Liew G, Wang JJ. *Visual impairment and Cognitive Function in an older population: longitudinal findings from the Blue Mountains Eye Study.*

Journal of the American Geriatric Society

Abstract

Purpose: To assess the associations of visual impairment (VI) and hearing loss (HL) with a decline in mini-mental state examination (MMSE) scores over time in older people.

Methods: Of the 3654 participants of the Blue Mountains Eye Study baseline examination, 2334, 1952 and 1149 were re-examined after 5-, 10- and 15-years. MMSE was assessed at all three follow-up visits. A decline ≥3 scores from 5-year to 10- or 15-year visits indicated probable cognitive decline. VI was defined as best-corrected visual acuity <6/12 in the worse-eye, HL was defined as pure-tone average >40 decibels in the worse-ear and dual sensory impairment (DSI) was defined by the co- presence of VI and HL, detected at 5-year follow-up (baseline of this report). Participants with no VI and HL over the corresponding period were controls. Associations of VI, HL and DSI with probable cognitive decline were assessed using logistic regression models adjusting for age and sex after excluding subjects with a stroke history.

Results: The presence of VI, HL or DSI was not associated with probable cognitive decline over 5 years (odds ratio (OR) 0.84, 95% confidence-intervals (CI) 0.40-1.79, OR 1.02, 95% CI 0.61-1.70 and 1.41, 95% CI 0.54-3.72, respectively) or 10 years (OR 1.09, 95% CI 0.52-2.30, OR 1.09, 95% CI 0.65-1.82 and 1.15, 95% CI 0.28-4.73, respectively). There were no changes to these findings after adjustment for other potential confounders. Age was significantly associated with probable cognitive decline (OR 1.07, 95% CI 1.04-1.10 for both periods).

Conclusion: Neither visual impairment, hearing loss or dual sensory impairment were independently associated with subsequent decline in cognition.

Background

Several cross-sectional studies previously reported associations between sensory impairments and cognitive decline[43;44;46], including a report using Blue Mountains Eye Study (BMES) baseline data[45] that showed a weak but significant cross-sectional association between sensory and cognitive function. However, findings of these associations using samples drawn from community dwelling or institutionalized older residents have been inconsistent after adjusting for potential confounding factors[43-46].

Only a limited number of longitudinal studies have assessed the associations between sensory and cognitive function decline in older persons, and conflicting findings have been reported from the few studies conducted[9;11;13]. Limitations of previous studies include unclear definitions of sensory impairment (the loss of visual or hearing impairment), use of non-standardized methods to assess visual and hearing function, and cognitive function assessment tools have included vision-related testing items.

In this report we aimed to determine whether longitudinal associations existed between visual, hearing and dual sensory impairment and probable cognitive decline over 5 and 10 years in a population-based cohort of older Australians, using the mini-mental state examination (MMSE) instrument, after removing visually dependent tasks (termed MMSE blind).

Specific Methods

Visual Impairment

Visual impairment definitions have been described previously in **chapter 3**, page 53. However, VA used in this chapter refers to the best-corrected acuity after subjective refraction.

Hearing Impairment

Hearing loss (HL) was defined as the pure-tone average of the audiometric hearing thresholds at 0.5, 1, 2 and 4 kilohertz (kHz) ($PTA_{0.5\text{-}4\ kHz}$) >40 decibels (dB)[9;272].

Dual Sensory Impairment

Dual sensory impairment (DSI) was defined at the co-presence of both VI and HL according to the definitions above.

Cognitive Function

We define a decline of ≥3 MMSE blind scores between the 5-year and 10- or 15-year follow-up visits to be indicative of probable decline in cognitive function, over either 5 years (between the 5- and 10-year) or 10 years (between the 5- and 15-year).

Statistical analysis

SAS 9.2 software (SAS Institute, Cary, NC) was used for statistical analyses. Logistic regression models (PROC LOGISTIC) were used to assess the associations between VI, HL and DSI with probable cognitive decline over 5 and 10 years. All measures, VI, HL and

MMSE were assessed at the 5-year and later follow-up examinations. VI and HL assessed at the 5-year follow-up examinations were used as the study factors, and MMSE assessed subsequently over the follow-up period were used to assess the decline in MMSE over time (outcome factor). In the primary analyses, VI was defined as VA<6/12 in the worse eye, and HL as average $PTA_{0.5\text{-}4\ kHz}$ >40dB in the worse ear, to include unilateral and bilateral impairment cases. In supplementary analyses, VI was defined as VA<6/12 in the better eye, and HL as average $PTA_{0.5\text{-}4\ kHz}$ >40dB in the better ear, to include bilateral impairment cases only.

All reported longitudinal associations were after adjusting for baseline age and sex initially. Further adjustments for factors known to be associated with cognitive impairment[61;273], including the presence of walking disability, living arrangements (whether or not they live alone), home ownership, the highest educational qualification obtained, baseline MMSE score,, having ≥3 major co-morbidities (angina, acute myocardial infarct, arthritis, hypertension and diabetes), history of depressive symptoms and having hospital admissions in the 12 month period prior to baseline. A history of stroke is known to be associated with a reduced cognitive function[161;274;275], hence persons with a past history of stroke were excluded (n=98). Odds ratios (OR) and 95% confidence intervals (CI) are presented.

Results

Of the 3654 baseline participants of the BMES, 2334 were re-examined at the 5-year follow-up visit. Of these 2334, 1605 (68.8%) had completed the MMSE in at least 2 follow-up examinations and therefore were included in this report. Compared to participants who attended the 5-year follow-up, participants who were alive but did not attend the follow-up examinations were more likely to be current smokers, have a history of diabetes, late age-related macular degeneration and VI. Participants who had died by the 5-year follow-up were more likely to have more chronic co-morbidities[201]. **Table 9.1** shows the baseline characteristics of those with VI, HL and DSI measured at the 5-year follow-up examination. Compared to participants with no sensory impairments, participants with DSI were more likely to be older, to live alone, to have a walking disability, self-reported history of depressive symptoms, 3+ major co-morbidities, hospital admissions 12 months prior to baseline, and a lower mean MMSE blind score.

Table 9.1: Characteristics of Blue Mountains Eye Study participants with visual impairment, hearing loss and dual sensory impairment compared to participants with no sensory impairment measured at the 5-year follow-up examination.

Baseline characteristics	No Sensory impairment n (%)	Visual impairment* n (%)	Hearing Impairment† n (%)	Dual Sensory impairment n (%)
N	1308	152	330	93
MMSE blind score‡	21.1 (1.5)	20.6 (2.1)	20.3 (2.3)	19.3 (2.8)
Age (years)‡	66.9 (7.4)	74.3 (8.4)	73.4 (7.8)	80.4 (7.0)
Gender (Female)	544 (41.6)	52 (34.2)	171 (51.8)	40 (43.0)
Lives alone	303 (23.2)	60 (39.5)	94 (28.5)	42 (45.2)
Walking disability	62 (4.7)	24 (14.6)	48 (14.6)	34 (36.6)
Home owner	1228 (94.0)	136 (89.5)	303 (91.8)	83 (89.3)
Hospital admissions 12 months prior	306 (23.5)	43 (28.5)	78 (23.8)	33 (35.9)
History of depressive symptoms	129 (10.7)	15 (11.5)	40 (13.1)	13 (18.1)
3+ major co-morbidities	140 (10.7)	33 (21.7)	53 (16.2)	19 (20.9)

MMSE – mini-mental state examination

* Visual impairment defined as (Visual acuity <6/12) in the worse eye
† Hearing loss defined as (>40 dB) in the worse ear
‡ mean (standard deviation)

Among 1352 participants who had MMSE assessed at both the 5- and 10-year follow-up examinations, probable cognitive decline was found in 9.5%, 11.1% and 18.8% of participants with VI, HL and DSI respectively, compared to 7.6% of controls over a 5-year period. Of 860 participants, who had MMSE assessed at both the 5- and 15-year follow-up examinations, probable cognitive decline was found in 21.9%, 20.8% and 30.0% of participants with VI, HL and DSI, respectively, compared to 16.0% of controls over a 10-year period.

Compared to participants with no sensory impairment, participants with VI, HL or DSI were not significantly associated with probable cognitive decline over 5 years (OR 0.84, 95% CI 0.40-1.79, OR 1.02, 95% CI 0.61-1.70 and 1.41, 95% CI 0.54-3.72, respectively) after adjusting for age and sex **(Table 9.2)**. Similarly, participants with VI, HL or DSI were not significantly associated with probable cognitive decline over 10 years (OR 1.09, 95% CI 0.52-2.30, OR 1.09, 95% CI 0.65-1.82 and 1.15, 95% CI 0.28-4.73 respectively) **(Table 9.3)**. Older age was found to be significantly associated with probable cognitive decline over both periods of 5 and 10 years, with an identical magnitude of association (per year increase in age, OR 1.07, 95% CI 1.04-1.10).

Table 9.2: Age- and sex-adjusted associations between sensory impairment and probable cognitive decline (≥3 units) in mini-mental state exam (MMSE) blind scores over 5 years (BMES II to BMES III)

	Decline ≥3 MMSE blind scores		
Sensory impairment	**n (%)**	**OR**	**95% CI**
Visual impairment	9 (9.5)	0.84	0.40-1.79
Hearing loss	24 (11.1)	1.02	0.61-1.70
Dual sensory impairment	6 (18.8)	1.41	0.54-3.72

Table 9.3: Age- and sex-adjusted associations between sensory impairment and probable cognitive decline (≥3 units) in mini-mental state exam (MMSE) blind scores over 10 years (BMES II to BMES IV)

	Decline ≥3 MMSE blind scores		
Sensory impairment	**n (%)**	**OR**	**95% CI**
Visual impairment	25 (21.9)	1.09	0.52-2.30
Hearing loss	10 (20.8)	1.09	0.65-1.82
Dual sensory impairment	3 (30.0)	1.15	0.28-4.73

There were no significant changes in these associations between VI, HL or DSI and probable cognitive decline after further adjusting for other co-variables: walking disability, living arrangements, home ownership, the highest educational qualification obtained, baseline MMSE score, a history of depressive symptoms, hospital admissions in the past 12 months and having 3 or more major chronic co-morbidities (data not shown). Supplementary analysis using VI in the better eye and HL in the better ear showed no significant associations with probable cognitive decline over either 5-years (OR 1.19, 95% CI 0.64-2.20 for bilateral VI and OR 1.04, 95% CI 0.22-4.93 for bilateral HL, respectively) or 10-years (OR 1.35, 95% CI 0.72-2.53 for bilateral VI and OR 2.08, 95% CI 0.46-9.43 for bilateral HL, respectively). Bilateral DSI, defined using VI in the better eye and HL in the better ear, showed similarly no significant associations with probable cognitive decline over 5 years (OR 6.48, 95% CI 0.37-113.0). We could not assess the association between DSI and probable cognitive decline over 10 years due to small numbers.

Discussion

In this older Australian cohort, we found that higher proportions of participants with visual, hearing or dual sensory impairment had a decline in 3+ MMSE blind scores after 5 and 10 years compared to participants with no sensory impairment. However, we did not find a significantly increased risk of probable cognitive decline after adjusting for age and sex, or after further adjusting for more potential confounding variables. Older age was significantly associated with a greater risk of cognitive decline.

Very few numbers of longitudinal studies on the associations between sensory impairment and cognitive function have been reported[9;11]. The Study of Osteoporotic Fractures (SOF)[9] examined 6112 women age 69+ years and reported a cognitive decline by ≥3 units

approximately after an average of 4.4 years, using a modified MMSE. Using comparable definitions of sensory impairments to our study, SOF study investigators found that VI and combined vision and hearing impairment at baseline was associated with probable cognitive decline (OR 1.78 95% CI 1.21-2.61 and OR 2.19 95% CI 1.26-3.81, respectively), after adjusting for education, smoking, vertebral fracture, body mass index (BMI), grip strength, social network and baseline cognitive status[9]. However, the modified version of the MMSE (3MS) used in the study did not exclude vision-related.

The Maastricht Aging Study [11] examined 418 participants aged 55+ years and found that a deterioration of VA was in parallel with deterioration in cognitive function over a 6-year period. Various cognitive performance tests were used in this study, though some tests were vision-related, the study investigators reported that the font size was large enough for all participants to perceive the words well. They found a parallel decline in both sensory and cognitive functions could suggest overall neurodegenerative changes associated with ageing.

The Hispanic Established Populations for Epidemiologic Studies of the Elderly[13] examined 2140 Mexican Americans aged 65+ years, and found that participants with near VI (<7-point type size) at baseline had an average decline of 0.13 more MMSE-blind points per year than the decline in persons with normal near vision over the 7 year period (p=0.045). They found no difference in per year change of MMSE-blind scores between persons with binocular distance VI and those with normal distant vision at baseline (p=0.14)[13]. Vision assessment methods used in this study were not standardised, nevertheless, the latter finding from this study is consistent with our findings.

Longitudinal studies on the associations between hearing loss and cognitive function have also been inconsistent. Both the Health, Aging and Body Composition study[276] (3075 participants aged 70-79 years), and the Maastricht Aging Study[11](418 participants aged 55+

years) found that baseline hearing impairment was associated with a decline in cognitive function after 5 and 6 years respectively. However, a study by Glennis et al[277] did not find any significant associations between hearing impairment and subsequent cognitive function after 5 years among 122 participants aged 60+ years. Different methods of cognitive function testing were used across the 3 studies, which makes comparison with our findings difficult.

Our negative findings on the associations of interest may suggest that previously reported positive associations between sensory function impairment and decreased cognitive function testing scores are unlikely due to true cognitive impairment but more likely due to the reduced ability to process stimuli in persons with sensory impairment that compromised the performance on cognitive function testing[11;278].

Strengths of our study include its large population-based sample with reasonable follow-up rates and standardized methods to assess vision and hearing. Limitations include the relatively small number of participants with visual or hearing impairment who were followed limiting the study power. We did not adjust for all potential variables which may have affected the associations between sensory impairment and cognitive decline. The MMSE is a screening tool, which should not be considered equivalent to specific diagnostic tools for cognitive impairment and a decline of 3 MMSE score may not be a valid representation of cognitive decline despite this level of change being used in previous studies[9]. Furthermore, reading letters off a vision chart may not be sufficiently cognitively challenging to detect any association between VI and subsequent cognitive decline. We could not adjust for other potential confounders. Although we adjusted for 3 or more major chronic co-morbidities as a potential confounding variable, each individual co-morbid condition may not have equal magnitude of association with cognitive decline. Furthermore, improvement in vision or hearing may have occurred subsequent to cataract surgery or the use of hearing aids during

the course of the follow-up period which may have contributed to the lack of association between sensory impairment and cognitive decline. Another limitation is survival bias: participants who were unable or refused to attend the follow-up visits, or who had died, would be more likely to have been older and have had more co-morbid conditions including sensory impairment, and may have been more likely to experience cognitive decline.

In summary, we did not find significant associations between sensory impairment and subsequent decline in MMSE scores after adjusting for age and sex or after additional adjustments for multiple potential confounders. We found, however, non-significantly higher proportions of participants with single or dual sensory impairment who had cognitive decline over time, which may warrant earlier detection and intervention. Longitudinal studies with larger sample sizes, clearly defined sensory impairment duration, and the use of appropriate testing tools to disentangle cognitive impairment from sensory impairments, are needed to confirm or refute the hypothesis that sensory impairment may lead to an increased risk of cognitive decline among older persons.

Section IV

Implications of the Study Findings

Section IV

Chapter 10: Implications of the Study Findings

This thesis has addressed a number of important issues relating to the long-term changes in visual acuity, the incidence of visual impairment and blindness, and the short- and long-term impacts of visual impairment among older Australians.

Together with other population-based longitudinal studies such as the Beaver Dam Eye Study[14], longitudinal data from the Blue Mountains Eye Study cohort provide an understanding of changes in visual acuity, and the changes over time in the impact of visual impairment on affected individuals, families and communities.

This thesis found a large proportion (approximately 40%) of people diagnosed with mild visual impairment were estimated to improve to normal vision over the course of 15 years. while only approximately 10% of older participants with moderate/severe visual impairment were estimated to improve to no visual impairment over the same follow-up period. The dynamic changes seen in vision over time accentuate how aging is not necessarily a downward slope, but a journey of ups and downs. These findings highlight the importance of early detection and treatment of visual impairment, and also the potential effectiveness of intervention and eye care services provided to older Australians.

This thesis explored the relationships between changes in visual acuity and the subsequent impact of visual impairment on affected individuals, families and the community over the short- and long-terms. Compared to older participants with normal vision, a greater short-term impact of visual impairment was observed on the following health outcomes, measured 5 years after visual impairment was detected: risk of having falls or fractures, self-reported depressive symptoms and the use of support services. However, these impacts were not sustained over the longer-term in 10 or more years. These findings suggest that early rehabilitation and support services provided shortly after visual impairment develops may maximize the benefit to the affected individuals and minimize the long-term burden to their families and communities. The lack of long-term associations found between visual impairment and risk of having falls or fractures, self-reported depressive symptoms and the use of support services may have also been due to an improvement of vision following treatment of visual impairment such as cataract surgery. As was estimated in Chapter 4, visual impairment can either worsen or improve over time. Furthermore, participants may or may not be classed as visually impaired depending on the definitions of visual impairment (bilateral or unilateral) used in the analysis. The fluctuation in vision and various definitions of visual impairment used incurs limitations when analysing long-term data. Further investigation in studies with much larger samples is warrant to allow for dynamic changes of vision (improvement or worsening) over time."

This thesis also explored the associations between sensory impairment and subsequent decline in cognitive function over 10 years. We did not find any increased risk of cognitive decline among older participants with visual, hearing, or dual sensory impairment in the subsequent 5 or 10 years, using a modified screening tool without vision function-dependent tests. This finding is consistent which some, but not all, previous reports[11;13]. Conflicting findings in this regard[9] may be due to the use of different cognitive function assessment tools,

and quite often visual function-dependent tasks were not excluded in previous studies. Further studies with large sample size, long-term follow-up durations and the use of more comprehensive and specific assessment tools are needed to confirm our findings.

This thesis also identifies a potential long term benefit of a healthy diet and lifestyle in prevention of visual impairment among older participants. Findings from this thesis may assist improving eye health services, planning and developing visual impairment prevention and rehabilitation programs for the older population sector. These findings also support the concept of precision medicine via tailoring the healthcare need for individual patients to optimise the cost-effectiveness of health and aged care services. With the ongoing development of more effective treatment strategies for causes of visual impairment such as anti-vascular endothelial growth factor (anti-VEGF) for age-related macular degeneration and less invasive cataract surgery, we may see a reduction in visual impairment rates in the future.

Like many developed countries, the Australian population is aging rapidly. In 2012, approximately 14% of the population were aged 65 years or older[170]. The anticipated increase in cost of, and the demand for, health and aged care will soon be beyond the capacity that the Medicare system can sustain. Prevention and early detection of visual impairment should be implemented into primary health care provision, and if detected, early treatment of amendable causes of visual impairment by eye health care professionals follows.

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