Impact of Individual and Combined Sensory Impairment in Older Australians

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Preface

This thesis describes the candidate’s full-time (three years, 2007-2009) work on the Blue Mountains Eye Study. The Blue Mountains Eye Study (BMES) is a population based cohort study of older Australians. The baseline examination (BMES 1) was conducted from 1992 to 1994 and included baseline visual acuity, collection of comprehensive lifestyle and health data and a complete eye examination including retinal photography. The five year follow up examination (BMES 2) was conducted from 1997 to 1999 and repeated previous data collection with the addition of hearing assessment. The ten year follow up (BMES 3) was conducted from 2002 to 2004 and repeated the previous data collection with the addition of olfactory assessment. The fifteen-year follow (BMES 4) was conducted from 2007 to 2009 and repeated the previous data collection. Professor Paul Mitchell (candidate’s supervisor) is the Principal Investigator, Professor Robert Cumming (candidate’s co-supervisor), Professor Stephen Leeder and Wayne Smith are the three Chief Investigators of the Study.

This thesis examined the associations of olfactory, auditory and visual impairments, individually and combined, with morbidity and mortality by both direct and indirect pathways in a representative older Australian population.
Abstract

**Purpose:** To estimate the prevalence and examine the clustering patterns of visual, auditory and olfactory impairments; to estimate the associations of olfactory impairment with neurodegenerative and other morbidities; to estimate the associations of visual and auditory impairments with morbidity and mortality using Cox regression; and to examine the associations of visual and auditory impairments with morbidity and mortality using structural equation modelling to identify potential indirect pathways and assess whether Cox regression underestimated the associations between VI, AI and mortality in a representative sample of older Australians.

**Methods:** The Blue Mountains Eye Study (BMES) examined 3,654 persons aged 49+ during 1992-1994, and after 5 and 10 years. The Blue Mountains Hearing Study (BMHS) invited participants who attended the second cross-sectional survey of the Blue Mountains Eye Study (BMES 2). Persons who moved into the study area or study age group, identified from a repeat door-to-door census in 1999, were also invited to participate. The Blue Mountains Hearing Study (BMHS) examined 2956 persons aged 49+ years (75.5% response) during 1997-2000. Vision, hearing and olfaction were assessed in BMES 3. Assessment was by interviewer administered structured questionnaire, clinical examination, audiometry, blood testing and the San Diego Odor Identification Test. A total of 1,497 (74.3% of all participants) had complete vision, auditory and olfactory data after BMES 3.

Visual impairment (VI) was categorized as either: presenting visual impairment (PVI), VA less than 6/12 Snellen equivalent (<39 letters read correctly) in the better eye using current glasses; or correctable visual impairment (CVI), PVI less than 6/12 Snellen equivalent correctable to 6/12 or better after subjective refraction; or non-correctable visual impairment
(NCVI), PVI correctable to less than 6/12 Snellen equivalent in the better eye, after subjective refraction.

Olfactory impairment (OI) was defined by San Diego Odour Identification Test score with subjects classified as having no impairment (score 6, 7 or 8), mild impairment (4 or 5), moderate impairment (≤3), or any impairment (<6). Auditory impairment (AI) was defined as the pure-tone average (0.5-4kHz) of air-conduction hearing thresholds >25 decibels hearing level (dBHL). Cognitive impairment was defined as mini mental state exam (MMSE) scores <24.

Log-linear models were used to assess the concomitant presence of the three sensory impairments (visual, auditory and olfactory). Observed frequencies of concomitant sensory impairments were compared to the expected frequencies estimated assuming they occurred independently (no clustering tendency). Multivariable adjusted logistic regression models were constructed to estimate associations between olfactory impairment and morbidities, including neurodegenerative conditions. Associations between visual impairment and mortality risk, and between hearing loss and mortality risk, were estimated using Cox regression and structural equation modelling (SEM). Odds ratios (OR), hazard ratios (HR) and 95% confidence intervals (CI) are presented. A p-value of less than 0.05 was considered statistically significant. Australian National Death Index data confirmed deaths until 2005.
**Results:** After 13 years from baseline, 1273 participants had died. After 5 years from BMES 2 (BMHS), 403 participants had died.

At BMES 3, the prevalence of PVI, CVI and NCVI was 11%, 8% and 3% respectively. The prevalence of any OI was 27.0% and the prevalence of AI was 43%. The observed prevalence of having all three sensory impairments in persons with PVI (or NCVI) was 2.6 (or 3.0) times greater than predicted if they clustered independently. VI, AI and OI clustered differently in women compared to men.

Inverse associations were observed between OI and body mass index (OR per 5 kg/m2 increase, 0.8, CI 0.7-0.9) and between moderate impairment and hypertension (OR 0.6, CI 0.4-0.9). There was no significant relationship with angina, previous myocardial infarction or diabetes. Persons with Parkinson disease had an increased likelihood of both mild (OR 9.8, CI 2.0-47.5) and moderate OI (OR 16.1, CI 3.8-68.2), as did persons with impaired cognitive function (OR 3.3, CI 1.3-8.6 and OR 3.7, CI 1.5-9.6, respectively).

After adjusting for mortality risk markers using Cox regression, higher mortality was associated with NCVI (HR 1.35, CI 1.04-1.75). This association was stronger for ages <75 years (HR 2.58, CI 1.42-4.69). Structural equation modelling revealed greater effects of NCVI on mortality risk (HR 5.25, CI 1.97-14.01 for baseline ages <75), with both direct (HR 2.16, CI 1.11-4.23) and indirect effects (HR 2.43, CI 1.17-5.03). Of the mortality risk markers examined, only disability in walking demonstrated a significant indirect pathway for the link between VI and mortality. Disability in walking acted both directly on mortality and via an association with self-rated health.
Using Cox regression, hearing loss was associated with increased risk of both cardiovascular (HR 1.36, CI 1.08-1.84) and all-cause mortality (HR 1.39, CI 1.11-1.79) after adjustment for age and sex, but not after multivariable adjustment. Structural equation modelling pathway analysis, however, revealed a higher all-cause mortality risk (HR 2.58, CI 1.64-4.05) in persons with hearing loss, which was mediated by two variables: cognitive impairment (HR 1.45, CI 1.08-1.94) and disability in walking (HR 1.63, CI 1.24-2.15). These variables increased mortality both directly and indirectly through effects on self-rated health.

**Conclusions:** In this representative population of older Australians, over one in ten persons had VI, over one in four persons had OI and almost one in two persons had AI. The prevalence of VI, AI and OI increased with increasing age. The prevalence of AI and OI was higher in males. The prevalence of VI was higher in females. Visual, auditory and olfactory impairments aggregated mutually and dependently.

Visual impairment and AI were significantly associated with morbidity and mortality. Visual impairment predicted mortality by both direct and indirect pathways. Auditory impairment predicted mortality via indirect pathways. Disability in walking, which can substantially influence general health, represented a major indirect pathway for both VI and AI. Auditory impairment was also associated with increased all-cause mortality via cognitive impairment and self-rated health. Adjustment for these co-variables using Cox regression underestimated the associations between VI and AI and mortality.

Olfactory impairment was inversely associated with BMI and hypertension. Olfactory impairment was significantly higher among persons with Parkinson disease and cognitive impairment.
It is important to recognise that persons with sensory impairments are at increased risk of important comorbidities and mortality. Dependent clustering of sensory impairments suggest the possibility of a common underlying mechanism and that separate hearing and vision services may not adequately support older persons.
Summary

Visual, auditory and olfactory impairments were frequent in this representative older Australian population. The prevalence of VI (11%), AI (43%) and OI (27%) increased with increasing age in both sexes. The prevalence of AI and OI was higher in males. The prevalence of VI was higher in females.

Visual, auditory and olfactory impairments aggregated mutually and dependently. Common mechanisms may underlie these sensory impairments. Persons with this combination of disabilities are at increased risk of social isolation, depression, low self-rated health and quality of life, functional difficulties, mobility problems, falls, fractures and mortality. Separate hearing and vision services may not adequately support older persons with multiple impairments.

Our data support a role for olfactory function in maintaining nutritional status and body weight and provide additional support to the link between impaired olfaction and neurodegenerative disorders.

These data reaffirm reports that visual impairment is associated with increased risk of all-cause mortality and suggest the association may be greater than previously reported with traditional regression modelling. Disability in walking was an indirect pathway to mortality for persons with visual impairment.

This study supports the contention that hearing loss is associated with an increased risk of mortality through the mediating variables disability in walking and SRH and identifies cognitive impairment as another potential mediating variable.
Acknowledgements

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Abbreviations

ADAS-cog    Alzheimer Disease Assessment Scale, cognitive subscale
ADL         Activities of Daily Living
ALMPT       Amiens, Lyon, Montpellier, Paris and Toulouse study in France
AMD         Age-Related Macular Degeneration
ANCOVA      Analysis Of Covariance
ANOVA       Analyses Of Variance
ARMD        Age-Related Macular Degeneration
AREDS       Age-Related Eye Disease Study
ARIC        Atherosclerosis Risk in Communities
B-SIT        Brief Smell Identification Test
BBES        Barbados Eye Study
BCRS        Brief Cognitive Rating Scale
BCVA        Best Corrected Visual Acuity
BCVI        Best Corrected Visual Impairment
BDES        Beaver Dam Eye Study
BDI         Beck Depression Inventory
BDI-II-NL   Beck Depression Inventory-II-Netherlands
BEHL         Better Ear Hearing Threshold
BES         Baltimore Eye Study
BISED       Barbados Incidence Study of Eye Diseases
BJES        Beijing Eye Study
BMES        Blue Mountains Eye Study
BMHS        Blue Mountains Hearing Study
CC-SIT      Cross-Cultural Smell Identification Test
CES-D-10  Center for Epidemiologic Studies Depression Scale
CFH  Complement Factor H
CHD  Coronary Heart Disease
CI  Confidence Interval
COP  Centre of Pressure
CSHA  Canadian Study of Health and Aging
CSME  Clinically Significant Macular Oedema
CVD  Cardiovascular Disease
CVI  Correctable Visual Impairment
dBALeq  decibels Equivalent Sound Level
  Time-weighted average of the level of sound (Leq) in decibels (dB) on scale A
  Scale A is relatable to human hearing denoting the frequency weighting
  Scale A audio frequency range = 20Hz - 20kHz
dBHL  decibels Hearing Level
dBHTL  decibels Hearing Threshold Level
dBSNR  dB of Signal to Noise Ratio
dBSPL  dB of sound pressure level
DR  Diabetic Retinopathy
DRR  Death Rate Ratio
EHLS  Epidemiology of Hearing Loss Study
EOTC  European Olfactory Abilities Test (ETOC)
ETDRS  Early Treatment of Diabetic Retinopathy Study
FES  Framingham Eye Study
FITSA  Finnish Twin Study on Ageing
GDS-K  Geriatric Depression Scale - Korean version
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<tr>
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<th>Description</th>
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<tr>
<td>GHS</td>
<td>Gallaudet Hearing Scale</td>
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<tr>
<td>GQoL</td>
<td>Geriatric Quality of Life</td>
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<tr>
<td>HAMD</td>
<td>Hamilton Depression Scale</td>
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<tr>
<td>HI</td>
<td>Hearing Impairment</td>
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<td>HRQOL</td>
<td>Health-Related Quality of Life</td>
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<tr>
<td>HSCL-25</td>
<td>25-item Hopkins Symptom Checklist</td>
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<tr>
<td>HUI3</td>
<td>Health Utilities Index Mark 3</td>
</tr>
<tr>
<td>IADL</td>
<td>Independent Activities of Daily Living</td>
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<tr>
<td>IRR</td>
<td>Incidence Rate Ratio</td>
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<tr>
<td>JLS</td>
<td>Jerusalem Seventy Year Olds Longitudinal Study</td>
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<tr>
<td>HRQOL</td>
<td>Health-related Quality Of Life</td>
</tr>
<tr>
<td>HUNT</td>
<td>Nord-Trøndelag Health Study</td>
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<tr>
<td>kHz</td>
<td>Kilohertz</td>
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<tr>
<td>LALES</td>
<td>Los Angeles Latino Eye Study</td>
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<td>LASA</td>
<td>Longitudinal Aging Study Amsterdam</td>
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<tr>
<td>LOCS II</td>
<td>Lens Opacities Classification System II</td>
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<tr>
<td>LQ</td>
<td>Life Quality domain of the QOD</td>
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<tr>
<td>LQrv</td>
<td>Life Quality raw score of the QOD</td>
</tr>
<tr>
<td>LQsc</td>
<td>Life Quality score of the QOD</td>
</tr>
<tr>
<td>MANOVA</td>
<td>Multivariate Analysis Of Variance</td>
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<td>MCS</td>
<td>Mental Component Score (of the SF-36)</td>
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<td>MDD</td>
<td>Major Depressive Disorder</td>
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<td>MI</td>
<td>Mood Inventory</td>
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<td>MMSE</td>
<td>Mini-Mental State Exam</td>
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<tr>
<td>MMSE-K</td>
<td>Korean version of the Mini-Mental State Examination</td>
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MVIP    Melbourne Visual Impairment Project
MR      Mortality Rate
NEI-VFQ25  National Eye Institute Visual Function Questionnaire
NHANES National Health Examination and Nutrition Survey
NCHS    National Center for Health Statistics
NCVI    Non Correctable Visual Impairment
NHIS    American National Health Interview Survey
NL-SH  Study on Hearing The Netherlands
NPHS    Statistics Canada National Population Health Survey
NPDR    Non-Proliferative Diabetic Retinopathy
NSHAP   National Social Life, Health, and Aging Project
OAG     Open Angle Glaucoma
OR      Odds Ratio
P       Parosmia domain of the QOD
P-SIT   Picture-Based Smell Identification Test
PCS     Physical Component Score (of the SF-36)
PDR     Proliferative Diabetic Retinopathy
Prv     Parosmia raw score of the QOD
Psc     Parosmia score of the QOD
PVA     Presenting Visual Acuity
PVI     Presenting Visual Impairment
QOD     Questionnaire of Olfactory Disorders
QOD-DS  Socially Desirable domain of the QOD
QOD-NS  Negative Statement domain of the QOD
QOD-PS  Positive Statement domain of the QOD
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tr>
<td>QOL</td>
<td>Quality of Life</td>
</tr>
<tr>
<td>RES</td>
<td>Rotterdam Eye Study</td>
</tr>
<tr>
<td>RR</td>
<td>Risk Ratio or Rate Ratio</td>
</tr>
<tr>
<td>S</td>
<td>Sincerity domain of the QOD</td>
</tr>
<tr>
<td>Srv</td>
<td>Sincerity raw score of the QOD</td>
</tr>
<tr>
<td>Ssc</td>
<td>Sincerity score of the QOD</td>
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<tr>
<td>SAHOS</td>
<td>South Australian Health Omnibus Survey</td>
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<tr>
<td>SDOIT</td>
<td>San Diego Odor Identification Test</td>
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<tr>
<td>SDV</td>
<td>Self-reported serious Difficulty with Vision</td>
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<tr>
<td>SEE</td>
<td>Salisbury Eye Evaluation</td>
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<td>SES</td>
<td>Shihpai Eye Study</td>
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<td>SF-12</td>
<td>Medical Outcomes Study 12 item Short-Form</td>
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<tr>
<td>SF-36</td>
<td>Medical Outcomes Study 36 item Short-Form</td>
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<tr>
<td>SMR</td>
<td>Standardised Mortality Rate</td>
</tr>
<tr>
<td>SNP</td>
<td>Single Nucleotide Polymorphism</td>
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<tr>
<td>SOA-II</td>
<td>Second Supplement On Ageing</td>
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<tr>
<td>SOIT</td>
<td>Scandinavian Odor Identification Test</td>
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<td>SRH</td>
<td>Self-Rated Health</td>
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<tr>
<td>SRS</td>
<td>Self-Rated Scale</td>
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<td>SRT</td>
<td>Selective Reminding Test</td>
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<tr>
<td>SRT-TR</td>
<td>Selective Reminding Test Total immediate Recall</td>
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<td>SRVI</td>
<td>Self-Reported Visual Impairment</td>
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<td>SSNHL</td>
<td>Sudden Sensorineural Hearing Loss</td>
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<tr>
<td>STAI</td>
<td>State-Trait-Anxiety-Inventory</td>
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<tr>
<td>TDI</td>
<td>Threshold Discrimination Identification score</td>
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<tr>
<td>Acronym</td>
<td>Full Form</td>
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<td>---------</td>
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<tr>
<td>UPSIT</td>
<td>University of Pennsylvania Smell Identification Test</td>
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<td>VAS</td>
<td>Visual Analogue Scales of the QOD</td>
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<td>VCM1</td>
<td>Vision-Related Quality of Life Core Measure 1</td>
</tr>
<tr>
<td>VI</td>
<td>Visual Impairment</td>
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<tr>
<td>VIP</td>
<td>Visually Impaired Person's</td>
</tr>
<tr>
<td>VRQOL</td>
<td>Vision-Related Quality Of Life</td>
</tr>
<tr>
<td>WESDR</td>
<td>Wisconsin Epidemiologic Study of Diabetic Retinopathy</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
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Publications Relating to this Thesis


Other BMES Publications Co-authored by the Candidate


Candidate’s Contribution

1. Professor Paul Mitchell and the candidate jointly contributed to the development of this thesis topic.

2. The candidate contributed to the revision of the questionnaires, ethics forms and examination booklet for BMES IV.

3. The candidate contributed to the application for ethics approval for BMES 4.

4. The candidate contributed to the publicity of BMES 4 including:
   a. Newspaper advertisements
   b. Newsletter to participants
   c. Advertisements to local medical officers
   d. Posters for local medical officers’ rooms
   e. Meetings with local medical officers, optometrists and interested parties

5. The candidate was responsible for finding and arranging rental of the field centre.

6. The candidate was responsible for arranging council approval to use the site.

7. The candidate contributed to procurement, logistics, placement, assembly and disassembly of the equipment and furniture for the entire field centre.

8. The candidate contributed to hiring, training and supervision of staff and investigators of the BMES 4.

9. The candidate performed the ocular examinations, lens grading and retinal photography for the entire BMES 4 data collection period.

10. The candidate performed lens photography and optical coherence tomography for a significant proportion of the BMES 4 cohort and trained another candidate in the performance of these duties.

11. The candidate performed the structured interview by questionnaire for a many of the BMES 4 cohort.
Professor Paul Mitchell and the candidate jointly contributed to every result letter sent to the participants and their local medical officers.

The candidate worked directly with the statisticians to design and interpret all statistical analyses.

The candidate wrote the first draft of all publications submitted in relation to this thesis with the candidate's name as first author.

The candidate collated revisions by other authors, wrote the final draft and submitted all papers in relation to this thesis with the candidate's name as first author.

The candidate contributed ideas and corrections for all publications co-authored by the candidate.
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Chapter One: Literature Review of the Prevalence and Associations of Visual, Auditory and Olfactory Impairment with Morbidity and Mortality in Older Persons
Visual, auditory and olfactory impairments are prevalent disabilities that are reportedly significantly and negatively associated with morbidity and mortality. The following review summarises representative examples from the literature that report the prevalence of visual, auditory and olfactory impairments and their associations with morbidity and mortality. The results of studies that report associations with morbidities examined in this thesis are included as background. This permits comparison of the results reported in this thesis with the literature current at the time of writing.

One of the difficulties in objectively scrutinizing these studies is that each differs in population demographics, particularly in age range and mean population. Each study also differs by the specific covariates used for adjustment in the multivariate models, and many differ in the definition of baseline visual impairment, by the methods of olfactory and auditory assessment. Some studies lacked objective measures of sensory function, using self and by proxy reporting of sensory impairments.
1.1 Visual Impairment
Prevalence

The visual impairment prevalence data presented in this review are derived from studies representative of the findings in the literature and that are similar in design and timing of data collection, when compared to the Blue Mountains Eye Study (BMES). Previous results from the BMES are also included. These studies were chosen to provide suitable background for the findings of this thesis and to illustrate the addition this thesis makes to the literature.
**The Prevalence of Visual Impairment**

The World Health Organisation estimated the global burden of visual impairment (best corrected visual acuity (BCVA) of <6/18 in the better eye) to be 161 million, including 37 million with blindness (BCVA of <3/60).9,10 If this definition is expanded to include persons with uncorrected refractive error then an estimated 259 million persons were visually impaired in 2002, including 42 million persons with blindness.11

The burden of visual impairment in Australia (BCVA <6/12) was estimated to be 297,800 persons, including 48,600 with blindness (BCVA 6/60) in 2004.12 If this definition is expanded to include persons with uncorrected refractive error, then this estimate increases to 480,300 with visual impairment, including 50,600 persons with blindness.12 The number of persons in Australia with low vision is projected to increase to 800,000 by 2020.12 These estimates were based on the combined results of the BMES and the Melbourne Visual Impairment Project (MVIP).12

The BMES is a population-based cohort study of common eye diseases and other health outcomes in a suburban Australian population located west of Sydney.2 The BMES baseline visual acuity data were collected during the years 1992-1994 and included persons aged from 49-97 years old. The baseline participation rate was 82%. The MVIP was a random cluster sample population based study of eye disease in urban and rural residents of Victoria.1 The MVIP baseline visual acuity data was collected during the years 1993-1995 and included persons aged 40-98 years old. The participation rate was 83%.

These studies defined levels of visual impairment differently. The BMES defined visual impairment as: blindness (BCVA <6/60); moderate visual impairment (BCVA ≤6/24->6/60)
and mild visual impairment (BCVA ≤6/12- >6/24). The MVIP definitions were: blindness (BCVI <3/60); visual impairment (BCVA <6/18); and visual impairment excluding blind persons (BCVA <6/18 ≥3/60).

The BMES reported prevalence rates for bilateral mild, moderate and severe best corrected visual impairment (BCVI) of 3.4%, 0.6% and 0.5% respectively. In the MVIP cohort, the prevalence of visual impairment (BCVI <6/18 ≥3/60) was 0.58% and the prevalence of blindness (BCVI <3/60) was 0.12%.

The Beaver Dam Eye Study (BDES) is a population based cohort study of common eye diseases and other health outcomes in an urban United States population located in Beaver Dam, Wisconsin. The BDES baseline visual acuity data were collected during the years 1988-1990 and included persons aged 43-84 years old. The baseline participation rate was 83%. The BDES utilised the same visual acuity limits as the BMES (mild (BCVA ≤6/12- >6/24), moderate (BCVA ≤6/24- >6/60) and severe (BCVA <6/60) and reported a similar prevalence of bilateral mild, moderate and severe BCVI of 3.9%, 0.8% and 0.5% respectively.

The Los Angeles Latino Eye Study (LALES) is a population based cohort study of eye disease in the predominately Latino population of Mexican ancestry in and around the city of La Puente, Los Angeles County. The LALES baseline data was collected during the years 2000-2003 and included persons aged 40 years or older. The baseline participation rate was 82%. The LALES reported the same visual acuity limits as the BMES and BDES (mild (BCVA ≤6/12- >6/24), moderate (BCVA ≤6/24- >6/60) and blindness (BCVA <6/60). The
The prevalence of visual impairment was found to increase significantly with increasing age in these population based studies. In addition, population based studies with older cohorts consistently report higher prevalence rates of visual impairment compared to the BDES, BMES, MVIP and the LALES including the RES and the SEE Project.
The Prevalence of Visual Impairment and Gender

With the exception of the Baltimore Eye Study (BES)\textsuperscript{14} and SEE\textsuperscript{3} study, the studies presented reported significantly higher prevalence of visual impairment in women compared to men after adjustment for age.\textsuperscript{1,3,5,8} The WHO reported women are more likely to have a visual impairment than men in every region of the world, with ratios ranging from 1.5 to 2.2.\textsuperscript{9}
The Prevalence of Visual Impairment, Race and Socioeconomic Status

The BMES, BDES, MVIP, LALES and the BES reported visual impairment to have higher prevalence in persons from lower socioeconomic backgrounds.4,6,15-17

The SEE study examined racial differences in the prevalence of visual impairment and blindness, but not socioeconomic status. The SEE study reported African Americans had two times higher likelihood of being visually impaired and more than three times higher likelihood of being blind when compared to white persons.18

The Baltimore Eye Study (BES) reported a higher prevalence of visual impairment and blindness in African Americans when compared to whites and that this increase was largely attributable to lower socioeconomic status rather than racial differences.6 Significantly, the increased prevalence of visual impairment found in African American or persons of lower socioeconomic status in this population was due to surgically treatable or potentially preventable causes such as cataract, diabetic retinopathy, glaucoma and refractive error.15,16,18,19

Comparing age specific rates of VI, the LALES authors reported the prevalence of VI to be higher in this population of predominately Latino persons of Mexican ancestry when compared to non-Hispanic whites in the BDES, BMES, Baltimore Eye Study (BES), Rotterdam Eye Study (RES) and the Salisbury Eye Evaluation (SEE) Project, but not as high as in African Americans.4

Socioeconomic status is a significant predictor of an increased prevalence of visual impairment worldwide. Studies of visual impairment in developing countries consistently
report higher rates of visual impairment compared to developed countries. In 2002, the WHO estimated prevalence of blindness was 9.0% in Africa compared to 0.4-0.6% in the United States, Western Europe and Australia, mostly due to cataract.9

The Beijing Eye Study (BJES) is a population based study of eye diseases in urban and rural areas of Northern China. It was carried out in seven communities, four from the Haidian urban district and three from the rural village area of Yufa.7 The baseline visual acuity data was collected during 2001 and included persons aged older than 40 years. The baseline participation rate was 83%. The Beijing Eye Study examined the same age group and reported the same visual acuity limits as the MVIP of bilateral visual impairment (BCVA <6/18-≥3/60) and blindness (BCVA<3/60).2

The BJES reported a higher prevalence compared to the MVIP of visual impairment (1.1% vs.. 0.58%) and blindness (0.3% vs.. 0.12%).1,7 The Beijing Eye Study also reported a significant inverse association with education level and that the largest cause of visual impairment was cataract.2 In contrast to western countries, age related macular degeneration and diabetic retinopathy played minor roles in causing visual impairment.2

Tables 1.1 and 1.2 summarise the prevalence of visual impairment these studies reported by category of visual impairment.
### Table 1.1 Summary of the prevalence of visual impairment in studies using the same categories of visual impairment† compared to the Blue Mountain Eye Study (BMES).

<table>
<thead>
<tr>
<th>Study</th>
<th>Participation Rate (%)</th>
<th>Mild (%)</th>
<th>Moderate (%)</th>
<th>Severe/Blindness (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMES(^a)</td>
<td>82</td>
<td>3.4</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td>BDES(^b)</td>
<td>83</td>
<td>3.9</td>
<td>0.8</td>
<td>0.5</td>
</tr>
<tr>
<td>LALES(^c)</td>
<td>82</td>
<td>2.1</td>
<td>0.5</td>
<td>0.4</td>
</tr>
</tbody>
</table>

† Visual impairment limits defined as mild (BCVA\(^d\) \(\leq\) 6/12 -> 6/24); moderate (BCVA\(^d\) \(\leq\) 6/24- >6/60); and severe/blindness (BCVA\(^d\) <6/60)

\(^a\) Blue Mountains Eye Study\(^2\)

\(^b\) Beaver Dam Eye Study\(^3\)

\(^c\) Los Angeles Latino Eye Study\(^4\)

\(^d\) Best corrected visual acuity

### Table 1.2 Summary of prevalence of visual impairment in studies using different categories of visual impairment† compared to the Blue Mountains Eye Study (BMES).

<table>
<thead>
<tr>
<th>Study</th>
<th>Participation Rate (%)</th>
<th>Visual Impairment (%)</th>
<th>Blindness (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVIP(^a)</td>
<td>83</td>
<td>0.58</td>
<td>0.12</td>
</tr>
<tr>
<td>RES(^b)</td>
<td>66</td>
<td>1.4</td>
<td>0.47</td>
</tr>
<tr>
<td>SEE(^c)</td>
<td>65</td>
<td>3.7</td>
<td>0.83</td>
</tr>
<tr>
<td>BJES(^d)</td>
<td>83</td>
<td>1.1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

† Visual acuity limits defined as visual impairment BCVA (<6/18-\(\geq\) 3/60); and blindness (BCVI <3/60)

\(^a\) Melbourne Visual Impairment Project\(^1\)

\(^b\) Rotterdam Elderly Study\(^5\)

\(^c\) Salisbury Eye Evaluation project\(^8\)

\(^d\) Beijing Eye Study\(^2\)
The Associations between Visual Impairment and Morbidity
Visual Impairment and Self-rated-health

Few studies have examined the associations of visual impairment with low self-rated health (SRH). The association has been estimated in the BMES population. During the baseline data collection, participants were asked: For someone of your age, how would you rate your overall health? Excellent, good, fair or poor. Self-rated health was dichotomised into excellent and good versus fair or poor. The answers fair or poor were scored as low SRH. Presenting and best corrected visual acuity were modelled as continuous independent variables using multivariable regression modelling. The model included all other co-variables found significantly associated with low SRH in this population and included socioeconomic variables, physical limitations, chronic diseases, risky health behaviours and hearing loss (17 co-variables in total).

After multivariable adjustment, there was a significantly increased likelihood of low SRH for both presenting and BCVI in persons younger than age 80 years. The association was not significant in persons older than 80 years. The likelihood of low SRH was greater when VI was modelled using best corrected visual acuity. For each one line (5 letters) decrease in visual acuity, there was a 10% increased likelihood of low SRH (odds ratio (OR) 1.1, 95% confidence interval (CI) 1.1-1.3) for PVA compared to a 20% increase (OR 1.2, CI 1.1-1.3) when visual acuity was modelled as BCVA.

The Jerusalem Seventy Year Old’s Longitudinal Study (JLS) also reported a significant association between visual impairment and poorer self-reported health. The JLS is a population-based cohort study of social and medical conditions of persons living in West Jerusalem born between June 1920 and May 1921. Baseline visual acuity data were collected from May 1990 to June 1991. Baseline participation rate was 61%. Visual impairment was
defined as BCVA in the better eye of ≤ 6/18. Self-rated health was measured in both absolute terms and in relation to others of the same age. Of the persons examined at baseline, 68% were re-examined in 1997 (Age = 77). A second cohort of persons aged 77 were also examined to maintain study numbers for future follow up.\textsuperscript{21}

The JLS reported that persons with visual impairment at age seventy (baseline examination) were significantly more likely to report poor SRH both in relative and absolute terms compared to persons with normal vision.\textsuperscript{21} The effect was significant in both sexes but stronger in women. Persons with visual impairment at age 70 were significantly more likely to subsequently report poor relative SRH at seven years follow up (OR 2.36, CI 1.09-5.10). In persons with visual impairment at age 77 (baseline participants plus additional cohort), only women were significantly more likely to report relative poor SRH.\textsuperscript{21}

Two studies have reported significant associations between self or by proxy-reported VI and SRH.\textsuperscript{22,23} Lee \textit{et al}, used pooled results from the American National Health Interview Survey collected over the years 1986 to 1996.\textsuperscript{22} In total, 140366 non-institutionalised civilian adults aged 18 years or older living in the United States were included in the study. Visual impairment was assessed by asking if participants were blind or had difficulty seeing in one or both eyes, even when wearing glasses. Visual impairment was defined as severe VI (self or by proxy-reported blindness in both eyes), some visual impairment (self or by proxy-reported visual impairment reported in one or both eyes or blindness in one eye with or without visual impairment in the other eye) and no visual impairment (no self or by proxy-reported difficulty with vision in either eye). Persons reporting excellent or good SRH were compared to persons reporting fair or poor SRH.\textsuperscript{22}
After adjusting for survey design, race, educational status and number of reported nonocular conditions, persons reporting some or severe VI had a greater likelihood of reporting low SRH compared to persons who reported no VI.\textsuperscript{22} Severe VI was associated with greater likelihood of low SRH compared to persons reporting some VI. Younger persons with VI were more likely to report low self-rated health compared to older persons. Women reporting VI had a greater likelihood of low SRH compared to men. For women reporting severe VI, the greater likelihood of low SRH was; OR 7.24, CI 2.91-18.07 for 18-44 year olds; OR 6.72, CI 2.90-15.55 for 45-64 year olds; and OR 2.14, CI 1.35-3.40 for 65+ year olds. For men reporting severe VI, the greater likelihood of low SRH was; OR 4.48, CI 2.22-9.03 for 18-44 year olds; OR 2.54, CI 1.20-5.39 for 45-64 year olds; and OR 2.50, CI 1.44-4.32 for 65+ year olds.\textsuperscript{22}

Wallhagen \textit{et al} studied two thousand four hundred forty-two community-dwelling persons aged 50 to 102 from the Alameda County Study (California).\textsuperscript{23} The aim of the study was to compare independent impacts of two levels of self-reported hearing impairment (HI) and VI on subsequent disability, mental health, physical and social functioning. Baseline data including self-reported VA was collected in 1994, with the one-year outcomes measured in 1995. Three questions were used to assess VI. Participants were asked how much difficulty they had (even with glasses) reading street signs at night, recognising a friend across the street and reading a newspaper. The possible responses (score) were: “a great deal” (3), “some” (2), “a little” (1), or “none” (0). Scores were summed and the resulting scale divided into three categories: no VI (score = 0), mild VI (score = 1-3), and moderate or more VI (score ≥ 4). Those reporting SRH as fair or poor were compared with those reporting good or excellent SRH.\textsuperscript{23}
The study reported no significant association between mild VI and low SRH, however, a significant association was reported between \( \geq \) moderate VI and Low SRH (OR 1.63, CI 1.07-2.48).\(^23\)

Table 1.3 summarises the findings of the studies that did not separate results by sex.

**Table 1.3** Summary of odds ratios (OR) and 95% confidence intervals (CI) of reporting low self-rated health in persons with visual impairment by study and age.

<table>
<thead>
<tr>
<th>Study</th>
<th>Participant Age (Years)</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMES (^a, c)</td>
<td>( \geq 49 )</td>
<td>1.20</td>
<td>1.10 – 1.30</td>
</tr>
<tr>
<td>JLS (^a, d)</td>
<td>( \geq 70 )</td>
<td>2.36</td>
<td>1.09 – 5.10</td>
</tr>
<tr>
<td>ACS (^b, e)</td>
<td>( \geq 50 )</td>
<td>1.63</td>
<td>1.07 – 2.48</td>
</tr>
</tbody>
</table>

\(^a\) Best corrected visual impairment <6/12 BMES; \( \leq 6/18 \) JLS
\(^b\) Self-reported visual impairment
\(^c\) Blue Mountains Eye Study\(^20\)
\(^d\) The Jerusalem Seventy-year old’s Longitudinal Study\(^21\)
\(^e\) Alameda County study\(^23\)
Visual Impairment, Measures of Function and Health Related Quality of Life

In comparison to SRH, more data has been reported for standardised measures of Health Related Quality of Life including the generic Medical Outcomes Study 36 item Short-Form (SF-36) and the vision specific National Eye Institute Visual Function Questionnaire (NEI-VFQ25). Both have been validated across a range of populations.\textsuperscript{24-28} These assess different dimensions of the same outcome measures and are reported to be valid and reliable measures of quality of life.\textsuperscript{24,29}

The SF-36 includes eight subscales: limitations in physical activities due to health problems; limitations in social activities because of physical or emotional problems; limitations in usual role activities because of physical health problems; bodily pain; general mental health; limitations in usual role activities because of emotional problems; vitality; and general health perceptions.\textsuperscript{26}

The NEI-VFQ25 includes twelve subscales: general health; general vision; near vision; distance vision; driving; peripheral vision; colour vision; ocular pain; role limitations; dependency; limitations in social functioning; and mental health.\textsuperscript{25}

Associations between visual impairment and health related quality of life measured by the SF-36 and the NEI-VFQ25 are reported for the BMES population.\textsuperscript{27,29,30} The SF-36 questionnaire was completed and visual acuity re-assessed in the BMES 2 data collection period in 1997 to 1999 in 2335 participants (75.1\% of the original cohort). A repeat door to door census found 1378 more persons had become eligible for inclusion into the study (age 50 years or older). Of these, 1174 persons (85\%) were interviewed and examined in the
BMES extension study (BMES 2B). The HRQOL of the BMES 2B cohort was assessed using both the SF-36 and the NEI-VFQ-25.27,29,30 Complete SF-36 and VA data were available from 3153 (90%) participants and complete NEI-VFQ-25 and VA data were available from 892 (76%) of the BMES 2B cohort.27,29,30 The impact of unilateral and bilateral visual impairment was examined. Presenting visual impairment was defined as VA <6/12. Correctable visual impairment was defined as PVI improving to ≥6/12 after subjective refraction and NCVI was defined as VI that persisted after subjective refraction. Levels of VI were defined as mild (<6/12 - ≥6/24), moderate (<6/24 - ≥6/60) and severe (<6/60).27,29,30

For unilateral VI, after age and sex adjustment, there were no statistically significant differences in SF-36 scores for unilateral VI, mild unilateral or correctable unilateral VI compared to persons without VI.29 Persons with moderate to severe unilateral NCVI had statistically significant lower SF-36 scores in three of the eight dimensions compared to persons without VI after age and sex adjustment; role limitations due to physical problems (15%), social functioning (7%), role limitations due to emotional problems (13%) and in the mental component score.29

There were no statistically significant decreases in any NEI-VFQ-25 scores for persons with unilateral CVI.28 Unilateral PVI was associated with statistically significant decreases in NEI-VFQ-25 scores in four dimensions compared to persons without PVI; general vision (6%); mental health (4%); dependency (2%); and driving (3%) and composite score (2%).28
Unilateral NCVI was associated with statistically significant lower NEI-VFQ-25 scores in eight dimensions after age and sex adjustment; general vision (11%); near vision (6%); distance vision (4%); social function (2%); mental health (10%); role difficulty (6%); dependency (2%); and peripheral vision (7%) and composite score (5%).

The following associations reported between bilateral VI and NEI-VFQ-25 were age and sex adjusted. The associations reported between bilateral VI and SF-36 scores were multivariable adjusted for age, sex, home ownership, current employment, marital status, tertiary education, receipt of a government pension, hospital admission in the preceding year, current smoking, and history of angina, stroke, hypertension, diabetes, arthritis, thyroid disease and cognitive impairment.

Bilateral CVI was associated with statistically significant lower SF-36 scores in two of the eight dimensions; physical functioning (8%); social functioning (6%); and the physical component score (5%) after multivariable adjustment. Bilateral CVI was also associated with statistically significant lower scores in seven of twelve dimensions of the NEI-VFQ-25; general vision (12%); near vision (9%); distance vision (5%); mental health (8%); role difficulty (8%); dependency (5%); peripheral vision (6%) and with the composite score (5%) after age and sex adjustment.

In comparison, bilateral NCVI was associated with statistically significant lower SF-36 scores in five of the eight dimensions; physical functioning (8%); general health (13%); vitality (18%); social functioning (9%); and mental health (9%) and the mental component score (8%) after multivariable adjustment. Bilateral NCVI was also associated with statistically significant lower scores in all dimensions of the NEI-VFQ-25; general health.
(24%) general vision (61%); ocular pain (16%); near vision (55%); distance vision (59%); social function (44%); mental health (49%); role difficulty (50%); dependency (33%); driving (74%); colour vision (33%); peripheral vision (47%) and composite score (45%) after age and sex adjustment.\textsuperscript{28,30} In addition, increasing severity of NCVI was associated with statistically significant decreases in SF-36 and NEI-VFQ-25 scores.\textsuperscript{28,30}

The 1958 British birth cohort assessed vision related quality of life (VRQOL) using the vision-related Quality of Life Core Measure 1 (VCM1).\textsuperscript{31} The cohort comprised everyone born in Britain during one week in 1958. The VCM1 is a validated 10 item self-completed VRQOL measure\textsuperscript{32} with a scoring range from 0 to 5. Higher scores represent lower VRQOL. Visual acuity and VCM1 data were obtained from 9324 of 11971 (78%) invited persons aged 44/45 years during 2002 to 2003.\textsuperscript{31} A score of greater than two was defined as impaired VRQOL. Visual acuity was defined as; normal (≥6/9.5 in both eyes); unilateral visual loss (normal VA one eye and ≤6/12 other eye); socially significant visual loss (≤6/12-≥6/18 better eye VA); visual impairment (≤6/19-≥6/60 in the better eye); severe visual impairment (<6/60-≥3/60 better eye VA); and blindness (<3/60 better eye VA).\textsuperscript{31}

In the 1958 British birth cohort study, the combined prevalence of VI and severe VI was 1.2%.\textsuperscript{31} After adjustment for age, sex, socio-economic, employment and marital status, all levels of presenting visual impairment were associated with significantly increased likelihood of impaired VRQOL. The likelihood of impaired VRQOL increased with increasing visual impairment (unilateral OR 2.94, CI 1.66-5.20; socially significant OR 3.49, CI 1.50-8.08; visual impairment OR 8.15, CI 3.00-22.40; and severe VI or blindness OR 10.03, CI 1.69-59.50).\textsuperscript{31}
The LALES examined associations between presenting visual impairment and NEI VFQ-25 and SF-12 scores. Complete data for the NEI VFQ-25 and SF-12 were available from 5377 (85%) of the LALES participants. Presenting visual impairment was categorised as unilateral or bilateral; no VI (>6/12); mild VI (≥6/12->6/24); and moderate/severe VI (≤6/24). Mean SF-12 and NEI VFQ-25 scores were adjusted for age, sex, education, employment status, income, acculturation, co-morbidities, health insurance status, vision insurance status, and visual field impairment.

In the LALES study, no significant differences were reported between persons with and without PVI for any SF-12 score and the NEI VFQ-25 item scores for general health and ocular pain. The remaining NEI VFQ-25 item mean scores were significantly lower in persons with any category of PVI compared with no VI, except for the item colour vision in persons with unilateral PVI. Compared to persons without VI, persons with moderate/severe PVI had the lowest mean NEI VFQ-25 scores in all items and the composite score; general vision (21%); near vision (28%); distance vision (30%); social function (20%); mental health (31%); role difficulty (23%); dependency (32%); driving (49%); colour vision (12%); peripheral vision (17%) and composite score (23%).

The MVIP examined the association of VI with performance of visually dependent functional tasks using the VF-14 and two vision related functional tasks. The VF-14 is a valid instrument for measuring difficulties with vision related activities. It is a 14-item questionnaire scored on a 100-point scale. Lower scores represent increasing difficulty performing vision related tasks. The two vision related tasks were identifying a ten cent coin from a group of three and reading a telephone number correctly from a telephone book. Participants from two test sites and with presenting visual acuity (PVA) of less the 6/18 (508
participants) completed the VF-14 and the two vision related functional tasks. Results for each VF-14 item were categorised dichotomously as moderate/great deal of difficulty/inability to perform task and little/no difficulty (control). Odds ratios were estimated using logistic regression.

Persons with PVI <6/12 had significantly higher odds of VF-14 total score < 90 and having ≥ moderate inability to perform tasks in all items except driving during the day when compared to persons with ≥6/12 VA. Participants with a VA of <6/12 were significantly more likely to be unable to recognise a 10 cent coin (OR 7.0, CI 2.6-19.3) or correctly read a telephone number (OR 10.1, CI 5.6-18.1). The mean VF-14 score was 59 for persons who could not identify a ten-cent coin compared to 95 for those who could. Similarly, the mean VF-14 score was 79 for those who could not read a telephone number correctly compared to 96 for those who could. The proportion of persons unable to correctly perform the functional tasks increased with decreasing VA.

The MVIP five-year follow-up study examined the impacts of unilateral and bilateral VI on various functional impairments. Of the 3040 surviving participants in the MVIP baseline study, 2594 (85%) participated in the 5-year follow-up study. For this study, VI was defined as unilateral correctable (PVI <6/12 correctable to ≥6/12), non-correctable (BCVI <6/12) and moderate to severe non-correctable VI (BCVI <6/24) and bilateral correctable and non-correctable VI.

After age and sex adjustment, unilateral CVI was associated with increased likelihood of problems watching television. Unilateral NCVI was associated with increased odds of falling away from home, needing help with chores, dependency, difficulties seeing faces,
reading the telephone book and newspaper and watching television. Similar associations were found for persons with moderate to severe unilateral NCVI except that watching television and falling away from home became non-significant.\textsuperscript{36}

Bilateral VI was associated with a greater number and likelihood of functional difficulties.\textsuperscript{36} Bilateral CVI was associated with increased likelihood of difficulties reading the telephone book and newspaper, watching television and seeing faces. Bilateral NCVI was associated with the greatest number and magnitude of increased likelihood of functional difficulties. Affected participants had increased likelihood of being in a nursing home, using supplied meals, needing help with chores, dependency, health/emotional problems, not feeling full of life, difficulties reading the telephone book and newspaper, watching television, seeing faces and doing other activities.\textsuperscript{36} There were no associations found between any form of VI and falling at home and hip replacement surgery.\textsuperscript{36} Multivariate adjustment for other outcome risk factors did not significantly attenuate the associations.\textsuperscript{36}

The SEE study reported associations between self-reported functional status and PVA \textless 6/12.\textsuperscript{37} Physical function was assessed using two standardised questionnaires; the Activities of Daily Living (ADL),\textsuperscript{38} which measures difficulties in basic areas of self-care such as dressing, bathing, toileting, mobility and feeding; and the Instrumental Activities of Daily Living (IADL),\textsuperscript{39} which measures difficulty in more complex tasks necessary for independent living such as house work, paying bills and shopping. Vision specific function was measured using the activities of daily vision scale (ADVS.) questionnaire.\textsuperscript{40}

The SEE study reported that after adjusting for age, sex and race, visual impairment was significantly associated with functional limitation in all measures of functional status and
with a decline in ADVS score (-6.73). The likelihood of reporting a lot of difficulty with ADL and IADL compared to no difficulties was greater in persons with PVI compared to persons without PVI (OR 1.82, CI 1.18-2.83 and OR 2.45 CI 1.77-3.40 respectively).

Lee et al, using pooled results from the American National Health Interview Survey (NHIS) collected over the years 1986 to 1996, estimated the associations between self or by proxy reported visual impairment and restricted activity days, bed days, doctor’s visits and hospital stays. They reported males with severe bilateral VI were significantly more likely to have one or more days of restricted activity or bed rest in the preceding two weeks or to have been admitted to hospital in the previous twelve months. They were also less likely to have seen a doctor in the previous 12 months. Females with some VI were significantly more likely to have one or more days of restricted activity or bed rest in the preceding two weeks or to have been admitted to hospital in the previous twelve months. There were no significant associations in females with severe bilateral VI.

Swanson et al, using the American 1995 NHIS and its supplement on Disability (NHIS-D) estimated the impacts of self-reported serious difficulty with vision (SDV) on ADLs and IADLS. For those who reported a serious difficulty with vision, 94% had a perfect or probable condition match consistent with their reported vision difficulty. The data used were for persons 18 years and older. In total 67570 persons were included in the study. The age range was 18-99 years old (mean = 44.6). The supplement included detailed questions on six ADLs; bathing; dressing; eating; toileting; getting in and out of chairs and getting around the house; and six IADLs; shopping; preparing meals; managing money; using the telephone; doing light house work and doing heavy house work. The results were dichotomised as no difficulty and any degree of difficulty.
After adjusting for age, gender, race, poverty, self-rated health, living arrangements, depression and mental status, SDV was significantly associated with difficulty in each of the ADLs and IADLs.\textsuperscript{41} For persons reporting difficulty in the following ADLs, the increased odds of reporting SDV were; bathing OR 3.64, CI 1.85-7.19; dressing OR 1.79, CI 1.40-2.29; eating OR 2.02, CI 1.32-3.07; toileting OR 1.70, CI 1.29-2.23; transfer OR 1.53, CI 1.20-1.96 and getting around OR 1.75, CI 1.36-2.25. For persons reporting difficulty in the following IADLs, the increased odds of reporting SDV were; shopping OR 2.53, CI 2.09-3.05; meals OR 1.92, CI 1.51-2.43; money OR 2.56, CI 1.98-3.33; telephone OR 2.65, CI 1.75-4.01; light housework OR 1.88, CI 1.53-2.31 and heavy housework OR 1.76, CI 1.51-2.05.\textsuperscript{41}

Laitinen \textit{et al} conducted a cross sectional survey of a representative Finnish population examining the associations between PVI with ADLs and IADLs.\textsuperscript{42} The data were obtained from the Health 2000 survey, a nationwide population based survey of health and functional capacity carried out in Finland in 2000-2001. The data used were from persons living on the mainland of Finland aged 55 years and older. Visual impairment was defined as VA ≤6/24 and good vision was defined as ≥6/7.5. Of 3392 eligible persons, 3185 were interviewed (93.9%) and 2781 (82.0%) had distance visual acuity assessed.\textsuperscript{42}

This study reported that compared to persons with good vision, persons with VI had a statistically significant increased likelihood of reporting difficulties with ADL’s (OR 4.36, CI 2.44-7.78) and IADLs (OR 4.82, CI 2.38-9.76) after adjustment for socio-demographic and behavioural factors and chronic conditions.\textsuperscript{42}
**Visual Impairment, Mobility, Falls and Fractures**

The association between distance vision and mobility in a population of 5143 older adults was examined by Salive et al in a cross sectional cohort study of three communities (Established Populations for the Epidemiologic Studies of the Elderly). Participants were interviewed in 1988-89 and residents of two communities were reinterviewed 15 months later (n = 3133, 97% of those eligible). After adjustment for age, sex, race, site, income, diabetes and a history of stroke, the relative odds of limitations in mobility was 3.1, CI 2.3-4.3 in persons with VA <6/60; 1.7, CI 1.4-2.0 for persons with VA ≥6/60 but <6/18 and 1.5, CI 1.3-1.8 for persons with VA ≥6/18 but <6/12 compared to persons with VA ≥6/12. In prospective analyses controlling for potential confounders, participants with severe visual impairment had 3-fold higher odds of incident mobility and activity of daily living limitations than those with acuity of 6/12 or better (P < 0.001). In prospective analyses investigating the relationship of VA with improvement in mobility, those with poor vision were about half as likely to improve as those with better acuity.

The association between VI and falls in the elderly has been examined in the BMES 1. After adjustment for confounding variables the prevalence ratio for two or more reported falls in the 12 months prior to the examination was 1.9 in persons with VI <6/9. Visual impairment was also associated with an increased risk of hip fracture in this population. Ivers et al reported an increased risk of fracture in the first two years after the initial eye examination in the BMES 1 cohort, but not after a longer period of time. The risk of hip fracture in those with BCVA worse than 6/18 was HR 8.4, CI 1.5-48.5 after adjustment for age, sex, health status, BMI, and Parkinson’s disease. In persons aged 75 and older, visual acuity worse than 6/18 gave an adjusted HR of 40.6, CI 5.6-292.5.
The BDES prospectively examined the associations of visual function with physical outcomes and limitations.\textsuperscript{46} Visual acuity and physical outcomes were measured at the five year follow up and again at the ten year BDES follow up. The outcomes measured were; change in 3m walk time (time at ten year minus time at five year examination); incidence of the use of walking aids; incidence of nursing home/assisted living facility placement; incidence of not driving at night; incidence of fracture; incidence of 2 or more falls in the 12 months preceding the ten year follow up; and the incidence of fear of falling.\textsuperscript{46}

After adjusting for confounding variables, there was no statistically significant association between measured walk time and visual impairment.\textsuperscript{46} The likelihood of the incidence of the use of walking aids and not driving at night was associated with decreasing PVA (p for trend 0.03 and 0.001 respectively) but not BCVA (p for trend = 0.17 and 0.11 respectively). The likelihood of the incidence of any fracture, nursing home placement and two or more falls increased with decreasing VA for both PVI (p for trend = 0.05, <0.0001 and 0.01 respectively) and BCVI (p for trend = 0.04, <0.0001 and 0.03 respectively). In persons with VA$\leq$6/12 in the better eye, the likelihood of any fracture was 1.75, CI 1.02-2.99 for PVI and 2.00, CI 1.10-3.62 for BCVI. The likelihood of two or more falls over the five-year periods was 2.02, CI 1.13-3.63 for PVI $\leq$6/12 and 1.55, CI 0.77-3.10 for BCVI $\leq$6/12. Change in time to walk the measured course was not significantly associated with any of the visual functions.\textsuperscript{46}

Dargent-Molina \textit{et al} \textsuperscript{47} examined the risk factors associated with hip fractures in 7575 women aged 75 years or older from the areas of Amiens, Lyon, Montpellier, Paris and Toulouse in France. They excluded women with previous hip fractures, previous bilateral hip replacement or women who were unable to walk independently.\textsuperscript{47} Visual impairment was
defined using best corrected binocular VA. The authors reported the relative risk of hip fracture increased with decreasing VA. Visual acuity of \(\leq 6/30\) was associated with a 2 fold increased risk of hip fracture (RR 2.0, CI 1.1-3.7) after adjustment for age, centre, bone mineral density, calf circumference, gait speed and tandem walk score.47

Felson et al reported the 10 year risk of hip fracture associated with visual impairment in those members of the Framingham Study Cohort who took part in the Framingham Eye Study (FES) in 1973-75.48 The authors reported that poor vision in one or both eyes was associated with an elevated fracture risk. The fracture rates in those with moderately impaired (6/9 to 6/24) vision (8.5%) and poor (6/60 or worse) vision (11.3%) were higher than in those with good (6/7.5 or better) vision (3.0%). After adjustment for age, sex, weight, alcohol consumption, and (in women) oestrogen use, the relative risk of fracture in those with moderate impairment was 1.54 (CI 0.95-2.49), while for those with poor vision, the relative risk was 2.17 (CI 1.24-3.80). In addition, persons with moderately impaired vision in one eye and good vision in the other remained at higher risk of fracture (RR=1.94) than those with a similar degree of binocular impairment (RR = 1.11). The risk of fracture with poor and moderately impaired vision combined was increased in women (RR 1.96, CI 1.23-3.11) but not in men (RR 0.79, CI 0.23-2.72).48

Cox et al reported that the prevalence of VI is significantly higher in a population of persons admitted to hospital for hip fractures compared to that estimated in the general community.49 This Scottish multicentre study examined all persons (537) admitted with hip fracture in four hospitals (Ayr, Dunfermline, Glasgow and Dundee) aged 65 years or older. They found a significantly higher prevalence of visual impairment (46%) in this population compared to that estimated to be present in the general community (15-30%) for the same age group. The
principal causes for visual impairment were preventable or potentially modifiable causes (untreated cataract (49%), macular degeneration (21%), uncorrected refractive error (17%), and glaucoma (3%)) and higher proportion of persons with visual impairment lived in areas of social deprivation (40 vs. 26%).

Table 1.4 summarises the reported risk of hip fracture in persons with visual impairment by study.

**Table 1.4** Summary of risk (odds ratios (OR) or risk ratios (RR) and 95% confidence intervals (CI) of risk of hip fracture in persons with visual impairment by study.

<table>
<thead>
<tr>
<th>Study</th>
<th>Visual Acuity</th>
<th>Risk</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMES a</td>
<td>&lt;6/18</td>
<td>8.40 b</td>
<td>1.50 – 48.50</td>
</tr>
<tr>
<td>ALMPT d</td>
<td>≤6/30</td>
<td>2.00 c</td>
<td>1.10 – 3.70</td>
</tr>
<tr>
<td>FES e</td>
<td>≥6/9–≤6/24</td>
<td>1.54 c</td>
<td>0.95 – 2.49</td>
</tr>
<tr>
<td>FES e</td>
<td>≤6/60</td>
<td>2.17 c</td>
<td>1.24 – 3.80</td>
</tr>
</tbody>
</table>

a Blue Mountains Eye Study
b OR
c RR
d Amiens, Lyon, Montpellier, Paris and Toulouse study in France
e Framingham Eye Study
Visual Impairment and Depression

A population-based cross-sectional study of 13,900 people aged 75 years or older in 49 family practices examined the associations of visual impairment with depression and anxiety in older people living in Britain. Visual impairment was defined as VA ≤6/18 and depression was defined using the Geriatric Depression Scale Short Form (GDS-SF), a set of 15 short questions with yes-or-no answers about feelings over the previous week. Evans et al reported that 13.5% of visually impaired persons were depressed (GDS-15 score of 6 or more) compared with 4.6% of people with good vision (age and gender adjusted OR 2.69, CI 2.03-3.56). This association was attenuated by adjusting for activities of daily living (OR 1.26, CI, 0.94-1.70).

Hayman et al estimated the prevalence of depression in a sample of older adults with impaired vision and associations between visual impairment and depression. The authors used cross-sectional baseline data from 391 participants aged ≥75 years with visual acuity of ≤6/24, recruited for the Visually Impaired Person’s (VIP) trial. Using the geriatric depression scale (GDS-SF) the authors reported that visual function was significantly worse for those with depression, independent of the effect of physical disability.

Tsia et al examined the associations between visual impairment and depression in persons aged ≥65 years in a population based survey of eye diseases in a metropolitan Taipei community using the Geriatric Depression Scale-Short Form (GDS-15). Visual impairment was defined as a BCVA of <6/12 in the better eye. Impaired vision was significantly associated with depression and was a significant predictor of four items of the GDS-S after multivariable adjustment. These were; feel unhappy most of the time (OR 1.73, CI 1.01-
2.88); do not think it is wonderful to be alive now (OR 2.13, CI 1.21-3.64); feel worthless the way they are now (OR 2.23, CI 1.24-3.90); and feel their situation is hopeless (OR 1.95, CI 1.03-3.52).⁵⁵
The Associations Between Visual Impairment and Mortality
Wang et al reported the association between VI and all-cause mortality in the Blue Mountains Eye Study at seven years from baseline. Visual impairment was defined as BCVI < 6/12. Australian National Death Index data were used to confirm persons who had died since baseline. Associations between mortality and presence of visual impairment at baseline were assessed using the Cox proportional hazards regression model, controlling for age, sex, demographic and socioeconomic status, medical history, and health risk behaviours.

Of the 3654 participants included at baseline, 604 participants (16.5%) had died before seven years. The age- and sex-standardized 7-year cumulative mortality rate from baseline was 26% among persons with any visual impairment and 16% in persons without visual impairment. After adjusting for factors found significantly associated with mortality, including age, male sex, low self-rated health, low socioeconomic status, systemic medical conditions, and negative health risk behaviours, the presence at baseline of any VI was independently associated with increased mortality risk (risk ratio (RR), 1.7, CI 1.2-2.3).

Cugati et al reported the eleven-year data for the association between VI and mortality in the Blue Mountains Eye Study population. Mortality occurring between baseline and December 31, 2003, were again obtained via data linkage with the Australian National Death Index. Age-standardized mortality rates were calculated, and hazard ratios (HRs) and 95% confidence intervals (CIs) were determined using Cox models. Similar to the seven-year data, age-standardised mortality was higher in persons with vs. without visual impairment (54.0% vs. 34.0%). At eleven years however, after adjusting for factors that predict mortality in this population, visual impairment (HR 1.3, CI 0.98-1.7) was no longer significantly associated with all-cause mortality in this cohort. However, among persons younger than 75 years, VI
remained associated with higher all-cause mortality (HR 2.9, CI 1.6-5.5). This association became non-significant after further adjustment for triglyceride level, fibrinogen level, educational level, and walking disability (HR 1.97, CI 0.8-4.8).\textsuperscript{57}

Kuang \textit{et al} examined the association between visual impairment and 3-year risk of mortality in a cohort of urban Chinese elderly individuals in the Shihpai Eye Study.\textsuperscript{58} Participants were aged ≥65 years at baseline. Baseline examinations were conducted between July 1, 1999 and December 31, 2000. Visual impairment was defined as PVI < 6/12. Of 2045 eligible persons randomly selected to participate in the study, 1361 (66.6\%) participated in both the questionnaire and eye examination. A follow-up of a fixed cohort was also conducted after 3 years. Deaths were confirmed through the household registration system.\textsuperscript{58}

During the three years before the follow-up, 54 (3.97\%) had died. After adjustments were made for age, sex, education, marital status, lifestyle factors, depression symptoms, fall history, and history of systemic diseases, visual impairment was not a significant predictor of 3-year mortality in elderly persons.\textsuperscript{58}

Lee \textit{et al} examined the associations between self-reported visual impairment (SRVI) and mortality in adults 18 years and older using data from the American National Health Interview Survey (NHIS).\textsuperscript{59} The NHIS is conducted annually by the National Center for Health Statistics (NCHS) and is a continuous, multipurpose and multistage probability survey of the US civilian non-institutionalised population. Approximately 50000 households are selected to participate with a response rate of 95-98\%. The study used data from 116796 adult participants for the years 1986-1994. Adults within households were administered questions about VI and selected eye diseases. Mortality linkage data with more than 96\% of the survey
participants were available. To determine the association of visual impairment with mortality, the study controlled for survey design, age, race, marital status, educational level, reported health status, glaucoma, cataract, and retinopathy. Statistical analyses used Cox proportional hazards regression analysis.\textsuperscript{59}

There were 8949 deaths in the study population from baseline before December 31 1997.\textsuperscript{59} In persons with severe bilateral visual impairment (SRVI), women, but not men, were at a significantly increased risk of death relative to their counterparts without VI (HR 2.21, CI 1.61-3.02 and HR 1.33, CI 0.96-1.84, respectively). In persons with some SRVI compared to those reporting no VI, the risk of mortality was significantly elevated in women and men (HR 1.35, CI 1.20-1.52 and HR 1.14, CI 1.01-1.29 respectively).\textsuperscript{59}

The association of visual impairment with all-cause mortality has been reported for the Beaver Dam Eye Study (BDES) population at 5 and 14 years from baseline.\textsuperscript{60,61} Baseline examinations took place between 1988 and 1990. Participants were aged 43 through 84 years at baseline. Visual impairment was defined as BCVA of 6/12 or worse. Deaths were ascertained by contacting family members, daily review of obituaries, and use of vital status records. Data were analysed using Cox Proportional Hazards Model.\textsuperscript{60} The association of visual impairment with five-year survival from baseline in the BDES population was reported by Klein \textit{et al.}\textsuperscript{60} At five years from baseline 9.5\% (467/4926) of the BDES population had died. After correcting for age and sex, poorer survival was associated with visual impairment (HR 1.57, CI, 1.18-2.08) however, after controlling for systemic factors, the association became non-significant (HR 1.08, CI 0.77-1.51).\textsuperscript{60}
The association of visual impairment with 14-year survival from baseline in the BDES population was reported by Knudtson et al. At fourteen years from baseline, 32% of the baseline population had died. After multivariate adjustment for age, sex, and systemic and lifestyle factors, poorer survival remained significantly associated with visual impairment (HR 1.24, CI 1.04-1.48).

In contrast to Lee et al, the associations tended to be stronger in males in the BDES cohort. The associations were also stronger in younger persons. By restricting the cohort to persons younger than 65 years, the relationship between visual impairment and decreased survival after multivariable adjustment increased (HR 2.18, CI 1.02-4.67).

McCarty et al reported the association of visual impairment with mortality in the 5 year follow up of the Melbourne Visual Impairment Project (MVIP) cohort. This population based study examined the distribution and determinants of age related eye disease in a cluster random sample of Melbourne residents. The participants were aged 40 years and older at baseline. The baseline examinations were conducted between 1992 and 1994. Causes of death were obtained from the National Death Index for all reported deaths. Visual impairment was defined as BCVA <6/12. Survival analyses were conducted with the Wilcoxon test for statistical significance of the survival curves. Before five years, 231 (7.1%) of the original 3271 participants had died. Visual impairment was associated with a significantly increased risk of mortality (OR 2.34, CI 1.03-5.32) after multivariable adjustment.

The Age-Related Eye Disease Study (AREDS) is a major clinical trial sponsored by the American National Eye Institute examining the natural history and risk factors of age-related macular degeneration (AMD) and cataract. The study also evaluated the effect of
antioxidant, vitamin and mineral supplements on the progression of AMD and cataract. A total of 4757 persons were enrolled. The baseline examinations were conducted between November 13, 1992, and January 15, 1998. Participants were aged 55 to 81 years at baseline. Visual impairment was defined as <6/12 BCVA. At baseline, participants had to be free of any condition that would make long-term follow-up unlikely or difficult. Persons with a history of cancer with a poor prognosis for 7-year survival or a major cardiovascular or cerebrovascular event within the year before enrollment were ineligible. Persons with more than minimal diabetic retinopathy or any other eye disease that could complicate assessment of the progression of lens opacities or AMD, or that could affect visual acuity (e.g. optic atrophy and acute uveitis) were also ineligible. All AREDS participants had at least 1 eye with 6/9 or better visual acuity at baseline.

Clemons et al reported the association of VI at baseline with all-cause mortality in the Age-Related Eye Disease Study population within 6.5 years from baseline. When mortality was reported, death was confirmed from hospital records and from death certificates. Associations between mortality and presence of VI in one eye at baseline were assessed using the Cox proportional hazards regression model controlling for statistically significant covariates in this population. During median follow-up of 6.5 years, 534(11%) of 4753 AREDS participants died. In the multivariable adjusted model, participants with VI to less than 6/12 in 1 eye had an increased risk of mortality (relative risk (RR) 1.36, CI 1.12-1.65). However, ninety-one percent of participants who had < 6/12 in 1 eye were in AMD Category 4. Thus, the association between all-cause visual impairment and mortality could not be distinguished from the association between AMD and mortality in this study.
Freeman et al reported the association of VI and 8-year mortality in the Salisbury Eye Evaluation (SEE) project.\textsuperscript{65} The authors also examined whether depressive symptoms acted as a mediator between visual impairment and mortality in this population. The Salisbury Eye Evaluation was a population-based cohort study of 2520 (65\% of those approached) older adult residents of Salisbury, Maryland. Participants were reexamined two years later, and of these, 1991 were eligible for the assessment of the association between VI, mortality and depression. Baseline examinations were conducted between September 1993 and September 1995. Participants were aged 65 to 84 years at baseline. Baseline presenting visual acuity (PVA) was examined categorically but then used as a continuous variable, as PVA was found to have a linear relationship with mortality in this population. Information on mortality was obtained by a report from family members, by the local newspapers, and by staff follow-up. All deaths reported by July 2003 were used in the analysis. Statistical analyses were performed with the Cox proportional hazards regression.\textsuperscript{65}

In the SEE, worse baseline acuity was associated with a higher mortality rate (HR 1.05, CI 1.01-1.09 per 0.1 logMAR (1 line) change in acuity) after multivariable adjustment.\textsuperscript{65} Change in PVA within two years from baseline was also significantly associated with mortality at eight years. Participants who gained two or more lines of visual acuity within two years from baseline had a lower multivariable adjusted risk of dying at eight years (HR 0.47, CI 0.23-0.95). Also, women, but not men, who lost three or more lines of visual acuity over a 2-year period, had a higher adjusted risk of dying (HR 3.97, CI, 2.21-7.15 vs. HR 1.32, CI 0.66-2.63 respectively). Depressive symptoms did not mediate the relationship between visual impairment and mortality in this population.\textsuperscript{65}
The Medical Research Council (MRC) trial of assessment and management of older people in the community is a cluster randomised trial comparing different methods of population-based multidimensional screening in 106 general practices (family practices) from the United Kingdom MRC General Practice Research Framework. Of these, 53 general practices were randomly allocated to the universal screening arm of the trial. Participants at these practices were given a visual acuity test as part of a detailed health assessment at baseline. The number of participants with baseline visual acuity measurements was 13569. Baseline examinations were performed between 1995 and 1999. Participants were aged 75 years and older at baseline. Visual impairment was stratified into three groups: binocular PVI <6/18; binocular PVI >6/9 but ≤ 6/18; and binocular PVI <6/6 but ≥ 6/9. Poisson regression modelling was performed with all-cause, cardiovascular disease, and cancer mortality rates as the outcomes of interest. All-cause mortality rates by level of visual acuity were modelled. Participants with a baseline PVA of 6/6 or better were used as the baseline reference group.

Thiagarajan et al reported the associations of visual impairment with mortality after 6 years from baseline in the MRC trial of assessment and management of older people in the community population. Rate Ratios of mortality for visually impaired participants after adjustment for confounding factors were determined. The incidence of mortality was significantly higher in participants with PVA <6/18 and in participants with PVI <6/9 but ≥ 6/18 when compared to participants with PVA of 6/6 at baseline after adjustment for all confounding variables in this population (RR 1.17, CI 1.07-1.27 and RR 1.10, CI 1.01-1.19 respectively). The association of mortality incidence with PVI <6/6 but ≥ 6/9 was not significant after multivariable adjustment (RR 1.01, CI 0.93-1.10).
The Copenhagen City Eye Study was a prospective population based cohort study of 946 persons. The study examined vision and common eye diseases in an urban population residing in the Østerbro district of Copenhagen, Denmark. The baseline examinations were conducted from 1986 to 1988. Participants were aged 60-80 years old at baseline. Mortality data was reported 14 years from baseline. Participants were followed until death or until May 1, 2002, whichever came first. At baseline, participants underwent an extensive ophthalmologic examination, including fundus photography, at Rigs Hospitalet, the National University Hospital of Copenhagen. Visual impairment was defined as ≤ 6/12. Data from the National Central Person Register, the National Death Register, and the National Patient Register were used, and information on the causes of death was obtained from the Danish National Death Register. The independent contribution of ARM, cataract, and visual loss to death, was estimated using Cox’s proportional hazards regression analysis.

In the Copenhagen Eye Study the presence of visual loss at baseline was not associated with increased mortality risk after adjustment for age and gender (RR 1.17, CI, 0.78-1.75).

The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) is a population based study of 996 persons (83% of all persons with type 1 diabetes who were receiving care in 11 counties in Wisconsin). Baseline examinations were conducted during the period 1980-1982. Follow up examinations were conducted 4, 10, 14 and 20 years later. Participants were aged > 0 years at baseline. Levels of visual impairment were defined as: BCVA > 6/12, none; 6/12 – 6/19, mild; 6/24 - 6/48, moderate; ≤ 6/60, severe. Mortality was determined yearly by telephone contact with study subjects or a contact person and monitoring of local newspapers for obituaries of study subjects. When unable determine subject vital status or last known address or death, the subjects name was submitted to the National Death Index.
Death certificates were obtained for those known to have died. Kaplan-Meier survival procedures were used for cardiovascular deaths. Cox proportional hazards regression analysis was used for multivariable models.69,70

After multivariable adjustment, visual impairment was associated with 16 year all-cause mortality in the younger-onset (Mild: HR 1.78, CI 1.02-3.11, Moderate: HR 1.41, CI 0.56-3.52, Severe: HR 1.94, CI 1.19-3.17) and the older-onset diabetes groups (mild: HR 1.48, CI 1.16-1.90, moderate HR 1.77, CI 1.25-2.51, severe: HR 2.14, CI 1.42-3.22).70 Table 1.5 summarises the results of these studies.
5 Table 1.5 Summary of mortality risk (risk ratios (RR), hazard ratios (HR) or odds ratios (OR) and 95% confidence intervals (CI) in persons with objectively measured visual impairment after multivariable adjustment.

<table>
<thead>
<tr>
<th>Study</th>
<th>Visual Acuity</th>
<th>Mortality Risk</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMES(^a)</td>
<td>&lt;6/12</td>
<td>1.70(^k)</td>
<td>1.50 – 48.50</td>
</tr>
<tr>
<td>BMES(^b)</td>
<td>&lt;6/12</td>
<td>1.30(^l)</td>
<td>0.98 – 1.7</td>
</tr>
<tr>
<td>SES(^c)</td>
<td>&lt;6/12</td>
<td>Not Significant</td>
<td>Not Significant</td>
</tr>
<tr>
<td>BDES(^d)</td>
<td>≤6/12</td>
<td>1.08(^l)</td>
<td>0.77 – 1.51</td>
</tr>
<tr>
<td>BDES(^e)</td>
<td>≤6/12</td>
<td>1.24(^l)</td>
<td>1.02 – 4.67</td>
</tr>
<tr>
<td>MVIP(^f)</td>
<td>&lt; 6/12</td>
<td>2.34(^m)</td>
<td>1.03 – 5.32</td>
</tr>
<tr>
<td>AREDS(^g)</td>
<td>&lt;6/12 in one eye, ≥6/9 fellow eye</td>
<td>1.36(^k)</td>
<td>1.12 – 1.65</td>
</tr>
<tr>
<td>MRC(^h)</td>
<td>&gt;6/9</td>
<td>1.01(^k)</td>
<td>0.93 – 1.10</td>
</tr>
<tr>
<td></td>
<td>&lt;6/9–≥6/18</td>
<td>1.10(^k)</td>
<td>1.01 – 1.19</td>
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<tr>
<td></td>
<td>&lt;6/18</td>
<td>1.17(^k)</td>
<td>1.07 – 1.27</td>
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<td>WESDR(^i)</td>
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<td>1.78(^l)</td>
<td>1.02 – 3.11</td>
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<tr>
<td></td>
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<td>1.41(^l)</td>
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<td></td>
<td>≤6/60</td>
<td>1.94(^l)</td>
<td>1.19 – 3.17</td>
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<tr>
<td>WESDR(^j)</td>
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<td>1.48(^l)</td>
<td>1.16 – 1.90</td>
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<td></td>
<td>≤6/60</td>
<td>2.14(^l)</td>
<td>1.42 – 3.22</td>
</tr>
</tbody>
</table>

\(^a\) Blue Mountains Eye Study 7-year follow-up\(^56\)
\(^b\) Blue Mountains Eye Study 11-year follow-up\(^57\)
\(^c\) Shihpai Eye Study 3-year follow-up\(^58\)
\(^d\) Beaver Dam Eye Study at 5-year follow up\(^60\)
\(^e\) Beaver Dam Eye Study 14-year follow-up\(^61\)
\(^f\) Melbourne visual impairment project 5-year follow-up\(^62\)
\(^g\) Age Related Eye Disease Study 7-year follow-up\(^64\)
\(^h\) Medical Research Council trial of assessment and management of older people 6-year follow-up\(^65\)
\(^i\) Wisconsin Epidemiologic Study of Diabetic Retinopathy 16-year follow-up in younger onset diabetics\(^70\)
\(^j\) Wisconsin Epidemiologic Study of Diabetic Retinopathy 16-year follow-up in older onset diabetics\(^70\)
\(^k\) RR
\(^l\) HR
\(^m\) OR
The Associations Between All-Cause Visual Impairment and Cause-Specific Mortality

Visual Impairment and Cardiovascular Disease

The United States National Health Interview Survey of adults within households found associations between self-reported visual impairment and cardiovascular disease related mortality, in women (HR 2.53, CI 1.68-3.81), but not men (HR 1.27, CI 0.78-2.07), who reported severe bilateral VI after multivariable adjustment.59 Risk of cardiovascular mortality was also significantly elevated in women (HR 1.36, CI 1.15-1.61) with some reported VI when compared with those reporting no VI after multivariable adjustment.59

The MRC trial of assessment and management of older people in the community did not report data for the association between all-cause visual impairment and cardiovascular mortality.67 There were however, statistically significant associations between VI and cardiovascular mortality after multivariable adjustment in participants with VI due to refractive error and VI of unknown cause (RR 1.37, CI 1.03-1.82 and RR 1.81, CI 1.17-2.78 respectively).67

The Blue Mountains Eye Study at 7 and 11 years follow up reported no association between baseline VI and vascular mortality.56,57 The BDES found no association between baseline VI and cardiovascular mortality at 13 years from baseline.61

The WESDR found significant associations with reduced baseline visual acuity and increased cardiovascular mortality risk in a diabetic population, after multivariable adjustment in both younger-onset and older-onset diabetic groups.70 Persons with severe visual impairment at baseline in the younger-onset diabetes group were at greatest risk (mild: HR 2.89, CI 1.42-5.87; severe: HR 3.21, CI 1.58-6.51). In the older-onset group, those with mild visual
impairment were at greater risk (mild: HR 1.81, CI, 1.29-2.54; severe: HR 1.22, CI, 0.57-2.61).\textsuperscript{20}

The AREDS was unable to determine the association between all cause visual impairment and cardiovascular mortality as ninety-one percent of participants who had reduced vision at baseline were in AMD Category 4.\textsuperscript{64} This group had a statistically significant risk of cardiovascular death.\textsuperscript{64}
Visual Impairment and Cancer

The United States National Health Interview Survey of adults within households found no association between self-reported visual impairment and cancer related mortality. The Blue Mountains Eye Study at 7 and 11 years follow up found cancer-related deaths were significantly less frequent in participants with baseline visual impairment (P=0.004 at 11 years from baseline). The BDES found no association between cancer related mortality and baseline visual impairment after 14 years follow up. The WESDR found no associations between baseline visual impairment and 16 year mortality in a diabetic population. There was no association reported between baseline visual impairment and cancer related deaths in the AREDS at 6 years. The MRC trial of assessment and management of older persons in the community found no association between baseline visual impairment and cancer related mortality.
The Associations Between Cause specific visual impairment and All-Cause Mortality

Cataract and All-Cause Mortality

The presence of cataract or previous cataract surgery has been associated with decreased survival in many populations studies, but not in other populations. 

Benson et al reported an increased risk of mortality associated with cataract surgery performed between 1979 and 1980 at the West Virginian University Medical Center, Morgantown. During this period, 193 patients aged 50 to 89 years of age had cataract surgery. Their mortality was compared to 182 patients who elected one of three other surgical procedures during the same period. Patients who had undergone cataract surgery at this institution during this time period had a significantly higher mortality rate (P = 0.0005) than control group patients according to life-table analysis estimates adjusted for age and sex.

Increased five-year mortality risk after cataract surgery was also reported in a cohort of patients undergoing cataract surgery at the Worthen Center for Eye Care Research, Center for Sight, Georgetown University Medical Center, Washington, D.C. during 1984. Participants were aged 65 to 79 years during 1984. The risk of dying within five years after cataract extraction in 1984 was compared to the five-year mortality risk of the same aged persons in the United States population in 1984. Street et al reported that cataract surgery at a younger age was associated with an increased risk of 5-year mortality compared to patients having surgery at older ages. Patients who had cataract extraction and who were younger than 75 years had significantly higher age-specific rates of mortality than predicted from United States life tables (P less than .001) (for age 65 years RR 1.34, CI 1.29-1.41). This risk progressively declined until the age of 75 years. At age 75 years and older, the risk of dying within five years of cataract surgery was not significantly different to that expected for the
However, cataract surgery did predict reduced five year mortality in women older than 79 years who had cataract surgery during 1984 (for age 79 years, RR 0.90, CI 0.82-0.99). Meddings et al reported the association between cataract surgery and mortality in persons who underwent surgery in British Columbia during either 1985 or 1989. Subjects were aged 50-95 years at time of cataract surgery. Mortality rates were compared with the provincial population of comparable age, who did not undergo cataract surgery during the study period. The 1985 cohort included 8,262 patients undergoing surgery and a comparison population of 804,303, and the 1989 cohort included 11,952 patients undergoing cataract surgery and a comparison population of 839,393. Cox regression analysis was used to determine hazard ratios.

For both cohorts, cataract surgery was associated with increased hazard ratios for dying during follow-up. In 1985, the results were similar between males and females for persons aged 50-54.9 years of age (HR 3.2, CI 2.0-5.0 and HR 3.3, CI 1.9-5.7 respectively). Hazard ratios decreased with older age, becoming nonsignificant for both males and females who were 80 years or older and who had cataract surgery in either 1985 or 1989.

McGwin et al examined a cohort of 384 persons with (n=286) and without cataract (n=98) from the Impact of Cataracts on Mobility (ICOM) Study. McGwin et al reported that persons with cataract had an increased rate of mortality at 6 years from baseline (crude mortality rate ratio (MRR) 2.5, CI 1.0-6.5). Of 286 participants who had cataract, 200 elected to have cataract surgery. Patients with cataract who did not elect to undergo surgery had a significantly higher mortality rate when compared to those who had surgery and those
without cataract (MRR 3.9, CI 1.5-9.8 and 7.3, CI 2.8-19.1 respectively) after age and sex adjustment. After multivariable adjustment, the no-surgery cataract group had an elevated mortality rate (MRR 3.2, CI 1.2-9.0) compared to the no-cataract group. Those who underwent cataract surgery had a nonsignificant elevation in mortality rate (MRR 2.0, CI 0.8-5.9). 74

In the AREDS study, nuclear opacity ≥4 and previous cataract surgery were associated with increased all-cause mortality that remained statistically significant after multivariable adjustment (RR 1.40, CI 1.12-1.75 and RR 1.55, CI 1.18-2.05 respectively). 64 Cortical cataract and posterior subcapsular cataract demonstrated no statistically significant association in this population. 64

The Nurses’ Health Study was established in 1976. 81 During baseline, 121,700 female registered nurses aged 30-55 years and residing in 11 large US states completed a mailed questionnaire on their medical history and lifestyle. Follow up questionnaires were sent every two years to update information on general health and to identify newly diagnosed coronary and other diseases. Cataract extraction was first assessed in 1984 and considered the baseline for the association between cataract surgery and mortality analysis. 75 Women who reported a diagnosis cancer or cardiovascular disease at this baseline were excluded. Women less than age 45 years were excluded. Women were added to the analysis after 1984 as they reached age 45 years. In 1984, 1986, 1988, 1990, and 1992, participants were asked if they had a cataract extraction since the previous questionnaire. When cataract extraction was reported, the authors requested permission to review medical records. The confirmation rate reached 100 percent for self-reported cataract extractions that occurred between 1984 and 1992. Only the first extraction was used as the exposure variable. In total, 60,657 women aged 45-63
years in 1984, 49.8% of the original cohort, were included in the analysis. Self-reported cataract extraction was used as the exposure variable. Deaths were reported by next of kin and the postal system or through the National Death Index. Fatal CHD was confirmed by hospital records or autopsy or if CHD was listed as the cause of death on the death certificate and evidence of previous CHD was available.\(^7\)

The Nurses’ Health Study demonstrated increased 10 year all-cause mortality after multivariable adjustment in women aged between 45 and 63 who had previous cataract surgery at baseline (RR 1.37, CI 1.13-1.66).\(^7\) In this population the entire increased mortality risk was explained by an increased coronary heart disease (CHD) mortality.\(^7\)

The BDES reported an association between increasing severity of nuclear sclerosis in nondiabetics and poorer 5 year survival from baseline (HR per level of severity 1.19, CI 1.00 to 1.40).\(^60\) There was no association between nuclear sclerosis and mortality in people with diabetes (HR 0.96, CI 0.68 to 1.36) or with other forms of cataract in this population after multivariable adjustment at five years from baseline.\(^60\) After 13 years, poorer survival was associated with cortical cataract (HR 1.21, CI 1.06-1.37), any cataract (HR 1.16, CI 1.03-1.32) but not with increasing severity of nuclear sclerosis (HR 1.07, CI 0.99-1.16, p = 0.06). Contrary to the results at five years, the associations tended to be slightly stronger in men compared to women after 13 years.\(^60,61\)

The MVIP study found no association between the presence of cataract and five year mortality in an Australian cohort aged 40 years and older.\(^62\) The Melbourne VIP study did previously report using the same data a significant increased risk of mortality in persons with cortical cataract at baseline (RR 1.45, CI 1.01-2.10), with the caveat that the reported risk
may be artifactual due to loss of significance when a more lenient definition of cortical cataract was used in the modelling.

The association between cataract and mortality has been reported in the BMES Cohort at 7 and 11 years after baseline. In this Australian cohort, participants were aged 49 years and older at baseline. After adjusting for factors found significantly associated with mortality, the presence of age-related cataract, either nuclear sclerotic (RR 1.5, CI 1.1-1.9), cortical (RR 1.3, CI 1.1-1.6), or posterior subcapsular cataract (RR 1.5, CI 1.1-2.0), was significantly associated with increased mortality risk at 7 years from baseline. Previous cataract surgery, was not associated with mortality after 7 years from baseline in this population study. At 11 years after baseline the associations remained statistically significant. (Nuclear sclerosis (HR 1.21, CI 1.00-1.46), cortical (HR 1.28, CI 1.10-1.48) and posterior subcapsular cataract (HR 1.46, CI 1.17-1.82)).

The North London Eye Study is a population-based cross-sectional survey of persons aged 65 years and older that aimed to estimate the magnitude of serious eye disorders and visual impairment in a defined elderly population of a typical metropolitan area in England. A random sample of people aged 65 years and older was drawn from a defined population of elderly people registered with 17 general practice groups. The baseline survey was carried out from April 1995 to October 1996. A total of 1547 people were examined and included in the sample. Mortality was monitored for three years by the Office for National Statistics. The monitoring covered a period from March 1995 (start of the survey) to December 1999 (3 years from the end of the survey). The lens status at the time of the survey was ascertained by ophthalmologists using a slit lamp biomicroscope and the lens opacity classification system (LOCSII). The age and sex-specific mortality from various causes was estimated
and compared in those with and without cataract. Hazard ratios were estimated using Cox proportional hazards regression models.77

This survey found an association between cataract and increased risk of 3-year mortality in nondiabetic women but not in nondiabetic men (HR 1.7, CI 1.1-2.7 vs. HR 0.9, CI 1.1-2.7) after age adjustment.77 The “sex cataract” interaction was apparent within each of the three main types of cataract. There was no significant effect modification by age. In diabetic patients, there was a significant association of cataract with mortality in both men and women after age and sex adjustment (HR 2.6, CI 1.1-6.0). Further adjustment for effects of smoking, for area of residence, and for ethnic group did not materially change the findings.77

The Barbados Eye Study measured the prevalence and evaluated risk factors for the major causes of visual loss. Four thousand seven hundred and nine persons were identified by random sampling of Barbadian-born citizens.84 The baseline examinations were conducted between 1988 and 1992. Participants were aged 40 to 84 years of age at baseline. Four years later, surviving members were reexamined in the Barbados Incidence Study of Eye Diseases (BISED). Three thousand four hundred and twenty-seven participants or 85% of those eligible were included. The Lens Opacities Classification System II (LOCS II),83 was used to grade opacities. Lens opacities were defined as LOCS II scores of 2 or more in at least one eye. Death certificate data were obtained from the Ministry of Health, including dates and specific causes of death. Cox proportional-hazards regression analyses were used to examine the associations of mortality and lens opacities, while controlling for potential confounding variables. These factors were first evaluated in univariate analyses and significant variables (P < 0.05) were then included in the multivariable Cox regression model.84
The Barbados Eye Study reported significant associations between mixed opacity cataracts and nuclear cataracts and all-cause mortality at 4 years from baseline (Death Rate Ratio (DRR) 1.6, CI 1.1-2.4; DRR 1.5, CI 1.1-2.0 respectively). No statistically significant associations between mortality and any cortical or any PSC cataract were found.

The Copenhagen Eye Study of persons aged 60-80 years at baseline found no association between the presence of baseline cataract and mortality after adjustment for age and sex at 14 years from baseline (RR 0.98, CI 0.82-1.17). Table 1.6 summarises the mortality risk of persons with cataract after multivariable adjustment.
Table 1.6 Summary of mortality risk (risk ratios (RR), hazard ratios (HR) or death rate ratios (DRR) and 95% confidence intervals (CI)) in persons with nuclear sclerosis (NS) cataract, cortical (CO) cataract and posterior subcapsular (PS) cataract after multivariable adjustment.

<table>
<thead>
<tr>
<th>Study</th>
<th>Cataract</th>
<th>Mortality Risk</th>
<th>95% Confidence Interval</th>
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<td>NS≥4</td>
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<td>1.12 – 1.75</td>
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<td></td>
<td>CO</td>
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<td></td>
<td>PS</td>
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<td>Not Significant</td>
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<td>MVIP b</td>
<td>Any</td>
<td>Not significant</td>
<td>Not significant</td>
</tr>
<tr>
<td>BMES c</td>
<td>NS</td>
<td>1.50 f</td>
<td>1.10 – 1.90</td>
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<tr>
<td></td>
<td>CO</td>
<td>1.30 f</td>
<td>1.10 – 1.60</td>
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<td></td>
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<td>BMES d</td>
<td>NS</td>
<td>1.21 g</td>
<td>1.00 – 1.46</td>
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<td>CO</td>
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a Age Related Eye Disease Study 7-year follow-up 64
b Melbourne Visual Impairment Project 5-year follow-up 62
c Blue Mountains Eye Study 7-year follow-up 56
d Blue Mountains Eye Study 11-year follow-up 57
e Barbados Eye Study 4-year follow-up 84
f RR
g HR
h DRR
Age-Related Macular Degeneration and All-Cause Mortality

The Blue Mountains Eye Study reported there was no association between all-cause mortality and baseline ARMD at 7 years from baseline. After 11 years, baseline ARMD was associated with increased mortality after multivariable adjustment in persons younger than 75 years at baseline (HR 1.59, CI 1.04-2.43) but not in persons older than 75 years at baseline (HR 0.90, CI 0.65-1.26).

An association between ARMD and all-cause mortality was reported for participants in AREDS. In this population, participants with advanced ARMD compared with participants with few if any, drusen at baseline had increased all-cause mortality (RR 1.41, CI 1.08-1.86) after multivariable adjustment.

The Copenhagen Eye Study of persons aged 60-80 year at baseline reported an association between the presence of baseline ARMD and 14-year mortality after multivariable adjustment. Adjustment was made for factors correlated to both age-related maculopathy and mortality, including visual impairment of ≤ 6/12. Buch et al reported the risk of mortality at 14 years was increased in persons with early but not late ARMD (HR 1.23, CI 1.02-1.49 early vs. HR 1.25, CI 0.84-1.87). When stratified by sex, baseline early ARMD was associated with increased mortality in women, but not men (HR 1.60, CI 1.20-2.13 vs. HR 0.97, CI 0.74-1.26 respectively). Late ARMD was not associated with significant increase in mortality in either sex.

The Beaver Dam Eye Study found no association between ARMD at baseline and mortality at five years and 13 years after multivariable adjustment (HR 0.88, CI 0.73-1.07; HR 0.97, CI 0.82-1.15).
0.87-1.07 respectively per one step increases of severity). Similarly the Melbourne VIP study found no association between ARMD and 5 year mortality (OR 1.36, CI 0.96-1.94).

The Medical Research Council (MRC) trial of assessment and management of older people in the community reported no association between ARMD and increased mortality risk. However, there was a significant association between those whose cause of visual impairment could not be ascertained with mortality (RR 1.33, CI 1.02-1.75). This may have led to an underestimation of the association between ARMD and mortality.

The Atherosclerosis Risk in Communities (ARIC) Study is a population-based cohort study that examined the relationship between AMD and risk of coronary heart disease (CHD) events and all-cause mortality in men and women. There were 15792 participants at baseline. The baseline period was 1987 to 1989. Participants were aged 45 to 64 years old at baseline. The study population was selected by probability sampling from 4 U.S. communities: Forsyth County, North Carolina; Jackson, Mississippi; suburbs of Minneapolis, Minnesota; and Washington County, Maryland. The Jackson sample included African Americans only; the remaining 3 were representative of the populations in these communities.

Of the 15792 participants at baseline, 14346 (93% of survivors) returned for a second examination in 1990 through 1992, and 12887 (86% of the survivors) returned for a third examination in 1993 through 1995. Participants had retinal photographs of one eye taken between 1993 and 1995. The reported associations between ARMD, cardiovascular events, cardiovascular and all-cause mortality were derived from individuals who participated at the third examination. Of the 12887 who returned for this examination 11414 participants were
used in the final analysis. Photographs were evaluated for the presence of early and late AMD signs according to the Wisconsin grading system.\textsuperscript{86} Incident CHD events (acute myocardial infarction, silent myocardial infarction, fatal CHD, and cardiac revascularization procedures) and all-cause mortality were identified prospectively using standardised methods.\textsuperscript{86} Cox proportional hazards models were used to estimate the RR and 95\% CIs for incident CHD and deaths by ARMD status, adjusting initially for age, gender, race, and centre, and then further for education, body mass index, systolic and diastolic BPs, diabetes status, total plasma cholesterol and HDL cholesterol, triglyceride, glucose, pack-years of cigarette smoking, and current alcohol consumption.\textsuperscript{85}

In the ARIC study, ARMD was not statistically significantly associated with all-cause mortality after multivariable adjustment (Early ARMD RR 0.95, CI 0.73-1.31; Late ARMD RR 1.95, CI 0.73-1.38).\textsuperscript{85}
Glaucoma and All-Cause Mortality

The United States NHIS examined the associations between self-reported glaucoma and survival in a nationally representative sample of U.S. adults over an average follow-up period of 7 years. After multivariable adjustment, participants with reported glaucoma, but without reported visual impairment, were at significantly increased risk of death relative to participants without reported glaucoma irrespective of visual impairment status (HR 1.35, CI 1.19-1.53). Similar associations were found for participants with reported glaucoma and visual impairment vs. participants with no reported glaucoma (HR 1.39, CI 1.14-1.71).

The Framingham Eye Study examined the relationship between high intraocular pressure (greater than or equal to 25 mm Hg) or history of treatment for glaucoma and survival. After adjustment for age and sex, this study demonstrated an association between high intraocular pressure or diagnosed glaucoma and increased mortality risk (DRR 1.56, CI 1.11-2.19). The association became non-significant after multivariable adjustment for other comorbidities linked to increased mortality.

The Barbados Eye Study reported no overall association between baseline open angle glaucoma and 9 year all-cause mortality after adjustment for confounders (RR 0.85, CI 0.64-1.15). However, there was a significant association between all-cause mortality and baseline OAG in persons being treated with timolol (RR 1.70, CI 1.08-2.68). There was also a smaller but statistically significant association between elevated IOP (> 21mm Hg) at baseline and all-cause mortality (RR 1.01, CI 1.00-1.03). The presence of ocular hypertension was not associated with a statistically significant increase in all-cause mortality.
A population based study of 32,918 elderly citizens of Malmo between 1992 and 1997 examined mortality rates in glaucoma patients and matched controls. Two controls of the same age and gender were chosen for each glaucoma patient. Deaths for each group were determined based on centrally administered registers. After a mean follow-up time of 7.75 years, the five-year mortality did not differ significantly between the groups (p=0.7406). Among glaucoma patients, neither IOP (p=0.1781) nor pseudoexfoliation (p=0.8882) was related to significantly increased mortality.

The BDES found no association between the presence of glaucoma at baseline and 5 year or 13 year mortality (HR 0.84, CI 0.57-1.26 and HR 1.04, CI 0.84-1.28 respectively). The Melbourne VIP similarly found no association between glaucoma and 5 year mortality risk after multivariate adjustment.62

The BMES reported no association existed between baseline glaucoma with seven and nine year all-cause mortality. The WESDR study found no association between baseline glaucoma and 16-year mortality after multivariable adjustment.
Diabetic retinopathy and All-Cause Mortality

The Early Treatment of Diabetic Retinopathy Study (ETDRS) is a randomized clinical trial that assessed photocoagulation and aspirin treatment for patients with diabetic retinopathy. Participants were recruited from April 1980 through July 1985 and aged 18-69 at baseline. The ETDRS enrolled 3,711 subjects over this period. Inclusion criteria included the diagnosis of diabetes and diabetic retinopathy in each eye. Diabetic retinopathy was graded as mild, moderate, or severe nonproliferative diabetic retinopathy (NPDR) or mild to moderate proliferative diabetic retinopathy (PDR) with or without macular oedema. Time to the occurrence of death of any cause during the period of the study was determined. The Mortality and Morbidity Classification Committee, composed of internists and cardiologists who were not ETDRS investigators, coded study deaths. Multivariable adjusted Cox proportional hazards models using all statistically significant covariates were used to estimate the associations between mortality diabetic retinopathy.

The ETDRS reported no association between diabetic retinopathy and mortality in participants with type 1 diabetes, defined as onset before 30 years old, after multivariable adjustment. In participants with type 2 diabetes, defined as onset of diabetes after 30 years of age, there was a significant association between severe nonproliferative diabetic retinopathy (NPDR) and severe proliferative diabetic retinopathy (PDR) with mortality after multivariable adjustment (HR 1.48, CI 1.03-2.15 and HR 2.02, CI 1.28-3.19 respectively). There were no associations between mild NPDR, moderate NPDR and mild PDR with mortality after multivariable adjustment in this population.

The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) reported an association between increased mortality risk and increasing severity of retinopathy.
Clinically significant macular oedema (CSME) was not significantly associated with all-cause mortality in this population. The BDES found a significant association between the presence of baseline diabetic retinopathy and 13-year mortality after multivariable adjustment (HR 1.36, CI 1.14-1.63). The BMES found a nonsignificant trend of increased mortality in people with diabetes with baseline diabetic retinopathy at seven years (RR 1.6, CI 1.0-2.7; p = 0.06). The EURODIAB prospective complications study found no significant association of diabetic retinopathy with mortality after multivariable adjustment.

A Finnish population of persons visually impaired due to diabetic retinopathy (DR) were reported to have a higher rate of cardiovascular mortality when compared to age and sex-matched control groups from the same geographic location over a period of 4 years. In this study, Rajala et al identified 34 men and 73 women living in northern Finland with visual impairment caused by DR on 31 December 1993. These subjects were aged 27 to 71 years at baseline (median 71 years). Visual impairment was defined as decimal visual acuity <0.3. The 4-year mortality rate of this group was compared with that of 3 age, and sex matched control groups. The first control group were subjects treated for DR by laser coagulation from 1990 to 1993 (decimal VA acuity was > 0.9 in 38 subjects, 0.6-0.9 in 30 subjects, 0.3-0.5 in 24 subjects and < 0.3 in 7 subjects). The second control group were diabetic subjects with fundus photographs taken from 1991 to 1992. The third control group comprised nondiabetic subjects from the population register. One-hundred and seven subjects from each control group were matched for age and sex with the study subjects. The subjects in the 4 groups were aged 27 to 88 years at baseline (median 71 years). Each group consisted of 34 (32%)
men and 73 (68%) women. Information on deaths was obtained from official death
certificates.\textsuperscript{98}

The 4-year mortality rate (MR) was highest in subjects with visual impairment caused by DR
at baseline (MR 477/1000, CI 382-571/1000).\textsuperscript{98} The 4-year mortality rates for diabetic
subjects with retinopathy previously treated by laser coagulation was higher than that of the
nondiabetic subjects but lower than subjects with VI and untreated DR at baseline (MR
224/1000, CI 145-303/1000 and MR 94/1000, CI 46-165/1000 respectively).\textsuperscript{98}

Compared with the nondiabetic control subjects, the risk of all-cause 4-year mortality was
highest in the diabetic subjects with visual impairment due to DR (OR 5.1, CI 2.6-11.0),
followed by diabetics with laser coagulation prior to baseline (OR 2.4, CI 1.1-5.6).\textsuperscript{98} The 4-
year mortality risk in diabetic subjects with fundus photographs taken, but without recorded
VI or previous laser treatment, was not significantly different to non-diabetics in this
population (OR 1.6, CI 0.68-4.0).\textsuperscript{98}
The Associations Between Cause-Specific Visual Impairment and Cause-Specific Mortality

**Cataract and Cause-Specific Mortality**

**Cataract and Cardiovascular Disease**

The Nurses’ Health Study cohort, found a significant association among women aged 45-63 years who had cataract surgery between 1984 and 1992, and coronary heart disease (CHD) morbidity and mortality.

Incidence rates of CHD were calculated for women who reported an extraction. The relative risk of CHD was estimated with adjustment for 5-year age categories. Pooled logistic regression across the five 2-year intervals was used to adjust simultaneously for potential confounding variables.

During 10 years follow-up, after adjustment for age, smoking, and other coronary risk factors, cataract extraction was significantly associated with higher risk of CHD (any CHD: RR 1.88, CI 1.41-2.50; fatal CHD: RR 2.44, CI 1.54-3.89; nonfatal CHD: RR 1.63, CI 1.14-2.34). The association between cataract extraction and total CHD may be greater among diabetic women (RR 2.80, CI 1.77-4.42 diabetic vs.. RR 1.51, CI 1.04-2.18 normoglycaemic). After multivariate adjustment, cataract extraction remained significantly associated with increased mortality from cardiovascular disease (RR 1.84, CI 1.29-2.64).

The North London Eye Study found significant associations between all three cataract morphologies and cardiovascular mortality in nondiabetic women, but not nondiabetic men, after adjustment for age. (HR for nuclear opacity (1.8); cortical opacity (1.9); and posterior subcapsular opacity (2.1) were all significant with p<0.04 for each cataract type vs. p>0.3 for each type in nondiabetic men).
The MRC trial of assessment and management of older people in the community reported no association risk of cardiovascular mortality and cataract in persons aged 75 years and older.\(^67\) However, there was a significant association between cardiovascular mortality and VI after multivariable adjustment in participants for whom the cause of VI was uncertain (RR 1.81, CI 1.17-2.78).\(^67\) This may have led to an underestimation of the association between cataract and cardiovascular mortality.

The BDES found a significant association between stroke mortality and increasing severity of nuclear sclerosis, but not cortical or posterior subcapsular cataract at 13 years from baseline.\(^61\) The association with heart disease related mortality and cataract was not significant after multivariable adjustment for any cataract subtype.\(^61\)

The BMES examined cause-specific VI and cause-specific mortality 7 and 11 years from baseline.\(^56,57\) At seven years, causes of death in persons with baseline visual impairment did not reveal any substantial differences compared to persons without baseline visual impairment.\(^56\) At 11 years, the BMES reported an association of increased risk of vascular mortality in participants with any cataract (HR 1.57, CI 1.13-2.19), nuclear cataract (HR 1.48, CI 1.06-2.07) and posterior subcapsular cataract (HR 1.46, CI 1.00-2.12) after multivariable adjustment for factors significantly associated with mortality in this population, including visual impairment.\(^57\) The association with cortical cataract was not significant after multivariable adjustment (HR 1.22, CI 0.94-1.59). There was no association between previous cataract surgery and 11-year vascular mortality after multivariable adjustment.\(^57\)
The Barbados Eye Study found no association between baseline cataract and cardiovascular mortality (RR 1.16, CI 0.67-2.02; RR 1.17, CI 0.79-1.75; RR 1.13, CI 0.76-1.67 for mixed opacity; any nuclear; and any cortical respectively, after age and sex adjust).\textsuperscript{84}

The AREDS study reported no statistically significant associations between the presence of nuclear sclerosis, cortical or posterior subcapsular cataract or previous cataract surgery and cardiovascular mortality.\textsuperscript{64}
**Cataract and Cancer**

In the AREDS study, grade ≥4 nuclear opacity (RR 1.56, CI 1.05-2.31) and previous cataract surgery (RR 2.29, CI 1.45-3.60) were associated with increased risk of cancer related death after multivariable adjustment.\(^{64}\) Grade ≥4 nuclear sclerosis, but not posterior subcapsular or cortical cataract, was also associated with non-cardiovascular and non-neoplastic causes of death (RR 1.64, CI 1.07-2.51; RR 1.63, CI 0.66-4.05; RR 0.82, CI 0.47-1.45 respectively).\(^{64}\)

In contrast to AREDS data, in the BMES population cancer-related deaths were significantly less frequent in participants with cataract (P<.001) at 11 years.\(^{57}\) No significant difference in respiratory or other causes of death between persons with and without cataract at baseline was observed at 11 years.\(^{57}\)

The North London Eye Study reported no association was present between cataract and cancer associated mortality after age and sex adjustment in their cohort.\(^{77}\) The MRC trial of assessment and management of older people in the community also found no significant association between cataract and cancer-related mortality after multivariable adjustment.\(^{67}\)

The Barbados Eye Study reported no significant associations between cataract and cancer-related mortality (RR 2.37, CI 0.98-5.71; RR 1.85, CI 0.98-3.52; RR 1.39, CI 0.76-2.55 for mixed, nuclear and cortical cataract respectively after age and sex adjustment).\(^{84}\)
**Age Related Macular Degeneration and Cause-Specific Mortality**

**Age Related Macular Degeneration and Cardiovascular disease**

In the BMES, cumulative 11-year vascular mortality was higher in participants with age related macular degeneration (ARMD) compared to those without ARMD at baseline (26.5% vs. 11.9%). After multivariable adjustment, the presence of any ARMD at baseline was associated with higher vascular mortality risk for participants younger than 75 years (HR 2.1, CI 1.17-3.77). The association remained significant after adjustment for the presence of visual impairment (HR 2.03, CI 1.07-3.84) but not after the addition of baseline fibrinogen and triglyceride levels and baseline disability in walking to the model (HR 1.41, CI 0.64-3.09). The authors reasonably suggested the loss of significance may reflect ARMD sharing common antecedents with cardiovascular disease.

The 11-year BMES data also demonstrated an association between level of baseline ARMD and 11-year cardiovascular mortality in participants younger than 75 years. In analyses using three categories for ARMD (none, early, and late), late ARMD predicted higher vascular mortality (HR 3.8, CI 1.4-10.4), although early ARMD did not (HR 1.4, CI 0.7-2.7) in participants younger than 75 years. There was no association between ARMD and cardiovascular mortality in participants aged ≥ 75 years at baseline.

Over a 10-year follow-up, after controlling for age, gender, race, systolic and diastolic blood pressure, pack-years of cigarette smoking, and other variables, early AMD was not associated with incident CHD (RR 1.08, CI 0.82-1.42) the ARIC study cohort. Individuals with late AMD were significantly more likely to have an incident CHD event, however the numbers were small. There were 4 CHD events among the 15 participants with late AMD at baseline giving a 10-year cumulative incidence of 30.9%. There were 918 CHD events among the
11,399 participants without late AMD giving a 10-year cumulative incidence of 10.0%. This was a statistically significant difference (P = 0.049, Fisher exact test).85

Participants in the Age-Related Eye Disease Study (AREDS) with advanced ARMD (Category 4 = unilateral advanced AMD or unilateral vision loss to worse than 20/32 attributable to AMD) compared with participants with few, if any, drusen had significantly increased risk of cardiovascular death after multivariable adjustment (RR 1.92, CI 1.18-3.12).64

The Leiden 85-plus Study is a prospective population based study consisting of two cohorts of inhabitants of Leiden, The Netherlands, aged 85 years and older. For cohort ‘87, subjects aged 85 years and over on November 1st 1987 were enrolled.99 For cohort ‘97, people of exactly 85 years were enrolled between September 1st 1997 and September 1st 1999.100 There were no inclusion criteria based on health or demographic characteristics.

The Y402H polymorphism is a Single Nucleotide Polymorphism (SNP) in codon 402 of the Complement Factor H gene (CFH Y402H) that is strongly associated with ARMD.101-104 The polymorphism has also been associated with cardiovascular disease mortality.105

Using the Leiden 85-plus Study population, Mooijaart et al examined the association of the CFH Y402H polymorphism with visual acuity and cardiovascular mortality. Mortality risks and 95% confidence intervals (CI) were calculated with a sex-adjusted Cox proportional hazards model.106
In this population, the risk of cardiovascular mortality was significantly increased in the HH haplotype compared to the YY haplotype (HR 1.51, CI 1.13-2.03). There was also a statistically significant association between visual impairment and CFH Y402H genotype (VA both eyes HH = 0.66 (0.62-0.69); HY = 0.63 (0.60-0.66); YY 0.58 (0.52-0.63) p = 0.020). There was no statistically significant association of the CFH Y402H polymorphism with any cardiovascular risk factor (Male sex, diabetes, smoking, cholesterol, triglycerides and BMI). This study did not directly report an association between visual impairment or ARMD and mortality.

The MRC trial of assessment and management of older people in the community reported no association between ARMD and cardiovascular mortality after multivariable adjustment in persons aged 75 years or older (RR 1.03, CI 0.72-1.45). There was a significant association between persons with an unknown cause of visual impairment and cardiovascular disease (RR 1.81, CI 1.17-2.78). This may have led to an underestimation of the association between ARMD and cardiovascular mortality in this study.

In the Copenhagen City Eye Study, death from respiratory conditions that included pulmonary disease caused by cardiac insufficiency was significantly higher in women with early and late ARM than in women without ARM at baseline (32% (28 of 87) vs. 19% (20 of 105), P = 0.045). However, women without ARM at baseline were more likely to have died from ischemic heart disease or stroke than women with early and late ARM (50% (52 of 105) vs. 32% (28 of 87), P = 0.019). There was no association between ARMD and cardiovascular mortality in the male participants.
**Age Related Macular Degeneration and Cancer**

The Age-Related Macular Degeneration and Cancer Mortality study, using data from the ARIC study population\(^8^6\) reported an association between the 10 year risk of cancer mortality and ARMD after multivariable adjustment (Early ARMD RR 1.68, CI 1.03-2.73).\(^1^0^7\) This association was larger in African American persons (RR 3.93, CI 1.67-9.22) and not significant in white persons (RR 1.28 CI 0.71-2.32). In African American persons, there was a statistically significant increased risk of lung cancer death (RR 5.28, CI 1.52-18.40). Associations between ARMD and lung cancer death were not statistically significant for white persons or the population as a whole.\(^1^0^7\) In this same population there was no association between ARMD and cardiovascular mortality.\(^8^5\)

There were no associations with ARMD and cancer-related mortality in the MRC trial of assessment and management of older people in the community.\(^6^7\) There were no significant associations between ARMD and cancer mortality in the BDES.\(^6^1\)
Glaucoma and Cause-Specific Mortality

Glaucoma and Cardiovascular Disease

The United States NHIS found an association between baseline glaucoma and seven-year cardiovascular mortality.87 Lee et al reported an increased risk of cardiovascular disease mortality for participants with reported glaucoma. The increased risk was present regardless of visual impairment status (without VI (HR 1.31, CI 1.11-1.55); with VI (HR 1.53, CI 1.15-2.05).87

The BMES reported a significant association between glaucoma and nine-year cardiovascular mortality in participants younger than 75 years with baseline open angle glaucoma.91 After multivariate adjustment, the increased cardiovascular mortality risk in glaucoma patients aged <75 years was RR 2.78 (CI 1.20-6.47). Further stratified analyses showed that cardiovascular mortality was higher among those with glaucoma diagnosed before baseline (RR 1.85, CI 1.12-3.04). An even greater risk of cardiovascular mortality was associated with glaucoma diagnosis before baseline and treatment with topical timolol (RR 2.14, CI 1.18-3.89).91

While the Barbados Eye Study found no statistically significant association between baseline open angle glaucoma and all-cause nine-year mortality, it did report an association with cardiovascular mortality.89 The association between baseline diagnosed OAG in all participants and cardiovascular mortality was not statistically significant (RR 1.38, CI 0.97-1.98). The association was significant in participants using timolol for IOP control (RR 1.91, CI 1.04-3.50). In persons with elevated IOP (>21mm Hg) at baseline (ocular hypertension and diagnosed glaucoma combined) there was a statistically significant association with cardiovascular death (RR 1.02, CI 1.00-1.04). The association between baseline ocular
hypertension and cardiovascular mortality was not statistically significantly (RR 1.28, CI 0.99-1.65).  

The WESDR found no associations between any glaucoma, open angle glaucoma and rubeotic glaucoma with 16-year cardiovascular mortality risk after multivariable adjustment.
Glaucoma and Cancer

Lee et al reported an association between baseline glaucoma and seven year cancer-related mortality in data drawn from the United States NHIS. The risk was increased only in participants with reported glaucoma but without reported visual impairment (HR 1.57, CI 1.25-1.98). Significantly, this association was stronger when the mortality analysis was restricted to cancers amenable to early screening, including breast, cervical, colon, and prostate cancer (HR 1.99, CI 1.41-2.81).

There were no significant associations between glaucoma and cancer mortality in the BDES. There were no significant associations between glaucoma and cancer mortality in the BMES.
Diabetic Retinopathy and Cause-Specific Mortality

Diabetic Retinopathy and Cardiovascular Disease

The BDES reported an association between increasing severity of diabetic retinopathy with increased risk of heart disease related mortality after multivariable adjustment.61

The BMES reported an association between any retinopathy at baseline and 12 year coronary heart disease mortality risk after adjusting for cardiovascular risk factors, both in persons with diabetes and without diabetes (HR 2.21, CI 1.20-4.05 and HR 1.33, CI 1.02-1.83 respectively).108 The presence of moderate retinopathy at baseline predicted a greater risk of cardiovascular death than any retinopathy (HR 6.68, CI 2.24-20.0 and HR 2.29, CI 1.10-4.76 in persons with and without diabetes respectively).108

The WESDR authors reported a significant increase in 20-year cardiovascular mortality risk with increasing severity of diabetic retinopathy after multivariable adjustment (HR 1.3, CI 1.1-1.5 per step increase in severity).95 This study also reported an association between CSME with increased risk of mortality due to ischaemic heart disease in participants diagnosed with diabetes after 30 years old and who were taking insulin after multivariable adjustment (HR 1.58, CI 1.07-2.35).96 An association between CSME and increased all-cause mortality risk after age and sex adjustment in participants of this cohort became nonsignificant after multivariable adjustment.96 There was no significant association between CSME and heart disease related mortality in participants diagnosed with diabetes before the age of 30 years old, nor in participants not taking insulin and diagnosed with diabetes after the age of 30 years after multivariable adjustment.96 In addition, CSME was not significantly associated with stroke mortality in this cohort.96
A Finnish population of persons with visual impairment caused by diabetic retinopathy (DR) were reported to have a higher rate of cardiovascular mortality, when compared to an age and sex matched control group without diabetes, over a period of 4 years (OR 5.6, CI 2.1-19).98
**Diabetic Retinopathy and Cancer**

There were no significant associations between DR and cancer mortality in the BDES.61

There were no significant associations between DR and cancer death in the WESDR population study of diabetics.70
Summary

The Prevalence of Visual Impairment

Visual impairment is a disability with high prevalence and significant negative impacts on the lives of persons in Australia and throughout the world. The global burden of BCVA <6/18 is estimated to be 161 million persons\(^9,10\) including 297,800 Australians with BCVA < 6/12.\(^12\) The number of persons with low vision in Australia is projected to increase to 800,000 by 2020.\(^12\)

The burden of visual impairment is not uniformly distributed. A higher prevalence is associated with older age,\(^1-5,8\) female sex,\(^1-3,5,8,9\) lower socioeconomic status,\(^4,6,15-17\) lower education level,\(^4,6,15-17,7\) minority race,\(^6,16,18,19\) and living in an underdeveloped nation.\(^7,9\) A larger proportion of visual impairment is due to potentially modifiable or treatable causes such as cataract, diabetic retinopathy and glaucoma in persons of lower socioeconomic status, lower education level or living in an underdeveloped nation.\(^4,7,15,16,18,19\)

The Associations Between Visual Impairment and Morbidity

Visual impairment has significant negative associations with function, independence, morbidity and mortality. Persons with visual impairment were significantly more likely to report lower self-rated health.\(^20-23\) This reported association appears greater in persons of younger age and female sex.\(^20-22\) The presence of visual impairment significantly negatively impacts measures of HRQOL,\(^27,29,30,33\) VRQOL,\(^29,31,33\) ADL,\(^37,41,42\) IADL\(^37,41,42\) and vision related functional tasks.\(^35,36\) Persons with visual impairment, were reported to have increased numbers of restricted activity days, bed days, doctors’ visits and hospital admissions.\(^22\)
Visually impaired persons were more likely to have or subsequently develop mobility problems,43,46 use walking aids46 and were less likely to improve their mobility over time.43 Visual impairment increases the risk of falls44,46 and fractures,46 including hip fractures.45,47-49 The association between hip fractures and VI increases with age45 and level of visual impairment.48 The majority of the principal causes of visual impairment associated with hip fractures may be potentially modifiable and associated with social deprivation.49 Persons with visual impairment were reported more likely to be placed into nursing homes,46 and to be depressed.50,53,55
The Associations Between Visual Impairment and Mortality

All-Cause Visual Impairment and Mortality

The association between all-cause VI and all-cause mortality after age and sex adjustment was consistently reported statistically significant in the included studies\textsuperscript{56-62,64,65,67,70} with the exception of the Copenhagen Eye Study.\textsuperscript{68} The majority of these studies report that statistical significance was attenuated, but not eliminated, by multivariable adjustment.\textsuperscript{56,57,59,62,64,65,67,70} Others reported statistical significance was lost after multivariable adjustment.\textsuperscript{57,58,60} In the BDES and BMES, the associations were reported as both significant and non-significant depending on the number of years until follow up,\textsuperscript{56,57,60,61} age stratification\textsuperscript{56,57,60,61} and confounder adjustment.\textsuperscript{56-57,60}

In studies that compared levels of VI, greater VI was associated with higher mortality risk.\textsuperscript{65,67,70} Conflicting results regarding sex, VI and the association with mortality were reported with some finding increased risk in women\textsuperscript{59,65} and others in men.\textsuperscript{61} Studies that stratified age found the presence of VI at a younger age was associated with increased risk of mortality when compared to VI in older age groups.\textsuperscript{57,61} Cohorts of older mean age or shorter duration follow up were less likely to report statistical significance after multivariable adjustment.\textsuperscript{56-62,64,65,67,68,70}

Studies differ by definition of visual impairment, mean age, age range, duration of follow up and confounding variables adjusted for.\textsuperscript{56-59,61,62,64,65,67,68,70} Visual impairment was reported to be independently associated with many of the confounding variables associated with mortality and corrected for in these studies.\textsuperscript{20,50,67,84,106,109-114} Correcting for these covariates using traditional regression techniques may underestimate the total effect of visual impairment on mortality.\textsuperscript{115}
All-cause visual impairment is associated with statistically significant increased risk of cardiovascular cause of death in some studies.\textsuperscript{59,70} Other studies reported no association between all-cause visual impairment and cardiovascular mortality.\textsuperscript{56,57,61} Women with visual impairment may be at higher risk of cardiovascular death.\textsuperscript{59}

All-cause visual impairment was not associated with cancer-related mortality in any of the included studies that examined this association except the BMES, which found an association between VI and lower cancer-related mortality risk.\textsuperscript{56,57,59,61,64,67,70}
Cataract and Mortality

In the studies reviewed that examined associations between previous cataract surgery and subsequent mortality, all reported increased mortality risk after multivariable adjustment except the BMES. One study of persons with baseline cataract found an increased risk of 6 year mortality that was significantly attenuated in persons who had undergone cataract surgery during the follow up period when compared to persons with cataract who did not elect to undergo surgery and with persons without baseline cataract. Cataract surgery at a younger age was associated with increased risk of mortality when compared to cataract surgery at older ages.

The presence of cataract was associated with increased all-cause mortality risk in most but not all included studies. The mortality risk associated with the presence of cataract or previous cataract surgery may be sex-dependent with two reviewed studies showing increased risk in women compared to men. The BDES reported the increased risk of mortality associated with baseline cataract was higher in women after five years follow-up but higher in men after 13 years follow-up. One study reported no sex difference in the association between all-cause mortality and the presence of cataract. The remaining studies did not report a difference in mortality risk between the sexes.

The reported associations between the morphology of baseline cataract and all-cause mortality were inconsistent after multivariable adjustment. In the BDES 5 year follow up, significant associations were reported between nuclear sclerosis and all-cause mortality but not between cortical or subcapsular cataract and all-cause mortality. At 13 years follow up,
the association between nuclear sclerosis and all-cause mortality was not significant, but the association between cortical cataract and all-cause mortality was. The BMES reported significant associations with nuclear, cortical and subcapsular cataract at 7 and 11 years follow up. Of the remaining studies examining morphology, only nuclear sclerosis was reported significantly associated with all-cause mortality.

Previous cataract surgery was reported associated with an increased risk of cardiovascular mortality in women after multivariable adjustment. In another study, all three morphologies of cataract were reported associated with cardiovascular mortality in nondiabetic women, but not men, after adjustment for age. The risk of 11-year vascular mortality in the BMES population was reported to be increased in participants with any cataract, nuclear and PSC after multivariable adjustment. This risk was not significant seven years from baseline.

The BDES found an increased risk of 13-year mortality due to stroke in participants with baseline nuclear sclerosis that increased with increasing severity of the cataract but the association with heart disease was not significant after multivariable adjustment. The Barbados Eye Study reported no significant increased risk of cardiovascular mortality in participants with baseline cataract after multivariable adjustment. The AREDS study reported no statistically significant increased risk of cardiovascular mortality and baseline presence of nuclear sclerosis, cortical or posterior subcapsular cataract or previous cataract surgery and cardiovascular mortality.

A significant association between ≥ grade 4 nuclear sclerosis or previous cataract surgery and cancer-related mortality was reported by the AREDS study. In contrast the BMES reported lower mortality risk (p < 0.001) in participants with cataract at 11 years from baseline.
Other studies examining cancer-related death reported no significant associations between baseline cataract and cancer-related mortality.67,77,84
Age Related Macular Degeneration and Mortality

The association between ARMD and all-cause mortality after multivariable adjustment was inconsistently reported. Of the seven studies reviewed that examined this association, only 2 reported a significant increase in all-cause mortality in persons with baseline age related macular degeneration.\textsuperscript{57,60,62,64,67,68,85}

Younger persons with ARMD may be at higher risk of all-cause mortality.\textsuperscript{57} The BMES reported no significant association between ARMD and all-cause mortality overall at 5 and 11 years from baseline. After age stratification, BMES participants younger than 75 years old were reported to have increased risk of all-cause mortality at 11 years from baseline.\textsuperscript{57} Women with ARMD may have higher mortality risk.\textsuperscript{68}

The risk of cardiovascular mortality was reported increased in BMES participants younger than 75 years with baseline ARMD\textsuperscript{57} and in the AREDS after multivariable adjustment.\textsuperscript{64} The reported risk increased with increasing severity of baseline ARMD in two studies.\textsuperscript{57,64} The association between ARMD and cardiovascular mortality became non-significant after adjustment for baseline fibrinogen level, triglyceride level and disability in walking in the BMES cohort.\textsuperscript{57} The ARIC study reported ARMD was associated with higher risk of cardiovascular events but not mortality.\textsuperscript{65} Age related macular degeneration was not associated with cardiovascular mortality in the Copenhagen City Eye Study.\textsuperscript{68}

The CFH Y402H polymorphism may offer a biologically plausible cause for excess cardiovascular risk in persons with ARMD after adjustment for cardiovascular risk factors.\textsuperscript{106}
One of the three included studies that examined the association between baseline ARMD and cancer-related mortality reported a statistically significant increased risk of cancer-related death after multivariable adjustment. In this population, there were no significant associations reported between ARMD and cardiovascular mortality after multivariable adjustment. The remaining two studies that examined the association between cancer-related mortality and ARMD reported no significant association.
Glaucoma and Mortality

Ten of the reviewed studies examined the association between glaucoma and mortality. A significant association between baseline glaucoma and increased all-cause mortality after multivariable adjustment was reported in only one of these studies. The remaining 9 studies reported no significant association between baseline glaucoma and all-cause mortality after multivariable adjustment.

Combined high intraocular (>21mmHg) or diagnosed glaucoma at baseline was found statistically significantly associated with increased all-cause mortality in the Barbados Eye Study. The Framingham Eye Study, using a definition of high intraocular pressure > 25mmHg, found no association between combined baseline glaucoma diagnosis or high intraocular pressure and all-cause mortality.

The Barbados Eye Study reported a statistically significant association in persons with elevated intraocular pressure or diagnosed glaucoma at baseline with an increased risk of cardiovascular mortality after multivariable adjustment. Glaucoma was found to be statistically significantly associated with increased risk of cardiovascular death in the BMES and an NHIS study. This associated risk may be higher in persons using timolol.

Two studies estimated the association of baseline timolol use and mortality, the Barbados Eye Study and the BMES. The Barbados Eye Study reported that participants with baseline open angle glaucoma using timolol had a significantly increased risk of all-cause and cardiovascular mortality. The BMES reported no increased risk of all-cause mortality, but did report an increased risk of cardiovascular mortality in participants using timolol for open angle glaucoma at baseline.
One of three reviewed studies reported a significant association between baseline glaucoma and an increased risk of cancer-related mortality.\textsuperscript{6,8,7,91}
Diabetic Retinopathy and Mortality

Diabetic retinopathy was reported to be associated with increased risk of all-cause mortality in all of the reviewed studies, with the exception of the BMES which found a non-significant trend towards increased mortality risk \( (p = 0.06) \) and the EURODIAB study which found strong associations between diabetic retinopathy and increased all-cause mortality risk that became non-significant after adjustment for cardiovascular risk factors. Two studies found increasing severity of diabetic retinopathy and greater VI due to diabetic retinopathy associated with higher all-cause mortality risk.

Baseline diabetic retinopathy was significantly associated with cardiovascular mortality risk in all five studies examining this association. Greater severity of diabetic retinopathy was associated with higher cardiovascular mortality risk. The presence of CSME was associated with increased risk of cardiovascular but not all-cause mortality after multivariable adjustment.

There were no significant associations found between baseline DR and cancer.

The associations between mortality risk markers, visual impairment and mortality using structural equation modelling have not been examined. This may have lead to overcorrection of the associations between visual impairment and mortality.
1.2 Auditory Impairment
The MRC Institute of Hearing Research reported the prevalence of various severities of measured hearing impairment, the prevalence of self-reported hearing disability and the variation in prevalence of hearing impairment with age, sex, occupational group and occupational noise exposure in a population based cohort study in Great Britain.\textsuperscript{116}

The study was a 2-stage sample survey conducted in the cities Cardiff, Glasgow, Nottingham and Southampton.\textsuperscript{116} The first stage was a postal questionnaire. The second consisted of a clinical examination, interview and audiological assessment. Participants for the first stage comprised a sample of 48,313 persons selected at random from the electoral registers compiled in 1980, 1981 and 1984 for the four cities. Participants for the second-stage samples (n=2910) were drawn from responders to the first-stage postal questionnaire. All participants tested underwent an audiological assessment, a clinical interview concerning hearing and general health and otoscopic examination. Attendance rate was 42\% of all people sampled for stage.\textsuperscript{116}

Audiological assessment was performed in sound-attenuating booths, conforming to ISO/DIS 8253\textsuperscript{18} for measurement of air conduction thresholds of 0 decibels hearing level (dBHL).\textsuperscript{116} Air-conduction thresholds were obtained at 0.25, 0.5, 1, 2, 3, 4, 6, 8 and 12 kHz. The analysis at stage 2 was restricted to subjects in the age-range 18-80 years.\textsuperscript{116}

Self-reported hearing disability was estimated from the stage 1 questionnaire and was associated with objectively measured hearing loss.\textsuperscript{116} Overall 26\% of adults report great difficulty hearing speech in noise. These participants on average had a 25 dBHL impairment in their better ear (averaged for the frequencies 0.5, 1, 2, 4 kHz). Over 3\% reported moderate or worse bilateral difficulty in quiet. These participants had an average of 45 dBHL HI in the
Overall, 16% of persons aged 17-80 years had a >25 dBHL, 4% a ≥ 45 dBHL and 1% a ≥ 65 dBHL impairment in both ears.\textsuperscript{116}

The prevalence of HI increased significantly with increasing age, male sex, manual occupation and occupational noise exposure > 90 dBA\text{Leq} (time weighted average of the level of sound in decibels on scale A).\textsuperscript{116} The prevalence of hearing impairment in the better ear doubled for each ten-year age band. There was no significant association between occupational noise exposure of 81-90 dBA\text{Leq}.\textsuperscript{116}

The Veneto Study is a random sample of 2700 noninstitutionalized persons aged 65 years and older, residing in the community in nine defined geographic areas of the Veneto region in northeast Italy on May 1, 1989.\textsuperscript{117} Five of these centres are rural, and four are urban. Eligible individuals were identified from the resident lists maintained by the municipalities. Random samples were taken from each of five age strata (65-69, 70-74, 75-79, 80-84, 85+ years). Eighty-nine percent (n = 2398) of eligible persons participated in the study. Participants were administered a questionnaire and a brief examination in their home. Self-reported assessment of Hearing Impairment included rate self-reported hearing impairment both at home (seven questions) and in a social environment (seven questions). Hearing impairment was assessed by speech intelligibility testing through speech audiometry using standard audiometric head phones (TDH 39) and a Hi-Fi portable tape voice recording set at 70 dB of sound pressure level (dBSPL) intensity. Intelligibility was indicated by the percentage of items repeated correctly. Hearing impairment was defined as intelligibility ≤75\%.\textsuperscript{117}

Four single forward stepwise logistic regression analyses were performed to identify the association of self-reported hearing impairment: at home, in a social environment, at home or
in a social environment, and hearing impairment assessed by speech audiometry with sociodemographic characteristics (sex, age, level of education), mental and physical status indicators (cognitive impairment, depressive symptomatology, ADL disability, mobility disability, and self-rated health), health behaviour (alcohol use), and all medical conditions (arthritis, diabetes, hypertension, chronic respiratory disease, stroke, heart disease, kidney diseases, Parkinsonism, and cancer). All analyses were performed using SAS procedures. In the Veneto study, speech audiometry testing detected a higher prevalence of hearing impairment than self-reporting by questionnaire. The prevalence of self-reported hearing impairment at home was 8.1% and 7.4% and in a social environment 11.1% and 9.3%, in men and women respectively. The prevalence of hearing impairment assessed by speech audiometry was 19% in both sexes.

Wilson et al reported the prevalence of hearing impairment, and the major demographic factors that influence its prevalence, in a representative South Australian adult population aged ≥ 15 years. This study used a 2 stage sample design. Stage 1 involved random sampling of persons aged ≥ 15 years from South Australian households using Australian Bureau of Statistics Census collectors’ districts as the sampling frame. The bi-annual South Australian Health Omnibus Survey (SAHOS) was then administered to the entire study cohort of 9027 persons over three consecutive SAHOS periods. Self-reported hearing impairment was defined as answering yes to either of the three following questions; Do you have trouble hearing what people say to you in a quiet room (a) when they speak loudly to you?; (b) if they speak normally to you?; (c) if they whisper to you? Audiological assessment was performed in sound-attenuated booths confirming to Australian Standard 1269-1983.
Cerumen that prevented view of the tympanic membrane was removed before audiological testing. Air conduction thresholds were obtained at 0.25, 0.5, 1, 2, 3, 4, 6 and 8 kHz. Of 1378 (15.3%) persons who self-reported hearing impairment, 689 (50%) completed stage 2, the audiological examination. Of those reporting no hearing impairment, 300 were asked and 237 (79%) completed the audiological examination assessed. Due to the complex recruiting process reweighting was required so that the data could be directly compared to the British National Study of Hearing data.\textsuperscript{116,119} The age range that allowed direct comparison was 15-50 years, 51-60 years, 61-70 years and 71+ years. Variance estimates were provided by the ultimate cluster variance estimator. Logistic regression models were used to estimate ORs and 95% CIs. Occupation was classified using the Australian Bureau of Statistics Standard Classification of Occupations (ASCO).\textsuperscript{119,120}

Wilson et al reported the prevalence of hearing impairment at $\geq 25$ dB Hearing Threshold Level (dBHTL) in this South Australian population to be 16.6% in the better ear and 22.2% in the worse ear to be.\textsuperscript{119} The self-reported prevalence was 15.3%. While this did not differ statistically from the measured prevalence of 16.6% in the better ear, the false positive rate for self-reported hearing impairment was 46% and the false negative rate 17%. The prevalence of hearing impairment increased significantly with age, approximately quadrupling for every 10 year age band in persons older than 50 years. The OR for the risk of $\geq 25$ dBHTL in persons $\geq 71$ years was 123.9, $p = 0.01$ when compared to the risk of hearing impairment in persons $\leq 50$ years of age. For $\geq 45$ dBHTL, the risk was OR, 369.3; $p = 0.01$ for the same age comparison. There was also a significant sex difference in the prevalence of hearing impairment in this population. The risk of being hearing impaired was 70% higher in males compared to females (OR, 1.7; $p = 0.01$) and increased with time exposed to noise.
There was no statistically significant association between risk of hearing impairment and socioeconomic status.\textsuperscript{119}

The Epidemiology of Hearing Loss Study (EHLS) is a population-based study designed to measure the prevalence of hearing loss in adults aged 48-92 years, residing in Beaver Dam, Wisconsin.\textsuperscript{121} To identify eligible participants aged 43-84 years, a private census was conducted during 1987-1988 of the township of Beaver Dam. This cohort was subsequently invited to participate in the Beaver Dam Eye Study. Of the 5,924 eligible people, 4,926 (83 percent) participated in the eye examination phase (1988-1990). The hearing study occurred during the five years follow up visit for the BDES. Participants alive as of March 1, 1993, were eligible for the hearing study (n = 4,541). Of those eligible, 3,753 (82.6 percent) participated in the hearing study. The hearing examination included an otoscopic examination, screening tympanogram and pure-tone air- and bone-conduction audiometry. Audiometric testing was conducted according to the guidelines of the American Speech-Language- Hearing Association using sound-treated booths. Pure-tone air-conduction thresholds were obtained for each ear at 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz. A questionnaire was administered via interview and included ear and hearing-related medical history, noise exposure and self-reported hearing function. Questionnaire data on socioeconomic status, medical history, lifestyle factors, and medication use were obtained as part of the Beaver Dam Eye Study examination.\textsuperscript{121}

The presence of a hearing loss was defined as a pure-tone average of thresholds at 0.5, 1, 2 and 4 kHz greater than 25 dB of hearing loss in the worse ear. Severity of hearing loss was classified as mild (>25 and \leq 40 dB of hearing loss), moderate (>40 and \leq 60 dB of hearing loss), or marked (>60 dB of hearing loss).\textsuperscript{121} The average age of participants was 65.8 years.
Fifty-eight percent of participants were female. The participant group was compared with 1990 Census data for US non-Hispanic whites and was similar to all US non-Hispanic whites in age and sex distributions, but less likely to report high household incomes. Analyses were conducted using the 1990 SAS version 6.09 software (SAS Institute, Inc., Cary, North Carolina). Univariate analyses used the chi-square test of association for categorical variables, Mantel-Haenszel test of trend for ordinal data and t tests of mean differences for continuous data. Logistic regression was used to evaluate the odds of having a hearing loss associated with age, sex, and socioeconomic factors.\textsuperscript{121}

The overall prevalence of hearing loss in this population was 45.9\%.\textsuperscript{121} The odds of hearing loss increased with age (OR 1.88 for 5 years, CI 1.80-1.97). The prevalence of hearing loss was 90\% in participants > 80 years of age compared to 21\% in persons aged 48-59 years old. The odds of hearing loss were greater in men (OR 4.42, CI 3.73-5.24). The greater odds of hearing loss in males remained statistically significant after adjusting for age, education, noise exposure, and occupation (OR 3.65, CI 2.97-4.49). Persons with occupational noise exposure had an increased likelihood of hearing loss (OR 1.31, CI 1.10-1.56).\textsuperscript{121}

The Blue Mountains Hearing Study (BMHS) is a population-based survey of age-related hearing loss in a representative older Australian community.\textsuperscript{122} The BMHS invited participants who attended the second cross-sectional survey of the Blue Mountains Eye Study (BMES 2). Persons who moved into the study area or study age group were identified by a repeat door-to-door census in 1999 and were invited to participate. The BMHS was conducted during 1997 to 2000. The hearing questionnaire and examinations for the Blue Mountains Hearing Study were identical to those described for BMES 2 onwards. During 1992 through 1994, 3654 participants 49 years or older were examined (82.4\% participation.
Surviving baseline participants were invited to attend 5- and 10-year follow-up examinations, at which 2335 (75.1% of survivors; 543 had died) and 952 (75.6% of survivors; 1103 had died) participants were reexamined, respectively. During 1997 through 2000, 2956 persons 50 years or older had audiometric testing performed.\textsuperscript{122}

A questionnaire eliciting medical history and information about occupational noise exposure, hearing and socioeconomic and lifestyle factors was administered to all participants by interview.\textsuperscript{122} An audiologist asked additional questions including the history of any self-perceived hearing problem, including its severity, onset, and duration. Pure-tone audiometry at both visits was performed by audiologists in sound-treated booths. Hearing impairment was determined as the pure-tone average (PTA) of audiometric hearing thresholds at 0.5, 1, 2, and 4 kHz (PTA0.5-4.0kHz). Hearing loss was defined as; (a) any hearing loss = PTA 0.5-4.0kHz > 25 dB HL (hearing level); (b) moderate to severe hearing loss = PTA > 40 dB HL in the better ear.\textsuperscript{122}

Of the 2956 participants, detailed audiometric data were available for 2940 subjects. Any level of hearing loss was present in 33.0% of participants.\textsuperscript{122} Hearing loss was more prevalent in men for each decade younger than 80 years (age adjusted OR 1.7, CI 1.4-2.0). The prevalence of any hearing loss doubled for each age decade (OR 3.5, CI 3.1-3.9). The odds of hearing loss for persons aged > 80 years was 50 times greater than the odds in persons aged 50-59 years (OR 50.7, CI 33.2-78.9). The prevalence of any hearing loss in persons aged 60-69 years was 28.7% in men and 17.0% in women. History of working in a noisy environment was associated with a 70% increased likelihood of any hearing loss (OR 1.7, CI 1.3-2.1) and a 90% increased likelihood of moderate to severe hearing loss (OR 1.9, CI 1.3-2.6).\textsuperscript{122}
The prevalence of hearing loss in the Framingham Heart Study Cohort\textsuperscript{123} has been reported\textsuperscript{124} The Framingham Heart Study is a prospective investigation of risk factors leading to the development of cardiovascular disease.\textsuperscript{123} The study population is located in Framingham, Massachusetts. The study included biennial physical examinations and extensive history taking for each subject. Six thousand and fifteen persons aged 30 to 59 were selected to participate. During the fifteenth cycle (exam 15) of examinations, from April 1978 to October 1979, a hearing study was conducted to report the hearing status of the cohort and assess associations between hearing loss and cardiovascular risk factors.\textsuperscript{124}

A total of 2351 of the 3510 persons in the cohort known to be alive received a hearing examination, yielding a response rate of 89.26\%.\textsuperscript{124} After exclusions, results from 2293 hearing study participants were used for data analysis (935 men aged 58 to 88 (mean age. 68) and 1358 women aged 57 to 89 (mean age. 69.1). A certified audiologist obtained a hearing history from each subject and performed an otoscopic examination. Pure-tone air conduction thresholds for eight frequencies, from 0.25 to 8 kHz were measured using a sound-treated booth. Hearing loss was defined as a threshold level greater than 20 dB above audiometric zero for at least one frequency from 0.5 to 4 kHz. A logistic regression model was used to determine risk factors associated with hearing loss in the better ear.\textsuperscript{124}

In this population of persons aged 57-89 years old, the prevalence of hearing loss was estimated to be 83\%.\textsuperscript{124} The prevalence of hearing loss was 94\% in men and 76\% in women. The risk factors for hearing loss in this population were age, sex, illness, family history of hearing loss, Meniere's disease, and noise exposure.\textsuperscript{124}
Table 1.7 lists the reported overall prevalence of HI for the summarised studies that defined hearing impairment as >25 dBHL.

<table>
<thead>
<tr>
<th>Study</th>
<th>Participant Age (Years)</th>
<th>Hearing Impairment (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRC&lt;sup&gt;a&lt;/sup&gt;</td>
<td>17 – 80</td>
<td>16&lt;sup&gt;†&lt;/sup&gt;</td>
</tr>
<tr>
<td>SAHOS&lt;sup&gt;b&lt;/sup&gt;</td>
<td>≥15</td>
<td>17&lt;sup&gt;†&lt;/sup&gt; 22&lt;sup&gt;‡&lt;/sup&gt;</td>
</tr>
<tr>
<td>EHLS&lt;sup&gt;c&lt;/sup&gt;</td>
<td>48 – 92</td>
<td>45&lt;sup&gt;‡&lt;/sup&gt;</td>
</tr>
<tr>
<td>BMHS&lt;sup&gt;d&lt;/sup&gt;</td>
<td>≥49</td>
<td>33&lt;sup&gt;†&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Medical Research Council Hearing Research study<sup>116</sup>
<sup>b</sup> South Australian Health Omnibus Survey<sup>119</sup>
<sup>c</sup> Epidemiology of Hearing Loss Study<sup>121</sup>
<sup>d</sup> Blue Mountains Hearing Study<sup>122</sup>
<sup>†</sup> In the better ear
<sup>‡</sup> In the worse ear
The Associations Between Auditory Impairment Morbidity
**Auditory Impairment, Self-rated-health and Cognitive Impairment**

The Veneto Study\textsuperscript{117} examined the associations between hearing impairment, and SRH, mini mental state exam (MMSE) and chronic systemic disease that could impair quality of life.\textsuperscript{125} Martini et al reported that persons with hearing impairment were twice as likely to report poor self-rated health. A MMSE score < 24 was associated with a higher prevalence of hearing impairment.\textsuperscript{125}

The Alameda County Study is a longitudinal study of factors related to health and mortality. The study began in 1965 by enrolling 6,928 persons aged 16 to 94 originally selecting participants by a random household survey in Alameda County, California.\textsuperscript{126} Data collection was by mailed questionnaire supplemented by telephone and in-person interviews for participants unable to complete the questionnaires. Survivors were resurveyed in 1974, 1983, 1994, and 1995. Response rates for these follow-up surveys were 85%, 87%, 93%, and 97%, respectively. Eligibility for the analyses of hearing impairment included the 2,504 participants aged 50 and older in 1994 who completed both the 1994 and 1995 questionnaires. After exclusions, the total remaining was 2,461 persons. Hearing Impairment was assessed by self-report. Participants were asked in 1994 how much difficulty they had (even with a hearing aid) hearing and understanding words in a normal conversation, hearing words clearly over the telephone, and hearing well enough to carry on a conversation in a noisy room. Responses were scored according to level of difficulty: a great deal (3), some (2), a little (1), or none (0) and summed. Hearing impairment was divided into three categories: no HI (score of 0), a little HI (score of 1-3), and moderate or more HI (score of 4 or higher). Outcomes were dichotomized for logistic regression analysis. Separate logistic regression models were performed for each functional outcome. Each 1995 outcome was regressed on
age, gender, education, chronic conditions, and hearing impairment with the two levels of 1994 HI coded as indicator variables; the reference category was no HI.\textsuperscript{126}

The Alameda County Study found no association between self-rated health and self-reported HI (little hearing impairment OR 1.20, CI 0.87-1.65; moderate or more hearing impairment OR 1.39, CI 0.97-2.00).\textsuperscript{126}
Auditory Impairment and Measures of Function and Health Related Quality of Life

The EHLS reported the associations between hearing loss and health related quality of life (HQORL) using the Short Form 36 Health Survey (SF-36).\textsuperscript{127} Severity of hearing loss was significantly associated with decreased function in both the Mental Component Summary (MCS) score and the Physical Component Summary (PCS) score of the SF-36, as well as with six of the eight individual domain scores. There was no significant association between severity of hearing loss and the SF-36 domain scores general health or bodily pain, although the scores in these domains did decline with increasing hearing loss.\textsuperscript{127}

The BMHS reported the associations of hearing loss with HRQOL using the SF-36.\textsuperscript{128} After multivariable adjustment, participants with bilateral HI had lower SF-36 scores in all dimensions when compared with those with unilateral HI (statistically significant in two SF-36 dimensions (physical functioning and role limitation due physical problems, \( p \leq 0.05 \)) or those with normal hearing (statistically significant in four SF-36 dimensions (physical functioning, social functioning, role limitation due physical problems, role limitations due emotional problems and the PCS, \( p \leq 0.05 \)). Persons with unilateral HI did not have significantly different SF-36 scores when compared to persons with normal hearing. A non-significant trend for lower SF-36 scores was present in persons with mild bilateral hearing loss compared to persons without hearing loss. Poorer scores in the PCS and MCS were significantly associated with higher levels of hearing impairment (PCS \( P_{\text{trend}} = 0.04 \); MCS \( P_{\text{trend}} = 0.003 \)).\textsuperscript{128}

Self-reported hearing loss was significantly associated with HRQOL.\textsuperscript{128} Persons with self-reported hearing loss had significantly poorer HRQOL compared to persons without self-reported hearing loss. The mean PCS was 44.3 (standard error 0.3) in persons with compared
to 45.6 (standard error 0.3) in persons without self-reported hearing loss (p = 0.001).

Similarly, the mean MCS was significantly lower (p = 0.001) in persons with (MCS = 51.5, standard error 0.3) compared to persons without self-reported hearing loss (MCS = 53.0, standard error 0.3).\textsuperscript{128}

Self-reported hearing disability in older people was reported associated with poorer PCS and MCS scores in the SF-12 in another Australian study.\textsuperscript{129} This study utilised data from the 2003 Australian Survey of Disability, Ageing, and Carers (n = 43,233), a weighted population-based survey providing of self-reported disability and quality of life. Participants were aged ≥ 55 years. The study reported that, compared with population norms, hearing disability at all levels was associated with poorer physical and mental health scores on the SF-12 measure. The effect was more marked with increasing levels of hearing loss.\textsuperscript{129}

The EHLS study reported significant associations between hearing loss and activities of daily living (ADLs) and instrumental ADLs (IADLs).\textsuperscript{127} This study found that individuals with moderate to severe hearing loss were more likely than individuals without hearing loss to have impaired ADLs and IADLs after multivariable adjustment. (ADL OR 1.54, CI 1.06-2.24; IADL OR 1.54, CI 1.18-2.00).\textsuperscript{127}

The BMHS also found significant associations between hearing loss and ADLs and IADLs.\textsuperscript{130} The BMHS reported a significantly higher proportion of hearing-impaired persons had difficulties in performing three out of the seven basic ADL (Can you get to places out of walking distance; Can you go shopping for groceries or clothes; Can you do your housework). Hearing impaired persons were also more likely to report difficulties in performing six out of the seven instrumental ADL tasks compared to participants without
hearing impairment. After multivariable adjustment, increasing severity of hearing loss was associated with impaired ADL ($P_{\text{trend}} = 0.001$). Participants with moderate to severe hearing loss were almost three times more likely to report difficulties with ADL when compared to persons without hearing loss. The association between hearing loss and difficulty in performing ADL was higher in younger persons with hearing impairment. The association was greater with increasing levels of hearing impairment. Participants aged <75 years with moderate to severe hearing loss had 8-fold higher odds of difficulty in ADL compared with those without hearing loss (OR 8.60, CI 3.12-23.70) after multivariable adjustment. After age stratification, significant associations were not observed in participants aged ≥ 75 years.

The second supplement on ageing (SDOA-II) examined the health, activity, and social participation of a US population aged 70 years or older with self-reported vision impairment, hearing loss, or both and compared the health and activities of these three groups to those without sensory loss. Data for the SDOA II was obtained from the 1994 National Health Interview Survey (NHIS) core questionnaire, the access to care supplement to the 1994 NHIS, phase I of the NHIS on disability and phase 2 of the NHIS on disability. A total of 9447 persons were interviewed. Participants were community dwelling (non-institutionalised) adults aged ≥ 70 years.

In this study, older people with self-reported hearing loss reported greater difficulties in various activities, and social roles. Persons with hearing loss were significantly more likely to report difficulty dressing (OR 1.5, CI 1.3-1.8), bathing (OR 1.4, CI 1.2-1.6), preparing meals (OR 1.5, CI 1.2-1.8), using the telephone (OR 3.6, CI 2.8-4.6) and difficulties taking medications (OR 1.6, CI 1.2-2.0) and managing money (OR 1.8, CI 1.4-2.3) when compared
to persons without HI. Persons with HI were also more likely to be confused (OR 1.4, CI 1.1-1.8).\textsuperscript{131}

The Alameda County Study found significant associations between both self-reported levels of hearing impairment (a little and moderate or more) and higher odds of ADL disability (OR 1.71, CI 1.22-2.39 and OR 1.85, CI 1.26-2.71 respectively).\textsuperscript{126} Moderate or more hearing impairment was also associated with significantly higher odds of disability in IADL and physical performance disability (OR 1.37, CI 1.01-1.86 and OR 1.98, CI 1.38-2.84 respectively).\textsuperscript{126}

In a prospective study of functional outcomes of 755 subjects presenting for Geriatric Assessment at the University of Nebraska Medical Center between January 1986 and December 1992, comparisons in mean ADL and IADL scores across mutually exclusive groups defined by sensory loss (i.e., no sensory impairment, hearing loss alone, vision loss alone, and both hearing and vision loss) were conducted using Bonferonni-adjusted multiple-comparison tests.\textsuperscript{132} To determine the relative contributions of vision and hearing loss to diminished ADL and IADL function, ordinary least squares (OLS) regression models were estimated on ADL and IADL scores.\textsuperscript{132}

In this prospective study, the prevalence of hearing impairment was 64%.\textsuperscript{132} The mean ADL and IADL scores were lower in hearing impaired persons compared with those without hearing impairment (19/24 vs. 21/24 (P < .001) and 11/23 vs. 13/23 (P < .001 respectively). The association between hearing impairment and IADL was independent of mental status and comorbid illness whereas the association with ADL score was not. An OLS regression model that included vision, hearing, sex, cognitive status, and comorbid illness accounted for 40%
of the explained variance in IADL scores and 31% of the explained variance in ADL scores. In this model, all factors except sex were found to be independently related to IADL score. A similar model for ADL score found both sex and hearing were not independently related to the ADL score. An OLS regression model constructed with only hearing as the explanatory variables for ADL and IADL found hearing contributed to 2% of ADL variance and 3% of IADL mean score variance.\textsuperscript{132}
**Auditory Impairment, Mobility, Falls and Fractures**

Hearing impairment was found to be associated with catastrophic decline in mobility in a longitudinal cohort study investigating the associations between chronic health conditions, psychosocial and environmental factors, and catastrophic decline in mobility of community dwelling persons aged ≥ 65 years.\textsuperscript{133} Data were obtained from a national cross-sectional survey of 999 individuals (response rate 68%) aged ≥65 years, representative of British households. Of these persons, 789 (79%) agreed to further contact, and 531 (68%) responded to the postal questionnaire follow-up survey 12 months later. This represented 36% of the original sample. The survey was conducted from July 2000 to February 2001.\textsuperscript{134} The mean age of participants was 73.4 (SD 6.4). Mobility dependency was defined as either needing help in doing or being unable to do any of the three ADL items: walk 400 yards; climb up or down stairs; and get on a bus. Catastrophic decline in mobility was defined as change from independence in all three activities at baseline to needing help or being unable to do at least one of the activities at follow-up. Associations with chronic health conditions and socio-demographic factors were examined individually. After exclusions, 427 individuals who reported intact mobility at baseline remained in the analysis. The annual incidence rates of catastrophic decline in mobility were calculated. The odds ratios (ORs) for catastrophic decline were adjusted for socio-demographic factors and health conditions.\textsuperscript{133}

Ayis \textit{et al} reported similar annual rates of catastrophic decline for men and women (4.8%, CI 2.7-8.3 and 4.6%, CI 2.4-8.6 respectively).\textsuperscript{133} Statistically significant associations were found between catastrophic decline and age > 70 years (OR 3.7, CI 1.1-11.8), hearing problems (OR 2.8, CI 1.1-7.3) and health deterioration (OR 4.3, CI 1.2-14.7) after multivariable adjustment.\textsuperscript{133}
The Alameda County Study compared the independent impacts of two levels of self-reported hearing impairment on subsequent disability, physical functioning, and social functioning. outcomes were measured in 1995 and included physical disability outcomes using questions concerning physical performance, mobility, and lack of participation in activities. Physical performance disability was defined as having a lot of difficulty or needing help with one of the following items; pulling or pushing large objects; writing; handling small objects; standing up from a chair; getting up from stooping or kneeling; reaching or extending arms above the shoulder; lifting or carrying weights over 10 pounds; stooping, crouching or kneeling. The category a lot of difficulty was used for the physical performance items as many functional middle-aged adults reported a little or some difficulty with one or more of these items. Mobility disability was defined as any difficulty walking one-quarter of a mile without help or walking up ten steps without resting. Never participating in activities was defined as never going out to entertainment, sports events, community, or volunteer activities. All 1995 outcomes were adjusted for baseline 1994 values.

The Alameda County study found no significant association between self-reported hearing impairment and mobility in persons with hearing impairment (Mild HI OR 1.21, CI 0.88-1.66 and ≥ moderate HI OR 1.07, CI 0.72-1.58). There was no significant association between self-reported hearing impairment and never participating in activities. There was no significant association between mild hearing impairment and physical performance (OR 1.12, CI 0.8-1.54). There was a significant association between ≥ moderate hearing impairment and physical performance (OR, 1.69, CI 1.15-2.48).

The second supplement on ageing (SDOA-II) reported that older people with self-reported hearing loss reported greater difficulties in various mobility associated activities and social
Persons with hearing loss were significantly more likely to report difficulty in walking (OR 1.5, CI 1.3-1.7), inability to walk 10 steps or a quarter mile (OR 1.4, CI 1.2-1.6 and OR, 1.5, CI 1.3-1.7 respectively), getting outside (OR 1.3, CI 1.1-1.5), buying groceries (OR 1.4, CI 1.2-1.6), difficulty in getting into and out of a bed or chair (OR 1.5 CI 1.3-1.8) and visiting relatives (OR 1.1, CI 1.0-1.3) when compared to persons without HI. There were no statistically significant increased odds of difficulties visiting friends, attending church, going to the movies, eating out or getting exercise. Self-reported hearing loss was associated with an increased risk of falling in the previous 12 months, but not with injury from a fall or hip fracture, when compared to persons without HI (OR 1.7, CI 1.5-1.9; OR 0.9, CI reported not significant; and OR 1.2, CI 0.9-1.5 respectively).

The Finnish Twin Study on Aging (FITSA), reported significant associations between severity of hearing loss and the incidence rate ratio of falls in women aged 63-76 years. The nationwide Finnish Twin Cohort comprises all same-sex twins born in Finland before 1958 with both co-twins alive in 1975. The FITSA participants were drawn from this cohort. Invitation to the hearing study was sent to 414 female twin pairs aged 63-76 years drawn on the basis of age and zygosity. The final FITSA sample consisted of 103 monozygotic (MZ) and 114 dizygotic (DZ) twin pairs. After refusals and exclusions 417 participants were included in the analysis. Audiometric measurements were performed by an audiology assistant in a sound-isolated booth using a clinical audiometer. Air conduction pure-tone hearing thresholds were measured at the frequencies of 0.125, 0.25, 0.5, 1, 2, 4, and 8 kHz for each ear separately. Better ear hearing threshold level (BEHL) was defined as a mean of the pure-tone air conduction thresholds at 0.5, 1, 2 and 4 kHz. At least mild hearing loss was defined as BEHL 0.5-4 kHz ≥ 21 dB.
Clinical examination by a physician and clinical tests on functional capacity and balance were performed. Postural balance was indicated as a centre of pressure (COP) movement in semi-tandem stance. Postural sway was measured and postural stability was recorded for 20 seconds by physiotherapists. A larger postural balance battery including measurements in side-by-side stance with eyes open and closed and tandem stance with eyes open was also performed. After the completion of the hearing and balance assessments, information on falls was gathered for 12 months by the participants marking daily on a calendar whether they fell or not. During the fall follow-up, three persons died and 12 persons did not return all of their calendar pages. Their data were included up to the month their participation ceased. An adjusted Wald test was used to compare whether centre of pressure movements and proportion of fallers differed between the hearing acuity quartiles. Incidence rate ratios (IRRs) for falls were computed from a negative binomial regression model.

The mean hearing acuity (better ear hearing threshold level at 0.5-4 kHz) for the population was 21 dB (standard deviation (SD) 12). There were statistically significant increases in COP movements in semi tandem stance associated with increasing HI. The means of the COP velocity moment from the best to the poorest hearing quartiles increased significantly and linearly from 40.7 mm²/s (SD 24.4) to 52.8 mm²/s (SD 32.0) (p<0.003).

After one year from baseline, 199 participants had reported 437 falls. Age-adjusted incidence rate ratios (IRRs) for falls using the best hearing quartile as a reference, increased with increasing HI, becoming statistically significant for persons with ≥ third quartile hearing impairment (IRR 1.2, CI 0.4-3.8 second quartile; IRR 4.1, CI 1.1-15.6 third quartile; IRR 3.4, CI 1.0-11.4 fourth quartile) after age adjustment. Adjustment for COP velocity moment led to...
the associations becoming non-significant. Twin analyses suggested the association between HI and postural balance was not explained by genetic factors.135

The FITSA also examined whether hearing acuity correlated with walking ability and whether impaired hearing at baseline predicted self-reported walking difficulties after 3 years.137 Maximal walking speed was measured over 10 m (m/s). Walking endurance was defined as the distance covered in 6 minutes. Difficulty in walking 2 km was assessed by self-report. At baseline, women with HI (n=179) had slower maximal walking speed (1.7 +/- 0.3 m/s vs. 1.8 +/- 0.3 m/s, p = 0.007), lower walking endurance (520 +/- 75 m vs. 536 +/- 75 m, p = 0.08), and more self-reported major difficulties in walking 2 km (12.8% vs. 5.5%, p = 0.02) when compared to those without HI. During follow-up, major walking difficulties developed for 33 participants. Women with hearing impairment at baseline had twice the age-adjusted risk for new walking difficulties when compared to those with normal hearing (OR 2.04, CI 0.96-4.33).137

A prospective study examined the prevalence and the association of HI with rehabilitation efficacy in 896 patients following hip fracture.138 Hearing impairment was defined as mean decibel level equal to or higher than 60dB in the better of the two ears. Hearing impairment was found in 231 (28.5%) of patients admitted for rehabilitation. In univariate analysis, the absolute efficacy of rehabilitation was significantly lower in patients in patients with HI compared to those without HI (p = 0.002). However, in multivariate analysis the association with HI became nonsignificant.138
Auditory Impairment and Depression

The Alameda County Study found significant associations between self-reported moderate or more HI and higher odds of depression (OR 2.05, CI 1.37-3.06).126

A community survey, carried out in Northern Italy by the Geriatric Research Group, Brescia, examined the associations between quality of life measures and sensory impairment in aged individuals living at home.139 A total of 1191 non-institutionalized persons age 70-75 years were given a comprehensive QOL questionnaire, free-field voice testing, and Snellen eye chart. The study reported that auditory impairment was significantly and independently associated with increased risk for depression (OR 1.8, CI 1.1-2.7).139

The Research Team for the Care of the Elderly, at the Welsh National School of Medicine reported results from a random sample (40%) of all patients aged ≥ 70 years in a large urban general practice in a medium sized town in South Wales.140 The study used trained fieldworkers to interview 657 (response rate 96%) in their own homes using a standardised interview schedule. Information was sought on hearing difficulty and mental state using standardised measures of anxiety, depression, and memory loss. Of the 657 subjects interviewed, 33% reported having some difficulty hearing normal conversations and 6% reported much difficulty. In this cohort, hearing difficulty was significantly associated with both depression and anxiety. These associations became non-significant after adjustment was made for physical disability.140

The Longitudinal Aging Study Amsterdam (LASA) is a longitudinal multidisciplinary study examining predictors and consequences of changes in autonomy and well-being in the ageing population.141 Of 3,805 participants approached, 3,107 (81.7%) took part in LASA at
baseline, including 1,506 men and 1,601 women. The age range at baseline was 55 to 85 years. Data were gathered by structured interview in the homes of participants by trained interviewers. Hearing status was based on self-report. The questions used for the determination of hearing impairment were 1. Can you follow a conversation with one person, with or without a hearing aid? 2. Can you follow a conversation with four people, with or without a hearing aid? 3. Can you use a normal telephone? Answers were given on a 4-point scale: 1 = without difficulty; 2 = with some difficulty; 3 = with much difficulty; 4 = no I cannot. Scores on the questions were summed. A summed score of 5 or more was defined as hearing impairment. The presence of depressive symptoms was measured by using the Dutch version of the Centre for Epidemiologic Studies Depression Scale (CES-D). Items were rated on a 4-point scale ranging from almost never to almost always, concerning the time in the past week. Multiple linear regression analyses were conducted to examine the strength of the associations between hearing impairment, the different types of chronic diseases, and the psychosocial health status.141

The overall prevalence of self-reported hearing impairment 12.2% (13.8% in men and 10.7 in women).141 After multivariable adjustment, hearing impaired elderly reported significantly more depressive symptoms, lower self-efficacy and mastery, more feelings of loneliness and a smaller social network when compared to persons with normal hearing.141

The Study on Hearing (NL-SH) conducted in The Netherlands, is an ongoing prospective cross-sectional cohort study examining the relationship between hearing impairment and several domains in life.142 The study is conducted over the Internet. The cohort for the reported study consisted of 1511 participants. Participants were invited to participate through advertisements and flyers distributed at audiological centres and hearing aid dispensers. The
study examined the association between hearing status and psychosocial health in adults aged between 18 and 70 yr. Hearing status was determined using a speech-in-noise screening test over the Internet (the National Hearing test). The test uses digit triplets presented against a background of masking noise, according to an adaptive procedure. Twenty-three triplets are presented. The speech reception threshold corresponds to 50% intelligibility calculated by the average signal to noise ratio (SNR) of the last 20 presentations. Self-reported psychosocial health was determined by online questionnaire. Baseline data of were analysed using regression models.142

After multivariable adjustment for all confounders, significant associations between hearing status and distress (b = 0.02, t = 2.16, p = 0.031) and somatization (b = 0.02, t = 3.96, p = 0.001) were identified.142 The odds for developing moderate or severe depression increased by 5% for every dB SNR reduction in hearing (OR 1.05, CI 1.00-1.09). The odds for developing severe or very severe loneliness significantly increased by 7% for every dB SNR reduction in hearing (OR 1.07, CI 1.02-1.12). The risk for depression was highest in persons with poorest hearing (OR 1.05, CI 1.00-1.09). The association between hearing status and depression was age dependent. When stratified by age, the association of poor hearing with depression was significant only for the 40-49 year old age group after multivariable adjustment (OR 1.18, CI 1.08-1.28).142

The Nord-Trøndelag Health Study (HUNT) is a population based study in which all adults in 24 municipalities of Nord-Trøndelag County, Norway, were invited to take part in a health screening survey during the period August 1995 to June 1997.143 The population of 17 of these 24 municipalities were invited to the hearing loss study. Participants were aged 20 to 101 years (mean, 50.2; SD, 17.0) at baseline. The participation rate was 68.7%. Valid
Audiometry and questionnaire data were available for 50,398 participants. Participation rate was less than 50% for subjects <30 years old. The participation rate increased with age to approximately 60 years. The participation rate ranged from 75% to 87% for people 50 to 80 years old.\(^{143}\)

Audiometric testing was performed in semi-portable, dismountable sound attenuation booths for the standard frequencies 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz.\(^{143}\) Three hearing scores were computed: a) low-frequency hearing level (0.25-kHz and 0.5-kHz thresholds, averaged over frequencies and both ears), b) middle-frequency hearing level (1 kHz and 2 kHz), and c) high-frequency hearing level (3 kHz, 4 kHz, 6 kHz, and 8 kHz). Participants completed a one-page questionnaire which included ten items from the 25-item Hopkins Symptom Checklist (HSCL -25),\(^{144,145}\) four examining symptoms of anxiety, and six examining symptoms of depression. Separate scores for anxiety and depression and a global score were determined by summing the values (1-4) from each item.\(^{143}\)

Regression analyses were performed separately for men and women in the age groups 20 to 44 years, 45 to 64 years, and older than 64 years. Multiple regression analyses were performed using occupational noise, educational level, marital status, and subjectively assessed health as covariates. Low, middle, and high-frequency hearing losses were entered as (continuous) independent variables. The analyses were run consecutively with anxiety, depression, self-esteem, and subjective well-being as dependent variables.\(^{143}\)

Low-frequency hearing coefficients were significantly associated with all ten items from the 25-item Hopkins Symptom (P = < 0.05) except for depression and self-esteem among the oldest men and women, and subjective well-being among young and middle aged women.\(^{143}\)
High-frequency hearing was significantly associated with low self-esteem among young and middle-aged women.\textsuperscript{143} Depressive symptoms and low self-esteem in young and middle-aged men were significantly increased among subjects with a 50-dB low-frequency hearing reduction. The effects of low-frequency hearing loss decreased significantly with age ($t \geq 2.78; p \leq .005$). Middle and high-frequency hearing level did not affect mental health significantly above what could be explained by low-frequency hearing level.\textsuperscript{143}

To assess for confounding, the covariates were entered stepwise into multiple regression analyses together with hearing loss.\textsuperscript{143} Noise and social background did not affect the results. Self-reported health decreased the association between hearing loss and the dependent variables anxiety, depression, self-esteem, and subjective well-being. After controlling for measured hearing loss, self-reported hearing loss was more significantly associated with self-reported mental health compared to measured hearing loss. This effect increased with age.\textsuperscript{143}

The Veneto Study reported an increased risk of depression in persons with self-reported hearing impairment in the home, social environment and in both environments (OR 1.84, CI 1.2-2.9; OR 2.05, CI 1.4-3.0; OR 2.29, CI 1.5-3.4 respectively).\textsuperscript{117} The second supplement on ageing (SDOA-II) reported no significant association between depression and self-reported hearing loss (OR 1.2, CI 0.9-1.5).\textsuperscript{131}

Hearing impairment was reported associated with the wish to die in an Australian epidemiological survey of people aged $\geq 70$ years.\textsuperscript{146} The sample was selected from the electoral rolls for the adjacent cities of Canberra and Queanbeyan. At least some interview data were obtained from 945 community residents and 100 nursing-home or hostel residents,
representing a response rate of 69% for the community residents and 70% for the nursing home and hostel residents. Wish to die was assessed by one question: 'In the last two weeks, have you felt as if you wanted to die?' If the subject answers 'yes' or 'depends', they are asked: 'Have you had such thoughts repeatedly?' Those who had repeated thoughts of wanting to die were defined as the case group and all other subjects (including those with a transient wish to die) as the control group. Data on this question were available from 923 subjects, 868 living in the community and 55 in residential care.146

The association between hearing loss and the wish to die was found to be independent of depression using multiple logistic regression with HI entered simultaneously as a predictor together with the count of depressive symptoms (OR 5.6, CI 2.3-13.9).146
Auditory Impairment and Age Related Macular Degeneration

The Beaver Dam Eye Study examined the association between hearing loss and the presence of age related macular degeneration (ARMD). Overall, the prevalence of ARMD was 25.4% and of hearing loss was 45.0% in this population. Both conditions were present in 15.1%. There was no statistically significant association between early ARMD lesions and hearing loss > 25dB. After multivariable adjustment, there was a statistically significant risk of hearing loss >25dB in persons with late ARMD (OR 3.17, CI 1.35-7.45).

The BMES also reported an association between hearing loss and age related macular degeneration. In this study population there was a significant association between any ARMD and the risk of hearing loss > 25 dB (OR 1.5, CI 1.1-2.0) after multivariable adjustment compared to persons without ARMD. This association was stronger in persons younger than 70 years (OR 2.0, CI 1.0-4.1).

Complement factor H Y402H is associated with increased risk of age related macular degeneration. This polymorphism has also been found associated with hearing loss in a Japanese population. Nishio et al conducted a case-control study of 72 persons with sudden sensorineural hearing loss (SSNHL) and compared them with 2161 control subjects selected randomly from the comprehensive Longitudinal Study of Aging (NILS-LSA). Participants in the NILS-LSA were selected randomly from resident registrations. The study region is located within 30 km of Nagoya University Hospital. Overall, 2161 participants aged 40-79 years who completed the first-wave examination of NILS-LSA between November 1997 and April 2000 and underwent CFH genotype analysis, were randomly selected as controls. The odds ratio (OR) for SSNHL risk was determined using the additive-genetic model of CFH Y402H polymorphism.
In this case control study, the OR for SSNHL in Japanese persons aged 40-79 years risk was OR 1.788, CI 1.008-3.172) with no adjustments and OR 1.820, CI 1.025-3.232) after adjusting for age and sex. SSNHL was also found significantly associated with diabetes but not hypertension or dyslipidaemia. After stratification of the cohort into diabetics and nondiabetics, the OR for SSNHL risk was significant in persons with diabetes but not in persons without diabetes (OR 6.326, CI 1.885-21.22 vs.. OR 1.214, CI 0.581-2.538).
The Associations Between Auditory Impairment, Noise Exposure and Mortality
Auditory Impairment and Mortality

A community survey, carried out in Northern Italy by the Geriatric Research Group, Brescia, examined the associations between sensory impairment in aged individuals living at home and mortality. The cohort was an urban population of 1,140 non-institutionalized elderly subjects, aged 70-75 years. Baseline information was collected in 1986 through a door-to-door interview with a standardized questionnaire. Sensory assessment was performed using bedside tasks: the whispered voice test for hearing and the Snellen chart for vision. The overall mortality rate at 6 years was 25.5%, with a significant sex difference (males = 37.5%; females = 19.8%). There was a significant interaction between sex and sensory impairment. Bivariate logistic regression showed that hearing deficit was associated with a significant increase in mortality risk in men but not women (OR 1.97, CI 1.02-3.77 vs. OR 0.77, CI 0.36-1.62). This increase remained significant after controlling for demographic variables and physical health status. Multivariate logistic regression showed that the effect of hearing deficit on mortality became nonsignificant after controlling for psychosocial parameters (mood and social relationships level).

Barnett et al used US NHIS data from 1990 and 1991 linked with National Death Index data for 1990-1995 to examine the association between age of onset of self-reported deafness and mortality. Deafness was considered present if the participant indicated on the self-rated scale (SRS) that they had at least "a lot of trouble hearing" in both ears or at least "a little trouble hearing" in their better ear and indicated on the Gallaudet Hearing Scale (GHS) that they could not hear or understand any speech. The control group comprised the non-deaf adults with hearing problems in the 1990 and 1991 NHIS samples and a 20% random sample of adult respondents without hearing problems. Non-deaf adults with hearing problems were
defined as those for whom the answer was yes to the question "Do you have a problem hearing?" but did not meet the definition of deafness.\textsuperscript{152}

The NHIS data demonstrated that the relative frequencies of the age at onset of hearing loss for 2449 deaf adults responding in 1990 and 1991, showed two peaks: one before age 3 and a second after age 60.\textsuperscript{152} The mortality rate was higher for adults with postlingual onset deafness, regardless of age group, compared to the control group after adjustment for socioeconomic status. (Prelingual OR 0.97, CI 0.58-1.64; Postlingual 19-64 years old OR 1.32, CI 1.05-1.49; Postlingual >65 years old OR 1.15, CI 1.03-1.27). After adjusting for health status, there was no significant relationship between deafness and mortality.\textsuperscript{152}

Lam et al used the US NHIS data to examine the association between reported hearing impairment and risk of mortality.\textsuperscript{153} Mortality linkage with the National Death Index of participants from 1986 to 1994 was performed through 1997. Mortality linkage identified 8949 deaths with an average follow-up of 7.0 years. Hazzard ratios were estimated for the entire cohort using both self- and proxy-reported interview results. After multivariable adjustment, African American men, but not women, nor white or other-race participants with proxy and or self-reported hearing impairment had significantly increased risk of mortality (Self- and Proxy-Reported HR 1.31, CI 1.00-1.73; Self-reported HR 1.40, CI 1.00-1.95).\textsuperscript{153}

Feeney et al used data from the longitudinal Statistics Canada National Population Health Survey (NPHS) for 1994/95 through 2006/07 to examine the associations between hearing impairment and mortality.\textsuperscript{154} The NPHS is a closed cohort survey of household residents in the 10 Canadian provinces, excluding persons living on Indian Reserves and Crown Lands, residents of health institutions, Canadian Forces bases, and some remote areas in Ontario and
Quebec. Using a stratified, multistage sampling procedure, 17,276 household members were randomly selected to be interviewed every two years regarding health status, health service utilisation, and sociodemographic data. Deaths up to December 31, 2005, were confirmed against the Canadian Vital Statistics Database. Disability in hearing was assessed by the self-reported level of disability in the HIU3 questionnaire. The Health Utilities Index Mark 3 (HUI3), includes eight attributes, vision, hearing, speech, ambulation, dexterity, cognition, emotion, and pain and discomfort, with five or six levels per attribute that vary from no to severe disability.

The levels for hearing are as follows:154

1. Able to hear what is said in a group conversation with at least three other people, without a hearing aid.
2. Able to hear what is said in a conversation with one other person in a quiet room without a hearing aid but requires a hearing aid to hear what is said in a group conversation with at least three other people.
3. Able to hear what is said in a conversation with one other person in a quiet room with a hearing aid and able to hear what is said in a group conversation with at least three other people, with a hearing aid.
4. Able to hear what is said in a conversation with one other person in a quiet room, without a hearing aid but unable to hear what is said in a group conversation with at least three other people even with a hearing aid.
5. Able to hear what is said in a conversation with one other person in a quiet room with a hearing aid but unable to hear what is said in a group conversation with at least three other people even with a hearing aid.
6. Unable to hear at all.
This study used HUI3 responses to estimate the association between self-reported hearing disability and 12 year mortality. Cox proportional hazards regression models were performed controlling for standard determinants of health and risk factors for two cohorts: those 18 years of age or older at baseline and those 60 years of age or older at baseline.

The study reported that among other HUI3 attributes, hearing impairment was significantly associated with increased mortality risk. This risk increased substantially and significantly with increasing level of hearing disability in a stepwise manner from level 1 (no disability) to level 6 (severe disability). The single-attribute utility score for hearing for the cohort as a whole was HR 0.18, CI 0.06-0.57 and for the cohort aged ≥60 was HR 0.14, CI 0.04-0.48.

A separate Canadian study, the Canadian Study of Health and Aging (CSHA) is a multicentre epidemiological study of dementia and other health problems in older Canadians. The study surveyed 10,263 randomly selected people aged 65 and older across Canada (excluding the Northwest and Yukon territories) in 1991. Deaths in the subsequent 5 years were determined from death certificates and interviews with the caregivers. Data from the CSHA found no associations between hearing impairment and mortality after multivariable adjustment.

The BMES reported no statistically significant association between hearing impairment and 10-year all-cause mortality after multivariable adjustment (HR 1.24, CI 0.99-1.54).
**Noise Exposure and Mortality**

Occupational exposure to noise may be associated with increased risk of CVD and death from myocardial infarction.\textsuperscript{158,159} Davies et al identified a cohort of 27,464 blue-collar workers from 14 lumber mills in British Columbia who worked at least one year between 1950 and 1995 and who were followed up over the same period.\textsuperscript{158} Cumulative noise exposure was quantitatively assessed. Vital status was ascertained from the Canadian Mortality Database. Standardised mortality ratios were estimated based on the general British Columbia population for the years 1950 to 1995. All person-years-at-risk calculations were begun one year after first employment. Ninety-five percent confidence intervals for the Standardised Mortality Rate (SMR) were estimated assuming the observed effect followed a Poisson distribution. Relative risks were estimated using an internal low-exposure group as controls. Subgroup analysis compared persons in the cohort employed before and after widespread use of hearing protection.\textsuperscript{158}

The mean age at entry into the cohort was 30 years, and mean follow-up period 24 years. During the follow-up period, 2510 circulatory disease deaths occurred. The association between noise exposure with acute myocardial infarction (AMI) mortality was not significant for the cohort as a whole (SMR 1.0, CI 0.97-1.1).\textsuperscript{158} There was a significant association found for persons who worked during the period before hearing protection became widely used (SMR 1.1, CI 1.0-1.2). There was also a statistically significant association between duration of exposure and cardiovascular mortality. The risk of fatal AMI increased significantly with increasing number of years of occupational noise exposure (85 dB(A) $p_{\text{trend}} = 0.003$; 90 dB(A) $p_{\text{trend}} = 0.004$; 95 dB(A) $p_{\text{trend}} = 0.001$). Persons working for $> 19$ years at noise levels $\geq 85$ dB had the highest statistically significant risk of mortality (85dB(A) SMR 4.0, CI 1.8-9.3; 90 dB(A) SMR 2.0, CI 1.0-3.7; 95dB(A) SMR 2.7, CI 1.4-4.9).\textsuperscript{158}
The BMES reported a statistically significant association between work related noise exposure and cardiovascular disease and mortality. There was no association between hearing impairment and mortality after multivariable adjustment reported in this study. The BMES examined cross-sectional (prevalence) and longitudinal relationships (5-year incidence and 10-year mortality) between workplace noise exposure and cardiovascular diseases (CVD). History of cardiovascular disease, workplace noise exposure and hearing protection was determined by questionnaire. Cardiovascular disease deaths were confirmed using the Australian National Death Index. Analyses were stratified by those who reported using and not using hearing protection devices in the workplace. Multivariable logistic regression analysis was used to calculate adjusted ORs and 95% CIs.

Of 1070 participants reporting workplace noise exposure, 937 reported non-use of hearing protection devices. After multivariable adjustment, the risk of mortality in all participants with self-reported workplace noise exposure did not reach statistical significance (HR 1.32, CI 0.99-1.76). There was a significantly higher risk of CVD and angina, but not AMI, in persons who reported tolerable workplace noise exposure (HR 1.53, CI 1.13-2.09; HR 1.75, CI 1.2-2.48; and HR 1.25, 0.84-1.84 respectively).

There was a significant difference in CVD risk by duration of exposure. Persons with 1-5 years of workplace exposure did not have statistically significant higher risk of all CVD and angina where as those with > 5 years of exposure did (CVD OR 1.27, CI 0.82-1.96; angina OR 1.54, CI 0.96-2.49 vs.. CVD OR 1.66, CI 1.17-2.35; angina OR 1.83, CI 1.23-2.71 respectively). Conversely, in participants with 1-5 years of workplace noise exposure, the association with increased CVD mortality was significant, while in those with > 5 years of exposure, the CVD mortality risk did not reach significance (HR 1.60, CI 1.10-2.33 and HR
1.10, CI 0.78-1.56 respectively). There was no association between self-rated severity of exposure and cardiovascular mortality.\textsuperscript{159}

Exposure to a tolerable level of workplace noise compared to no exposure was associated with a higher likelihood of having CVD and angina (OR 1.59, CI 1.13-2.23 and OR 1.75, CI 1.20-2.56 respectively).\textsuperscript{159} When both the duration and level of noise exposure were examined together, those exposed to a tolerable level of noise for >5 years were more likely to have CVD and angina when compared to those never exposed to workplace noise (OR 1.75, CI 1.23-2.49 and OR 1.78, CI 1.19-2.66 respectively).\textsuperscript{159}

Workplace noise exposure was not associated with the prevalence of stroke (OR 0.87, CI 0.61-1.26) or hypertension (OR 1.15, CI 0.79-1.64).\textsuperscript{159} Exposure to severe workplace noise for less than 1 to 5 years versus no exposure was associated with incident stroke (OR 3.44, CI 1.11-10.63) but not stroke related mortality.\textsuperscript{159}
Summary

*The Prevalence of Auditory Impairment*

The reported prevalence of hearing impairment varied between 19%-83% depending on the age and geographic location of the cohort studied. Older cohorts had higher prevalence of hearing impairment.\textsuperscript{116,117,119,121} The prevalence of hearing impairment was significantly increased in males,\textsuperscript{116,119,121,122,124} in persons in manual occupations,\textsuperscript{116} and with work related noise exposure\textsuperscript{116,119,121,122,124} and increased with increasing age.\textsuperscript{116,119,121,122,124}

The correlation between self-reported hearing loss and measured hearing loss in inconsistent. The Veneto study reported the prevalence of measured hearing loss to be double that of self-reported hearing loss.\textsuperscript{117} Two studies that examined the link between self-reported hearing impairment and measured hearing impairment reported opposing findings. Davies *et al* using MRC data reported that persons with great difficulty hearing speech in noise had on average a 25 dBHL impairment in the better ear. In persons reporting moderate or worse bilateral difficulty in hearing in quiet had an average of 45 dBHL hearing impairment.\textsuperscript{116} Wilson *et al* found that the while the prevalence of self-reported hearing loss and measured hearing loss did not differ significantly, the false positive rate was 46% and false negative rate was 17% for self-reported hearing loss.\textsuperscript{119}
The Associations Between Auditory Impairment and Morbidity

Hearing impairment is reported to be significantly associated with numerous morbidities including increased difficulties in physical and functional activities, lower QOL, greater social impairment and poorer mental health.

The physical and functional difficulties reported to be significantly associated with hearing impairment in the studies reviewed include: poorer HRQOL;\textsuperscript{125,127-129} increased difficulties in ADL and IADL;\textsuperscript{126,127,130-132} lower SRH;\textsuperscript{125} increased risk of institutionalisation;\textsuperscript{160} increased risk of falls\textsuperscript{131,135} and fractures; poor mobility\textsuperscript{23,131,137} and a decline in mobility;\textsuperscript{133,137} poorer balance;\textsuperscript{135} worse cognitive impairment;\textsuperscript{125,161} and an increased risk of car accidents.\textsuperscript{162}

Psychosocial impairments reported significantly associated with hearing impairment included: getting outside;\textsuperscript{131} visiting relatives;\textsuperscript{131} loneliness;\textsuperscript{141,142} depression;\textsuperscript{117,126,139-143} anxiety;\textsuperscript{140,143} and the wish to die.\textsuperscript{146}

Hearing loss is associated with ARMD in both the BMES\textsuperscript{148} and the BDES,\textsuperscript{147} and with the CFH Y402H polymorphism in a Japanese population.\textsuperscript{149}
The Associations Between Auditory Impairment and Mortality

Hearing impairment is independently associated with many mortality risk markers including stroke, ischemic heart disease, diabetes and smoking. In addition, occupational noise exposure is reported to be associated with a significant increased risk of CVD and death due to AMI. Despite these associations, the link between hearing impairment and mortality is inconsistently reported, with most studies finding the association to become non-significant after multivariable adjustment.

An Italian study found significant associations between hearing impairment and increased mortality risk in men but not women. The association became nonsignificant after multivariable adjustment for psychosocial parameters. Using NHIS data, one American study found significant associations between self-reported deafness and mortality that became non-significant after multivariable adjustment while another found the association remained significant in African American men after multivariable adjustment, but not with any other cohort grouping. Two Canadian studies also reported opposing estimates of the association between hearing impairment and mortality risk with one finding significant associations and the other reporting no association after multivariable adjustment. The BMES reported no statistically significant association between hearing impairment and 10 year all-cause mortality after multivariable adjustment.

The associations between mortality risk markers, hearing impairment and mortality using structural equation modelling have not been examined. This may have lead to overcorrection of the associations between hearing impairment and mortality.
1.3 Olfactory Impairment
Prevalence
The prevalence of olfactory impairment in the EHLS cohort at the 5-year follow up period (1998-2000) has been reported. The age of participants at this time was 53-97 years. The study utilised the San Diego Odor Identification Test (SDOIT), an 8-item odour identification test that uses common, natural odours typically found in the home (e.g., coffee, chocolate). Test-retest reliability of this test was $r=0.86$ when tested with a mean delay of 5 days in a sample of 92 subjects. The test was administered to participants with their eyes closed with odorants wrapped in gauze and kept in opaque containers to minimize visual clues. An interstimulus interval of 45 seconds was used to minimize adaptation. Participants identified the odorants from a picture board with illustrations of the target items as well as distracters. Olfactory impairment was defined as scoring <6 of 8 odorants correctly. This cut point corresponded to approximately 2 SDs less than the mean score in a group of 75 healthy adults aged 20 to 40 years. Information about self-assessed olfactory loss was obtained by a questionnaire administered as an interview. Self-reported smell impairment was determined by the question, “Do you have a normal sense of smell (compared to other people)?” The olfaction questions were asked before the administration of the SDOIT.

In the EHLS at five years follow up, the mean (SD) prevalence was 24.5% (1.7%). The prevalence increased with age (62.5% (CI 57.4%-67.7%) of 80-to 97-year-olds had olfactory impairment) and was more prevalent among men (adjusted prevalence ratio 1.92, CI 1.65-2.19). Despite the high prevalence, the sensitivity of self-report was low and became less accurate with age. The overall sensitivity of self-report was 20%, and the specificity was 94%. In the oldest group, aged 80 to 97 years, the sensitivity of self-report was 12% for women and 18% for men. After multivariable adjustment, age, sex, current smoking, nasal congestion or upper respiratory tract infection, stroke, and epilepsy were associated with
statistically significant increased odds of olfactory impairment. Olfactory impairment did not
differ for former smokers compared with those who had never smoked cigarettes.\textsuperscript{168}

The Skövde population-based study examined Rhinological disorders in the general
population in Sweden.\textsuperscript{170} In this study, a random sample of 1900 individuals aged 20 years or
older, drawn from the municipal roster in December 2000, was stratified by gender and seven
age groups: 20 to 29, 30 to 39, 40 to 49, 50 to 59, 60 to 60, 70 to 79, and 80 or more years of
age. Of 1900 randomly selected individuals, 1387 (73\%) participated in the clinical
investigation. The study was conducted between January and June 2001 at the University of
Gothenburg (Gothenburg, Sweden). Medical history was obtained by structured interview.
Olfactory function was assessed with the Scandinavian Odor Identification Test (SOIT). The
SOIT consists of 16 odours; pine needle, peppermint, juniper, violet, anise, clove, vanilla,
bitter almond, orange, cinnamon, lemon, lilac, vinegar, tar, ammonia, apple). There was four
response provided alternatives for each odour. The cut-off scores out of 16 for the level of
olfactory ability were defined as 10 to 12 for hyposmia and 9 or less for anosmia. Multiple
logistic regression was used to determine meaningful interactions between significant (p \leq
0.05) explanatory variables. Odds ratios including 95\% CIs were estimated for the
dichotomous explanatory variables.\textsuperscript{170}

The overall prevalence of olfactory dysfunction in the Skövde study was 19.1\% (CI 17.1\%-21.3\%), separated into hyposmia 13.3\% (CI 11.6\%-15.2\%) and anosmia 5.8\% (CI 4.7\%-7.1\%).\textsuperscript{170} Two-way ANOVA found that women performed better than men on the SOIT (P <
0.01) and that performance declined with age (P < 0.001).\textsuperscript{170}
The OR for olfactory dysfunction (hyposmia and anosmia) in men when compared to women was 1.7 (CI 1.3-2.3 OR) and in individuals with nasal polyps the OR was 2.1 (CI 1.0-4.3). There was no statistically significant association between olfactory dysfunction and diabetes mellitus, current smoking, or the number of pack-years smoked (including both current and previous smokers). In an additional analysis, current heavy smokers (≥ 20 pack-years) were compared with those who never had smoked, and after gender and age adjustment, no statistical difference in performance on the SOIT was observed.

The prevalence of anosmia (SOIT score ≤ 9) was found to be related to age, and the risk increased with the presence of nasal polyps (OR 3.8, CI 1.6-8.8) and diabetes mellitus (OR 2.6, CI 1.3-5.5), but there was no statistically significant relation to either gender or smoking. The sensitivity of self-reported olfactory dysfunction was 43.9% with a specificity of 85.4%.

Bhattacharyya et al reported the estimated prevalence of olfactory disturbance in the United States by performing a cross-sectional analysis of the National Health Examination and Nutrition Survey (NHANES). The NHANES is a nationwide survey administered by the National Centre for Health Statistics (NCHS). The data were collected during 2011 and 2012 and included all persons aged ≥40 years who completed the survey. The presence of olfactory disturbance was determined by self-report. Statistical analysis of the survey variables was used to estimate the national prevalence of olfactory disturbance. In this study, the prevalence of self-reported olfactory disturbance in persons aged ≥40 years during the 12 months prior data collection was reported to be 10.6%. The prevalence of self-reported olfactory disturbance increased with age (OR 1.147, CI 1.003 – 1.312 for each
decade increment in age). There was no statistically significant difference between the sexes (p = 0.146).171

A cross-sectional study of patients of the Otorhinolaryngology outpatient clinic of the Department of Otorhinolaryngology of the University Of Dresden Medical School reported the prevalence of olfactory dysfunction.173 One thousand two hundred and forty patients, with a mean patient age of 41.7 ± 0.5 years (range, 5-86 y) and almost equal sex distribution (52% men vs. 48% women), were included in the study. The included participants were exclusively outpatients with relatively mild and transitory conditions. Patients who required hospitalisation, had oncological otorhinolaryngology follow-up, complained of a Rhinological problem or chronic sinonasal problems were excluded. The 1240 selected otorhinolaryngological patients were representative of the German population regarding age and sex according to the data published by the German Federal Statistical Office. All participants completed a questionnaire concerning sociological and demographic data, smoking habits, general diseases, medications, ratings of olfactory function, and ratings of consequences on life quality in cases of smell loss. Self-rated olfactory function was defined as either “absent,” “attenuated,” “normal,” or “above average,” corresponding to scores of 0, 1, 2, or 3, respectively. After olfactory testing, all participants underwent a detailed, extensive nasal endoscopy.173

Patients with pathological findings on endoscopy were excluded.173 Olfactory function was assessed by means of the “Sniffin’ Sticks” test battery (Burghart, Wedel, Germany).174 Sixteen common odours were used, and participants selected the odour by a multiple-choice task with four descriptors per odour. Normative data for normosmia, hyposmia, and anosmia based on multicentric investigations in more than 1000 subjects174 were used to grade the
level of hyposmia. A score <8 was considered functionally anosmic, 8 to 12 hyposmic, and >12 normosmic. These participants were more likely to be hyposmic and more likely to rate reduced olfactory function than participants without nasal polyposis. Participants with nasal polyps were excluded from further analyses of the effect of general diseases on olfactory function.

The prevalence of undiagnosed and asymptomatic nasal polyps was 4.7%. These participants were more likely to be hyposmic and more likely to rate reduced olfactory function than participants without nasal polyposis. Participants with nasal polyps were excluded from further analyses of the effect of general diseases on olfactory function.

The prevalence of any olfactory loss was 21% in this population. The prevalence of functional anosmia was 4.7%. No significant sex-related difference in the rate of functional anosmia was detected. The prevalence of hyposmia was 16%. Hyposmia was more prevalent in men than women after adjustment for age. The prevalence of olfactory loss increased with age. There was no association between smoking and olfactory loss. After age adjustment, there was no association between olfactory loss and the number of drugs taken or the number of comorbid conditions.

Self-report was an inaccurate proxy for the prevalence of olfactory loss. While participants with measured olfactory loss were correctly able to identify olfactory deficit with statistical significance, (r55 = 0.34, P = 0.01 for anosmic and r189 = 0.18, P = 0.02 for hyposmic participants) the participants with normal olfaction were not accurate with statistical significance (r935 = 0.03, P = 0.3).
The Associations Between Olfactory Impairment and Morbidity
**Olfactory Impairment, Self-rated health status, measures of Function and health related quality of life**

Participants in a cross-sectional study of the prevalence of OI in an outpatient otorhinolaryngology clinic in Dresden Germany were asked about the impact on life quality attributable to self-reported sudden olfactory loss. The impact on life quality due to sudden olfactory loss was rated by participants as either none, slight, strong, or very strong, corresponding to scores of 0, 1, 2, or 3, respectively.

This study found no significant correlation between self-reported olfactory loss and measured olfactory loss in persons with normosmia. The association between measured OI and poorer QOL was not statistically significant. Participants who reported a higher loss of quality of life due to olfactory dysfunction were less likely to have an olfactory impairment. The impact on life quality due to self-reported olfactory loss was highest among normosmic participants and gradually decreased with hyposmia and anosmia. Participants with measured olfactory loss were less likely than normosmic participants to report that olfactory loss impacted their quality of life.

A cross sectional study of 127 non-institutionalised Korean elderly persons (85 women and 42 men) aged 65-89 years (mean ± SD: 73.8 ± 5.1 years) residing in Daejeon city of South Korea, estimated the association between measured olfactory dysfunction and quality of life. All participants were interviewed with regard to the presence of major olfactory problems. Olfactory sensitivity was assessed using the T&T olfactometer (Daiichi Yakuhin Sangyo Co., Tokyo, Japan) consisting of 5 test odorants: α-phenylethyl alcohol (odour A), methyl-cyclopentenolone (odour B), isovaleric acid (odour C), γ-undecalactone (odour D), and skatole (odour E). Each odorant was diluted in an 8 log step concentration series ranging
from $10^{-2}$ to $10^5$. Odorants were presented in ascending concentrations. Each odour was presented at eight concentrations. Following each odour concentration, subjects were asked whether they could detect an odorant (detection threshold) or identify it (recognition threshold). When the subject failed to detect or to recognize the odour at its highest level of concentration, an additional point was added to the detection or recognition threshold of that odour. Thresholds of detection and recognition were averaged across all odorants to estimate a general detection and recognition threshold, respectively. Based on the subject’s average recognition thresholds, olfactory function was classified as normal ($\leq 1.0$), slight impairment (1.1-2.5), moderate impairment (2.6-4.0), severe impairment (4.1-5.5), and functional anosmia ($\geq 5.6$).175

A questionnaire was administered to record demographics, and self-rated health and olfactory sensitivity in everyday life.175 Self-rated health and olfactory sensitivity were assessed using a five-point Likert scale (1: very unhealthy/very insensitive to 5: very healthy/very sensitive). Quality of life was examined by the Korean version176 of the Geriatric Quality of Life (GQoL) which includes 25 questions on physical and mental health, degree of independence, and social relationships. Subjects answered each question using four-point Likert scales: 1 = unsatisfied, 2 = moderate, 3 = satisfied, and 4 = very satisfied. The mean score was used as a measure of QOL.175

Associations between QOL and olfactory impairment were examined using t tests and analyses of variance (general linear model).175 Duncan’s multiple range test was performed to separate the means. Pearson and Spearman coefficients were used for correlation analyses between the degree of olfactory impairment and QOL. To control causal effects between the above variables, partial correlation analyses controlling the potential variables were
performed and stepwise linear regression models were used to explore the variables influencing QOL. The level of significance was set at $p < 0.05$.\textsuperscript{175}

The prevalence of olfactory impairment in this elderly population was 80.3% ranging from slightly impaired to functionally anosmic.\textsuperscript{175} Despite this very high prevalence, only 10.2% of the entire cohort self-reported olfactory loss. There were no sex-related differences in olfactory sensitivity. Higher olfactory detection and recognition thresholds were associated with higher age and lower education level. Lower SRH was associated with higher recognition, but not detection threshold. Subject groups with severely impaired olfaction and with functional anosmia rated their QOL significantly lower than the other groups ($F(4, 122) = 3.35, p = 0.01$). After partial correlation analyses controlling for depression and cognitive performance, no significant association between olfactory detection and recognition thresholds and QOL was found. Linear regression modelling confirmed no significant association between QOL and olfactory function in this population.\textsuperscript{175}

To investigate the hypothesis that persons with parosmia suffer more in their daily life than those who experience only quantitative olfactory loss, Frasnelli \textit{et al} developed the Questionnaire of Olfactory Disorders (QOD).\textsuperscript{177} The QOD was designed to address olfactory dysfunction and its impact on daily life. The study comprised of 205 patients (84 males and 121 females) of an outpatient Smell and Taste Clinic with self-reported olfactory loss and age and sex matched 25 healthy controls. The QOD was validated by comparison to three other standardised psychometric and QOL tests, the Beck Depression Inventory (BDI),\textsuperscript{178} the Befindlichkeitsskala (Mood Inventory, MI)\textsuperscript{179} and the SF-36 Health Survey (SF-36).\textsuperscript{180} Using these measures, Frasnelli validated the QOD; reported the associations of self-reported and quantitative OI with SRH and QOL; reported the associations of self-reported parosmia with
self-reported and measured OI; reported the associations between parosmia and QOL and SRH in persons with self-reported OI both with and without objective OI.\textsuperscript{177}

The QOD consists of 52 statements divided into three domains: 39 negative statements (QOD-NS), five positive statements (QOD-PS) and eight socially desired statements (QOD-DS).\textsuperscript{177} Negative statements estimate the negative impact of olfactory impairment; positive statements estimate coping with olfactory impairment; socially desired statements represent a lie scale estimating whether answers are influenced by desire to give a correct answer. All tests were paper and pencil tests that participants completed alone.\textsuperscript{177}

This study utilised the Sniffin Sticks Threshold Discrimination Identification (TDI) score to objectively assess olfactory function.\textsuperscript{181} Olfactory function was scored based on the aggregate of the individual Sniffin Sticks test TDI. Normosmia was defined as a TDI score $\geq 31$; Hyposmia was defined as $15 < $ TDI score $< 31$; Functional anosmia was defined as a TDI score $\leq 15$.\textsuperscript{177,181}

The mean age of the 205 patients (84 males and 121 females) was 53.6 (SD ±1.0 years).\textsuperscript{177} All were questioned for the presence of parosmia. Patients with parosmia are referred to as P+, patients without parosmia are referred to as P-. All participants completed the QOD, the MI and the BDI. Fifty patients and all 25 controls completed the SF-36. Results of the QOD were analysed for significant correlation with the parameters: duration of the olfactory disorder and age.\textsuperscript{Frasnelli, 2005 #94847}

Statistical analyses were performed using SPSS 10.0 (SPSS Inc., Chicago). The alpha level was 0.05.\textsuperscript{Frasnelli, #94847} After testing for normal distribution of the data for analysis of
group differences, Student’s t-test was applied; p values were adjusted according to Bonferroni. Pearson’s coefficient of correlation was calculated for analysis of bivariate correlations.\textsuperscript{177}

The QOD was found to be an appropriate and valid measure of the impact of olfactory dysfunction on daily life.\textsuperscript{177} Self-report of olfactory impairment was a poor predictor of olfactory function. All participants reported a significant loss of olfactory function, but only 90% overall had measurable olfactory loss using Sniffin sticks. Of these, 50% were hyposmic and 40% functionally anosmic. Correlation analysis found that normosmic subjects were unable to rate their olfactory function correctly, but that anosmic and hyposmic subjects were accurate in identifying their OI.\textsuperscript{177}

The results of the four psychometric tests correlated significantly.\textsuperscript{177} Compared to the 25 healthy subjects, self-reported olfactory loss demonstrated a non-significant trend towards reduced scores in all domains of the SF-36 (P = 0.068). The number of healthy subjects being limited to 25 subjects compared to 205 abnormal participants, may have led to a lack of power to detect a significant difference. Loss of quality of life also correlated with lower measured olfactory identification score.\textsuperscript{177}

In this female weighted study of 205 persons (84 males and 121 females) with self-reported olfactory loss, no gender difference in anosmia was identified. However, men were more likely to be hyposmic compared to women after adjustment for age.\textsuperscript{177} There were gender differences in QOL measured by MI, BDI and QOD-NS. In each measure, women reached statistically significant higher scores than men, indicating a significantly higher degree of
impairment (MI: P<0.001, BDI: P=0.038, QOD-NS: P<0.001). Quality of life measured by the QOD was not influenced by the duration of self-reported OI (r<0.078, P>0.28).

There were significant age effects on TDI score. Anosmic subjects (age, 52.9 ± 2.6 y) were older than normosmic subjects (age, 40.5 ± 0.5 y) (t = 4.6, P < 0.001). There was no significant association between OI and medications, smoking or individual comorbidities (diabetes, hypertension, depression, cardiovascular problems, liver problems) except a significant association of lower TDI in persons with a history of cancer and women taking the oral contraceptive pill.

There were significant differences in QOD scores of persons who inaccurately reported olfactory impairment (normosmic patients). Normosmic patients reporting OI had significantly higher QOD-NS scores when compared to hyposmic or functionally anosmic patients. No other psychometric test (BDI, MI, SF-36) demonstrated significant differences between normosmic, hyposmic and functionally anosmic patients. In persons with objective OI, the QOD-NS, but not the QOD-PS or QOD-DS, was significantly associated with the TDI score (r² = -0.15, P=0.034) meaning persons with measured OI by Sniffin Sticks had significantly higher QOD-NS score and therefore lower QOL.

Parosmia was reported by 28.3% of participants. Of these, 13.8% were functionally anosmic and 79.3% hyposmic leaving 6.9% of P+ who were normosmic. Comparing participants with quantitative olfactory loss and parosmia to those with quantitative olfactory loss without parosmia, parosmic participants had significantly more problems coping with their olfactory dysfunction (P+ had significantly lower scores on the QOD-PS vs. P-; p = 0.021). No other psychometric tests yielded significant differences between P+ and P- patient groups. Results
were not influenced by excluding participants with high QOD-DS scores. There was no significant association between parosmia and age (P+: 55.7; P-: 57.3; p = 0.57).

The organisation for anosmia is a Dutch organization founded in 2000 by volunteers experiencing problems in smelling and tasting. To compare health-related quality of life and depression between Dutch persons with anosmia and normosmia, all 105 members of the organisation were contacted in 2006 via an advertisement on the organisation's website and via a mailing letter. The response rate was 90%, and the final sample was 90 (86%) after exclusions. Smell dysfunction was self-reported. The age range was 24-86 years old (mean 58.8; SD = 12.5). A comparison group of 89 normosmic persons was recruited via an advertisement in a regional newspaper and from acquaintances of the study’s authors. The age range of this group was 32-78 years old (mean 56.8 years; SD = 9.4). The SF-36 and the QOD were administered to assess the degree of problems in daily life related to the smell impairment. Respondents also completed the questionnaire “Smell and Taste Impairments”, developed at Utrecht University, to diagnose and record smell and taste dysfunction. It consists of 52 items covering symptomatology and possible causes of olfactory impairment, duration of the impairment, comorbidities and medication use.

A multivariate analysis of variance (MANOVA) with between-subjects factor group (two levels: anosmia vs. comparison) was conducted on the three subscales of the QOD and the nine subscales of the SF-36. A significant MANOVA was followed by univariate ANOVA for each of the subscales. The scores on the BDI-II-NL were not normally distributed so the Mann-Whitney test was conducted. The corresponding effect size was calculated as follows: $r = Z/N^{\frac{1}{2}}$. A chi-square test was conducted to compare the division of scores from the two groups over the four categories from “no” to “severe” depression. Pearson product-moment
correlations were calculated between the various subscales to explore relevant associations. For all statistical tests, \( \alpha \) was set to 0.05; for correlations, \( \alpha \) was set to .001 to correct for multiple comparisons.\textsuperscript{182}

The study reported that persons who were members of the organisation for anosmia had significantly lower QOL related to situations involving taste and smell.\textsuperscript{182} Compared to the comparison group, scores in the anosmia group significantly differed on the QOD-subscale Life Quality (\( p < 0.001 \)). Scores on various subscales on the SF-36 indicated significant associations between anosmics and reduced energy, limitations in social activities and interactions, and a reduction of general health when compared to normosmics. Parosmia was associated with significantly reduced life quality concerning daily activities related to tasting and smelling, and health-related quality of life with significant correlations between the parosmia subscale of the QOD and other subscales of the QOD and SF-36, respectively.\textsuperscript{182}

To examine the impact of olfactory impairment in the UK, Phillcott et al enrolled members of the patient support organisation Fifth Sense in a study that utilised questions from the QOD to assess the associations between olfactory impairment and QOL.\textsuperscript{177,184} From a membership of over 1000 persons with olfactory disorders, 496 completed the online survey over 9-months. The age range was 8-95 years old (mean = 55).\textsuperscript{184}

Responding members of Fifth sense reported reduced appreciation of food and drink (92%), exposure to certain dangers (e.g., gas, rotten food) (85%), going to restaurants less often than they used to (55%) and relationship difficulties with partner/family/friends (54%) due to difficulties with smelling.\textsuperscript{184} There was a significant sex difference, with women being more likely to be affected by OI than men (\( p = 0.01 \)). There was also a high prevalence of
qualitative olfactory disorders with parosmia reported in 19% and phantosmia in 24% of Fifth Sense members. In both categories of qualitative disorders, there was a significant difference when compared to persons without qualitative disturbances for flavour perception, eating unhealthily, eating less, despair, being less sociable, and stress (P ≤ 0.05).

The BMES examined the associations of olfactory impairment with self-rated health, quality of life, functional disability and reduced independence in persons aged ≥ 60 years. Olfactory function was assessed during the BMES 10 year follow up period using the SDOIT. Self-rated health was assessed by questionnaire and QOL was assessed by SF-36 score. Use of community support services and dependence on informal supports was assessed by questionnaire. Dependence on community support services was defined as regular use of meals on wheels, home care or community nursing. Reliance on informal support was defined as receiving assistance from someone other than a spouse (family member/friend) for cleaning or shopping. Also, participants’ ability to go out alone was assessed. The Older American Resources and Services (OARS) ADL scale was used to assess functional disability. Participants reporting that they needed help with, or were completely unable to perform, one or more ADL activity were considered to have impaired ADL. Olfactory impairment was defined as identification of ≤ 5 out of 8 SDOIT odours.

In this cohort, persons with olfactory impairment were more likely to report low self-rated health when compared to participants with normal olfaction. After multivariable adjustment, persons with olfactory impairment had statistically significant lower SF-36 scores in physical functioning (p = 0.02), role limitation due to physical problems (p = 0.004), general health perception (p = 0.05), vitality (p < 0.0001), social functioning (p =
role limitation due to emotional problems \( (p < 0.0001) \) and mental health \( (p = 0.05) \). The association with bodily pain was not significant \( (p = 0.08) \).

The use of community support services was reported by 15.2\% of persons with OI compared to 5.2\% of persons without OI. After multivariable adjustment, participants with OI compared to those without OI were more likely to use community support services \( (OR \ 1.82, CI \ 1.16-2.86) \). Olfactory impaired persons were also significantly more likely to use informal supports \( (OR \ 1.62, CI \ 1.14-2.32) \). ADL difficulty was reported by 16.9\% of participants with olfactory impairment compared to and 4.4\% of participants without olfactory loss. After multivariable adjustment, olfactory impaired persons had an increased likelihood of experiencing ADL difficulty \( (OR \ 1.98, CI \ 1.10-3.57) \). Olfactory impaired participants reported statistically significant higher frequencies of difficulty in 12 of the 14 ADL items. Olfactory loss was significantly associated with impaired basic ADL \( (OR \ 1.57, CI \ 1.12-2.20) \). The severity of olfactory impairment was not associated with the use of community or informal supports, nor with impaired ADL. Olfactory impairment was not associated with instrumental ADL.

Using the database at the Department of Otorhinolaryngology, Friedrich-Schiller-University Jena, Germany, Neuland \textit{et al} recruited persons with \( \geq \) six months of severe hyposmia and anosmia as assessed by the Sniffin Sticks test. All had received a complete otorhinolaryngologic examination. Severe hyposmia or anosmia was defined as TDI score < 20. After exclusions, 527 patients were invited to participate via mail between May and October 2009 with a request to confirm their olfactory dysfunction and answer two questionnaires, the German version of the SF-36 Quality of Life Health Survey and the adapted version of the QOD, the QOD 29. The response rate was 53\% (280 persons). Three
hundred and twenty age and sex matched persons from the German population without
olfactory dysfunction were recruited as controls. The age range was 12-89 (mean = 60±14)
years. The interval between olfactory assessments and of QOL assessment was on average
3.6 ± 2.4 years (range, 0.3-9.7). 187

The QOD 29 has three-scale statements with three domains: 19 statements on life quality
(LQ), six statements on sincerity (S), four statements concerning parosmia (P), and five
visual analogue scales (VASs). 187

The sum of the LQ statements gives the LQ raw score (LQrv) with a maximum of 38 points.
LQrv is transformed into the LQ score (LQsc) by the formula LQsc = (LQrv/38) x 100 (%).
The sum of the S statements makes the S raw score (Srv) with a maximum score of 12 points.
Srv is transformed into the S score (Ssc) by the formula Ssc = (Srv/12) x 100 (%). Maximal P
raw score (Prv) is 8. Prv is transformed into the P score (Psc) by the formula: Psc = (Prv/8) x
100 (%). 187

High scores of LQrv/LQsc indicate a strong impairment. Low scores of Srv/Ssc indicate a
tendency toward giving socially desired answers. High scores of Prv/Psc indicate more
parosmia (P). 187

The five visual analogue scales (VAS) were: VAS 1 annoyance; VAS 2 perceivable; VAS 3
work-related impairment; VAS 4 recreational impairment; VAS 5 private impairment. 187 The
five VASs were 100-mm long. Absolute VAS values (in millimetres) were presented.
Bivariate correlations were determined by using Pearson’s product moment coefficient.
Mann-Whitney U tests for independent samples were used to analyse group differences. All
tests were two-tailed with a 5% significance level. Linear regression analysis, including all determinants significant in the univariate analysis, was performed to identify independent determinants of QOL.\textsuperscript{187}

Anosmia was present in 205 patients and severe hyposmia in 75 patients. The average TDI score was 12 ± 4 points.\textsuperscript{187} The average T score was 0.3 ± 1 points, the D score 6 ± 2 points, and the I score 6 ± 3 points. There was no sex interaction with overall TDI score. There was no age interaction for T and D scores. Participants older than the median study age of 62 years had higher I and TDI scores than participants younger than the median age (P = 0.014 and P = 0.009 respectively).\textsuperscript{187}

The values of all domains of the SF-36 were significantly lower than in the age- and sex-matched control group.\textsuperscript{187} The analysis of correlation (Pearson, bivariate) between SF-36 and TDI scores identified a significant correlation with the BP domain. Lower values in this domain correlated with lower TDI scores. There were no other significant correlations identified. Female participants had significantly lower values in several of the SF-36 physical health domains compared to male participants. Duration of olfactory dysfunction did not influence SF-36 measured HRQOL (all P > 0.05).\textsuperscript{187} The reported results for the different domains of the SF-36 questionnaire are summarised in Table 1.8.
8 Table 1.8 Comparison of the SF-36 Health Related Quality of Life between the anosmic/hyposmic patients (n = 280) and the age- and sex- matched control group$^a$ (n = 320)$^{187}$

<table>
<thead>
<tr>
<th>SF 36 Domain</th>
<th>Study Group</th>
<th>Control Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Functioning</td>
<td>71.53 ±27.50</td>
<td>75.89 ± 25.77</td>
<td>&lt; 0.042</td>
</tr>
<tr>
<td>Social Functioning</td>
<td>74.09 ± 25.72</td>
<td>86.76 ± 21.13</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Physical Role</td>
<td>56.52 ± 42.77</td>
<td>72.47 ± 39.64</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Emotional Role</td>
<td>63.10 ± 42.84</td>
<td>87.04 ± 31.04</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>General Mental Health</td>
<td>66.36 ± 19.77</td>
<td>74.43 ± 17.99</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Vitality</td>
<td>52.43 ± 20.69</td>
<td>60.93 ± 19.75</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Bodily Pain</td>
<td>61.51 ± 30.31</td>
<td>70.20 ± 30.62</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>General Health Perception</td>
<td>52.73 ± 20.08</td>
<td>58.83 ± 20.54</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

$a$ Subgroup of German normative data (median age, 63 years; 52% female).
The analysis of correlation (Pearson, bivariate) between TDI score and QOD domains (life quality (LQ), sincerity (S) and parosmia (P), and five visual analogue scales (VASs) found significant negative correlations between TDI score and LQrv ($r = -0.137; P = 0.022$), Prv ($r = 0.161; P = 0.007$), VAS 3 ($r = 0.129; P = 0.036$), and VAS 4 ($r = 0.136; P = 0.025$). A non-significant negative trend was found between TDI score and VAS 1 ($r = 0.102; P = 0.090$) and VAS 5 ($r = 0.114; P = 0.060$). Similar to the SF-36 physical health domains, female participants had worse QOD values than male participants and the duration of olfactory dysfunction had no influence on the QOD values (all $P > 0.05$).
**Olfactory Impairment and Depression**

Olfactory processing at the brain level recruits areas whose functioning is known to be altered in depression.\(^{188}\) These alterations may be reversed by antidepressants.\(^{188}\) Bilateral olfactory bulbectomy of a rat results in changes in behaviour, and in the endocrine, immune and neurotransmitter systems, that simulates many of those seen in patients with major depression.\(^{189}\) In addition, stress induces behaviour similar to some symptoms of depression and decreases neurogenesis in the hippocampus and olfactory bulbs.\(^{190}\) These findings describe possible biological pathways between depression and olfactory impairment.

The BMES examined the associations between depression and olfactory impairment at 10-year follow up.\(^{185}\) Participants were aged ≥ 60 years at the 10-year follow up. Olfactory impairment was assessed using the SDOIT. Olfactory impairment was considered present if the participant correctly identified ≤5 out 8 SDOIT odours. Depression was assessed using the Mental Health Index (MHI) component of the SF-36 and the Center for Epidemiologic Studies Depression Scale (CES-D-10).\(^{191}\) A score of ≥ 10 out of a total possible score of 30 was used to define significant depressive symptoms.\(^{185}\)

In the BMES cohort overall, there was no significant association between depressive symptoms and olfactory impairment after multivariable adjustment.\(^{185}\) When stratified by age, olfactory impaired persons older than 70 years had a significantly increased likelihood of depression if scored by the CESD-10 (OR 1.66, CI 1.03-2.66) but not the MHI.\(^{185}\)

A cross sectional study of 127 non-institutionalised Korean elderly persons (85 women and 42 men) aged 65-89 years (mean ± SD: 73.8 ± 5.1 years) residing in Daejeon city of South Korea, estimated the association between measured olfactory dysfunction and depression.\(^{175}\)
Depression was assessed using the Korean version of the Geriatric Depression Scale (GDS-K)\textsuperscript{192} developed by Yesavage et al.\textsuperscript{51} The GDS-K consisted of 30 questions, and the cut-off score for the determination of depression was 10 (maximum score 30).\textsuperscript{175}

For subjects with severely impaired olfactory function or functional anosmia, the mean depression scores exceeded the cut-off score of 10 points, indicating the presence of depression.\textsuperscript{175} When comparing olfactory thresholds between non-depressed and depressed subjects (above or below a score of 10 points on the GDS-K), depressed subjects exhibited significantly higher detection thresholds ($t_{69.48} = -2.51, p = 0.02$). For recognition thresholds, a nonsignificant trend was found for the same comparison ($t_{84.88} = -1.91, p = 0.06$). However, after partial correlation analyses controlling for cognitive performance and QOL, there was no significant association between olfactory detection and recognition thresholds and depression. Linear regression modelling confirmed no significant association between depression and olfactory function in this population.\textsuperscript{175}

To examine the effect of a major depressive episode on olfaction, Pause \textit{et al} recruited 24 inpatients with major depressive disorder (MDD) during their acute depressive phase.\textsuperscript{193} Persons were considered depressed if their symptoms met the DSM IV\textsuperscript{194} criteria for a major depressive episode and had a BDI $\geq 11$. The mean age was 48.4 (SD =13.2) and the mean BDI-score was 28.5 (SD = 11.4). Of these, 18 participated again after successful treatment, 2 participants refused the second examination and four patients did not subjectively recover from depression. Twenty-four non-depressed (BDI mean=4.8, SD = 2.5) age, sex, and smoking status matched controls were also recruited. The difference in BDI scores between the test and control subjects was statistically significant ($t (46) = 9.98; P<0.001$). No participant had neurological or endocrine disorders known to affect olfaction.\textsuperscript{193}
Olfaction was assessed with the following ten odorants: 5-a-androst-16-en-3-one (98%, Aldrich, body odour), butylcyclohexylacetate (99%, Aldrich, cedar-wood), citral (95%, Aldrich, citrus), eugenol (99%, Fluka, clove), isoamylacetate (98%, Aldrich, pear), isobutyraldehyde (99%, Aldrich, butter-acid), linalool (97%, Fluka, lavender), menthol (99%, Merck, peppermint), n-octyl-acetate (Aldrich, apple) and 2-phenyl-ethylalcohol (PEA, 99%, Fluka, rose).\textsuperscript{193} Olfactory thresholds for eugenol and PEA were determined using a two-alternative staircase detection procedure. Valence and intensity ratings were obtained for all ten odours. Ratings were measured using a 7-point scale (valence from -3 to +3; intensity from 0 to 6). All participants completed the BDI and an anxiety inventory (State-Trait-Anxiety-Inventory, STAI).\textsuperscript{193}

On average, depressed participants were examined 16.1 (SD 9.5) days after admission. On the day of the investigation, 20 participants were being treated with antidepressants and 4 were not.\textsuperscript{193} The second examination occurred after successful treatment (mean interval between sessions: 58.3 days, (SD 45.1). The reduction in the BDI score was statistically significant (P < 0.001). A control group of 18 healthy subjects was also tested again (mean interval between sessions: 49.5 days (SD 11.1). The reduced control group was matched by age, sex and smoking behaviour. The BDI score of the control group did not change between examinations (BDI mean = 4.6, SD = 3.4).\textsuperscript{193}

Participants with MDD had reduced sensitivity for odorants compared to controls, but this did not reach statistical significance.\textsuperscript{193} The BDI score trended negatively with olfactory sensitivity but was significantly reduced for eugenol threshold only. Measured intensity ratings for all odorants did not significantly differ between the test group and the controls. There was a non-significant trend for the valence ratings to differ between the groups. There
was a non-significant trend for olfactory scores to improve after the treatment of depression. The eugenol threshold of the MDD compared to the control group, which was significantly higher in MDD participants at the initial examination, became nonsignificant after treatment of depression.193

In a study to characterise and compare the psychophysical dimensions of olfaction in groups of patients affected by psychiatric disorders, Lombion-Pouthier et al compared olfactory ability of a sample population of 49 depressed persons (mean age = 43.4 years; SD = 17.54: 35 females) with 58 healthy subjects matched for sex, age and smoking habits (mean age = 38.4; SD = 13.96: 36 females).195 Severe depression was diagnosed using DSM IV194 criteria. Persons with other psychiatric diseases were excluded from the depression study. Olfactory assessment utilised the European Olfactory Abilities Test (ETOC).196 This test firstly evaluates the olfactory sensitivity with two odours: l-carvone and tetrahydrothiophene. Using a forced choice procedure for 5 successive concentrations, an overall score between 2 (high sensitivity) to 10 (low sensitivity) was calculated. The second part of the test evaluates detection and identification abilities using a panel of 16 odours (vanilla, lavender, eucalyptus, fuel, fish, violet, garlic, grass, orange, apple, cinnamon, lemon, anise, mulberry, chewing gum, mint). For each of odour, participants were required to select from four bottles, the bottle with an odour (detection test) and then identify the odour from a list of four names (identification test).195

This study reported that depressed participants had poorer olfactory sensitivity, but similar identification abilities when compared to healthy controls.195 The authors used Fisher's Protected Least Significant Difference to demonstrate a significant difference between the higher mean olfactory scores (lower sensitivity) of the depressed participants compared to the
control group. More depressed participants gave ≥1 incorrect identification responses when compared to the control group, but this difference did not reach statistical significance (14% depressive patients vs.. 2.5% control group; p <0.1).\textsuperscript{195}

The association between anosmia and parosmia and depression was examined in members of the organisation for anosmia.\textsuperscript{182} The SF-36\textsuperscript{183} and Beck Depression Inventory-II-NL (BDI-II-NL)\textsuperscript{178,197} were administered in addition to the QOD\textsuperscript{177} to assess levels of depression in both the anosmic and normosmic groups.\textsuperscript{182}

The study reported that persons with anosmia had higher scores on subscales of the SF-36 indicating increased feelings of depression and nervousness compared to the normosmic group.\textsuperscript{182} The BDI scores were significantly higher in the anosmic group indicating higher levels of depression in persons with anosmia than without anosmia. In the anosmic group, 22% were depressed (11% mildly depressed; 9% moderately depressed; 2% were severely depressed) compared to 5% overall in the normosmic group (4% mildly depressed; 1% moderately depressed).\textsuperscript{182} Persons with parosmia were also significantly more likely to be depressed compared to normosmic participants.\textsuperscript{182}

In a study of members of Fifth Sense, a UK patient support organisation for persons with olfactory impairment, the rate of depression as measured by the QOD was 43%, which is higher than the reported rate of depression in the adult population of 8-12% of the UK.\textsuperscript{184,198}

There were significant differences in depression and anxiety rates between the sexes in this group with women being significantly more likely than men to have depression and/or anxiety (47% (n = 151) vs.. 34% (n = 60) P = 0.003).\textsuperscript{184} There was also a significant age
effect. Members younger than 50 years were significantly more likely to report isolation ($P = 0.002$), depression ($P = 0.008$), and being scared of dangers ($P = 0.038$). Older sufferers had significantly higher rates of resignation to their sensory loss ($P = 0.03$).\footnote{184}

Phantosmic members reported significantly higher rates of depression ($P = 0.008$) compared to those without phantosmia.\footnote{184} Parosmic members did not show significantly different rates of depression when compared to those without parosmia, but did report a significantly higher rate of anxiety ($P = 0.007$).\footnote{184}

Amsterdam \textit{et al} found no significant association between olfactory function and MDD in a study of 51 depressed participants compared with 51 age and sex matched controls.\footnote{199} Depression was defined by the DSM-III criteria\footnote{200} for a major depressive disorder (MDD), with or without melancholic features, or atypical (bipolar II) depressive disorder. Olfaction was assessed using the University of Pennsylvania Smell Identification Test (UPSIT). Two-way ANOVA with age as the covariate and gender and subject group (depressed, controls) as factors, found no significant difference between the UPSIT test scores of depressed participants compared to the control subjects.\footnote{199}

To determine whether olfactory function could be useful in discriminating between the diagnoses of dementia or depression in elderly patients, Pentzek \textit{et al} compared the olfactory function of 20 patients from an old age psychiatric Ward with probable Alzheimer’s disease (AD); 20 elderly patients with a depressive disorder; and thirty healthy elderly subjects.\footnote{201} Participants in the depression group were mildly to moderately depressed overall. In this study, no significant difference in odour identification between the depressed group and the controls was identified.\footnote{201} This study is discussed at length in the following section.
A study of 48 persons with no history of neuropsychiatric diseases, including depression or anxiety disorders, examined the associations between olfactory sensitivity and olfactory identification with depressive symptoms. The mean age of participants was 28.2 years (SD 5.8 years). Olfactory function was assessed using the Sniffin' Sticks test. Depressive symptoms were assessed using the Beck Depression Inventory. Pleasantness and arousal during the olfactory assessments were assessed using a non-verbal self-report scale with scores ranging from 1 (very unpleasant or low arousing) to 9 (very pleasant or high arousing). Descriptive mean scores were calculated for olfactory sensitivity, olfactory discrimination, pleasantness, arousal and BDI score. Pearson's correlation analyses were used to examine the relationship between degree of depressive symptoms with olfactory sensitivity and olfactory discrimination. Regression analyses with the independent variable olfactory sensitivity and olfactory discrimination, respectively, and the dependent variables depressive symptoms, pleasantness and arousal were carried out.

The mean BDI score was 3.3 (SD 3.1; minimum 0, maximum 9). All subjects reported a small number of depressive symptoms (BDI score < 10). The mean perception threshold was 11.7 (SD 2.0) and the mean discrimination score 12.5 (SD 3.1) out of 16. There was a statistically significant (p = 0.05) inverse correlation between the degree of depressive symptoms and olfactory threshold score (r = −0.36) indicating reduced olfactory sensitivity in participants with a high degree of depressive symptoms. There were no significant correlations for olfactory discrimination.
A cross sectional study of 127 non-institutionalised Korean elderly persons (85 women and 42 men) aged 65-89 years (mean ± SD: 73.8 ± 5.1 years) residing in Daejeon city of South Korea, estimated the association between measured olfactory dysfunction and cognitive impairment. (Seo, Jeon et al. 2009) Cognitive performance was measured by the Korean version of the Mini-Mental State Examination (MMSE-K) originally designed by Folstein et al. Impaired cognitive function was defined as MMSE-K score < 24 out of 30 points.

Participants with severely impaired olfactory function and with functional anosmia, had a mean cognitive performance score < 24 points. This difference was statistically significant after partial correlation analyses controlling for depression and QOL when compared to participants with normal and slightly/moderately impaired olfaction. Linear regression modelling of cognitive performance found that detection threshold and education level were main modulators to account for the variance of cognitive performance (Y (degree of cognitive performance) = +23.892 - 1.020X1 (detection threshold) + 0.900X2 (education level).

To examine whether olfactory impairment was associated with cognitive impairment and subsequent cognitive decline, Swan et al assessed olfactory function and cognitive performance in 359 participants with a mean age of 74.3 (SD = 4.3) years in 1992 and again 4.5 years later. Participants were recruited from the Western Collaborative Group Study health and aging follow up which began in 1960 with 3152 healthy males aged 39 - 59 years. During 1986-1988, the wives of the participants were recruited and they form the basis for female participants. In 1992, 870 participants (712 men and 158 women) were
assessed for smell identification and cognitive performance. Of these, 52 (6.0%) participants had a positive history of stroke and 19 (2.2%) had a MMSE score of less than 23 and were excluded from further analysis. Of the remaining 802 individuals, eligible for inclusion in the follow-up 4.5 years later, 443 were either deceased (17.7%), too ill to participate (3.6%), refused participation (16.7%), participated by questionnaire only (23.9%), or lost to follow-up (2.9%). There were no cases of confirmed Alzheimer disease (AD). The remaining 359 individuals (286 men and 73 women) with repeat cognitive testing comprised the primary sample for the analysis of the association between odour identification and cognitive decline.

Odour identification was assessed using the CC-SIT. Impaired odour identification was defined as a CC-SIT score of ≤ 10 out of 12. Cognitive assessment was by means of a neuropsychological test battery consisting of several measures of executive control, verbal learning and memory, visual learning and memory, and global Function. The MMSE was performed by all subjects.

The association between olfactory dysfunction and potential confounders was examined with either chi-square or Student's t tests. Differences in variables of interest between the analysis sample and those not included in the analysis were examined with univariate tests. The primary analysis consisted of the use of the general linear model to examine differences between impaired and normal olfactory groups on mean change in cognitive performance on each of ten tests separately after multivariable adjustment.

Of all baseline participants, 53.3% had olfactory impairment at the initial assessment. Seventy three percent of participants with MMSE score < 23 had olfactory impairment.
compared to 52% of participants with MMSE ≥ 23. This difference was not statistically significant ($\chi^2(1) = 3.23; p < 0.072$). After exclusions, the prevalence of baseline olfactory impairment in the remaining 359 participants was 45.7%. After multivariable adjustment, there were no significant associations between baseline olfactory impairment and change in performance in any of the measures of executive control nor MMSE score. There were significant associations between baseline olfactory impairment and learning and memory tasks. After multivariable adjustment, persons with baseline olfactory impairment had significantly greater declines in visual memory and verbal learning and memory tasks compared to normosmic participants.205

A Japanese study compared olfactory function of 85 persons (mean age 76.3; SD = 7.2) with confirmed AD and 30 age-matched (mean age 74.8; SD = 8.5) non-demented elderly controls.207 Two tests of olfactory function were administered to all subjects, the cross cultural smell identification test (CC-SIT)208 and the picture-based smell identification test (P-SIT). The CC-SIT is a scratch-and-sniff test of 12 microencapsulated odorants with four forced choice alternatives per item. The P-SIT uses six distinctive odorants (ground coffee, incense, ground sesame, green tea, fermented soybean paste and soap) that were confirmed to be intense and familiar to cognitively intact Japanese elderly persons by preliminary trials.207 Twenty pictures of materials including six pictures corresponding to the smells and fourteen pictures unrelated to the odorants were presented. Subjects were asked to identify the odorants by choosing a corresponding picture after smelling each odorant. The number of correct choices was recorded as the score of the test. Cognitive impairment was assessed using the MMSE in all participants.207
The mean age of the two groups were compared by Student’s t-test. Gender difference of MMSE scores within each group and the mean P-SIT and CC-SIT scores of the two groups were compared by Mann-Whitney’s U-test. Differences were considered statistically significant if p < 0.05. The relationship between the age of the subjects and the scores of the P-SIT and the CC-SIT in both groups and the relationship between the MMSE scores and the scores of the two olfactory tests within the AD group were examined using Spearman rank of order correlation coefficients. Simple regression analyses were conducted for both olfactory tests within the AD group to calculate the predicted MMSE scores from the SIT scores as independent variables and compared coefficients of determination.

The mean MMSE score of the AD group (mean = 19.6; SD = 4.6) was significantly lower than that of the elderly controls (mean = 28.5; SD = 2.2) (p<0.0001). Within the AD group, there were no significant gender differences in age, MMSE scores and SIT scores. The AD group had significantly lower P-SIT and CC-SIT mean scores when compared to the control group (1.5; SD = 1.3 vs.. 4.4; SD = 1.2, and 4.1; SD = 2.5 vs.. 6.8; SD = 1.7 respectively; p < 0.0001 for both SITs). Chi square analysis estimated the P-SIT discriminated the AD group from elderly controls with a sensitivity of 94% and specificity of 81%. The positive predictive value was 0.93 and negative predictive value 0.83. The CC-SIT had lower sensitivity (90%) and specificity (51%) with a positive predictive value of 0.65 and negative predictive value of 0.83.

To examine the associations between olfactory impairment and Alzheimer disease, Doty et al compared olfactory function in 34 mildly to moderately severe AD patients with no other complicating diseases with 34 healthy non-institutionalised age, gender and ethnicity matched control subjects. Odour identification was assessed with the UPSIT. All AD
patients were administered a picture identification test identical in content and format to the UPSIT except that pictures, rather than odours, serve as stimulus items to identify individuals too demented to comprehend the non-olfactory components of the UPSIT. Nine AD patients failed or were unable to complete the picture identification test and were excluded, as were their matched controls, from further consideration. After exclusions, odour detection threshold was assessed in 25 AD patients and an equivalent number of age, race and gender matched controls using a single staircase, forced choice odour detection threshold test using the odorant phenyl ethyl alcohol.  

The average UPSIT test scores of the remaining 25 AD patients were significantly lower than their 25 age matched controls (Wilcoxon matched-pairs signed-ranks test. \( T = 3, p < 0.001 \)). A Mann-Whitney U-test found no association between stage of AD and UPSIT score (\( U=58.5; p > 0.20 \)). Alzheimer disease patients also had significantly higher detection thresholds when compared to matched controls (Wilcoxon matched-pairs signed-ranks test, \( T = 1, p < 0.001 \)). No significant differences were present between the stage of the disease and the odour detection threshold. Self-report of olfactory deficit was not a reliable measure of the presence of olfactory impairment in the AD patients; only two of the 34 AD patients reported olfactory loss.  

To compare olfactory impairment in vascular dementia (VD) with olfactory impairment in AD, Gray et al compared the UPSIT scores of age and sex matched AD patients, VD patients and a control group. There were 13 participants in each group. The age ranges for the groups were 71.6-79.2 years (mean 75.4) for the AD group, 76.1-86.4 (mean 79.2) for the VD group and 72.8-79.2 (mean 75.6) for the control group. The median UPSIT scores of the AD and VD were significantly lower than the UPSIT scores of the control group (Kruskal-
Wallace, $\chi^2 = 21.987$, df = 2; p = 0.001). Post hoc comparisons demonstrated significant differences between the UPSIT scores of the AD (Wilkinson paired: Z = -3.189; p = 0.001) and the control group and between the VD group and control group (Wilkinson paired: Z = -3.182; p = 0.001). There was no significant difference in the UPSIT score when comparing the AD with the VD groups in the post hoc comparisons (Wilkinson paired: Z = -0.980; p = 0.327).210

Pentzek et al compared the olfactory function of 20 patients from an old age psychiatric Ward with probable Alzheimer’s disease (AD), 20 elderly patients with a depressive disorder, and thirty healthy elderly subjects.201 A diagnosis of AD was made according to the NINCDS-ADRDA research criteria.211 A diagnosis of a depressive disorder was made according to the ICD-10 criteria.212 The 30 control subjects with no history of AD or depression were recruited from a general hospital (n=12) and a facility for assisted living (n=18). All participants were non-smokers aged $\geq$60 with no history of other psychiatric or neurological disease including stroke, head trauma, chronic exposure to toxic agents, and acute or chronic diseases of the upper respiratory tract.201

Cognitive status was assessed using the German version of the Alzheimer’s Disease Assessment Scale, cognitive subscale (ADAS-cog)213 and the German version of the Brief Cognitive Rating Scale (BCRS).214 Depressive symptoms were assessed using the Hamilton Depression Scale (HAMD).215 Odour identification ability was assessed with the 16-item identification subtest of the commercially available Sniffin’ Sticks.181 The total score ranged from 0 (no odour identified) to 16 (all odours correctly identified).201
Group means of the odour identification test, ADAS-cog score and HAMD score, were compared by univariate analyses of variance (ANOVA) and post-hoc Scheffé tests; diagnosis was treated as a between-subjects factor with three levels (AD, depression, healthy controls). The alpha level was set at 0.05. Non-parametric rank correlations (Kendall’s tau) of odour identification and the ADAS-cog score with age and years of education were calculated for the three groups.

The cognitive status of the AD group overall was in the mild to moderate dementia range. The depressed group overall were mildly to moderately depressed. Post-hoc Scheffé tests showed significant differences between AD and depression and the number of correct odorants identified (mean difference = -7.25; p<0.001) and between AD and controls (mean difference = -6.85; p<0.001), but not between depression and controls (mean difference = 0.40; p=0.72). The sensitivity of the odour identification test was estimated to be 100% for the differentiation of AD from both depressive patients and healthy subjects using a cut-off score of ≤10 correctly identified odours out of 16. Specificity was estimated to be 95% for the differentiation of AD from depression, and 100% from healthy controls.

Ansari et al were the first to describe olfactory deficits in PD in 1975. Twenty-two male PD patients aged 41-67 (mean 58), twenty with idiopathic Parkinson’s disease and two with a past history of encephalitis were examined. None had a past history of significant head trauma or nasal injury, acute or chronic sinusitis, recent upper respiratory tract infection, clinical evidence of liver dysfunction or other illnesses that might conceivably result in decreased olfactory acuity. Thirty-seven age-matched males (mean age 53, range 43-68 years) hospitalised on the Neurology Service for conditions that included seizure disorder, multiple sclerosis, stroke and headache were used as controls.
Olfactory loss was assessed by detection threshold for amyl acetate using a double blind testing procedure and serial binary dilutions of amyl acetate in odourless liquid paraffin. Participants were required to identify both test tubes containing the odorant to score correctly for that dilution. The highest dilution at which the subject correctly identified both tubes containing the odorant was designated as the olfactory threshold.

The mean detection threshold for PD patients was significantly lower (p < 0.05) when compared to the age matched control group. For PD patients, the threshold was 39 x 10^-2 vol per cent compared to 2.7 x 10^-2 vol per cent in the control subjects. There was a significant association (p < 0.05) between threshold score and rate of progression of PD, with the greatest decrease in olfactory acuity in patients with rapidly progressive Parkinson’s disease.

Lehrner et al compared olfactory function between AD patients and non-demented Parkinson disease (PD) and an age matched control group. Twenty-two AD patients (2 males, 20 females) and 21 nondemented patients with PD (13 males, 8 females) and 19 age matched controls were recruited into the study. Alzheimer disease patients were significantly older than controls and PD patients. The ages of the PD patients and the controls were not significantly different. All PD patients were taking anti-Parkinson medication. Cognitive status was assessed by MMSE. Olfactory assessment utilised a testing procedure previously described by the author. Olfactory threshold was assessed using 1-butanol and an ascending staircase, two-bottle, forced-choice method. Odour identification used 20 everyday
odours. An odour recognition memory task (retention time 15 min) was also administered to all participants.  

Statistical comparisons among groups employed analysis of covariance (ANCOVA) using age as a covariate, due to the older age of the AD patients, and disease group as the independent variable. One-way ANCOVA revealed significant differences in olfactory thresholds between the groups (P < 0.003). Post hoc analysis (Scheffé's, P < 0.05) found AD patients had significantly higher thresholds than the controls. Olfactory thresholds of the PD patients did not differ significantly from the control group (p < 0.073). For odour identification a one-way ANCOVA revealed significant differences between the groups (P < 0.001). Post hoc analysis (Scheffé's, P < 0.05) found that controls performed significantly better but there was no significant difference between the AD and PD groups in odour identification.

Lee et al compared olfactory function and brain volume of 40 right handed PD patients without dementia and 40 controls matched for age, years of education, gender, and handedness, using high-resolution T1-weighted brain MRIs and voxel based morphometry. Olfactory function was measured using the UPSIT. Thirty-eight PD and 39 controls completed the UPSIT.  

After adjusting for age, PD patients had significantly lower UPSIT scores compared to controls (mean UPSIT, 22.55/40; SD, 6.55 vs. mean UPSIT, 34.38/40; SD, 5.38; P < 0.0001). Compared to controls, PD patients sustained significantly greater grey matter loss localised to bilateral piriform cortex (P < 0.005) and orbitofrontal cortex (P < 0.05). Reduced olfactory performance in PD was significantly associated with lower grey matter volumes in
right piriform cortex and left orbitofrontal cortex ($R = 0.33$; uncorrected $P = 0.028$, one-tailed; $N = 38$ and $R = 0.37$; uncorrected $P = 0.015$, one-tailed; $N$

Olfactory impairment has been reported to predict cognitive decline and Alzheimer dementia. Devanand et al reported an increased risk of cognitive decline and Alzheimer dementia in a multiethnic community of North Manhattan, New York, in persons with olfactory impairment, at two and four years. Participants of the Washington Heights/Inwood Columbia Aging Project (WHICAP), a cohort study using a stratified random sample of 50% of all Medicare beneficiaries aged 65 years and older obtained from the Health Care Finance Administration, were recruited from a specific region of North Manhattan. Participants were recruited over two periods, one cohort recruited in 1992 (approximately 25% of subjects) and a new cohort recruited between 1999 and 2001 (approximately 75% of subjects).

Participants received a standardised neuropsychological test battery at each visit. The battery included measures of learning and memory, orientation, abstract reasoning, executive function, language, and visuospatial ability. A function score was determined by summing six items for instrumental activities of daily living. A standardised neurologic examination was performed at each visit and included a 10-item version of the Unified Parkinson’s Disease Rating Scale, used to diagnose Parkinson disease. Assessment of odour identification utilised the UPSIT. Participants were required to complete $\geq 38$ of the 40 UPSIT items to be included in the study. For participants who completed 38 or 39 items, a score of 0.25 was imputed for each missing item. Participants with a diagnosis of stroke or Parkinson disease were excluded.
The baseline UPSIT testing was administered between 2004 and 2006. The study sample comprised participants without dementia who received the UPSIT. Follow-up data was collected during 2006–2008 (2-year follow-up) and 2008–2010 (4-year follow-up). Diagnoses of dementia, including AD dementia, were made based on available clinical, cognitive, and functional information excluding UPSIT data. Cognitive decline was defined as a decline in the average of the three cognitive composite scores of 1 SD or greater for 4-year follow-up or a decline of 0.5 SD or greater if follow-up was limited to 2 years. Outcomes at the last available follow-up time point were used.  

Distributions and group differences in demographic and clinical variables were examined by $\chi^2$, t test, and general linear models. Spearman correlations between UPSIT scores and demographic, cognitive and functional measures were evaluated. The definition of cognitive decline was based on the trend in the composite cognitive domain scores during follow-up. Logistic regression analyses were used for the outcome of cognitive decline. Discrete time survival models were used to estimate associations between baseline UPSIT scores and the outcome AD dementia. The covariates used were age, sex, education, Selective Reminding Test (SRT) Total immediate Recall (SRT-TR) and functional impairment. Selective reminding test total immediate recall (SRT-TR) was a component of the composite cognitive domain scores for memory, selected a priori for inclusion in the modelling. Analyses were conducted in SAS 9.3 (SAS Institute, Cary, NC) and R (v.3.0.1) package pROC.

A total of 1,037 participants of 1,119 (92.7%) without dementia were evaluated. In 757 participants, follow-up occurred at 2 or 4-years. Of those 757 participants who completed at least one follow-up, 109 transitioned to dementia. Of those, 101 transitioned to AD dementia,
2 transitioned to vascular dementia, 3 transitioned to Lewy body dementia and 3 participants to other causes of dementia.\textsuperscript{220}

For participants with baseline status of no MCI, nonamnestic MCI, and amnestic MCI, transition rates to any dementia at final follow-up were; 35/498 (7.03%); 32/129 (24.81%); and 42/130 (32.31%) respectively ($\chi^2 = 67.11$, $p < 0.0001$) and for AD dementia were: 33/498 (6.64%), 31/129 (24.03%), and 37/130 (28.46%) respectively ($\chi^2 = 57.69$, $p < 0.0001$).

Participants with cognitive decline (n = 151) had a mean baseline UPSIT score of 24.28 (SD = 6.35) compared to a baseline UPSIT score of 27.33 (SD = 6.70) in nondecliners (n = 581).
Participants not followed (n = 25) had the lowest UPSIT mean score (21.24 (SD = 7.64)).

Logistic regression analyses found a strong association between lower baseline UPSIT score and subsequent cognitive decline (RR 1.067 per point interval, CI 1.040 - 1.095; $p = 0.0001$). Lower baseline UPSIT scores remained significantly associated with subsequent cognitive decline after adjusting for sex, age, test language, education, STR-TR and functional impairment (RR, 1.065 per point interval, CI 1.034 - 1.095).\textsuperscript{220} UPSIT, but not SRT-TR, predicted cognitive decline in participants without baseline cognitive impairment. Lower baseline UPSIT scores were significantly associated with transition to AD dementia in discrete time survival analyses, (HR 1.099 per point interval, CI 1.067 - 1.131; $p = 0.0001$) and remained significant (HR 1.072 per point interval, CI 1.036 - 1.109; $p = 0.0001$) after including demographic, cognitive, and functional covariates.\textsuperscript{220}
The Associations Between Olfactory Impairment and Mortality
Olfactory impairment has been termed the canary in the coal mine of human health.\textsuperscript{224} Several mechanisms have been suggested to explain the association between olfactory impairment and increased mortality risk. The olfactory nerve is exposed to the environment. Respiratory exposures could reach the central nervous system via the olfactory nerve and cause death due to direct injurious effects.\textsuperscript{224} Alternatively, these exposures could be absorbed and cause systemic effects that increase the risk of mortality while simultaneously damaging the olfactory system.\textsuperscript{224} To function normally, the olfactory system is dependent on stem cell turnover to repair damaged olfactory epithelium.\textsuperscript{225} Impaired olfaction may represent a deterioration in age-related regenerative capacity.\textsuperscript{224} In addition, olfactory impairment may lead to unhealthy food choices, malnutrition or an increased risk of accidents such as gas fires and explosions.\textsuperscript{226} It has been suggested that underlying neurodegenerative disease may explain the association between olfactory impairment and mortality\textsuperscript{227,228} however, longevity in Parkinson disease is similar to the general population\textsuperscript{229} and the decreased longevity in patients with dementia may not wholly explain for the magnitude of the association reported.\textsuperscript{224}
An association between olfactory impairment and mortality was reported in participants of the Rush Memory and Aging Project, a longitudinal study involving annual clinical evaluations and brain donation at death.\textsuperscript{227,230} Participants were recruited from retirement communities and subsidised housing facilities in the Chicago metropolitan area starting in 1997 and expanded in 2001.\textsuperscript{230} At the time of the analyses, 1232 individuals had completed olfactory testing during their baseline testing.\textsuperscript{227} Persons with dementia and PD were excluded from the analysis (n = 58 and n = 12 respectively) leaving 1162 participants. The mean age at the time of olfactory testing was 79.7 years (SD = 7.7) and 74.5% were women. Olfaction was assessed using the brief smell identification test (B-SIT). This test was previously known as the CC-SIT.\textsuperscript{208} The association of olfactory score with mortality was assessed with Cox proportional hazards models. All analyses included terms for age, sex, and education. Multivariable adjusted models for other significant covariates were also performed.\textsuperscript{227}

After a mean of 4.2 years (SD = 2.6; range 0-9) follow up, 321 (27.6\%) participants had died.\textsuperscript{227} Those who died were older, more likely to be male, and more cognitively impaired than survivors. Baseline mean B-SIT scores were higher in survivors compared to those who died (9.2/12; SD = 2.1 vs. 8.4/12; SD = 2.3 respectively). After adjustment for age, sex and education level, the risk of death decreased by about 6\% for each additional correct choice on the B-SIT (HR 0.94, CI 0.90-0.98). Participants with a B-SIT score of 6 correct were $\approx$36\% more likely to die than a participant with a score of 11. Further analyses examined confounding by naming ability on the Boston Naming Test, disability on the Katz scale, cardiovascular risk factors and conditions, characteristic patterns of cognitive, social, and physical activity and depressive symptoms. In each analysis the association of olfactory impairment with mortality remained significant.\textsuperscript{227}
The association between olfactory impairment and 5-year all-cause mortality has been reported for the BMES population. Olfactory assessment was performed using the SDOIT. Olfactory impairment was defined as mild in participants scoring greater than 3 but less than 6 and moderate as 3 or less out of a total of eight possible responses. At baseline, persons with olfactory loss were more likely to be older and male and to have visual impairment, cognitive impairment, diabetes, angina, stroke, lower BMI, and poor self-rated health and higher serum total cholesterol. The mortality rate was more than double in the olfactory impaired group when compared to participants with normal olfaction (21.8%, n = 96 vs. 8.3%, n = 99). After adjustment for age and sex, mortality risk was significantly increased in persons with any olfactory loss compared to normosmics (HR 1.69, CI 1.26-2.27). This risk was higher in persons with moderate olfactory loss (HR 1.99, CI 1.42-2.80). After multivariable adjustment for other covariates associated with increased mortality, the increased risk associated with moderate olfactory loss remained statistically significant (HR 1.68, CI 1.10-2.56). The association became non-significant after the addition of cognitive impairment to the model (HR 1.51, CI 0.96-2.38).

The Washington Heights/Inwood Columbia Aging Project is a prospective cohort study of a stratified random sample of 50% of all Medicare beneficiaries aged 65 years and older from a specific region of North Manhattan, New York. Participants were recruited originally in 1992 and a new cohort recruited between 1999 and 2001. The associations between olfactory impairment and 4-year mortality (mean = 4.1 years, standard deviation = 2.6, range = 0-9.8 years), have been reported for this cohort. Participants with a history of stroke, PD, atypical Parkinsonian syndrome diagnoses, schizophrenia, and other psychotic disorders were excluded from the analysis of olfactory impairment and mortality.
All participants completed standardised neuropsychological testing of learning and memory, orientation, abstract reasoning, executive function, language, and visuospatial ability. Assessment of odour identification utilised the UPSIT. Mortality was ascertained and confirmed with family members and via the National Death Index. Age, gender, race/ethnicity, education and language of UPSIT administration were covariates in all analyses. Participant medical and social histories and qualitative grading of self-reported vision and hearing impairments were determined via interview.

Demographic and clinical variables were compared by chi-square tests and general linear models. The association of the UPSIT score with mortality was estimated using Cox proportional hazard models. The initial model included the UPSIT score alone. Subsequent models then estimated the association after adjustment for individual demographic covariates. The association of UPSIT score with mortality within 5 years was estimated by logistic regression analysis.

In the proportional hazard model (UPSIT score alone) the mortality risk was significantly increased with decreasing UPSIT score (HR, 1.068 per point interval, CI 1.053-1.083, p<0.001). After dividing UPSIT scores into quartiles, (0-20, 20-26, 26-31, and 31-40), compared to the fourth quartile with the highest UPSIT scores, HRs for mortality were 3.81 (CI 2.71-5.34), 1.75 (CI 1.23-2.50) and 1.58 (CI 1.09-2.30) for the first, second, and third quartiles respectively. The association between lower UPSIT score and mortality remained significant after adjustment for age, gender, education, ethnicity, language, modified Charlson medical comorbidity index, dementia, depression, alcohol abuse, head injury, smoking, body mass index, and vision and hearing impairment (HR 1.05 CI 1.03-1.07).
The National Social Life, Health, and Aging Project (NSHAP) is a nationally representative study of 3005 community-dwelling male and female older adults aged ≥57-≤85-years. The study was designed to examine associations between covariates and intimate social relationships, including marriage, family, social ties, and sexuality. The study collected information on physical and cognitive health, health behaviours, medications, and health service utilisation and a selection of biomarkers and other physiological assessments, including sensory functions.

Baseline data were collected during 2005 – 2006 by in-home interview. Data were collected from 1454 men and 1551 women living throughout the US. Five-year mortality data were collected by either speaking with the respondent (alive) or by conducting a proxy interview with a family member or neighbour or examining public records or news sources. Cases were pursued to determine whether respondents were likely alive, but not accessible for re-interview, or deceased. At 5-year follow-up, 430 participants were determined to be deceased and 2,565 were determined to be alive, leaving 10 cases in which it was unknown whether the participant was alive or not. These participants were excluded from the analyses. An additional 77 participants were excluded from the analyses due to missing data in one of the primary independent variables (odour identification, demographics and comorbidity index) A total of N=2,918 participants remained for analyses of the association between olfactory impairment and 5-year mortality risk.

Olfactory function was assessed using a validated abbreviated five item version of the Sniffin’ Sticks odour identification test. Each odorant was presented one at a time and participants were asked to identify each odorant by choosing from a set of four picture/word
prompts in a forced choice protocol. Refusals were coded as incorrect. The target odours were rose, leather, orange, fish, and peppermint. The number of errors made was used to categorise olfactory impairment as follows: anosmic = 4–5 errors; hyposmic = 2–3 errors; and normosmic = 0–1 error.

Adjustment was made for covariates known to be associated with mortality. Age was categorised into three groups: 57–64 years; 65–74 years and 75–85 years. Socioeconomic status was measured by education (highest degree or certification earned). Comorbid diseases were assessed with the Charlson Index modified for NSHAP. In addition, participants were asked whether a doctor had ever told them they had a particular disease. Nutrition measures included self-reported taste, the presence of poor appetite and body-mass index (BMI). Inability to perform one or more of seven activities of daily living (ADL) quantified frailty. Cognitive function was measured with a modified version of the Short Portable Mental Status Questionnaire (SPMSQ). Self-rated mental health was measured by a standard 5-point scale (excellent, very good, good, fair, or poor). Health behaviours affecting olfaction were current smoking, based on either salivary cotinine level or self-report, and problem drinking.

Statistical analyses were conducted with Stata Version 13.0 (Stata Corp LP, College Station, Texas, USA). Olfactory dysfunction (anosmia, hyposmia, or normosmia) or the number of odours incorrectly identified (0–5) was treated as the independent variable and death as the dependent variable in separate analyses. Multivariate logistic regression was used to estimate the associations between olfactory dysfunction and covariates of interest present at the baseline examination and 5-year mortality. P-values and 95% confidence intervals were based on the corresponding Wald statistic.
The response rate was 75.5% and nonresponders were similar demographically to the responders. The 5-year mortality rates stratified by baseline olfactory function were 12.5% overall, 39% for participants with anosmia, 19% for participants with hyposmia and 10% for participants with normosmia (p = 0.001). The risk of 5-year mortality was significantly increased for participants with anosmia and hyposmia compared to normosmics (OR 3.37, CI 2.04 – 5.07 and OR 1.47, CI 1.00 – 2.17 respectively) after adjustment for age, sex, comorbidity index and common diseases causing death.
Summary

The Prevalence of Olfactory Impairment

The prevalence of olfactory impairment is reported to be 10.6-24.5%\textsuperscript{168,170,171,173} although one small Korean study reported a prevalence of 80% in persons aged 65-89 years old.\textsuperscript{175} In most studies the prevalence was higher in males\textsuperscript{168,170,173} and increased with age,\textsuperscript{168,170,171,187} upper respiratory tract infection,\textsuperscript{168} previous stroke,\textsuperscript{168} the presence of nasal polyps\textsuperscript{173} and a diagnosis of epilepsy.\textsuperscript{168}

The association with current smoking is inconsistent. Murphy \textit{et al} reported a significant association\textsuperscript{168} while two other studies reported no statistically significant association.\textsuperscript{170,173} There were no significant associations reported between former smoking and olfactory impairment.\textsuperscript{168,170}

The sensitivity of self-reported olfactory impairment is low\textsuperscript{168,170,173,175,177} (20-44%) and decreases with age.\textsuperscript{168} The specificity of self-reported olfactory impairment is reported to be 85-94\%.\textsuperscript{168,170}
**The Associations Between Olfactory Impairment and Morbidity**

Normosmic persons with self-reported olfactory loss were found to be more likely to report an impact on quality of life when compared to hyposmic persons.\textsuperscript{173,177}

The BMES reported persons with quantitative olfactory impairment had statistically significant lower self-rated health and SF-36 scores after multivariable adjustment.\textsuperscript{185}

Olfactory impaired persons were also more likely to use community and informal supports and more likely to report difficulty in ADL.\textsuperscript{185}

In a study of persons with \( \geq \) six months of severe hyposmia or anosmia, participants were reported to have significantly lower SF-36 and QOD scores when compared to age and sex matched normosmic controls.\textsuperscript{187}

Significant associations between OI and QOL were also identified in patients of an outpatient clinic for taste and smell disorders.\textsuperscript{177} Frasnelli et al reported patients with quantitative olfactory impairment had statistically significant reduced NS-QOD scores when compared to age and sex matched normosmic controls. No significant associations were found with PS-QOD. Parosmia was significantly associated with reduced PS-QOD scores when compared to persons without parosmia, but there was no association between parosmia and NS-QOD.\textsuperscript{177}

No significant correlation was reported between measured olfactory loss and QOL after multivariable adjustment in a small cross sectional Korean population based study.\textsuperscript{175}

Study participants who voluntarily joined a support organisation for persons experiencing problems with smell were reported to have lower HRQOL in two studies when compared to
normosmic persons from the general population. Olfaction was not measured in these studies.

Women with self-reported or objective OI were reported to have significantly lower QOL when compared to their male counterparts.

Biological pathways linking olfactory impairment with depression have been proposed. Despite this, statistical associations in between olfactory impairment and depression appear weak. Few large population based studies exist.

The BMES reported no significant associations between olfactory impairment and depression overall. In persons older than 70 years, olfactory impairment increased the likelihood of depression if scored by the CESD-10 but not the MHI component of the SF-36. A Korean population based study of persons aged 65-89 years reported no significant association between olfactory impairment and depression after multivariable adjustment. A study of elderly persons with mild to moderate depression found no significant association with odour identification when compared to age and sex matched controls.

Three studies of persons with diagnoses of major depression were reviewed and had conflicting results. One study compared 51 depressed patients with 51 age and sex matched controls; no significant associations were found between olfactory impairment and depression. Another study of 18 persons with major depression and 18 age and sex matched controls reported a statistically significant association between lower BDI score and higher olfactory sensitivity to the odorant eugenol. In this study, persons with major depression had lower sensitivity to all odorants assessed when compared to matched controls.
but the differences were not significant. After treatment of depression, the statistically significant lower threshold score for eugenol in depressed patients became non-significant.\textsuperscript{193} The third study of persons with major depression compared 49 depressed persons with 58 age, sex and smoking matched controls. This study reported statistically significant associations between olfactory sensitivity, but not identification, and depression.\textsuperscript{195}

A study of 48 persons with no current or previous history of depression reported a statistically significant negative correlation between olfactory sensitivity and the BDI score (persons with higher BDI score having lower olfactory sensitivity) but not between olfactory discrimination and BDI score.\textsuperscript{202}

Two included studies examined the associations with olfactory impairment and depression in support groups for persons with olfactory impairment.\textsuperscript{182,182} Olfactory function was not formally assessed in these studies. Persons who were members of the organisation for anosmia were reported to be significantly more likely to have depression when compared to normosmic matched controls.\textsuperscript{182} The rates of anxiety and depression were also reported to be higher in members of the UK support group for persons with olfactory impairment, Fifth Sense, when compared to the reported rate of depression in the general population of the UK.\textsuperscript{182,198}
The Associations Between Olfactory Impairment, Cognitive Impairment and Parkinson Disease

Strong associations have been reported between olfactory impairment and cognitive impairment, vascular dementia, Alzheimer disease, subsequent cognitive decline and Parkinson Disease. Loss of olfactory function correlates with loss of brain volume in PD patients.

Olfactory dysfunction may differ between AD and PD. One study comparing Alzheimer disease with non-dementing Parkinson disease and an age and sex matched control group reported both the Alzheimer and Parkinson groups had statistically significant reduced odour identification scores when compared to the control group. Alzheimer, but not Parkinson disease participants had statistically significant increased olfactory threshold compared to the age and sex matched control group.
**The Associations Between Olfactory Impairment and Mortality**

Higher mortality rate has been reported in persons with olfactory impairment.\textsuperscript{224,226-228} Gopinath \textit{et al} reported the association between olfactory impairment and mortality rate to be statistically significant after multivariable adjustment for covariates associated with mortality, but not after further adjustment for cognitive impairment.\textsuperscript{228} Two other studies excluded persons with dementia and PD. Both reported significant associations between olfactory impairment and mortality after multivariable adjustment including cognitive impairment.\textsuperscript{226,227} Pinto \textit{et al}

Olfaction and neurodegenerative diseases are linked clinically and pathologically. Cognitive deficits may be one small component explaining the effect of odour identification on mortality, but may not account for the majority of the role olfaction plays on this outcome. Correcting for cognitive deficit may lead to underestimation of the association between OI and mortality.\textsuperscript{224,226-229}
Chapter Two: Methods
2.1 Study population: the Blue Mountains Eye Study
Choice of Site and Sampling Method

The Beaver Dam Eye Study is a population based study of eye disease in a small United States community that began in 1987 that a very high response rate of 88%. It was thought that an Australian study could obtain a similarly high response rate in a compact urban “town” population. It was also thought that using a single well defined geographical sample would achieve a higher response rate and lower costs compared to a multisite random cluster sample such as that used in the Melbourne Visual Impairment Project. It was determined that a sample size of greater than 4000 would be required to provide a power of 90-99% to detect the major risk factors of visual impairment and blindness.

The adjoining Blue Mountains urban townships of Katoomba, Leura and Medlow Bath (postcode 2780) and Wentworth Falls (postcode 2782), approximately 100 kilometres west of Sydney, were subsequently chosen. When the study commenced in 1991, this area had an older age distribution compared to the state of NSW average, a population size that was adequate to provide greater than 4000 participants and relatively stable, and was representative of the state of New South Wales in terms of ancestry, occupation, education and income level.\textsuperscript{236} The choice was reinforced by the enthusiastic support of eye care and general practitioners canvassed when planning the study.
Identification of Eligible Participants
Eligibility Criteria

To be eligible for the survey, three criteria were set:

1. Resident in the postcode areas at the time of the door to door census.
2. Permanent residency (residing at the address for more than 6 months per calendar year). Current residence was accepted if recently moved to the address.
3. Born before January 1, 1943. Aged 49 years or older at the time of the commencement of the survey.

There was no upper age limit.
Census of the Population

To identify eligible persons, a census was conducted by sequential door knock of all dwellings in the area by a trained team of 14 census collectors, many of whom had worked as census collectors for the Australian Bureau of Statistics (ABS). Census methods were identical to those used in the ABS national census (Census 91) on August 6, 1991. The census was conducted from November to December 1991 in the Blue Mountains urban townships of Katoomba, Leura and Medlow Bath (postcode 2780), and repeated from March to April 1993 in the Blue Mountains township of Wentworth Falls (postcode 2782). In total, 38 Census Collector Districts (CCDs) were surveyed including 28 in postcode area 2780 and 10 in postcode area 2782.

The census was preceded by a local newspaper article (Blue Mountains Gazette) and notification by mail to every residential and business address in the study area. Posters providing information about the study were displayed in prominent public places, optometrist offices and general practitioner surgeries. Detailed information regarding the Eye Study was also supplied to all healthcare providers servicing the area.

The aim of the census was to determine the names, birthdates, addresses and telephone numbers of all eligible permanent residents living in each CCD. Call-back visits to each house were made until contact was made with the resident either by door knocking or by telephone. An electronic telephone directory and council listings of rate payers sorted by street were obtained for this purpose. Leaflets were left in the letterbox at each visit that failed to contact the resident requesting them to telephone the Study information line. Subsequently, a letter addressed to “The Resident” that included a reply paid envelope was sent to each dwelling where no contact had been made. The letter explained the study and
requested an indication of whether or not eligible persons lived at the residence, regardless of whether they wished to participate. Final classification of no contact was made after five separate calls to the house were made at different times (morning, afternoon, evening) on different days of the week (including weekends) and after a total of three mail outs to the household identified no eligible residents.

An attempt was made at initial contact to complete a short questionnaire for each eligible resident. In some cases it was completed at the time of booking an appointment for the examination. Questions identified the person’s general practitioner, self-reported vision or hearing problems and past diagnoses of cataract, glaucoma, macular degeneration and diabetic retinopathy. Past medical history and last attendance to an optometrist or ophthalmologist was also determined. In some cases the questionnaire was completed by the spouse or relative of persons who were unable or refused to attend.

Persons who refused to provide answers to the door step questionnaire or to participate in the Eye Study were re-contacted up to ten times. Evening and weekend appointments, home visits and transport were offered at all stages of the recruitment process. Financial incentives were not offered at any time.
2.2 Interview and Examination Procedures
Baseline Study

After the initial contact and interview, an information sheet was given to each eligible resident. This provided details about the Eye Study, and indicated that they would be invited to take part at a later date. All identified eligible residents were subsequently invited to attend the study examinations at the Blue Mountains District ANZAC Memorial Hospital. The protocol received ethical approval from the Western Sydney Area Health Service Human Research and Ethics Committee. Signed informed consent was obtained from all participants at the time of the examination.
**Study Protocol**

The examinations were conducted according to a standardised study protocol based on the Beaver Dam Eye Study protocol. This allowed meaningful comparison with other Australian and international population based studies. The Blue Mountains Eye Study questionnaire and flow sheet is provided in appendix A. The examinations began in January 1992 and were completed in January 1994. Trained interviewers administered a comprehensive demographic and medical questionnaire for each participant. The questionnaire detailed past and current medications, family and social history, medical and surgical history, alcohol and smoking history and a self-rating of global health and vision. The questionnaire also assessed independence, mobility and exercise, women’s health, coffee and tea intake, driving ability and sun exposure. Questions detailing previous diagnoses of, or a family history of, specific eye diseases were also asked.

The examination and interview procedures were divided into four sections conducted in four separate rooms to facilitate completion. The whole procedure took on average one and a half hours to complete.
Measurement of Visual Acuity and Refractive Error

The current glasses of each participant were neutralised using the Humphrey automatic lens analyser model 330 (Allergan Humphrey, San Leandro, CA) and the printout affixed to the study flow sheet. The type of glasses was also coded.

Objective refraction of each participant was performed using the Humphrey 530 Automatic Refractor (Allergan Humphrey, San Leandro, CA). The sphere, cylinder and a reflex reading was measured for each eye and the printout affixed to the study flow sheet.

Visual acuity was measured using a retro-illuminating logarithm of the minimum angle of resolution (LogMAR) chart (Vectorvision CSV-1000™ Vectorvision Inc, Dayton, Ohio) read at 2.4 metres. The CSV-1000 uses a fluorescent light source and monitors and calibrates the light level to 85 candelas per square metre ± 0.1 log units using a series of photocells.

Distance visual acuity was first assessed for each eye using current distance glasses if worn, then with a 1.2mm pinhole aperture held over the current distance glasses and finally after subjective refraction. If no letters could be read at 2.4 metres, the chart was moved to 0.95 metres (0.4 log units closer to the participant). If no letters could be read at 0.95 metres, vision was assessed as “count fingers” at 0.5 metres, “hand movements”, “perception of light”, or “no perception of light. Table 2.1 lists the equivalent scores for the LogMAR and Snellen charts.

Distance visual acuity was first measured in the right eye and then the left, using a different test face for each eye. With the opposite eye covered, the participant was asked to slowly read from the first letter on the left hand side at the top of the chart. Each letter that was read
correctly was circled on a scoresheet identical to the face of the chart. Only one attempt was allowed for each letter. If the participant had difficulties with any letter they were encouraged to guess.
Table 2.1 Equivalent letter scores comparing the logarithm of the minimum angle of resolution (logMAR) and Snellen charts

<table>
<thead>
<tr>
<th>Letter Score 2.4 metres</th>
<th>Snellen Visual Acuity 2.4 metres</th>
<th>logMAR Visual Acuity 2.4 metres</th>
<th>Snellen Visual Acuity 0.95 metres</th>
<th>logMAR Visual Acuity 0.95 metres</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>6/60</td>
<td>1.0</td>
<td>6/150</td>
<td>1.4</td>
</tr>
<tr>
<td>10</td>
<td>6/48</td>
<td>0.9</td>
<td>6/120</td>
<td>1.3</td>
</tr>
<tr>
<td>15</td>
<td>6/38</td>
<td>0.8</td>
<td>6/95</td>
<td>1.2</td>
</tr>
<tr>
<td>20</td>
<td>6/30</td>
<td>0.7</td>
<td>6/75</td>
<td>1.1</td>
</tr>
<tr>
<td>25</td>
<td>6/24</td>
<td>0.6</td>
<td>6/60</td>
<td>1.0</td>
</tr>
<tr>
<td>30</td>
<td>6/19</td>
<td>0.5</td>
<td>6/48</td>
<td>0.9</td>
</tr>
<tr>
<td>35</td>
<td>6/15</td>
<td>0.4</td>
<td>6/38</td>
<td>0.8</td>
</tr>
<tr>
<td>40</td>
<td>6/12</td>
<td>0.3</td>
<td>6/30</td>
<td>0.7</td>
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</tr>
<tr>
<td>50</td>
<td>6/7.5</td>
<td>0.1</td>
<td>6/19</td>
<td>0.5</td>
</tr>
<tr>
<td>55</td>
<td>6/6</td>
<td>0.0</td>
<td>6/15</td>
<td>0.4</td>
</tr>
<tr>
<td>60</td>
<td>6/4.8</td>
<td>-0.1</td>
<td>6/12</td>
<td>0.3</td>
</tr>
<tr>
<td>65</td>
<td>6/3.8</td>
<td>-0.2</td>
<td>6/9.5</td>
<td>0.2</td>
</tr>
<tr>
<td>70</td>
<td>6/3.0</td>
<td>-0.3</td>
<td>6/7.5</td>
<td>0.1</td>
</tr>
</tbody>
</table>
Distance visual acuity was recorded as the number of letters read correctly from 0 to 70 and then calculated according to the test distance. Participants with 54 letters or better read correctly at 2.4 metres without glasses were recorded as emmetropic. Participants with 54 letters or better read correctly at 2.4 metres with their current glasses were not refracted. The results from the automatic lens neutraliser were recorded as the refractive error. If visual acuity was less than 54 letters read correctly then subjective refraction was performed using the Beaver Dam modification of the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol using the 0.5D and 0.25D Jackson cross cylinder. Refractive error was tested in 0.25D steps. Cylinder powers were measured and recorded in the negative form. Astigmatic axes were measured to the nearest 2.5 degrees for powers of 1D or less, or to the nearest degree for higher power. The result from the automatic lens neutraliser was used as the initial trial lens.
Examination of the Eye

The eye lids, conjunctiva and anterior chamber of the eye were examined using a slit-lamp. Participants with a shallow anterior chamber or iris clip intraocular lens were identified and excluded from the dilated examination. The remaining participant’s pupils were dilated with Tropicamide 1% and Phenylephrine 10% and the lens and retina examined. The examination included retro-illumination photographs of the lens and stereoscopic photographs of the optic disc and retina.
Identification of Eye Disease

The presence of cataract was determined by slit-lamp examination and documented with both slit-lamp (TopconSL-7e camera, Topcon Optical Co., Tokyo, Japan) and retro-illumination (Neitz CT-R cataract camera, Neitz Instrument Co., Tokyo, Japan) lens photographs. Details of the cataract photographs and grading system used in the Blue Mountains Eye Study have been previously reported and closely follow the Wisconsin Cataract Grading System.

Retinal diseases were diagnosed by the examining ophthalmologist (PM) and confirmed by grading of stereoscopic retinal photographs. Details of the age related maculopathy photographs and grading system used in the Blue Mountains Eye Study have been previously reported and closely follow the Wisconsin Age-Related Maculopathy Grading System. Inter-grader and intra-grader reliability was assessed on a random subsample of gradable photographs with good agreement achieved. Diabetic retinopathy was diagnosed if typical retinopathy lesions were present in subjects with a history of diabetes or with fasting blood glucose ≥ 7.8 mmol/l. Retinopathy lesions were also graded in non-diabetic participants.

Intraocular pressure (IOP) was measured using Goldmann applanation tonometry. Open-angle glaucoma was diagnosed by the presence of glaucomatous visual field changes using automated perimetry (Humphrey 30-2 test) with matching optic disc rim thinning and an enlarged cup to disc ratio (>0.6) or cup to disc ration asymmetry (>0.3) between the two eyes.

Spherical equivalent refraction, measured in dioptres, was calculated using the spherical dioptric power plus half the cylindrical power. Myopia was defined as a mean spherical equivalent of the two eyes ≥ -1 dioptre. Unilateral amblyopia was diagnosed if the best-
corrected visual acuity was $\geq 6/9$ in the affected eye and was not attributable to any underlying structural abnormality of the eye or visual pathway.

Estimation of the proportional causes contributing to decreased visual acuity was made for each eye with impaired vision by the examining ophthalmologist (PM). Confirmation of these causes was made during masked grading of the lens and retinal photographs.
**Socio-demographic variables**

Socio-demographic variables were evaluated and defined dichotomously. Attainment of higher education was determined by the achievement of a trade certificate or higher qualification, according to the ABS Classification of Occupation. Occupational prestige was assessed based on the participant’s principle occupation using the Daniel Occupational Prestige Scale. Occupational prestige was categorised as “average to high” if the score was $\leq 4.0$ (equivalent to a trade certificate or better) or low if the score was $> 4.0$. It was also determined by questionnaire whether the participant owned their own home, was renting or was living in a relative’s home. The participant’s marital status, whether they lived alone, or with a spouse or other persons was also determined by questionnaire.
**Medical, Smoking and Alcohol History**

Medical, alcohol and smoking histories were determined by interviewer-administered questionnaire by a trained examiner. A history of angina, myocardial infarction, diabetes, hypertension, stroke, arthritis, asthma, migraine, gout, thyroid disease, Parkinson disease, dementia, kidney disease, liver disease or cancer was determined by responses to the question “Has a doctor advised you that you have….?” History of smoking was defined as never, past or current smoking. Current smokers included those who had stopped smoking within the past year. Alcohol consumption was categorised as none or light to moderate (≤4 standard drinks per day) and heavy (>4 standard drinks per day). Participants were also asked if they had hearing loss.
Anthropometric Variables, Self-Rated health, Functional Disability and use of Support Services

Weight in kilograms, height in meters, and systolic and diastolic blood pressures (Auscultatory) were recorded. Body mass index was calculated using the formula: weight (kg)/height (m)². Functional assessments were performed for all participants by asking questions about the participant’s ability to complete activities of daily living, such as driving, cleaning, and shopping and whether they received home help or whether they were able to do out alone and how frequently. Disability in walking was assessed by one trained examiner based on an observed difficulty in walking or the use of a cane, walking frame or wheelchair. Participants were also asked if they had fallen in the previous twelve months and whether they walked regularly for exercise. Self-rated health was assessed by questionnaire and dichotomised into two levels: poor or fair vs. good or excellent.
Use of Eye Care Services

Details of the proceeding two visits to either an ophthalmologist or optometrist were documented, including the name and office address of the eye care practitioner. If an ophthalmologist had not been seen in the previous two visits the participant was asked if they had ever seen an ophthalmologist.

The designation of the optometrist and ophthalmologist was verified by reference to a booklet of ophthalmologist members of the Royal Australian College of Ophthalmologists. The interviewer was trained regarding the names of ophthalmologists and optometrists working in the local area and in Western Sydney and then referred to the booklet as required. The names of the ophthalmologists and optometrists given by the participants were again cross checked to confirm their status during data entry and cleaning procedures.
Examination of Nursing Home Residents

To provide a representative sample of nursing home residents, three Blue Mountains nursing homes (Burlington, Martyn Claver and Sans Souci) were selected from the postcode area 2870. Questionnaires and examinations were attempted on all eligible nursing home residents after obtaining informed consent form the either the resident or their legal guardian. The nursing home medical records were also reviewed to complete the questionnaires. Visual acuity was assessed with the CSV-1000 logMAR with current glasses if worn and a subjective refraction attempted if their visual acuity was less than 54 letters read correctly. Participants who were unable to read letters on the vision chart were assessed using the Sheridan-Gardiner letter matching test, providing Snellen equivalent visual acuity. Bjerrum visual field testing was attempted in all nursing home participants. The eye lids, conjunctiva and anterior chamber of the eye were examined using a slit-lamp (standard or portable). Intraocular pressure was measured using either Goldmann applanation or Tonopen tonometry. The pupils were dilated with 1% Tropicamide and 10% Phenylephrine. Direct and indirect ophthalmoscopy was performed and biomicroscopy of the retina and optic disc attempted in all nursing home participants.
Longitudinal Studies

The Blue Mountains Eye Study has been repeated every five years since the baseline examinations began in 1992. The baseline study examined 3654 residents aged >49 years during 1992 to 1994 (BMES 1), representing a participation rate of 82.4%. Of the baseline participants, 2335 (75.1% of survivors) returned for five year follow-up examinations during 1997-9 (BMES 2), and 1952 participants (53.4% of the original cohort, or 76.6% of survivors) returned for ten year follow-up examinations during 2002-4 (BMES 3). At the BMES 2, a detailed hearing questionnaire and the mini mental state examination was added to the study protocol and repeated at follow-up (BMES 3 and 4). At BMES 3 a detailed olfactory questionnaire and examination was also added to the study protocol. The study questionnaires and flow sheets for BMES 4 are provided in appendix A.
Identification of Deaths

To identify and confirm persons who died after the baseline examination, demographic information including surname, first and second names, gender and date of birth of the 3654 participants were cross-matched with Australian National Death Index (NDI) data for deaths, to the end of 2005. A probabilistic record linkage package was used, adopting a multiple pass procedure in which both data sets were grouped based on different characteristics (e.g. date of birth, name, sex) each time. Matches were divided into exact and non-exact. A pair of records matched on each demographic characteristic was defined as an exact match. All non-exact matched records were examined manually and accepted if there was only one non-exact matched characteristic that was not critical. Information provided by family members during follow-up was also included if the participant was reported to have died on or before December 2005. The *International Classification of Diseases, Ninth Revision* 245 and *International Statistical Classification of Diseases, 10th Revision* 246 cause of death codes were also obtained. The primary cause of death was used in statistical modelling.
Hearing Questionnaire

An audiologist-administered questionnaire (Appendix A2) included history of any self-perceived hearing problem, including its severity, onset and duration, whether primary care practitioners or other professionals had been consulted and if a hearing aid had been provided. Hearing-related questions included family history of hearing loss, past medical or surgical treatment of otologic conditions, diseases associated with hearing loss and risk factors for ear disease. Other questions addressed exposure to noise at work, or during military service or leisure activities, the presence of tinnitus and past use of ototoxic drugs. The severity of the noise exposure was subjectively classified in three ways: mostly quiet, tolerable level, unable to hear speech. The duration of the noise exposure was categorised in years.
**Hearing Examination**

Pure-tone audiometry was performed by audiologists in sound treated booths, using TDH-39 earphones and a Madsen OB822 audiometer (Madsen Electronics, Copenhagen, Denmark). Audiometer calibration was conducted regularly and complied with the International Standards Organization protocol 389 (1991). Audiometric thresholds for air conducted stimuli (right and left ears) were established for frequencies at 250, 500, 1000, 2000, 4000, 8000, and 8000 Hz, with 3000 Hz added if a 20 dB difference existed between the 2000 & 4000 Hz thresholds. Bone conduction was measured if AC thresholds were greater than 15 dB HL for the frequencies 500, 1000, 2000, and 4000 Hz. Acoustic impedance and speech discrimination testing was also conducted.
Olfactory Examination

Participants were tested individually with the San Diego Odour Identification Test (SDOIT), an 8-item odor identification test with a test-retest reliability relatively similar to the 40-item UPSIT ($r = 0.86$ SDOIT; $r = 0.94$ UPSIT). Odorants were presented to participants in random order, in an opaque container covered with gauze. An inter-stimulus pause of 45 seconds was used to prevent adaptation. A picture board illustrating the odorants as well as distracters was used for participants to identify each odorant. Scores were calculated by the number of odorants identified correctly. Self-reported olfactory loss was also determined by interviewer-administered questionnaire (Appendix A).
The Blue Mountains Hearing Study

The Blue Mountains Hearing Study (BMHS) is a population-based survey of age-related hearing loss in a representative older Australian community. The BMHS invited participants who attended the second cross-sectional survey of the Blue Mountains Eye Study (BMES 2). Persons who moved into the study area or study age group were identified by a repeat door-to-door census in 1999 and were invited to participate. The BMHS was conducted during 1997 to 2000. The study was approved by the Human Research Ethics Committee of the University of Sydney and was conducted adhering to the tenets of the Helsinki Declaration. Signed informed consent was obtained from all the participants at each examination. The hearing questionnaire and examinations for the Blue Mountains Hearing Study were identical to those described for BMES 2 onwards.
2.3 Definitions

- Visual impairment was defined as: presenting visual impairment (PVI), VA less than 6/12 Snellen equivalent (<40 letters read correctly) in the better eye using current glasses; correctable visual impairment (CVI), PVI correctable to 6/12 Snellen equivalent or better by subjective refraction; and non-correctable visual impairment (NCVI), PVI correctable to worse than 6/12 Snellen equivalent in the better eye after subjective refraction.

- Hearing impairment was defined as: any hearing impairment, the pure-tone average of air-conduction hearing thresholds >25 decibels hearing level (dB HL) for the pure tone average (PTA) of four frequencies (0.5, 1, 2, and 4 kHz) in the better ear; mild hearing impairment, >25 to ≤45 dB HL; moderate to severe hearing impairment, >45 dB HL for the average of four frequencies (0.5, 1, 2, and 4 kHz) in the better ear.

- Olfactory impairment was defined as: any olfactory impairment, less than 6 correct responses; mild olfactory impairment, less than six but greater than three correct responses; and moderate, three or less correct responses out of a total of eight possible responses in the SDOIT.

- The definition of hypertension was based on the 2003 World Health Organization/International Society of Hypertension guidelines. Hypertension was defined as: any hypertension, systolic blood pressure was greater than 140 mm Hg or diastolic greater than 90 mm Hg or previously diagnosed with hypertension and taking antihypertensive medications; hypertension stage 1, systolic blood pressure 140 to 159 mm Hg or if diastolic blood pressure 90 to 99 mm Hg; Hypertension stage 2, previously diagnosed with hypertension and taking antihypertensive medications or systolic blood pressure 160 mmHg or greater or diastolic blood pressure 100mmHg or greater.
• Body mass index (BMI) was calculated using the formula weight (kg)/ height (m)² and was defined as; underweight, <20 kg/m²; normal weight, 20-25 kg/m²; overweight, 26-30 kg/m²; and obese (>30 kg/m²)

• Disability in walking at baseline was defined as present if the participant was observed by a trained examiner to have walking difficulties, or used walking aids or a wheelchair

• Cognitive impairment was defined as mini mental state examination score of ≤24

• One unit of alcohol was defined as 12 grams

• High serum urate was defined as serum urate >0.5 mmol/l

• Renal impairment was defined as GFR<30 mL/minute/1.73m². There was no significant difference when estimating GFR using the Cockcroft-Gault or the Modification of Diet in Renal Disease (MDRD) equation. Results of Cockcroft-Gault estimation are used

• Hypercholesterolemia was defined as total cholesterol >5.2 mmol/l
2.4 Data Handling and Statistical analysis

Data were entered into Dbase IV (BMES 1) or Microsoft Access (BMES 2, BMES 3) using automatic skips and range checks. Statistical analyses were performed using SAS software v9.13 (SAS Institute, Cary, NC) and Mplus.\textsuperscript{250}

Simple statistics included student t tests for comparing means and chi-square tests for comparing proportions. Age and sex and multivariable adjusted Cox regression models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI). Age and sex and multivariable adjusted logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals.

Log-linear models were used to assess the concomitant presence of the three sensory impairments (visual, auditory and olfactory). Observed frequencies of concomitant sensory impairments were compared to the expected frequencies estimated assuming that they occur independently (no clustering tendency). Models that included two- and three-way interactions among the three impairments were used to test the significance of these interaction terms. The likelihood ratio was used to choose the best fitting models.\textsuperscript{251}

Structural equation modelling (SEM) pathway analysis\textsuperscript{252} was used to model the relationship between visual or hearing impairment with mortality and co variables found to be significantly associated with mortality by Cox regression. The model was fit using maximum likelihood and Monte Carlo integration methods. Standard errors were calculated using the delta method and hazard rates obtained from the coefficients by exponentiation. Each mediating variable was adjusted for age, gender and sensory impairment (visual or hearing). The indirect effect of the sensory impairment was then calculated for each co-variable by
multiplying the effects of that co-variable on mortality and the sensory impairment on that co-variable. The total indirect effect of the sensory impairment was then calculated by summing the coefficients of the estimated indirect effects of each mediating variable, and then converting to hazard ratios. The total estimated effect of the sensory impairment on mortality was calculated by summing the coefficients of the indirect and direct effects, and then converting to hazard ratios (Figure 2.2). Models were simplified by removing indirect pathways for individual co-variables that were not significant at a p value level of 0.1.

A p value of less than 0.05 was considered statistically significant.
1 Figure 2.1 Calculation of direct, indirect and total effects using structural equation modelling pathway analysis

\[ \gamma = \text{regression coefficient} \]

Direct = \( \gamma_1 \)

Indirect = \( \gamma_2 \gamma_3 \)

Total = \( \gamma_1 + \gamma_2 \gamma_3 \)
Chapter Three: *Prevalence and Neurodegenerative or Other Associations with Olfactory Impairment in an Older Community*
Abstract

**Purpose:** To determine the prevalence of olfactory impairment and its associations with neurodegenerative and other conditions in an older population.

**Methods:** Olfactory ability, medical conditions and cognitive function were assessed in 1636 participants, aged ≥60 years and enrolled in the Blue Mountains Eye Study (2002-4). Assessment was by questionnaire, clinical examination, blood testing and the San Diego Odor Identification Test, with subjects classified as having no impairment (score 6, 7 or 8), mild impairment (4 or 5), moderate impairment (≤3), or any impairment (<6).

**Results:** The prevalence of any olfactory impairment was 27.0% (95% confidence interval, CI 22.9-31.4%). After multivariate adjustment, the likelihood increased 2-fold with each decade of life after 60 years (odds ratio, OR, 2.22, CI 1.8-2.7) and was higher in men than women (OR 2.0 CI 1.5-2.7). Inverse associations were observed between olfactory impairment and body mass index (OR per 5 kg/m² increase, 0.8, CI 0.7-0.9) and between moderate impairment and hypertension (OR 0.6, CI 0.4-0.9). There was no significant relationship with angina, previous myocardial infarction or diabetes. Persons with Parkinson disease had an increased likelihood of both mild (OR 9.8, CI 2.0-47.5) and moderate impairment (OR 16.1, CI 3.8-68.2), as did persons with impaired cognitive function (OR 3.3, CI 1.3-8.6 and OR 3.7, CI 1.5-9.6, respectively).

**Conclusions:** Over one in four older persons had olfactory impairment. The prevalence was higher in males, increased with age and decreasing BMI, and was substantially higher among persons with Parkinson disease and cognitive impairment.
Background

The sense of smell is clinically under-appreciated and infrequently tested but makes a significant contribution to the quality of life and the ability to experience pleasure. Olfaction determines flavor and serves as a warning for smoke, toxic fumes and spoiled foodstuffs. It has been long presumed that loss of olfaction in older persons is a consequence of the normal biological aging process. The prevalence of impaired olfaction in the “healthy” ageing population may, however, be greater than previously thought, and co-morbidities that increase with advancing age may be responsible for the observed increase in the prevalence of impaired olfaction.

Olfactory dysfunction in older age is associated with impaired global cognition and a more rapid decline in perceptual processing speed, and in episodic and verbal memory. Olfactory impairment and the lack of ability to self-report such impairment predicts future cognitive decline and predates Parkinson disease by four or more years. Olfactory testing may therefore be a useful screening tool to detect individuals at-risk for neurodegenerative disorders in older persons.

Olfactory dysfunction is also linked to numerous other disorders including diabetes, renal disease, epilepsy, and many others. Olfactory dysfunction also correlates with food intake and nutrition in the elderly, and is associated with nursing home placement. Very few studies to date have examined the link between cardiovascular risk factors or disease with olfactory impairment despite their adverse effect on cognitive function. To our knowledge, no study has examined the potential association between total cholesterol level and olfaction despite there being a link
between olfaction, Alzheimer Disease and APOE ε4 which also predicts familial hypercholesterolemia.

In this study, we examine the prevalence of olfactory impairment in the surviving participants of the Blue Mountains Eye Study (BMES) who returned to 10-year follow-up examinations during 2002-2004. We aimed to investigate the association of olfactory impairment with cardiovascular risk factors and disease, and to confirm the relationship between neurodegenerative disease and olfactory dysfunction in this population. We hypothesized that due to the adverse effect of cardiovascular risk factors and disease on cognitive function, their presence would be positively associated with the prevalence of smell impairment in older persons. Further, given that APOE ε4 increases the risk of developing hypercholesterolemia and Alzheimer disease, we hypothesized that there would be a positive correlation between total cholesterol level and smell impairment.
Methods

The San Diego Odour Identification Test (SDOIT) and related olfactory and taste questions were a component of the BMES 3 examination. Complete olfaction and taste data were obtained from 1636 of 1952 (83.8%) BMES 3 participants.

Participants were tested individually with the SDOIT, an 8-item odor identification test with a test-retest reliability relatively similar to the 40-item UPSIT (r = 0.86 SDOIT; r = 0.94 UPSIT). We defined mild olfactory impairment as less than six but greater than three correct responses and moderate as three or less correct responses out of a total of eight possible responses.

Information about self-reported olfactory abnormality medical problems and cognitive function was obtained from an interviewer administered questionnaire (Chapter 2, Methods and Appendix A, BMES 4 Study Questionnaire and Flow Sheet). Patients who answered that they had a reduced or no sense of smell were considered to have self-reported olfactory impairment. Participants with mini mental state exam scores <24 were considered cognitively impaired. Body mass index (BMI) was calculated using the formula weight (kg)/ height (m)^2 and was categorized as underweight (<20 kg/m^2), normal weight (20-25 kg/m^2), overweight (26-30 kg/m^2) and obese (>30 kg/m^2). Fasting blood samples were used to determine creatinine, blood glucose, total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL) and triglyceride levels. There was no significant difference when estimating GFR using the Cockcroft-Gault or the Modification of Diet in Renal Disease (MDRD) equation. Results of Cockcroft-Gault estimation are used.
All statistical analyses were performed using Statistical Analysis System software v9.13 (SAS Institute, Cary, NC). Chi-square tests were used for proportions and Student-t tests for means, to examine categorical and continuous variable characteristics of participants with and without olfactory impairment. Multivariable-adjusted logistic regression models were constructed to estimate associations between cardiovascular disease risk factors, cardiovascular disease and neurodegenerative conditions. Co-variables included age, sex, smoking, nasal congestion, BMI, GFR <30, hypercholesterolemia (>5.2 mmol/L), stage I and II hypertension, stroke, Parkinson disease, impaired cognitive function (MMSE <24) and epilepsy. Odds ratios (OR) and 95% confidence intervals (CI) are presented. A p value of less than 0.05 was considered statistically significant.
Results

The mean age of the 316 subjects who did not have olfaction data collected was 75.7 years and 65.2% were female, compared with a mean age 73.5 years among participants included in this report, 58.1% of whom were female.

Of the 1636 participants, 441 participants had impaired olfaction (27.0%, CI 22.9-31.4%). The age- and sex- specific prevalence of olfactory impairment is shown in Figure 3.1. Of the 8 odors tested, honey and cinnamon were the most difficult for impaired participants to detect as shown in Figure 3.2. The highest prevalence of mild and moderate olfactory impairment was observed in persons aged 80 years and over and both levels were more frequent in men than in women (16.8% vs. 11.7% and 18.0% vs. 9.7%, respectively).
2 Figure 3.1 Prevalence of mild and moderate olfactory impairment stratified by age, sex and severity in BMES participants.
Figure 3.2 The frequency distribution of odors correctly identified by those with impaired olfactory function.
Baseline characteristics of participants with and without olfactory impairment are shown in Table 3.1. Compared to those with normal olfaction, participants with impaired olfaction were more likely to be male, aged older than 70 years, or to smoke. They were also more likely to have current nasal congestion, be underweight or cognitively impaired. They were also more likely to have Parkinson disease, renal failure, diabetes or a previous history of stroke or angina (Table 3.1).
Table 3.1 Characteristics of the Blue Mountains Eye Study 10-year follow-up examination participants by olfactory impairment

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Olfactory impairment</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>Yes (n=441)</td>
<td>No (n=1195)</td>
<td>p value</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>238 (54.0)</td>
<td>447 (37.4)</td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Women</td>
<td>203 (46.0)</td>
<td>748 (62.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-69</td>
<td>73 (16.6)</td>
<td>468 (39.2)</td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>70-79</td>
<td>191 (43.3)</td>
<td>530 (44.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥80</td>
<td>177 (40.1)</td>
<td>197 (16.5)</td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Self reported loss of smell</td>
<td>103 (32.2)</td>
<td>70 (7.0)</td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>83 (18.8)</td>
<td>150 (12.6)</td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>202 (46.5)</td>
<td>679 (57.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>197 (45.4)</td>
<td>417 (35.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>35 (8.1)</td>
<td>76 (6.5)</td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Body mass index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>25 (5.8)</td>
<td>34 (2.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>175 (40.2)</td>
<td>501 (42.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>73 (16.8)</td>
<td>311 (26.4)</td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>301 (68.9)</td>
<td>849 (71.4)</td>
<td></td>
<td>0.58</td>
</tr>
<tr>
<td>Diabetes</td>
<td>71 (18.9)</td>
<td>154 (14.3)</td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>Stroke a</td>
<td>37(8.5)</td>
<td>57 (4.8)</td>
<td></td>
<td>0.005</td>
</tr>
<tr>
<td>Angina a</td>
<td>79 (18.2)</td>
<td>159 (13.4)</td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>Myocardial infarction a</td>
<td>50 (11.6)</td>
<td>112 (9.5)</td>
<td></td>
<td>0.22</td>
</tr>
<tr>
<td>Mean total cholesterol (mmol/L)</td>
<td>4.7 ± 1.6</td>
<td>5.1 ± 1.5</td>
<td></td>
<td>0.09</td>
</tr>
<tr>
<td>Glomerular filtration rate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-60</td>
<td>176 (47.4)</td>
<td>333 (31.0)</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&lt;30</td>
<td>20 (5.4)</td>
<td>15 (1.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impaired cognitive function b</td>
<td>32 (7.6)</td>
<td>17 (1.5)</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Parkinson disease</td>
<td>19 (4.3)</td>
<td>3 (0.3)</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Epilepsy a</td>
<td>4 (0.93)</td>
<td>3 (0.3)</td>
<td></td>
<td>0.07</td>
</tr>
</tbody>
</table>

aSelf-reported
bMini mental state exam score <24
Table 3.2 lists the odds ratios with 95% confidence intervals for associations after adjusting for age and sex. Increasing age, male sex, current nasal congestion, past and current smoking, BMI >30, impaired cognitive function and Parkinson disease were all significantly associated with increased odds for mild and, except for smoking and BMI, moderate smell impairment, after adjusting for age and sex (Table 3.2). Glomerular Filtration Rate (GFR) <30, stroke and epilepsy were associated with increased odds of moderate smell impairment only. Hypercholesterolemia and stage II hypertension were associated with decreased odds of moderate smell impairment. When analyzed separately, significant associations were not observed between fasting HDL or triglyceride levels and olfactory impairment (data not shown). There was no significant association between other cardiovascular risk factors or diabetes and smell impairment, after adjusting for age and sex. After adjusting for variables listed in Table 3.3, all of the age-sex-adjusted associations remained, with the exception of epilepsy (Table 3.3).
### Table 3.2: Age- and sex-adjusted associations (odds ratios, OR, and 95% confidence intervals) with olfactory impairment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mild Impairment n (%)</th>
<th>p Value</th>
<th>Moderate Impairment n (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td></td>
<td>OR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Age per 10 years</td>
<td>-</td>
<td>&lt;0.001</td>
<td>-</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male Sex</td>
<td>115 (17)</td>
<td>&lt;0.001</td>
<td>123 (18)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nasal Congestion</td>
<td>45 (19)</td>
<td>0.003</td>
<td>38 (16)</td>
<td>0.01</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>104 (17)</td>
<td>0.01</td>
<td>93 (15)</td>
<td>0.95</td>
</tr>
<tr>
<td>Current</td>
<td>26 (23)</td>
<td>&lt;0.001</td>
<td>9 (8)</td>
<td>0.84</td>
</tr>
<tr>
<td>BMI a &lt;20</td>
<td>13 (22)</td>
<td>0.16</td>
<td>12 (20)</td>
<td>0.04</td>
</tr>
<tr>
<td>20-25</td>
<td>84 (17)</td>
<td>1.0 (Ref)</td>
<td>78 (16)</td>
<td>1.0 (Ref)</td>
</tr>
<tr>
<td>26-30</td>
<td>85 (13)</td>
<td>0.08</td>
<td>90 (13)</td>
<td>0.61</td>
</tr>
<tr>
<td>&gt;30</td>
<td>40 (10)</td>
<td>0.02</td>
<td>33 (9)</td>
<td>0.08</td>
</tr>
<tr>
<td>Impaired cognitive function b</td>
<td>10 (5)</td>
<td>0.01</td>
<td>22 (45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Parkinson disease</td>
<td>7 (32)</td>
<td>0.001</td>
<td>12 (55)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>1 (14)</td>
<td>0.66</td>
<td>3 (43)</td>
<td>0.01</td>
</tr>
<tr>
<td>GFR c ≥60</td>
<td>103 (11)</td>
<td>1.0 (Ref)</td>
<td>72 (8)</td>
<td>1.0 (Ref)</td>
</tr>
<tr>
<td>&lt;60-30</td>
<td>87 (17)</td>
<td>0.77</td>
<td>89 (17)</td>
<td>0.47</td>
</tr>
<tr>
<td>&lt;30</td>
<td>4 (11)</td>
<td>0.90</td>
<td>16 (46)</td>
<td>0.01</td>
</tr>
<tr>
<td>Hypercholesterolaemia (&gt;5.2 mmol/L)</td>
<td>6 (8.3)</td>
<td>0.30</td>
<td>18 (25)</td>
<td>0.02</td>
</tr>
<tr>
<td>Stroke</td>
<td>17 (18)</td>
<td>0.15</td>
<td>20 (21)</td>
<td>0.04</td>
</tr>
<tr>
<td>Angina</td>
<td>36 (15)</td>
<td>0.80</td>
<td>43 (18)</td>
<td>0.24</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>25 (15)</td>
<td>0.84</td>
<td>25 (15)</td>
<td>0.64</td>
</tr>
<tr>
<td>Hypertension d Stage I</td>
<td>24 (11)</td>
<td>0.16</td>
<td>29 (14)</td>
<td>0.47</td>
</tr>
<tr>
<td>Stage II</td>
<td>133 (14)</td>
<td>0.20</td>
<td>115 (12)</td>
<td>0.01</td>
</tr>
<tr>
<td>Diabetes</td>
<td>34 (15)</td>
<td>0.38</td>
<td>37 (16)</td>
<td>0.07</td>
</tr>
<tr>
<td>Gout</td>
<td>30 (16)</td>
<td>0.97</td>
<td>36 (19)</td>
<td>0.49</td>
</tr>
</tbody>
</table>

a Per 5 kg/m² increase in body mass index (BMI)
b Mini-mental state exam score <24
c Glomerular filtration rate - GFR
d Hypertension stage I - 140/90-160/100; stage II: >160/100 or treated
Table 3.3 Multivariable-adjusted associations (odds ratios, OR, and 95% confidence intervals) for all characteristics found to be significant in age-sex-adjusted models

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Any impairment OR (95% CI)</th>
<th>Mild OR (95% CI)</th>
<th>Moderate OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age per 10 years</td>
<td>2.22 (1.82-2.71)</td>
<td>1.89 (1.48 - 2.42)</td>
<td>2.71 (2.04 - 3.60)</td>
</tr>
<tr>
<td>Male Sex</td>
<td>2.02 (1.50-2.71)</td>
<td>1.81 (1.26 - 2.60)</td>
<td>2.26 (1.49 - 3.42)</td>
</tr>
<tr>
<td>Nasal Congestion</td>
<td>1.99 (1.39-2.87)</td>
<td>1.84 (1.18 - 2.87)</td>
<td>2.16 (1.32 - 3.56)</td>
</tr>
<tr>
<td>Smoking a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>1.31 (0.97-1.77)</td>
<td>1.57 (1.09 - 2.28)</td>
<td>1.03 (0.68 - 1.54)</td>
</tr>
<tr>
<td>Current</td>
<td>1.59 (0.91-2.76)</td>
<td>2.68 (1.47 - 4.87)</td>
<td>0.49 (0.16 - 1.49)</td>
</tr>
<tr>
<td>BMI b</td>
<td>0.77 (0.66-0.91)</td>
<td>0.74 (0.60 - 0.91)</td>
<td>0.81 (0.64 - 1.02)</td>
</tr>
<tr>
<td>GFR &lt;30 c</td>
<td>2.41 (1.13-5.14)</td>
<td>1.04 (0.32 - 3.36)</td>
<td>4.22 (1.82 - 9.77)</td>
</tr>
<tr>
<td>Hypercholesterolaemia d</td>
<td>0.71 (0.54-0.94)</td>
<td>0.87 (0.61-1.23)</td>
<td>0.54 (0.36-0.79)</td>
</tr>
<tr>
<td>Hypertension e Stage I</td>
<td>0.87 (0.55-1.37)</td>
<td>0.77 (0.42 - 1.40)</td>
<td>0.99 (0.54 - 1.80)</td>
</tr>
<tr>
<td>Stage II</td>
<td>0.73 (0.53-1.00)</td>
<td>0.91 (0.61 - 1.35)</td>
<td>0.58 (0.37 - 0.90)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.31 (0.78-2.21)</td>
<td>0.97 (0.49 - 1.95)</td>
<td>1.94 (1.01 - 3.75)</td>
</tr>
<tr>
<td>Impaired cognitive function f</td>
<td>3.70 (1.68-8.14)</td>
<td>3.31 (1.28 - 8.57)</td>
<td>3.73 (1.45 - 9.57)</td>
</tr>
<tr>
<td>Parkinson Disease</td>
<td>13.21 (3.49-50.0)</td>
<td>9.76 (2.01 - 47.5)</td>
<td>16.11 (3.80 - 68.2)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>2.59 (0.45-14.9)</td>
<td>0.87 (0.08 - 9.13)</td>
<td>6.38 (0.85 - 47.7)</td>
</tr>
</tbody>
</table>

a Compared to non-smokers

b Body Mass Index - per 5 kg/m² increase

c Glomerular filtration rate - GFR estimated by Cockcroft-Gault formula.

d Serum total cholesterol >5.2 mmol/L

e Hypertension Stage I - 140/90-160/100; Stage II - >160/100 or treated

f Mini-mental state exam score <24
Self-report of poor smell correlated poorly with measured olfactory impairment. Only 32.2% of participants with measured olfactory impairment reported they had lost their sense of smell. Of participants who reported an abnormal sense of smell, 48.6% (CI 39.7-57.5) had no measured impairment (SDOIT scores 6 or greater). Similarly, of participants who did report smell loss, 40.5% (CI 33.1-48.2) had no measured impairment.
**Discussion**

We observed a high prevalence of olfactory impairment (27.0%) in a population-based sample of Australians aged 60 years and over. Based on these data and the 2006 Australian census, we estimate that 868,000 Australians aged 60 years or older have impaired odor perception.

There have been only two other large-population based studies that have assessed the prevalence of olfactory impairment, the Wisconsin Epidemiology of Hearing Loss Study (EHLS) and the Swedish Skövde study, with only the former having focused on an older population. The size and response rates of these studies were comparable to ours (73% of 1900 persons in Skovde; 82% of 3407 persons in the EHLS; 77% of 2548 persons in the BMES). The BMES olfactory impairment prevalence is comparable to the 24.5% rate observed in the EHLS for persons aged 43-86 years, but slightly lower than the reported prevalence of 32.9% in persons aged 53 years or older in the Skövde study. These differences could be due to different age ranges and distributions of the three study samples. After age and sex standardizing our BMES prevalence to the EHLS, we observed a slightly lower prevalence of olfactory impairment of 24.3% (22.4-26.3) in our study compared with 29.8% (27.8-31.9) in the EHLS (for participants aged >60 years).

In agreement with the greater prevalence of olfactory impairment observed among men in the EHLS, Skövde and other smaller cross-sectional studies, we found that men were twice as likely to have impaired olfaction compared with women, after multivariable adjustment.
As in previous studies, we also observed a significant age-associated increase in the prevalence of olfactory impairment, with the highest prevalence of mild (19.8%) and moderate impairment (27.5%) seen in those aged 80 years and over. Factors that co-vary with age, such as medication use and medical conditions could be responsible, at least in part, for the increased prevalence of olfactory impairment with age. We found, however, a significant inverse association between hypertension, total cholesterol and measured olfactory impairment. This apparent protective association is difficult to explain. It may be confounded by premature death in participants with these co-morbidities, by the medications used to control these risk factors, or some shared mechanistic pathway. This association with olfaction warrants further investigation given the previously reported relationship between blood pressure and cholesterol and the incidence of cognitive decline. We did not find associations between other cardiovascular risk factors including diabetes, cardiovascular diseases, except stroke, and prevalent olfactory impairment in our older population.

BMES participants with moderate olfactory impairment were twice as likely to be underweight (BMI <20 kg/m²) than those without impaired olfaction. Several smaller studies demonstrated similar findings. Elderly patients with a poor sense of smell may be much less likely to enjoy food and more likely to subsequently eat inadequately, resulting in lower body weight. Olfactory capabilities may stimulate appetite and interest in eating and thus protect individuals against under-nutrition.

Ours is the first community-based study to demonstrate that older people with mild renal impairment are much more likely to have moderate (but not mild) olfactory impairment. A previous inpatient clinic study demonstrated similar findings and postulated the cause to be the accumulation of uremic toxins.
BMES participants with cognitive impairment had approximately 3-fold higher odds of mild and approximately 6-fold higher odds moderate olfactory impairment. Participants with a diagnosis of Parkinson disease had a 10- and 16-fold higher risk of having mild and moderate olfactory impairment, respectively, after multivariable adjustment, consistent with previous literature.257,272

We found that self-reported smell loss was an unreliable indicator of measured olfactory decline. Of those with olfactory deficit, 67.8% did not report a loss of smell function. Of participants that did report smell deficit, 40.5% had no measurable loss. This is in agreement with previous population reports.168,170

Strengths of this study are its high participation and follow-up rates. Two limitations are that the study sample represents survivors of this population-based cohort and that the data are cross-sectional in nature. As with any olfactory function test, the SDOIT tests only a limited number of stimulants, possibly resulting in under-detection of deficits in the rare spectrum of the olfaction function. In addition, olfactory threshold is not assessed with this measure. It is, however, substantially more reliable than self-reported methods. This simple and quick test may be useful in screening older persons at risk of neurodegenerative disease and malnutrition. Our study could have under-estimated the true prevalence as those who did not have olfaction data collected tended to be older and therefore more likely to have olfactory impairment.
Summary

Olfactory impairment was frequent in this older Australian population, with over one in four having impaired olfaction. Male gender and aging were the most important risk factors for olfactory impairment. Our data support an essential role for olfactory function in maintaining a healthy nutritional status and body weight. We provide additional data to support the link between impaired olfaction and neurodegenerative disorders, including dementia and Parkinson disease. Of note in our study, over 50% of participants with olfactory impairment had a normal BMI and did not have cognitive impairment or Parkinson Disease. Given that olfactory impairment may be a biomarker for both these neurodegenerative conditions and malnutrition, longitudinal studies are needed to assess the prognosis of older persons with olfactory deficit. These data may be useful in identifying persons at risk of certain conditions in their pre-clinical stage with the aim of initiating protective therapy.
Chapter Four: *Prevalence and Dependent Clustering*

*Characteristics of Visual, Auditory and Olfactory Impairments in Older Persons*
Abstract

**Purpose:** To assess the clustering patterns of visual, auditory and olfactory impairments in an older population sample.

**Methods:** The Blue Mountains Eye Study (BMES) examined 3,654 persons aged 49+ during 1992-1994, and after 5 and 10 years. At the 10-year follow-up (during 2002-4), 1,497 (74.3% of all participants) had complete vision, auditory and olfactory data, and were included in the current study. Visual impairment (VI) was defined as either presenting (PVI) or non-correctable (NCVI). Auditory impairment (AI) was defined as the pure-tone average (0.5-4kHz) of air-conduction hearing thresholds >25 decibels hearing level (dB HL). Olfactory impairment (OI) was defined as a San Diego Odour Identification Test score <6/8.

**Results:** The observed prevalence of having all three sensory impairments in persons with PVI (or NCVI) was 2.6 (or 3.0) times greater than predicted if this occurred independently. VI, AI and OI clustered differently in women compared to men. OI was associated with concomitant PVI and NCVI while AI associated with concomitant OI in men only; Visual impairment was associated with concomitant OI in women and AI in men.

**Conclusion:** Visual, auditory and olfactory impairments aggregate mutually and dependently in older persons. Separate hearing and vision services may not adequately support older persons with multiple impairments.
**Background**

Visual, auditory and olfactory impairments are common disabilities associated with significant morbidity and mortality in older persons. The prevalence of non-correctable visual impairment (NCVI) is estimated at between 2% and 4%,\(^{13,223,274}\) while the prevalence of reduced presenting visual acuity is 8 to 12% among persons aged ≥40 years.\(^{275,276}\) Auditory (hearing) impairment (AI) is the third most frequent chronic condition reported by elderly persons in the 2002 United States National Health Interview Survey,\(^{277}\) affecting between 35% and 45% of persons aged 50+ years.\(^{121,278}\) The prevalence of olfactory impairment (OI) is estimated to be 25% in older persons in persons aged older than 53 years.\(^{168}\)

Visual, auditory and olfactory impairments share common risk factors and consequences. Shared risk factors include increasing age, poorer cognitive status, lower education level, diabetes, workplace exposures, diet, cerebrovascular disease and smoking.\(^{121,170,253,279-288}\) Shared impacts include measures of independence, functional and physical decline, low SRH, quality of life, and nursing home placement.\(^{47,133,289,290}\) Visual and hearing impairments are also reported to be associated with an increased risk of all-cause mortality.\(^{56,57,60,61,64,151,152,156}\)

Despite the high prevalence of these disabilities and their similar associations, no studies have examined the prevalence of aggregated visual, auditory and olfactory impairments in older persons, or whether they aggregate dependently or randomly. Dependent aggregation of sensory impairments could indicate common underlying mechanisms. The presence of more than one sensory impairment may lead to greater negative impacts on the health-related quality of life\(^ {148}\) and mortality risk\(^ {151,153,156,291}\) of affected individuals. A trend for multiple sensory impairments in older persons may also imply particular needs for health care service provision to older persons. Identifying this aggregation could lead to improved interventions.
Using an Australian population based study of older persons, we aimed to assess the prevalence of aggregated visual, auditory and olfactory impairments and determine whether presence of a single impairment was associated with an increased likelihood of concomitantly having other sensory impairments; i.e. whether these three impairments tended to cluster.
Methods

Vision, hearing and olfaction were assessed in BMES 3. Visual impairment (VI) was categorized as either presenting visual impairment (PVI), VA less than 6/12 Snellen equivalent (<39 letters read correctly) in the better eye using current glasses, or non-correctable visual impairment (NCVI), PVI correctable to 6/12 Snellen equivalent or worse in the better eye, after subjective refraction.

Auditory impairment (AI) was defined as the pure-tone average of air-conduction hearing thresholds >25 decibels hearing level (dB HL) for the four frequencies (0.5, 1, 2, and 4 kHz) in the better ear (bilateral hearing loss). Olfactory impairment (OI) was defined as less than 6 correct out of a total of 8 possible responses. The presence of multiple sensory impairments was defined either as: a) >1 impairment using PVI, this included two or three of the impairments (AI, OI and PVI); and b) >1 impairment using NCVI, this includes two or three of the impairments (AI, OI and NCVI).

Statistical analyses were performed using SAS software v9.13 (SAS Institute, Cary, NC). Simple statistics included student t-tests for comparing means and chi-square tests for comparing proportions. Log-linear models were used to assess the concomitant presence of the three sensory impairments (visual, auditory and olfactory). Observed frequencies of concomitant sensory impairments were compared to the expected frequencies estimated assuming that they occur independently (no clustering tendency). Models that included two- and three-way interactions among the three impairments were used to test the significance of these interaction terms. The likelihood ratio was used to choose the best fitting models.

Logistic regression models were used to examine the presence of a single sensory impairment and the likelihood of other concomitant sensory impairments. Hypotheses tested were that: a) persons with AI are more likely to have concomitant OI or VI (compared to persons without AI); b) persons with OI are more likely to have concomitant AI or VI (compared to persons without OI); c) persons
with VI are more likely to have concomitant AI or OI (compared to persons without VI). Finally we wished to examine potential gender differences in the clustering patterns of sensory impairment in analyses stratified by gender. Associations are presented as odds ratios (OR) with 95% confidence intervals (CI).
Results

Study Population

Participants with a history of hearing loss from birth, otosclerosis or conductive hearing loss were excluded from the analyses. Of the remainder at BMES 3, 1497 (74.3% of all participants) had complete vision, auditory and olfactory data.

Table 4.1 presents the prevalence of single and combined sensory impairments in the study population. Auditory impairment was the most frequent sensory impairment followed by OI, PVI and then NCVI. The prevalence of single and multiple sensory impairments increased with age. Auditory and OI were more frequent in men than in women, while VI was more frequent in women. Associations were universally greater for persons with NCVI compared to PVI (Tables 4.1-4.4). Men were also more likely to have multiple sensory impairments than women (for multiple impairments, including PVI, OR 1.66, CI 1.26-2.20; for multiple impairments, including NCVI, OR 1.96, CI 1.46-2.63) after multivariable adjustment.
<table>
<thead>
<tr>
<th>Sensory Impairment</th>
<th>% (n)</th>
<th>60-69 % (n)</th>
<th>70-79 % (n)</th>
<th>≥80 % (n)</th>
<th>p value</th>
<th>Female % (n)</th>
<th>Male % (n)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auditory Impairment</td>
<td>43.1 (646)</td>
<td>18.7 (95)</td>
<td>47.0 (311)</td>
<td>73.0 (240)</td>
<td>&lt;0.0001</td>
<td>41.0 (351)</td>
<td>46.0 (295)</td>
<td>0.0534</td>
</tr>
<tr>
<td>Presenting Visual Impairment (PVI)</td>
<td>10.7 (160)</td>
<td>3.9 (20)</td>
<td>9.2 (61)</td>
<td>24.0 (79)</td>
<td>&lt;0.0001</td>
<td>12.1 (104)</td>
<td>8.7 (56)</td>
<td>0.0342</td>
</tr>
<tr>
<td>Non Correctable Visual Impairment (NCVI)</td>
<td>3.1 (46)</td>
<td>0.4 (2)</td>
<td>2.3 (15)</td>
<td>8.8 (29)</td>
<td>&lt;0.0001</td>
<td>3.9 (33)</td>
<td>2.0 (13)</td>
<td>0.0436</td>
</tr>
<tr>
<td>Olfactory Impairment</td>
<td>26.9 (403)</td>
<td>13.4 (68)</td>
<td>27.8 (184)</td>
<td>45.9 (178)</td>
<td>&lt;0.0001</td>
<td>21.1 (181)</td>
<td>34.6 (222)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&gt; 1 impairment using PVI</td>
<td>20.7 (310)</td>
<td>4.9 (25)</td>
<td>19.5 (129)</td>
<td>47.4 (156)</td>
<td>&lt;0.0001</td>
<td>18.4 (158)</td>
<td>23.7 (152)</td>
<td>0.0132</td>
</tr>
<tr>
<td>&gt; 1 impairment using NCVI</td>
<td>17.4 (61)</td>
<td>4.1 (21)</td>
<td>16.8 (111)</td>
<td>39.3 (129)</td>
<td>&lt;0.0001</td>
<td>14.5 (124)</td>
<td>21.4 (137)</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

* n total 661 for 70-79 and 328 for ≥ 80 for NCVI
Table 4.2 Frequencies of none, single and multiple sensory impairments identified compared to predicted if sensory impairments occurred independently, stratified by visual impairment and sex.

<table>
<thead>
<tr>
<th>Number of Impairments</th>
<th>% (n) identified</th>
<th>% Predicted if independent*</th>
<th>% (n) identified</th>
<th>% Predicted if independent*</th>
<th>% (n) found</th>
<th>% Predicted if independent*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presenting Visual Impairment</td>
<td>All</td>
<td>Female</td>
<td>Male</td>
<td>All</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>0</td>
<td>43.1 (646)</td>
<td>37.2</td>
<td>46.7 (400)</td>
<td>41.0</td>
<td>38.3 (246)</td>
<td>32.1</td>
</tr>
<tr>
<td>1</td>
<td>36.2 (543)</td>
<td>46.3</td>
<td>34.9 (299)</td>
<td>44.9</td>
<td>38.0 (244)</td>
<td>47.5</td>
</tr>
<tr>
<td>2</td>
<td>17.6 (264)</td>
<td>15.3</td>
<td>16.0 (137)</td>
<td>13.1</td>
<td>19.8 (127)</td>
<td>18.9</td>
</tr>
<tr>
<td>3</td>
<td>3.1 (46)</td>
<td>1.2</td>
<td>2.5 (21)</td>
<td>1.1</td>
<td>3.9 (25)</td>
<td>1.4</td>
</tr>
<tr>
<td>Non Correctable Visual Impairment</td>
<td>All</td>
<td>n total = 857</td>
<td>n total = 642</td>
<td>All</td>
<td>n total = 857</td>
<td>n total = 640</td>
</tr>
<tr>
<td>0</td>
<td>45.5 (681)</td>
<td>40.3</td>
<td>49.6 (425)</td>
<td>44.8</td>
<td>40.0 (256)</td>
<td>35.0</td>
</tr>
<tr>
<td>1</td>
<td>37.1 (555)</td>
<td>46.7</td>
<td>35.9 (308)</td>
<td>44.8</td>
<td>38.6 (247)</td>
<td>47.7</td>
</tr>
<tr>
<td>2</td>
<td>16.2 (243)</td>
<td>12.7</td>
<td>13.4 (115)</td>
<td>10.0</td>
<td>20.0 (128)</td>
<td>16.9</td>
</tr>
<tr>
<td>3</td>
<td>1.2 (18)</td>
<td>0.4</td>
<td>1.1 (9)</td>
<td>0.4</td>
<td>1.4 (9)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*If visual, auditory and olfactory sensory impairments cluster independently of each other, this is the predicted % of having none, single or multiple sensory impairments
Table 4.3 The likelihood of concomitant olfactory, auditory and visual impairments expressed as age-sex adjusted and multivariable adjusted odds ratios (OR) with 95% confidence intervals (95% CI) given the presence of the initial listed (conditional) impairment.

<table>
<thead>
<tr>
<th>Conditional impairment</th>
<th>Concomitant impairment</th>
<th>Age-sex adjusted OR (95% CI)</th>
<th>p value</th>
<th>Multivariable adjusted* OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olfactory</td>
<td>Auditory</td>
<td>1.44 (1.11-1.88)</td>
<td>0.0064</td>
<td>1.44 (1.07-1.94)†</td>
<td>0.0174</td>
</tr>
<tr>
<td></td>
<td>Presenting visual impairment</td>
<td>1.33 (0.92-1.92)</td>
<td>0.1326</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Non correctable visual impairment</td>
<td>1.66 (0.88-3.13)</td>
<td>0.1182</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Auditory</td>
<td>Olfactory</td>
<td>1.46 (1.12-1.90)</td>
<td>0.0054</td>
<td>1.43 (1.10-1.88)†</td>
<td>0.0098</td>
</tr>
<tr>
<td></td>
<td>Presenting visual impairment</td>
<td>1.13 (0.77-1.65)</td>
<td>0.5428</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Non correctable visual impairment</td>
<td>1.84 (0.88-3.88)</td>
<td>0.1068</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Presenting visual acuity‡</td>
<td>Olfactory</td>
<td>1.13 (1.05-1.20)</td>
<td>0.0005</td>
<td>1.11 (1.04-1.19)</td>
<td>0.0030</td>
</tr>
<tr>
<td></td>
<td>Auditory</td>
<td>1.09 (1.01-1.17)</td>
<td>0.0201</td>
<td>1.09 (1.01-1.18)</td>
<td>0.0380</td>
</tr>
<tr>
<td>Non correctable visual acuity‡</td>
<td>Olfactory</td>
<td>1.17 (1.07-1.28)</td>
<td>0.0004</td>
<td>1.14 (1.04-1.24)</td>
<td>0.0042</td>
</tr>
<tr>
<td></td>
<td>Auditory</td>
<td>1.15 (1.04-1.26)</td>
<td>0.0070</td>
<td>1.14 (1.02-1.28)</td>
<td>0.0241</td>
</tr>
</tbody>
</table>

* Olfactory impairment adjusted for sex, age, smoking, nasal congestion, Parkinson disease and presence of other sensory impairment; auditory impairment adjusted for low education (no post-school qualifications), family history of hearing loss (including parents and siblings), history of work in noisy industry and presence of other sensory impairment

† Adjusted for decreasing PVA

‡ Continuous 1 line (5 letter) decrease
Table 4.4 The likelihood of concomitant olfactory, auditory and visual impairments expressed as sex-stratified multivariable adjusted odds ratios (OR) with 95% confidence intervals (95% CI), given the presence of the listed (conditional) initial impairment.

<table>
<thead>
<tr>
<th>Conditional impairment</th>
<th>Concomitant impairment</th>
<th>Women OR (95% CI)*</th>
<th>p value</th>
<th>Men OR (95% CI)*</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olfactory</td>
<td>Auditory†</td>
<td>1.45 (0.94-2.22)</td>
<td>0.0921</td>
<td>1.46 (0.96-2.21)</td>
<td>0.0800</td>
</tr>
<tr>
<td></td>
<td>Presenting visual impairment</td>
<td>1.34 (0.83-2.16)</td>
<td>0.2369</td>
<td>2.34 (1.28-4.27)</td>
<td>0.0056</td>
</tr>
<tr>
<td></td>
<td>Non correctable visual impairment</td>
<td>0.81 (0.36-1.82)</td>
<td>0.6132</td>
<td>15.5 (1.96-122.50)</td>
<td>0.0094</td>
</tr>
<tr>
<td>Auditory</td>
<td>Olfactory†</td>
<td>1.28 (0.86-1.89)</td>
<td>0.2249</td>
<td>1.58 (1.08-2.32)</td>
<td>0.0180</td>
</tr>
<tr>
<td></td>
<td>Presenting visual impairment</td>
<td>1.34 (0.83-2.16)</td>
<td>0.2369</td>
<td>0.84 (0.45-1.58)</td>
<td>0.5957</td>
</tr>
<tr>
<td></td>
<td>Non correctable visual impairment</td>
<td>1.70 (0.69-4.14)</td>
<td>0.2473</td>
<td>1.78 (0.50-6.87)</td>
<td>0.4050</td>
</tr>
<tr>
<td>Presenting visual acuity†</td>
<td>Olfactory</td>
<td>1.13 (1.01-1.25)</td>
<td>0.0260</td>
<td>1.03 (0.90-1.18)</td>
<td>0.6538</td>
</tr>
<tr>
<td></td>
<td>Auditory</td>
<td>1.05 (0.96-1.14)</td>
<td>0.2794</td>
<td>1.24 (1.09-1.39)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Non correctable visual acuity†</td>
<td>Olfactory</td>
<td>1.18 (1.02-1.35)</td>
<td>0.0221</td>
<td>1.06 (0.86-1.31)</td>
<td>0.5913</td>
</tr>
<tr>
<td></td>
<td>Auditory</td>
<td>1.05 (0.95-1.16)</td>
<td>0.3571</td>
<td>1.47 (1.21-1.78)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

*Olfactory impairment adjusted for sex, age, smoking, nasal congestion, Parkinson disease and presence of other sensory impairment; auditory impairment adjusted for low education (no post-school qualifications), family history of hearing loss (including parents and siblings), history of work in noisy industry and presence of other sensory impairment; Visual impairments adjusted for age and presence of other sensory impairment
†Adjusted for decreasing presenting visual acuity
‡Continuous 1 line (5 letter) decrease.
**Concomitant Sensory Impairments**

Analysis using log-linear models assuming that these three sensory impairments occur independently estimated the predicted prevalence of two or more concomitant sensory impairments, which was found to be significantly lower than the observed prevalence (Likelihood Ratio = 92.39, p<0.001) (Table 4.2). The observed prevalence of having all three sensory impairments was 2.6 times more likely than the predicted proportion for persons with PVI and 3.0 times more likely than the predicted proportion for those with NCVI, had these impairments occurred independently (Table 4.2). The best-fitting model (Likelihood Ratio = 0.27, p=0.60) was the one that included the three main effects (AI, OI, VI) and all two-way interaction terms (AI*OI, AI*VI, OI*VI, p<0.002).

**Associations between Sensory Impairments**

No significant increase in the likelihood of other concomitant types of sensory impairment was found, given the presence of either PVI or NCVI (data not shown). However, when decreasing visual acuity (DVA) was modelled as a continuous variable (per 5 letter /1 line reduction), significant associations with other sensory impairments were found (Tables 4.3 and 4.4). The presence of OI was significantly associated with an increased likelihood of concomitant AI, but not VI, after age-sex and multivariable adjustment (Table 4.4). Similarly, the presence of AI was significantly associated with an increased likelihood of concomitant OI but not VI, after age-sex and multivariable adjustment (Table 4.3).

For each 1-line (5-letter) reduction in presenting visual acuity (PVA), there was an 11% (CI 4-19%) increased likelihood of concomitant OI and a 9% (CI 1-18%) increased likelihood of concomitant AI, after multivariable adjustment (Table 4.4). Similarly, for each 1-line (5-
letter) reduction in non-correctable visual acuity (NCVA) there was a 14% (CI 4-24%) increased likelihood of concomitant OI and a 14% (CI 2-28%) increased likelihood of concomitant AI, after multivariable adjustment (Table 4.3).

When analyses were performed for men and women separately, we found that the increased likelihood of concomitant AI, given the presence of OI, was not significant but that there was a trend towards a non-significantly increased likelihood of concomitant AI that was of similar magnitude in both genders. Visual, AI and OI appeared to cluster differently in women compared to men (Table 4.4). After adjusting for age and other co-variables, OI was associated with concomitant PVI and NCVI while AI associated with concomitant OI in men, but not in women (Table 4.4). The increased likelihood of concomitant AI and OI was not significant after gender stratification, but there was a trend towards a marginally non-significantly increased likelihood of AI, given the presence of OI, with similar magnitude in both sexes. The presence of AI did not increase the likelihood of either PVI or NCVI in men or women. In women, each one-line reduction in PVA and NCVA increased the likelihood of concomitant OI, but not AI. In contrast, each one-line reduction in PVA and NCVA increased the likelihood of concomitant AI but not OI in men (Table 4.4).
Discussion

We recorded prevalence rates for NCVI, PVI, OI and AI in our population of persons aged 49+ years to be 3.1, 10.7%, 26.9% and 43.1% respectively. Consistent with previous reports, we also found that auditory and olfactory impairments were both more frequent in men, visual impairment was more frequent in women and the prevalence of VI, AI and OI increased with age.13,273

In this study, we found that the prevalence two or more sensory impairments in older persons was higher than the predicted prevalence if these impairments were assumed to have occurred randomly and independently, suggesting that sensory impairments tend to occur in clusters in older persons. The clustering tendencies of these sensory impairments suggest that common mechanisms may underlie VI, AI and OI. The finding of stronger associations in persons with NCVI compared to PVI supports this hypothesis. That sensory impairments are known to share common risk factors including increasing age, poorer cognitive status, lower education levels, diabetes, workplace exposures, diet, cerebrovascular disease and smoking, adds further weight to the possibility of common pathways.121,170,253,278-288,292-294 Auditory and VI have been associated with oxidative stress,106,111,295 but to date, this risk factor has not been investigated for OI.

We also found that the clustering patterns differed between men and women. In women, VI was associated with an increased likelihood of AI. Similar gender differences were reported for age-related macular degeneration and AI, which could reflect a common cause.147 These data suggest that the mechanisms and/or exposures (e.g. workplace or environmental exposures, smoking status, genetic, hormonal or other sex differences) potentially underlying these sensory deficits could differ between men and women. The finding that OI strongly
tends to co-exist with either PVI or NCVI in men, but not in women, could indicate that OI is a marker of gender-specific exposures that also increase the likelihood of VI. However, due to the relatively small numbers with two or more impairments in women and men separately, we cannot exclude the possibility that these are chance findings, so that confirmation will be important.

While not examined in this study, it is important to consider that presence of all three sensory impairments may increase the burden of shared adverse health outcomes on affected individuals and their families and carers. Associations of each impairment, VI, AI or OI, with measures of independence, functional and physical decline, low SRH and nursing home placement have been previously reported. Combined vision and auditory impairments have also been reported to cumulatively decrease health-related quality of life and to increase mortality risk. Evidence on whether correcting these sensory impairments with hearing or low vision aids would reduce their negative impact is limited with further studies needed.

Our findings highlight some public health concerns for individuals suffering from multiple sensory impairments. Specifically, the current imperfect care system inhibits the effective delivery of services and rehabilitation to older people with multiple sensory impairments. There has been no active screening using case-finding strategies to detect older persons with sensory impairment. Further, older persons with these impairments tend to think that sensory function loss is part of aging, which are thus likely to be under-reported. By the time affected individuals seek services, they are often at a relatively late stage, and may have already been socially isolated and have had a substantially reduced quality of life and limitations in daily functioning for some period of time. While separate vision and hearing rehabilitation systems...
currently operate in Australia and the U.S., such systems often fail to service and support older people with multiple sensory impairments in a coherent and collaborative manner. The bewildering complexity of current systems for the care of older people with two or more sensory impairments highlights the need for clearer, and better co-ordinated health policies.

Strengths of our study include its large population-based dataset, with high participation and standardized measurements of visual acuity, olfactory and hearing assessments. Among limitations, the study sample consisted of a survivor cohort and the data were cross-sectional in nature. Our study may also have underestimated the true prevalence of sensory impairment as those who did not have a complete collection of sensory data tended to be older and were therefore more likely to have multiple sensory impairments. In addition, the small number of persons with combined sensory impairment in the two gender subgroups could have led to chance findings in the different clustering patterns of these sensory impairments between men and women, and limits our ability to detect weak associations that could have been significant.
Summary

Visual, olfactory and auditory impairments tend to aggregate mutually and dependently in older persons. This implies that once a sensory impairment is detected, screening for other concomitant sensory impairment may be warranted. The higher than expected frequency of combined sensory impairment implies that the current health care provision may not have met the needs of older persons with sensory impairment. It may not have provided appropriate, coherent rehabilitation services to these older individuals with multiple sensory losses. Our study findings advocate for greater attention from health care providers and health policy makers to improve health care services to older persons with multiple sensory impairments.
Chapter Five: *Direct and Indirect Effects of Visual Impairment on Mortality Risk in Older Persons*
Abstract

**Purpose:** To investigate pathways from visual impairment to increased all-cause mortality in older persons.

**Methods:** The Blue Mountains Eye Study examined 3654 persons aged 49+ years (82.4% response) during 1992-1994 and after 5 and 10 years. Australian National Death Index data confirmed deaths until 2005. Visual impairment was defined as presenting (PVI), correctable (CVI), and non-correctable (NCVI), using better-eye visual acuity. Associations between visual impairment and mortality risk were estimated using Cox regression and structural equation modelling (SEM).

**Results:** After 13 years, 1273 participants had died. Adjusting for mortality risk markers, higher mortality was associated with NCVI (hazard ratio (HR), 1.35, 95% confidence interval (CI) 1.04-1.75). This association was stronger for ages <75 years (HR 2.58, CI 1.42-4.69). SEM revealed greater effects of NCVI on mortality risk (HR 5.25, CI 1.97-14.01 for baseline ages <75), with both direct (HR 2.16, CI 1.11-4.23) and indirect effects (HR 2.43, CI 1.17-5.03). Of mortality risk markers examined, only disability in walking demonstrated a significant indirect pathway for the link between visual impairment and mortality.

**Conclusions:** Visual impairment predicted mortality by both direct and indirect pathways, particularly for persons with NCVI aged <75. Disability in walking, which can substantially influence general health, represented a major indirect pathway.
Background

Visual impairment has consistently been associated with a higher risk of dying. Visual impairment is also reportedly associated with many factors also linked to increased mortality. These include unintentional injury, reduced walking speed, depression, lower body mass index, increased risk of falls, SRH, self-reported difficulty in physical activity, systemic inflammation, cardiovascular disease, dementia and cancer. Correction for these “confounders” has been found to attenuate the association between visual impairment and mortality, but the mechanisms behind the association between visual impairment and mortality remain to be determined.

Due to the complex interactions of other mortality risk factors with visual impairment, correcting for these covariates using traditional regression techniques could underestimate the total effect of visual impairment on mortality. For example, persons with visual impairment may be more likely to use walking aids because of an increased risk or fear of falling. If true, then adjustment for the use of walking aids, an independent marker of mortality, would underestimate the effect of visual impairment. This covariate is an intermediate variable, a variable that lies on the causal pathway between visual impairment and mortality. Simple adjustment for such variables in a traditional statistical model is not appropriate.

Structural equation modelling (SEM) is a modern statistical method that permits modelling of complex relationships that are difficult to estimate using traditional regression techniques. SEM facilitates the examination and quantification of direct pathways, plus indirect pathways via intermediate variables. Estimates for such variables can be summated to determine the total indirect effect of the variable of interest on the outcome. Adding the indirect and direct
effects then estimates the total effect of the variable of interest on the outcome. To our knowledge, only one study has utilized SEM to examine the associations between visual impairment and mortality. This large population survey relied on self- or proxy-reporting of visual impairment and co-morbidities. The authors reported that in addition to a direct effect on mortality, visual impairment increased mortality risk indirectly through intermediate variables, SRH and disability. To confirm the findings by Christ et al., we aimed, in an older Australian population-based cohort, to examine association between visual impairment, mortality risk markers and the 13-year risk of mortality, using a SEM approach
Methods

Medical and smoking histories were determined by interviewer-administered questionnaire at baseline (Methods, Chapter 2). To identify and confirm persons who died after the baseline examination, demographic information including surname, first and second names, gender and date of birth of the 3654 participants were cross-matched with Australian National Death Index (NDI) data for deaths, to the end of 2005. A probabilistic record linkage package was used, adopting a multiple pass procedure in which both data sets were grouped based on different characteristics (e.g., date of birth, name, sex) each time. Matches were divided into exact and non-exact. All non-exact matched records were examined manually and accepted if there was only one non-exact matched characteristic that was not critical. Information provided by family members during follow-up was also included if the participant was reported to have died on or before December 2005.

Statistical analyses were performed using SAS software v9.13 (SAS Institute, Cary, NC) and Mplus. Simple statistics included Student t tests for comparing means and chi-square tests for comparing proportions. Cox regression models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI). Multivariable-adjusted models included variables found significantly associated with mortality after age adjustment. These were previous history of acute myocardial infarction (AMI), stroke, angina and hypertension, current smoking, low body mass index (BMI), cancer, diabetes, walking disability, home ownership, tertiary qualification and SRH. Additional stratified analyses were conducted by age-group (age <75 years vs. 75+ years) to assess whether the impact from visual impairment was stronger on premature mortality of the relatively younger age group at baseline (<75 years). A p value of less than 0.05 was considered statistically significant.
Structural equation modelling pathway analysis\textsuperscript{252} was used to model the relationship between visual impairment, survival and co-variables found significantly associated with mortality by Cox regression. The SEM was fit using the MPlus\textsuperscript{250} statistical package with maximum likelihood and Monte Carlo integration methods. Standard errors were calculated using the delta method and hazard rates obtained from the coefficients by exponentiation. The co-variables used in the model were previous history of acute myocardial infarction (AMI), stroke, angina and hypertension, current smoking, low body mass index (BMI), cancer, diabetes, walking disability, home ownership, tertiary qualification and SRH. The multiple potential pathways to mortality are shown in Figure 5.1. Each variable was adjusted for age and gender. Models were simplified by removing indirect pathways for individual co-variables that were not significant at the p value level of 0.1.
4 **Figure 5.1** Path model of the SEM for the relationship between non-correctable visual impairment, risk markers and all-cause mortality in all ages showing hazard rates and 95% confidence intervals (Total Indirect 1.68 (1.21-2.33)).

Covariates are corrected for age, gender
*Other covariates include the mortality risk markers angina, myocardial infarction stroke, cancer, hypertension, smoking, diabetes, home ownership, tertiary education and self-rated health
**There was no significant relationship between visual impairment and self-rated health independent of walking disability
Results

Study Population

As of 31/12/2005, 1273 BMES participants had died. Table 5.1 shows the distribution of known mortality risk markers in persons with and without visual impairment. Compared to those with normal vision, participants with non-correctable visual impairment at baseline were more likely to be female, older (age ≥75 years) and underweight. Persons with correctable visual impairment were more likely to be older (age ≥75 years), but there was no difference in the proportions of women or persons with low body mass index. They were more likely to have a self-reported history of angina, myocardial infarction, stroke, cancer, low SRH and an observed difficulty in walking or use of walking aids. They were less likely to have tertiary education or to own their home. There were no significant differences in the proportions of current smokers or history of hypertension or diabetes between the groups with and without visual impairment.
### Table 5.1 Prevalence of mortality risk markers in participants of the Blue Mountains Eye Study 10-year follow-up examination by visual impairment.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>None (n=3224)</th>
<th>Visual impairment</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Correctable (n=269)</td>
<td>Non Correctable (n=130)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>n(%)</td>
<td>n(%)</td>
<td>n(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1412 (43.8%)</td>
<td>119 (44.2%)</td>
<td>38 (29.2%)</td>
<td>0.004</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>1812 (56.2%)</td>
<td>150 (55.8%)</td>
<td>92 (70.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;75</td>
<td>2743 (85.1%)</td>
<td>155 (57.6%)</td>
<td>27 (20.8%)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥75</td>
<td>481 (14.9%)</td>
<td>114 (42.4%)</td>
<td>103 (79.2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking(^a)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1492 (48.4%)</td>
<td>128 (49.6%)</td>
<td>67 (59.8%)</td>
<td>0.13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>1122 (36.4%)</td>
<td>88 (31.3%)</td>
<td>35 (34.1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>471 (15.3%)</td>
<td>42 (16.3%)</td>
<td>10 (8.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index(^b)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>168 (5.3%)</td>
<td>18 (6.9%)</td>
<td>19 (17.9%)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1183 (37.6%)</td>
<td>110 (42.3%)</td>
<td>45 (42.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>1250 (39.7%)</td>
<td>97 (37.3%)</td>
<td>24 (22.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>549 (17.4%)</td>
<td>35 (13.5%)</td>
<td>18 (17.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension(^a,(^b))</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>926 (28.9%)</td>
<td>69 (25.7%)</td>
<td>30 (24.4%)</td>
<td>0.41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage I</td>
<td>843 (26.3%)</td>
<td>65 (24.2%)</td>
<td>34 (27.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage II</td>
<td>1437 (44.8%)</td>
<td>135 (50.2%)</td>
<td>59 (48.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes(^a)</td>
<td>244 (7.6%)</td>
<td>23 (8.6%)</td>
<td>13 (10.0%)</td>
<td>0.52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke(^a)</td>
<td>150 (4.7%)</td>
<td>23 (8.6%)</td>
<td>16 (12.7%)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina(^a)</td>
<td>366 (11.4%)</td>
<td>54 (20.1%)</td>
<td>25 (20.0%)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction(^a)</td>
<td></td>
<td>275 (8.6%)</td>
<td>34 (12.7%)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer(^a)</td>
<td>260 (8.1%)</td>
<td>27 (10.0%)</td>
<td>19 (14.6%)</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking Disability(^b)</td>
<td>173 (5.4%)</td>
<td>41 (15.2%)</td>
<td>44 (33.8%)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home Ownership(^a)</td>
<td>2807 (89.3%)</td>
<td>219 (83.9%)</td>
<td>103 (83.1%)</td>
<td>0.004</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher Education(^a)</td>
<td>1810 (59.7%)</td>
<td>116 (47.2%)</td>
<td>48 (41.7%)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fair or Poor Self-Rated Health(^a)</td>
<td>766 (24.1%)</td>
<td>83 (31.4%)</td>
<td>47 (38.8%)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Self-reported \(^b\)Examiner assessed
**Association between Visual Impairment and Mortality**

Table 5.2 shows all-cause mortality rates and mortality risk after age and sex adjustment, which were higher in persons with visual impairment compared to those with normal vision. This difference was greater in persons younger than 75 years compared to those aged ≥75 years at baseline. Persons aged <75 years with visual impairment were at greater risk of (for PVI: Hazard Ratio (HR), 1.69, 95 % confidence interval (CI) 1.32-2.17; for CVI: HR 1.60, CI 1.23-2.09; for NCVI: HR 2.58, CI 1.42-4.69). The associations for all ages combined remained either significant or marginally significant after multivariable adjustment (Table 2), although were substantially attenuated in magnitude (for PVI: HR 1.29, CI 1.09-1.52; for CVI: HR 1.26, CI 1.04-1.53; for NCVI: HR 1.35, CI 1.04-1.75). In persons aged <75 years, only PVI and NCVI were statistically associated with mortality, while for those age ≥75 years, only PVI was significantly associated with mortality, after multivariable adjustment.
**Table 5.2** The association of visual impairment (VI) and all-cause mortality assessed using Cox regression by visual impairment category and expressed as hazard ratios with 95% confidence intervals (CI): reference group is persons without any visual impairment.

<table>
<thead>
<tr>
<th>Age</th>
<th>Mortality rate</th>
<th>Age and Sex Adjusted</th>
<th>Multi-variable Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No VI n of deaths/ n at risk</td>
<td>VI n of deaths/ n at risk</td>
<td>Hazard Ratio (CI)</td>
</tr>
<tr>
<td></td>
<td>995/3224</td>
<td>273/399</td>
<td>1.49 (1.29-1.73)</td>
</tr>
<tr>
<td>&lt;75</td>
<td>595/2680</td>
<td>72/170</td>
<td>1.69 (1.32-2.17)</td>
</tr>
<tr>
<td>≥75</td>
<td>400/544</td>
<td>201/229</td>
<td>1.39 (1.17-1.67)</td>
</tr>
</tbody>
</table>

**Presenting Visual Impairment**

<table>
<thead>
<tr>
<th>Age</th>
<th>Mortality rate</th>
<th>Age and Sex Adjusted</th>
<th>Multi-variable Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No VI n of deaths/ n at risk</td>
<td>VI n of deaths/ n at risk</td>
<td>Hazard Ratio (CI)</td>
</tr>
<tr>
<td></td>
<td>995/3224</td>
<td>163/269</td>
<td>1.47 (1.24-1.74)</td>
</tr>
<tr>
<td>&lt;75</td>
<td>595/2680</td>
<td>61/147</td>
<td>1.60 (1.23-2.09)</td>
</tr>
<tr>
<td>≥75</td>
<td>400/544</td>
<td>102/122</td>
<td>1.36 (1.09-1.70)</td>
</tr>
</tbody>
</table>

**Correctable Visual Impairment**

<table>
<thead>
<tr>
<th>Age</th>
<th>Mortality rate</th>
<th>Age and Sex Adjusted</th>
<th>Multi-variable Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No VI n of deaths/ n at risk</td>
<td>VI n of deaths/ n at risk</td>
<td>Hazard Ratio (CI)</td>
</tr>
<tr>
<td></td>
<td>995/3224</td>
<td>110/130</td>
<td>1.56 (1.25-1.94)</td>
</tr>
<tr>
<td>&lt;75</td>
<td>595/2680</td>
<td>11/23</td>
<td>2.58 (1.42-4.69)</td>
</tr>
<tr>
<td>≥75</td>
<td>400/544</td>
<td>99/107</td>
<td>1.45 (1.15-1.83)</td>
</tr>
</tbody>
</table>

*Covariates include the mortality risk markers angina, myocardial infarction, stroke, cancer, hypertension, walking disability, low body mass index, smoking, diabetes, home ownership, tertiary education corrected for age, gender and visual impairment.
Structural Equation Modeling (SEM) pathway analysis confirmed that visual impairment influenced mortality by both direct and indirect pathways. Table 5.3 shows the hazard ratios and 95% confidence intervals using this model. The pattern was similar to the Cox regression models, except that the hazard ratios were higher when estimated using SEM.
**Table 5.3** The association of visual impairment (VI) and all-cause mortality assessed using structural equation modelling by visual impairment category and expressed as hazard ratios (HR) with 95% confidence intervals (CI): reference group is persons without any visual impairment.

<table>
<thead>
<tr>
<th>Age</th>
<th>Total Hazard Ratio (CI)</th>
<th>p value</th>
<th>Direct Hazard Ratio (CI)</th>
<th>p value</th>
<th>Indirect* Hazard Ratio (CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Presenting Visual Impairment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>1.80 (1.38-2.35)</td>
<td>&lt;0.001</td>
<td>1.29 (1.09-1.52)</td>
<td>0.0028</td>
<td>1.40 (1.13-1.73)</td>
<td>0.0019</td>
</tr>
<tr>
<td>&lt;75</td>
<td>2.14 (1.39-3.28)</td>
<td>&lt;0.001</td>
<td>1.42 (1.07-1.87)</td>
<td>0.0150</td>
<td>1.51 (1.07-2.12)</td>
<td>0.0179</td>
</tr>
<tr>
<td>≥75</td>
<td>1.46 (1.04-2.05)</td>
<td>0.030</td>
<td>1.24 (1.01-1.53)</td>
<td>0.0416</td>
<td>1.18 (0.90-1.54)</td>
<td>0.2438</td>
</tr>
<tr>
<td></td>
<td>Correctable Visual Impairment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>1.60 (1.18-2.17)</td>
<td>0.002</td>
<td>1.26 (1.04-1.53)</td>
<td>0.0174</td>
<td>1.27 (1.00-1.61)</td>
<td>0.0501</td>
</tr>
<tr>
<td>&lt;75</td>
<td>1.81 (1.15-2.85)</td>
<td>0.011</td>
<td>1.33 (0.99-1.80)</td>
<td>0.0607</td>
<td>1.36 (0.95-1.93)</td>
<td>0.0891</td>
</tr>
<tr>
<td>≥75</td>
<td>1.34 (0.89-2.03)</td>
<td>0.16</td>
<td>1.20 (0.94-1.55)</td>
<td>0.1462</td>
<td>1.12 (0.80-1.55)</td>
<td>0.5126</td>
</tr>
<tr>
<td></td>
<td>Non-correctable Visual Impairment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>2.27 (1.50-3.43)</td>
<td>&lt;0.001</td>
<td>1.35 (1.04-1.75)</td>
<td>0.024</td>
<td>1.68 (1.21-2.33)</td>
<td>0.002</td>
</tr>
<tr>
<td>&lt;75</td>
<td>5.25 (1.97-14.01)</td>
<td>&lt;0.001</td>
<td>2.16 (1.11-4.23)</td>
<td>0.024</td>
<td>2.43 (1.17-5.03)</td>
<td>0.017</td>
</tr>
<tr>
<td>≥75</td>
<td>1.63 (1.03-2.59)</td>
<td>0.039</td>
<td>1.30 (0.97-1.73)</td>
<td>0.08</td>
<td>1.25 (0.87-1.81)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

*Covariates include walking disability, low body mass index
Of the risk markers investigated by SEM, only disability in walking represented a significant indirect pathway from visual impairment to mortality. Table 5.4 lists the hazards ratios and 95% confidence intervals for the indirect effects of disability in walking on mortality. Figures 5.1, 5.2 and 5.3 illustrate the detailed pathways that could explain the associations found between visual impairment and mortality. There was a significant indirect pathway from visual impairment to mortality via disability in walking, through poorer SRH, to mortality (Table 5.4, Figures 5.1, 5.2, 5.3). An indirect pathway through lower body mass index (BMI) bordered on significance for NCVI in all age groups (HR 1.21, CI 0.99-1.48, p=0.06) but was not significant for other forms of visual impairment or after age stratification (data not shown). There was no indirect pathway through any other mortality risk markers: e.g. past history of angina, acute myocardial infarction, stroke, hypertension, diabetes, cancer or smoking. There were also no indirect pathways from visual impairment to mortality through lower home ownership or education levels. There was no indirect pathway from visual impairment to mortality through poorer SRH that was independent of disability in walking.
20 **Table 5.4** Total indirect effects of visual impairment to all-cause mortality using structural equation modelling pathway analysis expressed as hazard ratios (HR) with 95% confidence intervals (CI) stratified by pathway: reference group is persons without any visual impairment.

<table>
<thead>
<tr>
<th>Age</th>
<th>Total Indirect Effect</th>
<th>Disability in Walking Pathway</th>
<th>Disability in Walking via Poor Self-rated Health Pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard Ratio (CI)</td>
<td>p value</td>
<td>Hazard Ratio (CI)</td>
</tr>
<tr>
<td>All</td>
<td>1.29 (1.09-1.53)</td>
<td>0.004</td>
<td>1.20 (1.05-1.37)</td>
</tr>
<tr>
<td>&lt;75</td>
<td>1.35 (1.01-1.80)</td>
<td>0.041</td>
<td>1.22 (0.99-1.51)</td>
</tr>
<tr>
<td>≥75</td>
<td>1.18 (0.95-1.47)</td>
<td>0.12</td>
<td>1.14 (0.96-1.34)</td>
</tr>
</tbody>
</table>

**Presenting Visual Impairment**

<table>
<thead>
<tr>
<th>Age</th>
<th>Total Indirect Effect</th>
<th>Disability in Walking Pathway</th>
<th>Disability in Walking via Poor Self-rated Health Pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard Ratio (CI)</td>
<td>p value</td>
<td>Hazard Ratio (CI)</td>
</tr>
<tr>
<td>All</td>
<td>1.24 (1.03-1.51)</td>
<td>0.025</td>
<td>1.17 (1.02-1.35)</td>
</tr>
<tr>
<td>&lt;75</td>
<td>1.27 (0.94-1.71)</td>
<td>0.11</td>
<td>1.08 (0.97-1.21)</td>
</tr>
<tr>
<td>≥75</td>
<td>1.19 (0.92-1.53)</td>
<td>0.19</td>
<td>1.14 (0.94-1.38)</td>
</tr>
</tbody>
</table>

**Correctable Visual Impairment**

<table>
<thead>
<tr>
<th>Age</th>
<th>Total Indirect Effect</th>
<th>Disability in Walking Pathway</th>
<th>Disability in Walking via Poor Self-rated Health Pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard Ratio (CI)</td>
<td>p value</td>
<td>Hazard Ratio (CI)</td>
</tr>
<tr>
<td>All</td>
<td>1.39 (1.07-1.80)</td>
<td>0.013</td>
<td>1.27 (1.04-1.54)</td>
</tr>
<tr>
<td>&lt;75</td>
<td>1.82 (0.99-3.34)</td>
<td>0.05</td>
<td>1.23 (0.98-1.54)</td>
</tr>
<tr>
<td>≥75</td>
<td>1.18 (0.88-1.57)</td>
<td>0.26</td>
<td>1.13 (0.91-1.41)</td>
</tr>
</tbody>
</table>
Figure 5.2 Path model of the SEM for the relationship between presenting visual impairment, risk markers and all-cause mortality in all ages showing hazard rates and 95% confidence intervals (Total Indirect 1.40 (1.13-1.73)).

Covariates are corrected for age and gender
*Other covariates include the mortality risk markers angina, myocardial infarction stroke, cancer, hypertension, smoking, diabetes, home ownership, tertiary education and self-rated health**.
** There was no significant relationship between visual impairment and self-rated health independent of walking disability.
Figure 5.3 Path model of the SEM for the relationship between correctable visual impairment, risk markers and all-cause mortality in all ages showing hazard rates and 95% confidence intervals (Total Indirect 1.27 (1.00-1.61)).

Covariates are corrected for age and gender
*Other covariates include the mortality risk markers angina, myocardial infarction stroke, cancer, hypertension, smoking, diabetes, home ownership, tertiary education and self-rated health**.
** There was no significant relationship between visual impairment and self-rated health independent of walking disability.
Discussion

In agreement with previous reports, we observed that the presence of visual impairment predicted mortality in older persons. Using Cox regression models, PVI predicted mortality independent of age, sex and the presence of known mortality risk markers. Using SEM analysis, we confirmed that visual impairment increased mortality via both direct and indirect pathways. The relationship between visual impairment and mortality was strongest for NCVI among persons with baseline ages <75 years.

Compared with estimates from SEM, Cox regression appears to underestimate the effect of visual impairment on mortality by over-correcting for intermediate variables that were associated with both visual impairment and mortality. To determine which indirect effects were important in predicting mortality for visually impaired persons, we modelled each covariate as a pathway to mortality (Table 5.4). Of the mortality risk markers we assessed, only disability in walking represented a significant indirect pathway. For this association, two possible pathways were identified, one pathway involved only disability in walking; the second also involved an effect through low SRH (Table 5.4, Figure 5.1). Because of reduced power through fewer events, we were unable to differentiate indirect effects via age. The age-related trend for mortality, however, suggests that in persons younger than 75 years at baseline, the pathway through SRH may be more important than the pathway directly from disability in walking to mortality (Table 5.4).

Weaker associations were consistently found in persons aged 75+ years at baseline, and are not unexpected. Many studies have reported no associations between visual impairment and mortality after correcting for covariates in older populations or in analyses that included all ages in one model. Similar findings are reported for cardiovascular risk factors where
risk factors lose their predictive power after ages of 80+ years.57,301-303 One explanation is a ceiling effect, where mortality risk is already high in persons aged 75+ years because of multiple mortality risk factors so that there is a limit to the additional contribution from visual impairment to mortality. Another explanation is "selective survival", that is persons genetically predisposed to die from causes related to visual impairment will do so at a relatively younger age, leaving those without this predisposition to survive into very old age.

We found that CVI also increased mortality risk via both direct and indirect pathways. Although the direct effect of CVI on mortality risk seems counterintuitive, it is important to recognize that the association may occur in both directions. The SEM model provides information on the magnitude of the association but not its direction. There are several mechanisms that could explain the associations we found between visual impairment and mortality. Persons with various disabilities in walking may be less likely to see a doctor regularly, or to have prescriptions for critical medications filled. They may be more socially isolated, have a poorer and relatively unvaried diet and may be less able to seek urgent help when needed. They may also be less likely to exercise regularly, leading to lower cardiorespiratory reserve and greater risk of death during the stress of illness. Disabilities in walking are also associated with increasing risk of falls and fractures (e.g. hip fractures),45 which may lead to an increased risk of death.

For the direct pathway, there are probably many unidentified covariates that were not accounted for. One example is poor diet, which is associated with AMD,304-306 cataract,307-308 and with cancer,309 310 diabetes,311,312 and cardiovascular disease.309,311,313 We found some evidence of an indirect association through lower BMI to mortality for non-correctable visual impairment, which may support this speculation.
The direct pathway may also be explained by some systemic processes that are common to both visual impairment and mortality, such as chronic inflammation. For example, the CFH Y402H polymorphism is associated with ARMD and cardiovascular death independent of cardiovascular risk factors. Possession of this polymorphism is a biologically plausible cause for excess cardiovascular mortality in persons with VI due to ARMD after adjustment for cardiovascular risk factors.

To our knowledge, only one other study has used SEM to examine the pathways from visual impairment to mortality. In agreement with their findings, this study reported a small but significant indirect effect through disability. In contrast to our results, however, these authors reported that SRH was a significant indirect pathway that was independent of disability in walking. Other notable differences from this earlier study were that the indirect pathways had a lower magnitude than the direct pathway and the hazard ratios were much lower in comparison to those estimated from our study sample. There were two main differences between this earlier study and ours that may explain this disagreement. First, while the earlier study was comparable to ours in many ways, there was no objective measure of VA. Visual function was assessed by self and proxy reporting of visual impairment by asking whether each person was blind or had difficulty seeing from one or both eyes. This could have introduced bias as persons with lower SRH and/or disability might have been more likely to overestimate visual impairment and vice versa. Second, the earlier study included persons aged 18+ years in comparison to 49+ years in our study.

The strengths of our study include its large population based dataset, with high participation and long follow-up period, standardized VA assessment, use of Australian National Death Index mortality and causes of death data, and detailed data on the health and functional status...
of participants. Limitations include the possibility that not all potential mortality markers were included in the model, such as exercise, diet and nutrition variables. Also, the relatively low number of persons with visual impairment after age stratification limits our ability to detect weak associations that could be significant. Limitations of structural equation modelling include the assumption that relationships between variables in the model are linear and that the directions of the arrows in the path model are assumed but cannot be proven.
Summary

This study reaffirms that visual impairment is associated with an increased risk of all-cause mortality. Analysis using SEM suggests both direct and indirect pathways for this relationship. Disability in walking may represent an important indirect pathway to mortality for persons with visual impairment, and adjusting for this factor in statistical analysis may over-adjust for the indirect effect of visual impairment on mortality risk. It is important to recognize that the impact of visual impairment on mortality may in fact be greater than that reported from previous studies that have used traditional statistical models.
Chapter Six: *Direct and Indirect Effects of Hearing Impairment on Mortality Risk in Older Persons*
Abstract

Purpose: To assess whether hearing loss predicts an increased risk of mortality.

Methods: The Blue Mountains Hearing Study (BMHS) examined 2956 persons aged 49+ years (75.5% response) during 1997-2000. The Australian National Death Index was used to identify deaths until 2005. Hearing loss was defined as the pure-tone average (0.5-4kHz) of air-conduction hearing thresholds >25 decibels hearing level (dB HL) in the better ear. Associations between hearing loss and mortality risk were estimated using Cox regression and structural equation modelling (SEM).

Results: After 5 years, 403 participants had died. Using Cox regression, hearing loss was associated with increased risk of both cardiovascular (hazard ratio (HR) 1.36, 95% confidence interval (CI) 1.08-1.84) and all-cause mortality (HR 1.39, CI 1.11-1.79) after adjustment for age and sex, but not after multivariable adjustment. Structural equation modelling pathway analysis, however, revealed a higher all-cause mortality risk (HR 2.58, CI 1.64-4.05) in persons with hearing loss, which was mediated by two variables: cognitive impairment (HR 1.45, CI 1.08-1.94) and disability in walking (HR 1.63, CI 1.24-2.15). These variables increased mortality both directly and indirectly through effects on self-rated health. Adjusting for these co-variables in Cox regression underestimated the impact of hearing loss on mortality.

Conclusions: Hearing loss was associated with increased all-cause mortality, via three mediating variables: disability in walking, cognitive impairment and SRH. It is important to recognise that persons with combined disabilities are at increased risk of cardiovascular and all-cause mortality.
Background

Hearing impairment increases with age and was the third most frequent chronic condition reported by elderly persons in the 2002 United States National Health Interview Survey,277 affecting between 35% and 45% of persons aged 50+ years.121,278,314,315 This common disability is independently associated with many mortality risk markers including stroke163, ischemic heart disease164, diabetes165,166 and smoking.167 Hearing impairment is also associated with increased functional, physical and psychosocial impairment,316,317 poorer health related quality of life;128 increased risk of institutionalization,160 increased risk of falls,318 cognitive impairment,161 increased risk of car accidents162 and a poorer understanding of one’s health and its treatment.319 In addition, occupational noise exposure is reported to be associated with a significant increased risk of CVD and death due to AMI.158,159

Despite these associations, the link between hearing impairment and mortality is inconsistently reported, with most studies finding the association to become non-significant after multivariable adjustment.151-153,156,157 Consistent with these reports,151-153,156,157 There are no reports that assess potential pathways between hearing impairment and mortality. Better understanding of this association may help guide mortality lowering interventions in persons with hearing loss.

Prospective studies suggest that hearing impairment increases the mortality risk associated with visual impairment.151,153,291,320 However, the association with mortality independent of visual impairment is lost after adjustment for co-morbidities and self-reported health status.151,152,156,291 The association with mortality has been attributed to the effect of hearing loss on contextual variables such as self-rated health (SRH), mood, functional status and social relationships.151,152,156,291 This was based on the finding that the association was lost
after adjustment for these variables. To our knowledge there have been no reports using structural equation modelling to identify mediating variables between hearing impairment and mortality.

We aimed, using structural equation modelling in an older Australian population-based cohort, to confirm firstly, that no direct link existed between hearing impairment and mortality and secondly, to determine whether indirect associations existed through mediating variables associated with increased mortality risk.
Methods

The Blue Mountains Hearing Study (BMHS) is a population-based survey of age-related hearing loss in a representative older Australian community. The BMHS invited participants who attended the second cross-sectional survey of the Blue Mountains Eye Study (BMES 2). Persons who moved into the study area or study age group, identified from a repeat door-to-door census in 1999, were also invited to participate. Of the original 3654 participants, 575 (15.7%) died before the 5-yr follow-up eye examinations commenced, whereas 383 subjects (10.5%) moved from the study area. This left 2696 subjects still living in the region and eligible to participate. Of these, 2015 (74.7%) agreed to take part in hearing examinations, whereas 681 (25.3%) refused. At the time of participating, the mean age of hearing study subjects was 69.8 years, and there were 1156 women and 859 men. The BMHS was conducted during 1997 to 2000. Medical, alcohol and smoking histories were determined by interviewer-administered questionnaire (Methods, Chapter 2).

To identify and confirm persons who died after the baseline examination, demographic information including surname, first and second names, gender and date of birth of the 2965 participants were crossmatched with Australian National Death Index (NDI) data for deaths, to the end of 2005.

Statistical analyses were performed using SAS software v9.13 (SAS Institute, Cary, NC) and Mplus. Simple statistics included student t tests for comparing means and chi-square tests for comparing proportions. Cox regression models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI). Multivariable-adjusted models included variables found significantly associated with mortality after age adjustment. These were previous history of acute myocardial infarction (AMI), stroke, angina and hypertension, current smoking, BMI,
cancer, diabetes, walking disability, high serum urate, alcohol consumption, cognitive impairment, depression and SRH. A p value of less than 0.05 was considered statistically significant.

Structural equation modelling (SEM) pathway analysis was used to model the relationship between hearing impairment, mortality and co variables found to be significantly associated with mortality by Cox regression. Co variables used in the model were previous history of acute myocardial infarction (AMI), stroke, angina and hypertension, current smoking, BMI, cancer, diabetes, walking disability, high serum urate, alcohol consumption >1 unit per day, cognitive impairment, depression and SRH. For this model, the cardiovascular risk factors acute myocardial infarction (AMI), stroke, angina and hypertension were modelled as latent variables. Each mediating variable was adjusted for age, gender and hearing loss. The multiple potential pathways to mortality are shown in Figure 6.1.
Figure 6.1 Path model of the structural equation model for the relationship between hearing loss, risk markers and mortality.

Hearing loss

Other co-variates

Mortality

Significant co-variates

Poor Self-Rated

Covariates are corrected for age and gender

* Other covariates were smoking, alcohol intake, home ownership, low body mass index (<20 kg/m²), previous history of diagnosed angina, acute myocardial infarction, fair or poor self-reported health, high serum urate.

** Significant co-variates were disability in walking and cognitive impairment.
Results

Study population

As of 31/12/2005, 403 BMHS participants with detailed cause of death data available had died. Table 6.1 shows the distribution of significant mortality risk markers in persons with and without hearing loss. Compared to those with normal hearing, participants with hearing loss at baseline were more likely to be male, older, cognitively impaired, diabetic or underweight. They were more likely to have a self-reported history of angina, myocardial infarction, stroke, low SRH, an observed difficulty in walking or use of walking aids and reported lower alcohol consumption. There were no significant differences in the proportions of current smokers or persons with a history of cancer between the groups with and without hearing loss.
**Table 6.1** Prevalence of mortality risk markers in participants of the Blue Mountains Hearing Study by hearing impairment.

<table>
<thead>
<tr>
<th>Mortality Risk Marker</th>
<th>All Subjects</th>
<th>Hearing Impairment n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%) (n=2815)</td>
<td>No (^b) n (%)</td>
</tr>
<tr>
<td>Male</td>
<td>1218 (43.3)</td>
<td>750 (39.8)</td>
</tr>
<tr>
<td>Age Mean (SD)</td>
<td>66.6 (9.3)</td>
<td>63.5 (8.0)</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>267 (9.6)</td>
<td>188 (10.0)</td>
</tr>
<tr>
<td>Body Mass Index (^e) &lt;20</td>
<td>74 (2.6)</td>
<td>36 (1.9)</td>
</tr>
<tr>
<td>Body Mass Index (^e) 20-30</td>
<td>2023 (72.4)</td>
<td>1343 (71.6)</td>
</tr>
<tr>
<td>Body Mass Index (^e) &gt;30</td>
<td>696 (24.9)</td>
<td>497 (26.5)</td>
</tr>
<tr>
<td>Alcohol &gt;1 unit/day</td>
<td>2160 (76.7)</td>
<td>1480 (78.3)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>289 (11.0)</td>
<td>163 (9.3)</td>
</tr>
<tr>
<td>Stroke</td>
<td>119 (4.2)</td>
<td>55 (2.9)</td>
</tr>
<tr>
<td>Angina</td>
<td>291 (10.3)</td>
<td>144 (7.6)</td>
</tr>
<tr>
<td>Previous Myocardial Infarction</td>
<td>210 (7.5)</td>
<td>114 (6.0)</td>
</tr>
<tr>
<td>History of Cancer</td>
<td>314 (11.2)</td>
<td>208 (11.0)</td>
</tr>
<tr>
<td>Disability in Walking</td>
<td>194 (6.9)</td>
<td>58 (3.1)</td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td>79 (2.9)</td>
<td>21 (1.2)</td>
</tr>
<tr>
<td>Self-Rated Health Fair-Poor</td>
<td>536 (19.1)</td>
<td>319 (17.0)</td>
</tr>
</tbody>
</table>

\(^a\) Excludes subjects with hearing loss from birth, otosclerosis or conductive hearing loss.

\(^b\) ≤25 decibel hearing loss

\(^c\) >25 decibel hearing loss

\(^d\) For comparison between normal hearing and hearing impaired

\(^e\) Body Mass Index calculated in standard international units of kg/m\(^2\)
**Association between hearing loss and mortality**

Table 6.2 shows age and sex adjusted as well as multivariable adjusted cardiovascular and all-cause mortality rates, stratified by severity of hearing loss, expressed as hazard ratios (HR) with 95% confidence intervals (CI). After age and sex adjustment, cardiovascular (CV) and all-cause (AC) mortality was higher in persons with any hearing loss compared to those with normal hearing (for CV: HR 1.36, CI 1.00-1.84; for AC: HR 1.39, CI 1.11-1.75). There was no difference in the association with mortality between any, mild or moderate-severe hearing loss. There was no statistically significant association between hearing loss and cardiovascular or all-cause mortality, however, after multivariable adjustment using Cox regression (Table 6.2). There was no significant association between other causes of death (including cancer, cerebrovascular, respiratory, renal, liver, gastrointestinal, injury, neurological, diabetes and other) and hearing impairment (data not shown).
### Table 6.2

Association between the severity of hearing loss \(^a\) and mortality by cause after co-variable adjustment in the Blue Mountains Hearing Study using Cox regression, expressed as hazard ratio (HR) with 95% confidence intervals (CI): the Reference group is persons without hearing loss\(^b\) (n=1886).

<table>
<thead>
<tr>
<th>Cause of Mortality</th>
<th>Any hearing loss (n=929)</th>
<th>Mild hearing loss (n=635)</th>
<th>Moderate-severe hearing loss (n=294)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Deaths</td>
<td>HR (CI)</td>
<td>Deaths</td>
</tr>
<tr>
<td>Age and Sex Adjusted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>144</td>
<td>1.36 (1.00-1.84)</td>
<td>0.048</td>
</tr>
<tr>
<td>All-cause</td>
<td>245</td>
<td>1.39 (1.11-1.75)</td>
<td>0.004</td>
</tr>
<tr>
<td>Multivariable Adjusted (^c)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>122</td>
<td>1.06 (0.76-1.48)</td>
<td>0.73</td>
</tr>
<tr>
<td>All-cause</td>
<td>208</td>
<td>1.12 (0.88-1.44)</td>
<td>0.36</td>
</tr>
</tbody>
</table>

\(^a\) Excludes subjects with hearing loss from birth, or with otosclerosis or other causes of conductive hearing loss.

\(^b\) >25 decibel hearing loss

\(^c\) Adjusted for age, sex, smoking, alcohol, home ownership, low body mass index (<20 kg/m\(^2\)), previous history of diagnosed angina, acute myocardial infarction, walking disability, cognitive impairment (mini mental state examination <24), fair or poor self-reported health, high serum urate.
Table 6.3 shows the association between hearing loss and mortality using SEM pathway analysis. In contrast to the Cox multivariable adjusted model, SEM identified a significant association between hearing impairment and mortality after adjusting for confounders. This occurred only via indirect links to mortality through the mediating variables of disability in walking and cognitive impairment. The pathways from disability in walking and cognitive impairment to mortality occurred both directly and indirectly, via a third mediating variable, SRH. Figure 6.2 shows the path model with hazard rates and 95% confidence intervals. However, there was no significant link between mortality and SRH that was independent of disability in walking or cognitive impairment. Other co-variables including smoking, alcohol intake, home ownership, low BMI (<20 kg/m²), prior history of diagnosed angina or acute myocardial infarction, hypertension or high serum urate, were found not to be associated with either hearing loss or mortality.
**Table 6.3** The association of hearing loss\(^a\) and all-cause mortality assessed using structural equation modelling and expressed as hazard ratios with 95% confidence intervals (CI) stratified by pathway: reference group is persons with normal hearing\(^b\).

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Hazard Ratio (CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2.58 (1.64-4.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Direct</td>
<td>1.09 (0.84-1.41)</td>
<td>0.51</td>
</tr>
<tr>
<td>Indirect</td>
<td>2.37 (1.58-3.54)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Covariates of Indirect Pathway**

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Hazard Ratio (CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disability in Walking</td>
<td>1.63 (1.24-2.15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td>1.45 (1.08-1.94)</td>
<td>0.014</td>
</tr>
</tbody>
</table>

**Direct Through Covariate to Survival**

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Hazard Ratio (CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disability in Walking</td>
<td>1.37 (1.11-1.68)</td>
<td>0.003</td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td>1.25 (1.00-1.57)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

**Through Covariate via Poor Health to Survival**

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Hazard Ratio (CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disability in Walking</td>
<td>1.19 (1.05-1.37)</td>
<td>0.009</td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td>1.16 (1.01-1.32)</td>
<td>0.034</td>
</tr>
</tbody>
</table>

\(^a\) Excludes subjects with hearing loss from birth, otosclerosis or conductive hearing loss

\(^b\) >25 decibel hearing loss
Figure 6.2 Detailed path model showing estimated hazard rates and 95% confidence intervals for the relationships between hearing loss, risk markers and all-cause mortality (Total indirect effect 2.37 (1.58-3.54)).

Covariates are corrected for age and gender
* Other covariates include smoking, alcohol intake, home ownership, low body mass index (<20 kg/m²), previous history of diagnosed angina, acute myocardial infarction, fair or poor self-reported health, high serum urate.
Discussion

Consistent with previous reports using Cox regression, we observed that hearing loss predicted mortality after adjustment for age and sex, but the association became non-significant after adjusting for other co-variables associated with mortality in the study population (mortality risk markers). Using structural SEM pathway analysis we found no direct pathway between hearing loss and mortality but identified disability in walking and cognitive impairment as mediating variables for the increased mortality risk associated with hearing loss. These variables acted both directly on mortality and via a third mediating variable, SRH.

While previous studies concluded that the association between hearing loss and mortality was likely to be mediated by contextual variables such as SRH and functional status, these conclusions were based on findings that the association was lost after adjustment for these variables. In a further advancement in this field, our study using SEM has now documented that disability in walking and SRH are two mediating factors likely to account for the link between hearing impairment and mortality. To our knowledge, this is the first report to suggest that cognitive impairment may be a mediating variable between hearing loss and mortality.

Our proposed model is supported by previous work. Studies suggest that both functional and physical decline as well as cognitive impairment are associated with low SRH. Functional and physical impairment, cognitive impairment and low SRH are each independently associated with increased mortality. In keeping with these findings, our study showed that disability in walking and cognitive impairment are associated with an increased mortality risk, both directly and indirectly via SRH. Associations between hearing...
loss and measures of functional and physical decline have also been reported previously.\textsuperscript{47,132,133,289,296,318,327,328} Mechanisms that could explain the association of hearing loss with disability in walking include increased fear of falling, infirmity due to declining physical and social activities associated with hearing loss, reflecting a decreased ability to seek professional help for hearing impairment\textsuperscript{319} and impaired balance from accompanying decreased vestibular function.\textsuperscript{318}

Associations between hearing loss and cognitive impairment have also been reported.\textsuperscript{289,329-332} These may be explained by sensory underload (lack of intellectual stimulation reducing cognitive ability),\textsuperscript{329,333} attentional demands of sensory measurement (measurement of hearing loss is sensitive to negative age differences in cognitive processes such as sustained attention and discrimination),\textsuperscript{329} or some common cause (hearing loss and cognitive function are both measures of the physiological architecture of the brain).\textsuperscript{331} These reports support our finding that associations exist between hearing loss and cognitive impairment. Our study adds a new dimension to these associations and extends the hearing loss-cognitive impairment association to mortality risk by identifying pathways from hearing loss to mortality through cognitive impairment and disability in walking.

Our finding that hearing loss increased the odds of cardiovascular death but not other causes may be explained by the pathways through disability in walking and cognitive impairment. Affected persons are more socially isolated and may be less likely to see their doctor regularly, or to have prescriptions for preventive medications filled. They may also have a poorer understanding of their own health issues and its treatments.\textsuperscript{310} They may have relatively poorer diets and be less able to seek urgent help when needed. They may also be less likely or unable to exercise regularly, leading to lower cardiorespiratory reserve and
greater risk of cardiovascular death. Other causes of death may either be less susceptible to these associations, or because of fewer events, we may have had insufficient statistical power to detect associations.

Our results also suggest that severity of hearing impairment may not be so important in predicting mortality risk. This is significant as persons with mild hearing loss may not report it or the loss may go unnoticed by treating clinicians, particularly if they have cognitive or functional impairment. This makes identification of at risk groups more difficult. It also raises the possibility of some unidentified common mechanism leading to an increased risk of hearing loss, cognitive and functional impairments and mortality.

The strengths of our study include its large population based dataset, with high participation and long follow-up period, standardized hearing assessment, use of Australian National Death Index mortality and causes of death data, and detailed data on the health and functional status of participants. Limitations include the possibility that not all potential pathways were included in the model, such as the variables, exercise, and diet and nutrition variables.
Summary

This study supports the contention that hearing loss is associated with an increased risk of mortality through mediating variables, including disability in walking and SRH and identifies cognitive impairment as a further mediating variable between hearing loss and mortality risk. We could not, however, document a gradient effect from the severity levels of hearing loss on mortality risk. It is important for clinicians to recognise that persons with this combination of disabilities are at increased risk cardiovascular and all-cause mortality so they can implement strategies that may reduce mortality risk.
Chapter Seven: *Implications of the Findings of this Thesis*
This thesis provides prevalence data in a representative population based cohort of older Australians for VI, AI and OI. To our knowledge, this study is the first population based cohort study to document the prevalence of concurrent VI, AI and OI and is the first to document the prevalence of OI in a representative Australian population cohort.

We observed a high prevalence of PVI (11%), AI (43%) and OI (27.0%) in this cohort of Australians aged 60 years and over. Based on these data and the 2006 Australian census, we estimate that among Australians aged 60 years or older, 354,000 have VI, 1,383,000 have AI and 868,000 have OI.

Only two other large-population based studies have assessed the prevalence of olfactory impairment. The EHLS reported a prevalence of 24.5% rate for persons aged 43-86 years. The Skövde study reported prevalence of 32.9% in persons aged 53 years or older. After age and sex standardising our BMES prevalence to the EHLS, we observed a slightly lower prevalence of olfactory impairment of 24.3% (22.4-26.3) in our study compared with 29.8% (27.8-31.9) in the EHLS (for participants aged >60 years).

This thesis supports the reported significant age-associated increases in the prevalence of VI, AI and OI. We found the prevalence of VI, AI and OI to increase significantly with increasing age.

This thesis supports reported gender biases for VI, AI and OI. We found auditory and olfactory impairments were more frequent in men and visual impairment more frequent in women.
To our knowledge, we are the first to examine the clustering patterns of VI, AI and OI. We observed that the prevalence of two or more sensory impairments in older persons was higher than the predicted prevalence if these impairments were assumed to have occurred randomly and independently. This suggests common mechanisms may underlie VI, AI and OI.

We observed different clustering patterns between men and women. This finding suggests mechanisms and/or exposures (e.g. workplace or environmental exposures, smoking status, genetic, hormonal or other sex differences) underlying these sensory deficits may differ between men and women.

This thesis supports previous reports of increased mortality risk in persons with VI. We observed that the presence of visual impairment predicted mortality in older persons using Cox regression.

This thesis supports previous reports that hearing loss is associated with increased mortality after adjustment for age and sex, but not after adjustment for co-variables associated with mortality in the study population. Using SEM pathway analysis, we confirmed that PVI, CVI and NCVI increased mortality via both direct and indirect pathways. Based on our estimates from SEM, Cox regression underestimates the association of visual impairment with mortality by over-correcting for intermediate variables associated with both visual impairment and mortality. Visual impairment was reported to be independently associated with many of the confounding variables associated with mortality and corrected for in previous studies.
When modelling these associations, it must be considered that due to complex interactions between other mortality risk factors and visual impairment, correcting for these covariates may underestimate the association between visual impairment and mortality.\textsuperscript{115}

To our knowledge, only one other study has used SEM to examine the pathways from visual impairment to mortality.\textsuperscript{299} This study reported a small but significant indirect effect through disability. We identified disability in walking as a potential mediating variable for the association between VI and mortality. Two possible pathways were identified, one involved only disability in walking; the second also involved an effect through low SRH. We found evidence of an indirect association through lower BMI to mortality for non-correctable visual impairment.

To our knowledge, ours is the first study to examine the association between hearing impairment and mortality risk using SEM pathway analysis. We found no direct pathway between hearing loss and mortality but identified indirect pathways via two mediating variables: disability in walking and cognitive impairment. These variables acted both directly on mortality and via a third mediating variable, SRH.

To our knowledge, ours is the first to document that disability in walking and SRH are two mediating factors likely to account for the link between hearing impairment and mortality. Previous studies concluded the association between hearing loss and mortality was likely mediated by contextual variables such as SRH and functional status.\textsuperscript{151,152,156,291} These reports support our findings.
To our knowledge, ours is the first report to suggest cognitive impairment may be a mediating variable between hearing loss and mortality. Associations between hearing loss and cognitive impairment have been reported previously. These reports support our finding that associations exist between hearing loss and cognitive impairment.

Our finding that disability in walking is a mediating variable between VI, AI and mortality has important implications for the care of older persons. Affected persons are reportedly more socially isolated and may be less likely to see their doctor regularly, or to have prescriptions for preventive medications filled. They may have relatively poorer diets and be less able to seek urgent help when needed. They may also be less likely or unable to exercise regularly, leading to lower cardiorespiratory reserve and greater risk of illness and death. It is important for clinicians to recognise this combination of disabilities may increase morbidity and mortality so treatment strategies are formulated and implemented early.

Our data support an essential role for olfactory function in maintaining a healthy nutritional status and body weight. Our finding that participants with moderate olfactory impairment were twice as likely to be underweight (BMI <20 kg/m²) than those without impaired olfaction has important implications for the care of older persons. Ours is the first community-based study to demonstrate that older people with mild renal impairment are significantly more likely to have moderate (but not mild) olfactory impairment. It is important for clinicians to recognise that persons with renal impairment are at higher risk of OI and that persons with OI may be at increased risk of nutritional deficiencies so they can
implement strategies that may reduce this risk. Several smaller studies demonstrated similar findings.263,270,271

This thesis provides additional data to support the link between impaired olfaction and neurodegenerative disorders, including cognitive impairment and PD.175,201,205,207,209,210,216,217,219,257,272 After multivariable adjustment, BMES participants with marked cognitive impairment had approximately 3-fold higher odds of mild and approximately 6-fold higher odds of moderate OI. Participants with a diagnosis of Parkinson disease had a 10- and 16-fold higher risk of having mild and moderate olfactory impairment, respectively.

This thesis supports a previous population studies168,170,173,175,177 that self-reported OI was an unreliable indicator of measured olfactory decline. Of those with olfactory deficit, 67.8% did not report a loss of smell function. Of participants that did report smell deficit, 40.5% had no measurable loss.

While not examined in this study, it is important to consider that presence of all three sensory impairments may increase the burden of shared adverse health outcomes on affected individuals and their families and carers. Combined vision and auditory impairments have been reported to cumulatively decrease health-related quality of life148,296 and to increase mortality risk.151,153,291 Associations of each impairment, VI, AI or OI, with measures of independence, functional and physical decline, low SRH and nursing home placement have been previously reported.20-23,27,29,31,33,37,41,42,125-129,131,132,160,173,177,182,184-187,253,289 Evidence on
whether correcting these sensory impairments with hearing or low vision aids would reduce their negative impact is limited with further studies needed.

Our findings highlight several public health concerns for individuals suffering from multiple sensory impairments. Specifically, the current imperfect care system inhibits the effective delivery of services and rehabilitation to older people with multiple sensory impairments. Visual, olfactory and auditory impairments tend to aggregate mutually and dependently in this cohort of older Australians. This implies that once a sensory impairment is detected, screening for other concomitant sensory impairment may be warranted. The higher than expected frequency of combined sensory impairment implies that current health care provision may not meet the needs of older persons with sensory impairment. Self-report is an inaccurate measure of sensory impairment in older persons so they are likely to be under-reported. There has been no active screening using case-finding strategies to detect older persons with sensory impairment. By the time affected individuals are identified they may already be socially isolated and have substantially reduced quality of life and limitations in daily functioning.

Separate vision and hearing rehabilitation systems currently operating in Australia and the U.S. fail to service and support older people with multiple sensory impairments in a coherent and collaborative manner. The bewildering complexity of current systems for the care of older people with two or more sensory impairments highlights the need for clearer, and better co-ordinated health policies. Our study findings advocate for greater attention from health care providers and health policy makers to improve health care services to older persons with sensory impairments.
The strengths of our study include its large population-based dataset with high participation rate; the use of standardised measurements of vision, olfaction and hearing; the use of Australian National Death Index mortality and cause of death data; and detailed data on the health and functional status of participants.

The limitations of our study design include the study sample being a survivor cohort and the data being cross-sectional in nature. Our study may underestimate the prevalence of sensory impairment as those who did not have complete sensory data tended to be older and therefore more likely to have individual or multiple sensory impairments. In addition, the small number of persons with combined sensory impairment in the two gender subgroups could have led to chance findings in the different clustering patterns of these sensory impairments between men and women, and limits our ability to detect weak associations that could have been significant.

The SDOIT tests a limited number of “common” stimulants, possibly resulting in under-detection of deficits. In addition, the SDOIT assesses odour identification but not threshold. It is, however, substantially more reliable than self-reported methods. This simple and quick test may be useful in screening older persons at risk of neurodegenerative disease and malnutrition. The presence of nasal polyps, known to reduce olfactory function, was not assessed in our study. This may have led to an underestimation of the associations with other comorbid conditions.

The limitations of the SEM include the possibility that not all potential pathways were included, such as the variables, exercise, diet and nutrition.
Chapter Eight: *Summary*
Visual, auditory and olfactory impairments were frequent in this representative older Australian population. We estimate that among Australians aged 60 years or older, 354,000 have visual impairment, 1,383,000 have auditory impairment and 868,000 have olfactory impairment. The prevalence of VI, AI and OI increased with increasing age in both sexes. The prevalence of AI and OI was higher in males. The prevalence of VI was higher in females.

Visual, auditory and olfactory impairments aggregated mutually and dependently. If one sensory impairment is detected, screening for other concomitant sensory impairment seems warranted. Common mechanisms may underlie these disabilities and their associated morbidities and mortality. Separate hearing and vision services may not adequately support older persons with multiple impairments.

Our data support an essential role for olfactory function in maintaining a healthy nutritional status and body weight and provide additional support to the link between impaired olfaction and neurodegenerative disorders, including cognitive impairment and Parkinson disease. Olfactory assessment may be a simple to administer, useful clinical tool, in older persons.

This data reaffirms that visual impairment is associated with an increased risk of all-cause mortality and suggests the impact of visual impairment on mortality may be greater than that reported by previous studies using traditional statistical models. Analysis using SEM suggests both direct and indirect pathways for this relationship. Disability in walking may represent an important indirect pathway to mortality, both directly and via SRH, for persons with visual
impairment. Adjustment for these mediating variables in statistical analysis may over-adjust for the association between visual impairment and mortality risk.

This study supports the contention that hearing loss is associated with an increased risk of mortality through mediating variables, including disability in walking and SRH and identifies cognitive impairment as another mediating variable between hearing loss and mortality risk.

Studies of sensory impairment using self-report do not correlate have poor correlation with objective measures of sensory impairment overall. Importantly, self-reported sensory impairment is associated with higher risk of morbidity compared to objectively measured impairment. This may lead to overestimation of the significance of the associations between sensory impairment and morbidity. It is important for clinicians to recognise this and that formal testing is preferred. It is also important that clinicians recognise that persons with this combination of disabilities, particularly self-reported sensory impairment with normal objective measures of the senses, are at increased risk of social isolation, depression, low SRH and QOL, functional difficulties, mobility problems, falls, fractures and mortality so they may implement strategies that reduce these risks.
Chapter Nine: *Future Studies*
Over 50% of participants with OI had normal BMI and no neurodegenerative disease. Longitudinal studies in this cohort to assess the incidence of neurodegenerative disease in persons with and without OI will provide useful data regarding the sensitivity and specify of this simple test in predicting neurodegenerative disease risk in a representative population of older adults.

Olfactory impairment was associated with low BMI in this cohort. Longitudinal studies in this cohort assessing whether persons with normal BMI and OI are at increased risk of subsequent low BMI are needed. If OI predicts subsequent weight loss then this simple test may allow early nutritional intervention in persons at risk.

The significant inverse association between hypertension, total cholesterol and measured olfactory impairment, may be confounded by premature death in participants with these co-morbidities, by medications used to control these risk factors, or some shared mechanistic pathway. The associations warrant further investigation given the previously reported relationship between blood pressure, cholesterol and the incidence of cognitive decline.

Associations between VI, AI or OI individually and of VI and AI combined and measures of independence, functional and physical decline, low SRH, nursing home placement and mortality have been previously reported. Evidence if possession of all 3 sensory impairments further increases the observed negative impacts and whether correcting sensory impairments reduces significantly these negative associations is limited. Longitudinal studies are needed to address this question.
Our study found VI, AI and OI clustered dependently and that AI and VI were associated with increased mortality risk indirectly via disability in walking. Studies examining the clustering behaviour of these sensory impairments with disability in walking in this cohort would add weight to our findings. If disability in walking did dependently cluster with these sensory impairments then underlying biological mechanisms could be postulated and investigated.

Whether sensory impairments are independent risk factors for mortality remains unknown. One of the difficulties in objectively scrutinising the literature is that study populations significantly differ and co-variables adjusted for are not standardised. Biologically plausible mechanisms need to be postulated and investigated to help elucidate this question. Such research may identify potential drug targets to reduce morbidity and mortality. The CFH Y402H polymorphism has been reported associated with ARMD, CVD and hearing impairment suggesting a biologically plausible explanation for the association between VI and HI and mortality, particularly cardiovascular mortality after adjustment for cardiovascular risk factors in ARMD. Studies examining the associations and clustering behaviour between CFH Y402H polymorphism and VI, HI, OI, walking disability and low SRH in this cohort would help determine whether this polymorphism has potential as one biological explanation for the dependent clustering characteristics of these sensory impairments and their direct and indirect associations with morbidity and mortality.

Overall the literature suggests glaucoma is not associated with increased mortality, all though one study did report a significant association. Glaucoma is underdiagnosed in the community and one large study found significant associations with mortality when combining baseline
IOP >21mmHg and diagnosed glaucoma as the at risk group. Neither elevated IOP nor glaucoma predicted mortality in this study. Studies that have assessed only baseline diagnosed glaucoma may have underestimated an association between IOP and mortality. Over adjustment of mediating co-variables is another possible cause for underestimating this association and SEM would be useful in this regard. The association of baseline elevated IOP and glaucoma with mortality warrants further investigation. That timolol may be associated with higher mortality in glaucoma patients also warrants further investigation.
Appendix A: *Blue Mountains Eye Study Questionnaires*  
*and Flow Sheets*
1. Identity
1-1 (Identif) ID number □□□□
1-2 (hosp) Blue Mountains Hospital No. ..............................
1-3 (hosp2) Westmead Hospital No. .................................
1-4 (name) Surname ......................................................
1-5 (name) First name(s) ................................................
1-6 (sex) Sex: Female □1 Male □2
1-7 (dob) Date of birth …/…/……
1-8 (address) Your current address? ........................................

...........................................................................................................

1-9 (postcode) Postcode □□□□
1-10 (usual) Is this your usual address (live here more than 6 months of the year)? □Y 1 □N 2
1-11 (phone) Your phone number? ...................................................

1-12 (otherd) Do you have another address? □Y 1 □N 2 □ DK 8 □ Missing 9
1-13 (otherd) If yes, other address: ..............................................

...........................................................................................................

1-14 (postcode) Postcode □□□□
1-15 (private) Are you a member of a private health fund? □Y 1 □N 2 □ DK 8 □ Missing
1-16 (yearBM) How long have you lived in the Blue Mountains? …….. years □ DK 8 □ Missing 9
1-17 (marital) What is your current marital status?
never married ..................... □1 divorced ............. □ 4
married............................... □2 widowed .......... □ 5
separated but not divorced ........ □ 3 DK .................. □ 8
missing ..................... □ 9

1-18 (family) Have we seen any of your family members previously in the Eye Study?
□Y 1 □N 2 □ DK 8 □ Missing 9
1-19 (family) If yes, who (name and relationship)
Person 1.......................................................... (rel1type) relationship..............................
Person 2.......................................................... (rel2type) relationship ..............................
For person 1

1-20  {(1st/2nd)}  Has or will he/she been seen in the 10-year follow up study?
□ Y  □ N  □ DK  □ Missing

1-21  {(1st/2nd)}  If no, do you know why he/she has not returned?
.................................................................................................................. | code

1-22  {(1st/2nd)}  If deceased, do you know the date of his/her death?  ....../.....

For person 2

1-23  {(2nd/2nd)}  Has or will he/she been seen in the 10-year follow up study?
□ Y  □ N  □ DK  □ Missing

1-24  {(2nd/2nd)}  If no, do you know why he/she did not return?
.................................................................................................................. | code

1-25  {(2nd/2nd)}  If deceased, do you know the date of his/her death?  ....../.....

1-26  {(2nd)}  Is anyone else in your household eligible for the Study (i.e. aged 50 or older and has not previously participated in the Study)?  □ Y  □ N  □ DK  □ Missing

1-27  {(2nd/come)}  If yes, do you think he would be interested in participating at a later date?
□ Y  □ N  □ DK  □ Missing

1-28  {(2nd/come)}  Name and contact details?
..............................................................................................................................................
..............................................................................................................................................

Could you please give us the name and addresses of two people we could contact to get a forwarding address for you if you move?

Contact 1

1-29  {(fname1)}  Name.................................................................

1-30  {(fph1)}  Telephone...........................................................

1-31  {(fadd1)}  Address..............................................................................................................
..............................................................................................................................................

1-32  {(frel1)}  Relationship....................................................

Contact 2

1-33  {(fname2)}  Name.................................................................

1-34  {(fph2)}  Telephone...........................................................

1-35  {(fadd2)}  Address..............................................................................................................
..............................................................................................................................................

1-36  {(frel2)}  Relationship....................................................
General Practitioner

1-37 (Opium) Who is your GP? .................................................................

1-38 (addGP) What address is his/her surgery? ................................................

1-39 (IntGP) When did you last visit your GP? ...............months ago

1-40 (freqGP) How often do you visit your GP? ..............................................per...

Ophthalmologist / optometrist

1-41 (whoeve) Who was the last person you saw for your eyes, for glasses or any eye treatment?

1-42 (wheneve) When? (Specify month & year if in the last 1 year) ....../.....

1-43 (adreme) In which suburb are his/her rooms? ...........................................

1-44 (optoph) Was it, an optometrist...........☐1 ☐DK ...... ☐8

            an eye specialist?...........☐2 go to 1-46 missing ..................☐9

1-45 (sezoph) If not an eye specialist, have you previously seen an eye specialist?
              ☐Y ☐N ☐go to 1-49 ☐DK ☐Missing

1-46 (whooph) If yes, who was the last eye specialist you saw? .....................

1-47 (wheneoph) When? (Specify month & year if in the last 1 year) ....../.....

1-48 (locoph) In which suburb are his/her rooms? ........................................

Report

1-49 (report) We plan to send a report of your eye and hearing results to you and your GP.

Are you happy with this? Yes, participant only ☐1

GP only ☐2

Both ☐3

No ☐4

1-50 (repo) Are there any other practitioners (ophthalmologist, optometrist, ENT doctor, audiologist) you would like us to send a copy of the report?

........................................................................................................

........................................................................................................

........................................................................................................

........................................................................................................

........................................................................................................
Station 1

2. Demography

2-1 (examday) Exam Date …… /……
2-2 (first) Start Time ………………hrs (24 hr time)
2-3 (examloc) 70 Great Western Highway, Leura in nursing home/ hostel…
    Westmead Hospital…
    other site…………………
    ☐ 1 Specify……………………………
    ☐ 3 Specify…………………………… | code………..

Thank you for attending the Eye Study. Before we commence the eye exam, we'd like to collect some general information about you. The information you provide is strictly confidential. If you have any queries or don't understand any questions please ask. I will first ask you to read and sign the consent form.

2-4 (trnscp) How did you get to the study today?
    ☐ 1 Walked.
    ☐ 2 Bus.
    ☐ 3 Taxi.
    ☐ 4 drove self.
    ☐ 5 friend/ rel drove.
    ☐ 6 hospital bus.
    ☐ 7 study driver.
    ☐ 8 don't know.
    ☐ 9 missing.
    ☐ 10 other.
    ☐ specify…………………………… | code………..

2-5 (jobstat) Are you retired or still employed?
    ☐ 1 house duties.
    ☐ 2 retired go to 2-7
    ☐ 3 employed go to 2-8
    ☐ 4 medical disability
    ☐ 5 unemployed
    ☐ 6 other
    ☐ 7 DK
    ☐ 8 missing
    ☐ 9 code

2-6 (retired) If retired, how old were you when you retired?………years ☐ DK ☐ Missing

2-7 (prejob) If employed, what is your present occupation?……………………………… | code………..

2-8 (spnjob) If now married or widowed, what kind of work does/did your spouse do for most of his/her life?………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………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The next question concerns your current income and is identical to the income question in the 2001 Census. All information you provide is confidential. However, as these questions involve personal details, which you may not wish to disclose, you can choose not to answer this question if you wish.

3-4 (place) What sort of a place do you live in?
- own house ............... 1
- own flat/unit ............. 2
- rented house ............. 3
- rented flat ............... 4
- hostel .................... 5
- boarding house .......... 6
- nursing home ............ 7
- with relatives ............ 8
- other ..................... 9
- specify .................. 88
- missing ................. 99

3-5 (wholive) Who lives with you? (multiple answers possible)
- nobody .......................... 1
- friend .......................... 6
- spouse .......................... 2
- pets ............................ 7
- partner ......................... 3
- other .......................... 8
- daughter ....................... 4
- DK ............................. 88
- son ............................ 5
- missing ...................... 99

Do you get regular help at home from .......?

<table>
<thead>
<tr>
<th>yes</th>
<th>no</th>
<th>DK</th>
<th>missing</th>
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<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
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</tbody>
</table>

3-6 (now) Meals on Wheels 1 2 8 9
If yes, no. of visits....... per week

3-7 (nurse) community nurse 1 2 8 9
If yes, no. of visits ....... per week

3-8 (home) Home Care 1 2 8 9
If yes, no. of visits ......... per week

3-9 (othhelp) others 1 2 8 9
If yes, specify....................
      no. of visits ........ per week

3-10 (clean) Who usually cleans your house?
- you .......................... 1
- friend ........................ 6
- spouse/partner .............. 2
- others ........................ 7
- daughter ..................... 3
- DK ............................ 8
- son ............................ 4
- missing ...................... 9
- other relatives .......... 5

3-11 (shop) Who usually does your shopping?
- you .......................... 1
- friend ........................ 6
- spouse/partner .............. 2
- others ........................ 7
- daughter ..................... 3
- DK ............................ 8
- son ............................ 4
- missing ...................... 9
- other relatives .......... 5

Are you able to go out alone....?

3-12 (go) to do the shopping Y 1 N 2
3-13 (visit) to visit someone Y 1 N 2
3-14 (town) to go to 'town' Y 1 N 2

4. Check whether this collected previously

4-1 (medica) If not obtained: Medicare number

5 344
5. Present Medications

5-0 (cussed) Are you currently taking any medications?  
☐ Y  □ N  go to 6-0  ☐ DK  □ Missing

<table>
<thead>
<tr>
<th>Name</th>
<th>code</th>
<th>strength (mg) per tablet</th>
<th>no. of tablets/day</th>
<th>duration (months)</th>
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<tbody>
<tr>
<td>5-1 (tab1)</td>
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<td>5-2 (tab2)</td>
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<td>5-3 (tab3)</td>
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<td>5-4 (tab4)</td>
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<td>5-5 (tab5)</td>
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<td>5-6 (tab6)</td>
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<td>5-7 (tab7)</td>
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<td>5-8 (tab8)</td>
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<td>5-9 (tab9)</td>
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<td>5-10 (tab10)</td>
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<tr>
<td>5-11 (tab11)</td>
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<td>5-12 (tab12)</td>
<td></td>
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</tbody>
</table>
Medication List
(please attach securely)
6. Past Medications
6-0 (post) Can you recall any other tablets, vitamins, drops, or other medications that you are not taking now that you have taken for more than 3 months in the past 5 years?
☐ Y ☐ N → go to 7-0 ☐ DK ☐ Missing

If yes, request to see list prepared (sent with confirmation of appointment)

<table>
<thead>
<tr>
<th>Name</th>
<th>code</th>
<th>strength (mg)</th>
<th>no./day</th>
<th>duration (months)</th>
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<td>6-1</td>
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<td>6-8</td>
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7. Eyedrop Medications
7-0 (eyesed) Are you currently using any eyedrops for any eye conditions?
☐ Y ☐ N → go to 8-1 ☐ DK ☐ Missing

<table>
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<tr>
<th>Name</th>
<th>yes</th>
<th>no</th>
<th>DK</th>
<th>missing</th>
<th>code</th>
<th>strength (%)</th>
<th>drops/day</th>
<th>duration (months)</th>
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<tbody>
<tr>
<td>7-1 (drop1)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>N/A</td>
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<tr>
<td>7-2 (drop2)</td>
<td></td>
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<td>2</td>
<td>8</td>
<td>9</td>
<td>N/A</td>
<td></td>
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<tr>
<td>7-3 (drop3)</td>
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<td></td>
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<td>specify.......</td>
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<td>7-4 (drop4)</td>
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<td>specify.......</td>
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<td>7-5 (drop5)</td>
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<td>7-6 (drop6)</td>
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<td>specify.......</td>
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</table>
8. Specific Medications

Aspirin
I am now going to ask questions about your use of aspirin. Aspirin-based drugs include: solpin, cardiprin, diprin, ecolotin, but not panadol or dymadon.

<table>
<thead>
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<th>Code</th>
<th>Question</th>
<th>Options</th>
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<tbody>
<tr>
<td>8-1</td>
<td>Have you taken aspirin in the last 12 months?</td>
<td>Y</td>
</tr>
<tr>
<td>8-2</td>
<td>If yes, how many aspirin would you typically consume per month?</td>
<td>tablets per month</td>
</tr>
<tr>
<td>8-3</td>
<td>For how many years have you been taking this amount?</td>
<td>yrs</td>
</tr>
</tbody>
</table>

Steroids

<table>
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<tr>
<th>Code</th>
<th>Question</th>
<th>Options</th>
</tr>
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<tbody>
<tr>
<td>8-4</td>
<td>Have you ever taken steroid tablets such as Prednisone for asthma, arthritis or other conditions for more than one month?</td>
<td>Y</td>
</tr>
</tbody>
</table>

If yes, which tablets?

<table>
<thead>
<tr>
<th>Code</th>
<th>Name</th>
<th>yes</th>
<th>no</th>
<th>DK</th>
<th>missing</th>
<th>code</th>
<th>strength (mg)</th>
<th>no./day</th>
<th>duration (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-5</td>
<td>Prednisone</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-6</td>
<td>Other</td>
<td>specify</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

8-7 What condition were you taking steroid tablets for?

8-8 Have you ever used any steroid inhalers for more than one month in the form of nasal sprays, puffers, turbulahers or nebulisers? This does not include ventolin, intal or Bricanyl.

If yes, have you taken....

<table>
<thead>
<tr>
<th>Code</th>
<th>Name</th>
<th>yes</th>
<th>no</th>
<th>don't</th>
<th>missing</th>
<th>know</th>
<th>strength</th>
<th>Puffs</th>
<th>duration (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-9</td>
<td>Beconase (nasal spray for hay fever)</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-10</td>
<td>Beflote (yellow), without spacer</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-11</td>
<td>Beflote (yellow), with spacer</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-12</td>
<td>Becotide (brown), without spacer</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-13</td>
<td>Becotide (brown), with spacer</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-14</td>
<td>Pulmicort (white, makes a clicking noise)</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-15</td>
<td>Pulmicort (brown), without spacer</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-16</td>
<td>Pulmicort (brown), with spacer</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Name</td>
<td>yes</td>
<td>no</td>
<td>don’t</td>
<td>missing</td>
<td>strength</td>
<td>Puffs/day</td>
<td>duration (months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>-----</td>
<td>----</td>
<td>-------</td>
<td>---------</td>
<td>----------</td>
<td>-----------</td>
<td>------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-17 Pulmicort via a nebuliser, with a mask</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-18 Pulmicort via a nebuliser, with a mouthpiece</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-19 Flixotide puffer (orange)</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-20 Aldecin puffer (white/maroon)</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-21 Other: specify</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Antidepressants**

8-22 Have you ever taken tablets for depression? ☐ Y 1 ☐ N 2 ☐ DK 8 ☐ Missing 9

Have you ever taken any of the following tablets?

<table>
<thead>
<tr>
<th>Name</th>
<th>yes</th>
<th>no</th>
<th>DK missing</th>
<th>code</th>
<th>strength (mg)</th>
<th>Freq.</th>
<th>duration (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-23 Zoloft (sertraline)</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-24 Prozac, Erocap, Auscap, Fluohexal, Lovan, Zactin (fluoxetine)</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-25 Aropax (paroxetine)</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-26 Cipramil (citalopram)</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-27 Luvox (fluvoxamine)</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-28 Endepr, Tryptanol (amitriptyline)</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-29 Other: specify</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**B12 and Folate**

8-30 Do you have B12 (Neocytamen) injections? ☐ Y 1 ☐ N 2 go to 8-33 ☐ DK 8 ☐ Missing 9

8-31 If yes, how often do you receive them? ........months

8-32 how many years have you been receiving them? ........years

8-33 Have you been taking folate tablets? ☐ Y 1 ☐ N 2 go to 9-1 ☐ DK 8 ☐ Missing 9

8-34 If yes, how often do you take them? ...........

8-35 how many years have you been taking them? ........years
Medical and Surgical History

I would like to ask some questions about your general health, to find whether this is related to eye disease.

9. General

9-1 (health) For someone of your age, how would you rate your overall health? Is it?
   - ☐ Excellent 1  ☐ Good 2  ☐ Fair 3  ☐ Poor 4  ☐ DK 8  ☐ Missing 9

9-2 (bed) Have you spent more than a week in bed because of illness or injury in the past 3 months?
   - ☐ Y 1  ☐ N 2  ☐ DK 8  ☐ Missing 9

9-3 (hospad) Have you had any admissions (at least overnight) to a hospital in the last 12 months?
   - ☐ Y 1  ☐ N 2  ☐ go to 9-7  ☐ DK 8  ☐ Missing 9

9-4 (hospadm) If yes, number of times________times
   - ☐ DK 8  ☐ Missing 9

9-5 What were you admitted for?
   - (hosres1)............................................................................................................ code.......
   - (hosres2)............................................................................................................ code.......
   - (hosres3)............................................................................................................ code.......

9-6 Which hospital(s)?
   - (hosnam1)............................................................................................................ code.......
   - (hosnam2)............................................................................................................ code.......
   - (hosnam3)............................................................................................................ code.......

9-7 (outpad) Have you had any visits to an outpatient department in the last 12 months?
   - ☐ Y 1  ☐ N 2  ☐ go to 10-1  ☐ DK 8  ☐ Missing 9

9-8 (outpada) If yes, number of times________times
   - ☐ DK 8  ☐ Missing 9

9-9 What medical condition were you visiting OPD for?
   - (outopd1)............................................................................................................ code.......
   - (outopd2)............................................................................................................ code.......
   - (outopd3)............................................................................................................ code.......

9-10 Which hospital?
   - ☐  ☐ DK 8  ☐ Missing 9

   - (outnam1)............................................................................................................ code.......
   - (outnam2)............................................................................................................ code.......
   - (outnam3)............................................................................................................ code.......

350
10. Medical Conditions

Has a doctor advised you that you have any of the following conditions........

<table>
<thead>
<tr>
<th>10-1</th>
<th>(angina) “angina”?</th>
<th>□ Y  □ N  □ DK  □ Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>If yes,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-1.1</td>
<td>(angyr) When was it first diagnosed? ........ years ago</td>
<td></td>
</tr>
<tr>
<td>10-1.2</td>
<td>(angrcq) Was the diagnosis confirmed with an ECG? □ Y  □ N  □ DK  □ Missing</td>
<td></td>
</tr>
<tr>
<td>10-1.3</td>
<td>(angrd) Name &amp; address of Dr. who made diagnosis?</td>
<td></td>
</tr>
<tr>
<td>10-1.4</td>
<td>(angrb) How often do you take anginine tablets or sprays? ...... times per ......</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>10-2</th>
<th>heart attack?</th>
<th>□ Y  □ N  □ DK  □ Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>If yes,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-2.1</td>
<td>(miyu) When was it diagnosed? ........ years ago</td>
<td></td>
</tr>
<tr>
<td>10-2.2</td>
<td>(miqig) Was the diagnosis confirmed with an ECG? □ Y  □ N  □ DK  □ Missing</td>
<td></td>
</tr>
<tr>
<td>10-2.3</td>
<td>(mildd) a blood test? □ Y  □ N  □ DK  □ Missing</td>
<td></td>
</tr>
<tr>
<td>10-2.4</td>
<td>(milh) Name &amp; address of Dr. who made diagnosis?</td>
<td></td>
</tr>
</tbody>
</table>

| 10-2.5 | (milgo) Were you admitted to hospital? □ Y  □ N  □ DK  □ Missing |
| 10-2.6 | (milpmd) Which hospital?................................. |
| 10-2.7 | (milopt) For how long?.............days |
| 10-2.8 | (mirx) Treatment for your heart attack? |
| | □ Bypass...................years ago at ....................................hospital |
| | □ Angioplasty..........years ago at ..............................................hospital |
| | □ Pacemaker ............years ago at ................................................hospital |
| | □ Valve replacement ..........years ago at ...........................................hospital |
| | □ Other: specify................................................................. |

<table>
<thead>
<tr>
<th>10-3</th>
<th>stroke?</th>
<th>□ Y  □ N  □ DK  □ Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>If yes,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-3.1</td>
<td>(cswrt) When was it diagnosed? ........ years ago</td>
<td></td>
</tr>
<tr>
<td>10-3.2</td>
<td>(csCT) Was the diagnosis confirmed with a CT scan? □ Y  □ N  □ DK  □ Missing</td>
<td></td>
</tr>
<tr>
<td>10-3.3</td>
<td>(csck) Name &amp; address of Dr. who made diagnosis?</td>
<td></td>
</tr>
</tbody>
</table>

| 10-3.4 | (cswio) Were you admitted to hospital? □ Y  □ N  □ DK  □ Missing |
| 10-3.5 | (cswpmd) Which hospital?................................. |
| 10-3.6 | (cswopt) For how long?.............days |
| 10-3.7 | (cswaff) How did the stroke affect you? □ Mild □ Moderate □ Severe |
| 10-3.8 | (cswood) Part of body affected: Arm □ right □ left Leg □ right □ left Speech □ Other ................. |
| 10-3.9 | (csweso) How well have you recovered from the stroke?.....% (100% is full recovery) |
| 10-3.10 | (csw0m) How long did it take? ..........months |
10-3.11 Treatment for your stroke?

- ☐ Aspirin, clopidogrel, persantin
- ☐ Anticoagulation (heparin, clexane and warfarin)
- ☐ Don’t know

**Has a doctor advised you that you have any of the following conditions?**

<table>
<thead>
<tr>
<th>10-4</th>
<th>Mini-Stroke or TIA?</th>
<th>☐ Y 1</th>
<th>☐ N 2</th>
<th>☐ DK 8</th>
<th>☐ Missing 9</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Stroke-like episodes with weakness in your face, fingers, hands, arms which last for short periods of time transient loss of vision in one eye)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If yes

10-4.1 When was the first attack? .......... years ago
10-4.2 Did you ever have surgery to the brain or neck to correct or prevent a stroke? 

10-4.3 Which hospital did you have this surgery at? ................................................. years ago
10-4.4 Surgery ................... years ago

<table>
<thead>
<tr>
<th>10-5</th>
<th>high blood pressure?</th>
<th>☐ Y 1</th>
<th>☐ N 2</th>
<th>☐ DK 8</th>
<th>☐ Missing 9</th>
</tr>
</thead>
</table>

If yes

10-5.1 When was it first diagnosed? ........ years ago
10-5.2 For how many years has it been treated with medications? ............... years

<table>
<thead>
<tr>
<th>10-6</th>
<th>high cholesterol?</th>
<th>☐ Y 1</th>
<th>☐ N 2</th>
<th>☐ DK 8</th>
<th>☐ Missing 9</th>
</tr>
</thead>
</table>

If yes

10-6.1 When was it first diagnosed? ........ years ago
10-6.2 Are you taking tablets?

- ☐ Gemfibrozil (lipid, ausgem)
- ☐ Fluvastatin (lescol, vastin)
- ☐ Simvastatin (lipex, zocor)
- ☐ Other

No ☐ DK ☐

(Colestipol, Atorvastatin, Cerivastatin, Pravastatin, Probucol, Cholestryamine, Nicotinic Acid)

**Has a doctor advised you that you have any of the following conditions?**

<table>
<thead>
<tr>
<th>10-7</th>
<th>asthma?</th>
<th>☐ Y 1</th>
<th>☐ N 2</th>
<th>☐ DK 8</th>
<th>☐ Missing 9</th>
</tr>
</thead>
</table>

If yes

10-7.1 When was it first diagnosed? .......... years ago

<table>
<thead>
<tr>
<th>10-8</th>
<th>gout?</th>
<th>☐ Y 1</th>
<th>☐ N 2</th>
<th>☐ DK 8</th>
<th>☐ Missing 9</th>
</tr>
</thead>
</table>

If yes

10-8.1 When was the first episode of gout? ........ years ago
10-8.2 Are you taking a medicine for gout?

- ☐ Allopurinol
- ☐ Colchicine
- ☐ Probenecid
- ☐ Other

No ☐ DK ☐

<table>
<thead>
<tr>
<th>10-9</th>
<th>arthritis?</th>
<th>☐ Y 1</th>
<th>☐ N 2</th>
<th>☐ DK 8</th>
<th>☐ Missing 9</th>
</tr>
</thead>
</table>

If yes

10-9.1 When was it first diagnosed? .......... years ago
10-9.2 Has your doctor told you what type of arthritis it is? .................. ☐ DK 8

☐ Missing 9
10-10 (ca)
Have you been diagnosed with cancer?☐ Y ☐ N ☐ DK ☐
☐ Missing ☐

If yes
10-10.1 Cancer 1
a (extry) year of diagnosis…………………
b (extryp) Type of cancer……………………………
c (extri) Chronological treatment details (plus year)……………………………
………………………………………………………………………………………………
d (extri) Name and address of Doctor treating you……………………………
………………………………………………………………………………………………
10-10.2 Cancer 2
a (extry) year of diagnosis…………………
b (extryp) Type of cancer……………………………
c (extri) Chronological treatment details (plus year)……………………………
………………………………………………………………………………………………
d (extri) Name and address of Doctor treating you……………………………
………………………………………………………………………………………………
10-10.3 Cancer 3
a (extry) year of diagnosis…………………
b (extryp) Type of cancer……………………………
c (extri) Chronological treatment details (plus year)……………………………
………………………………………………………………………………………………
d (extri) Name and address of Doctor treating you……………………………
………………………………………………………………………………………………

10-11 (dca) Have you ever had sunspots or skin cancers treated by either surgery or freezing over the last 12 months only? ☐ Y ☐ N ☐ DK ☐
☐ Missing ☐

If yes
10-11.1 (skmcno) how many lesions? ……………… lesions

10-12 (thy) thyroid condition?☐ Y ☐ N ☐ DK ☐
☐ Missing ☐

If yes
10-12.1 (thyry) When was it first diagnosed? ……………… years ago
10-12.2 (thylry) What was your thyroid problem due to? ………………………specify
10-12.3 (thyst) At the time of diagnosis, was your thyroid problem …
☐ underactive ☐ overactive ☐ normal activity
☐ DK ☐ Missing ☐

10-12.4 (thygoi) Did you have a goitre (enlarged thyroid gland)? ☐ Y ☐ N ☐ DK ☐
☐ Missing ☐

10-12.5 (thyt) Indicate which treatment you received (can tick more than one box):
☐ Surgery ☐ 1 ............ age…………………………… type of surgery
☐ Radioactive iodine ☐ 2 from ............... years old for ........... months
☐ Thyroxine tablets ☐ 3 from ............... years old to ........... years old ☐ still

taking

Carbimazole/ Neo-mercazole (anti-thyroid medication)
☐ 4 from ............... years old to ........... years old

Propylthiouracil ☐ 5 from ............... years old to ........... years old
no treatment… ☐ 7

DK ……☐ 8 missing…………☐ 9

10-12.6 (thydr) Name and address of Doctors treating your thyroid problem currently?
………………………………………………………………………………………………
<table>
<thead>
<tr>
<th>10-13 (diab) Do you have Diabetes?</th>
<th>☐ Y 1</th>
<th>☐ N 2</th>
<th>☐ DK 8</th>
<th>☐ Missing 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>(High sugar in the blood or urine)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**If yes**

10-13.1 (diab) When was it first diagnosed? ............... years ago

In what year did you begin and finish each type of treatment? (if currently on treatment put 7777 as year finished)

<table>
<thead>
<tr>
<th>10-13.2 (diet) Diet alone</th>
<th>Yes 1</th>
<th>No 2</th>
<th>DK 8</th>
<th>Miss'g 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-13.3 (tablet) Tablets</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-13.4 (insulin) Insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-13.5 (diabst) No treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Has a doctor advised you that you have any of the following conditions? ........... |

10-14 (park) Parkinson disease? | ☐ Y 1 | ☐ N 2 | ☐ DK 8 | ☐ Missing 9 |
10-14.1 (park) When was it first diagnosed? ............... years ago

10-15 (dement) Dementia? | ☐ Y 1 | ☐ N 2 | ☐ DK 8 | ☐ Missing 9 |
10-15.1 (dement) When was it first diagnosed? ............... years ago
10-15.2 (dementtype) Was it diagnosed as ☐ 1 Alzheimer’s Disease? ☐ Other

10-15.3 (dementdr) Name and address of doctor who diagnosed dementia:

10-15.4 (dementTel) Telephone number of the doctor who diagnosed dementia:

10-16 (kidstc) Kidney Disease? | ☐ Y 1 | ☐ N 2 | ☐ DK 8 | ☐ Missing 9 |
10-16.1 (kidstc) When was this first diagnosed? ........ years ago
10-16.2 (kidstc) What was it caused by? ........................................
10-16.3 (kidstc) Name and address of treating kidney doctor:

10-16.4 (kidstc) What type of treatment are you receiving?

- ☐ None 1
- Dietary measures 2
- Medication 3
- Peritoneal dialysis 4 commenced ........ years ago at .......... hospital
- Haemodialysis 5 commenced ........ years ago at .......... hospital
- Kidney transplant 6 .......... years ago at .......... hospital
- Other 7
- Missing 8
<table>
<thead>
<tr>
<th>10-17</th>
<th>Liver disease</th>
<th>☐ Y ☐ N ☐ DK ☐ Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-17.1</td>
<td>When was this first diagnosed?</td>
<td>☐ Y ☐ N ☐ DK ☐ Missing</td>
</tr>
<tr>
<td>10-17.2</td>
<td>What was it caused by?</td>
<td>☐ Y ☐ N ☐ DK ☐ Missing</td>
</tr>
<tr>
<td>10-17.3</td>
<td>Name and address of treating liver doctor?</td>
<td>☐ Y ☐ N ☐ DK ☐ Missing</td>
</tr>
<tr>
<td>10-17.4</td>
<td>Treatment received?</td>
<td>☐ Y ☐ N ☐ DK ☐ Missing</td>
</tr>
</tbody>
</table>

**10-18** Have you had any other serious illnesses? ☐ Y ☐ N ☐ DK ☐ Missing

- (illnes1) If yes, specify illness and year: code:________ year:____
- (illnes2) code:________ year:____
- (illnes3) code:________ year:____
- (illnes4) code:________ year:____
- (illnes5) code:________ year:____

**10-19** Have you had any major operations? ☐ Y ☐ N ☐ DK ☐ Missing

- (urg1) If yes, specify operation and year: code:________ year:____
- (urg2) code:________ year:____
- (urg3) code:________ year:____
- (urg4) code:________ year:____
- (urg5) code:________ year:____
12. Sleep Questions

12-1 (snore) Have you ever been told that you snore in your sleep?
☐ Y ☐ N ☐ DK ☐ Missing

12-2 (choke) Have you ever been told that you choke or gasp in your sleep at night?
☐ Y ☐ N ☐ DK ☐ Missing

12-3 (sphy) Have you ever been told that you stop breathing during your sleep?
☐ Y ☐ N ☐ DK ☐ Missing

12-4 (snoo) Do you often feel sleepy during the day?
☐ Y ☐ N ☐ go to 12-5 ☐ DK ☐ Missing

If yes, how likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired?

<table>
<thead>
<tr>
<th>Situation</th>
<th>Chance of dozing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting and reading</td>
<td>None</td>
</tr>
<tr>
<td>Watching T.V</td>
<td>0</td>
</tr>
<tr>
<td>Sitting inactive in public place (eg theatre or meeting)</td>
<td>0</td>
</tr>
<tr>
<td>As a passenger in a car for an hour without a break</td>
<td>0</td>
</tr>
<tr>
<td>Lying down to rest in the afternoon when circumstances permit</td>
<td>0</td>
</tr>
<tr>
<td>Sitting and talking to someone</td>
<td>0</td>
</tr>
<tr>
<td>Sitting quietly after lunch without alcohol</td>
<td>0</td>
</tr>
<tr>
<td>In a car, whilst stopped for a few minutes in traffic</td>
<td>0</td>
</tr>
</tbody>
</table>

12-5 (slepn) Have you been told by a doctor that you have sleep apnoea?
☐ Y ☐ N ☐ go to 13-1 ☐ DK ☐ Missing

12-6 (slepny) If yes, for how many years? ................. yrs

12-7 (slepno) Was the diagnosis confirmed on nocturnal polysomnogram/ sleep study?
☐ Y ☐ N ☐ DK ☐ Missing

12-8 (slepdnc) If yes, was this study done at home or in a laboratory?
☐ Y ☐ N ☐ DK ☐ Missing

12-9 (slepdnc) Name & Address of doctor who made diagnosis?

12-10 (slepnrs) What treatment have you received and year of treatment?

- Weight reduction ☐ 1 ......... years ago
- Alcohol reduction ☐ 2 ......... years ago
- Surgery ☐ 3 .................................. specify ..... years ago
- Nasal CPAP/ Bi PAP ☐ 4 ............... years ago
- Other ☐ 5 .................................. specify ..... years ago
- DK ☐ 8
- Missing ☐ 9

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13. Migraines

13-1 (migrain) Has a doctor ever told you that you suffer from migraine? (severe headaches, usually on one side, at least 5 attacks during lifetime, lasting at least 4 hours and less than 3 days, may have changes in vision like zig-zag lines or blurring, often nausea or vomiting and you usually need to lie down with the lights off)

☐ Y ☐ N go to 14-1 ☐ DK ☐ go to 14-1 ☐ Missing 9

13-2 (migrain) Age started................ years old

13-3 (migrain) How old were you when you stopped getting migraines? ...................... years old

☐ still getting them ☐ DK ☐ Missing 9

14. Falls and Fractures

General – falls and fractures

14-1 (fallsh) During the past 12 months, have you had any falls where you have landed on the ground or floor?

☐ Y ☐ N go to 14-4 ☐ DK ☐ Missing 9

14-2 (fallsh) If yes, number of falls ................ during the past 12 months

14-3 (fallvis) How many of these falls do you think were due to problems with your vision? ..............

14-4 (fear) Are you afraid of falling?

☐ Y ☐ N go to 14-6 ☐ DK ☐ Missing 9

14-5 (fear) How afraid are you of falling?

Little ☐ 0
Moderately ☐ 1
Very ☐ 2
DK ☐ 8

14-6 (fract) Have you broken or fractured a bone since your last exam here?

☐ Y ☐ N ☐ DK ☐ Missing 9

If yes, please give details (type of fracture, operation?, name of doctor, hospital, complications):

---------------------------------------------------------------------------------------------
---------------------------------------------------------------------------------------------
---------------------------------------------------------------------------------------------
---------------------------------------------------------------------------------------------

18
15. Women’s Health

Check previous questionnaire to confirm details

15-1 (menorr) How old were you when you stopped having your menstrual periods? ..........years old

15-2 (menorr) Did you stop naturally or because of a hysterectomy?
- naturally ................................... 1
- other reason ................................ 3

15-3 (hyster) Have you had a hysterectomy?
- Y 1
- N 2 go to 15-6
- DK 8
- Missing 9

15-4 (hyster) If yes, how old were you when you had a hysterectomy? .......... years
- DK 8
- Missing 9

15-5 (hystov) Have you had both ovaries removed?
- Y 1
- N 2 go to 15-8
- DK 8
- Missing 9

15-6 (hystov) If yes, how old were you when you had both ovaries removed? ....... years
- DK 8
- Missing 9

15-7 (hrt) Did you take hormone replacement therapy after the menopause or for menopausal symptoms?
- Y 1
- N 2 go to 15-17
- DKs
- Missing 9

If yes, for HRT 1:

15-8 (hrt1) When did you start? ..........(year)
- DK 8
- Missing 9

15-9 (hrtfin) When did you stop? ..........(year)
- still taking 7
- DK 8
- Missing 9

15-10 (hrtpp1) Was it estrogen only, or estrogen and progesterone combined?
- estrogen only 1
- combined 2 (estrogen and progesterone) 8
- Missing 9

15-12 (hrtname1) What was/is its name ........................................ code............
- DK 8
- Missing 9

for HRT 2:

15-13 (hrt2) When did you start? ..........(year)
- DK 8
- Missing 9

15-14 (hrtfin) When did you stop? ..........(year)
- still taking 7
- DK 8
- Missing 9

15-15 (hrtpp1) Was it estrogen only, or estrogen and progesterone combined?
- estrogen only 1
- combined 2 (estrogen and progesterone) 8
- Missing 9

15-16 (hrtname1) What was/is its name ........................................ code............
- DK 8
- Missing 9

Pap Smear Test

15-17 (papksm) Have you ever heard of a Pap Smear Test?
- Y 1
- N 2
- DK 8
- Missing 9

A Pap Smear Test, sometimes called a Pap test, is a routine test carried out by a doctor. It is recommended for all women to detect cancer of the cervix.

15-18 (paphad) Have you ever had a Pap Smear Test?
- Y 1
- N 2 go to 15-20
- DK 8
- Missing 9

15-19 (paphw) When did you have your last Pap Smear Test?
Less than 1 year ago .......... 1
1 year to less than 3 years ago . 2
5 years to less than 5 years ago ... 3
DK 8

Mammogram

15-20 (mamksm) Have you ever heard of a mammogram?
- Y 1
- N 2
- DK 8
- Missing 9

A mammogram is an x-ray taken of the breasts by a machine that presses against the breast while the picture is taken.

15-21 (mamhod) Have you ever had a mammogram?
- Y 1
- N 2 go to 16-1
- DK 8
- Missing 9

15-22 (mamw) When did you have your last mammogram?
Less than 1 year ago .......... 1
1 year to less than 3 years ago . 2
5 years to less than 5 years ago ... 3
DK 8

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16. Visual Function and change in visual function

Use of Glasses

16-1 (glass) Do you wear glasses of any kind?  
☐ Y  ☐ N ☐ go to 16-7 ☐ DK ☐ Missing  

16-2 (typical) If yes, are they:  
☐ single vision distance glasses only.........☐ ☐ don’t know ......☐  
☐ single vision reading glasses only.........☐ ☐ missing.........☐  
☐ separate reading and distance glasses...........☐  
☐ bifocals............................................☐  
☐ multifocals...........................................☐  

16-3 (typical) How old were you when you first needed to wear glasses to see clearly in the distance?  
.........years old ☐ don’t wear distance glasses ☐ DK ☐ Missing  

16-4 (typical) How old were you when you first needed reading glasses, bifocals or multifocals?  
.........years old ☐ don’t wear reading glasses ☐ DK ☐ Missing  

16-5 (typical) How long have you had your current glasses?  
Glasses are.............years old ☐ DK ☐ Missing  

16-6 (typical) When did you last have the strength of your glasses checked? ..........years ago ☐ DK ☐ Missing  

16-7 (typical) Can you read the ordinary print in the newspaper reasonably well, with or without glasses?  
☐ Y: go to 16-9 ☐ N: ☐ DK ☐ Missing  

16-8 (bound) If no, when were you last able to do this? ..........years ago ☐ DK ☐ Missing  

16-9 (bound) Do you use a magnifier to read?  
☐ Y  ☐ N  ☐ DK ☐ Missing  

Eye Symptoms

17-1 (typical) Are you aware of a deterioration of vision in one or both eyes?  
yes; R eye...........☐ ☐ go to 17-2 ☐ no.............☐ ☐ go to 17-4  
yes; L eye...........☐ ☐ go to 17-3 ☐ don’t know {...} ☐  
yes; both eyes ......☐ ☐ go to 17-3 ☐ missing...........☐  

17-2 (typical) When did your right eye worsen? .......mths ago  

17-3 (typical) When did your left eye worsen? ..........mths ago  

Are you aware of:  

<table>
<thead>
<tr>
<th>Any distortion of straight lines?</th>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Right) ☐ yes ☐ no ☐ ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>If yes, for how long? ..........mths</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>A dark patch?</th>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Lentic) ☐ yes ☐ no ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>If yes, for how long? ..........mths</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Flashing lights?</th>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Right) ☐ yes ☐ no ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>If yes, for how long? ..........mths</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Floaters?</th>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Lentic) ☐ yes ☐ no ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>If yes, for how long? ..........mths</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Any other changes?</th>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Lentic) ☐ yes ☐ no ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>If yes, for how long? ..........mths</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐</td>
</tr>
</tbody>
</table>

| Sensible | Do you think you have more difficulty seeing in the dark than others of your age?  
|-----------|------------------------------------------|
| ☐ Y ☐ N ☐ DK ☐ Missing  

| Sunlight | Do you think you are more sensitive than others of your age to sunlight or glare?  
|-------------|------------------------------------------|
| ☐ Y ☐ N ☐ DK ☐ Missing  

359
In the **last 12 months** have you noticed any of the following **eye problems**?

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>DK</th>
<th>Missing</th>
<th>Which eye?</th>
<th>Duration of symptoms?</th>
<th>Severity of symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-11 <strong>Discomfort</strong></td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td>Right</td>
<td>months</td>
<td>Mild</td>
</tr>
<tr>
<td>17-12 <strong>Grittiness</strong></td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td>Right</td>
<td>months</td>
<td>Mild</td>
</tr>
<tr>
<td>17-13 <strong>Itchiness</strong></td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td>Right</td>
<td>months</td>
<td>Mild</td>
</tr>
<tr>
<td>17-14 <strong>Watering</strong></td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td>Right</td>
<td>months</td>
<td>Mild</td>
</tr>
</tbody>
</table>

17-15 (dry eye) For the past 3 months or longer, have you had dry eyes? (foreign body sensation with itching and burning; sandy feeling, not related to allergy)

- Y
- N
- DK
- Missing

If yes, which eye was affected?

- Right
- Left
- Both
- Missing

17-16 (colour) Are you colour blind?

- Y
- N
- DK
- Missing

17-17 (coltype) If yes, do you know what type of colour blindness?

- Code

17-18 (coltest) Has this been confirmed by tests?

- Y
- N
- DK
- Missing

17-19 (emoney) To which eye would you normally hold a telescope to?

- R
- L
- Either
- DK
- Missing
18. Family History

Some eye diseases run in families, so I would like to ask about eye problems in your relatives, that is: your parents, children, or brothers and sisters.

Have any been diagnosed with?:

<table>
<thead>
<tr>
<th>Code</th>
<th>Diagnosis</th>
<th>yes</th>
<th>no</th>
<th>don’t know</th>
<th>missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-1</td>
<td>glaucoma (high pressure in the eyes)</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>18-2</td>
<td>cataract</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>18-3</td>
<td>macular degeneration</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td></td>
<td>(ageing at the back of the eye)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-4</td>
<td>diabetes</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>18-5</td>
<td>blindness from any other cause</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>18-6</td>
<td>other eye problem</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

If yes to 18-1 to 18-6 of the above please complete the following table:

**N.B. Include age of cataract surgery**

<table>
<thead>
<tr>
<th>Relative</th>
<th>Code</th>
<th>Diagnosis</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>eg. brother</td>
<td></td>
<td>glaucoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>diabetes</td>
<td></td>
</tr>
<tr>
<td>18-7a (fam1)</td>
<td></td>
<td></td>
<td>18-7 (fam1)</td>
</tr>
<tr>
<td>18-8 (fam2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-9a (fam)</td>
<td></td>
<td></td>
<td>18-9 (fam3)</td>
</tr>
<tr>
<td>18-10 (fam4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-11a (fam5)</td>
<td></td>
<td></td>
<td>18-11 (fam5)</td>
</tr>
<tr>
<td>18-12 (fam6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-13a (fam7)</td>
<td></td>
<td></td>
<td>18-13 (fam7)</td>
</tr>
<tr>
<td>18-14 (fam8)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

18-15 (father) Is your father? ☐ alive 1 ☐ dead 2 (age at death …… years old) ☐ DK ☐ Missing
18-16 (mother) Is your mother? ☐ alive 1 ☐ dead 2 (age at death …… years old) ☐ DK ☐ Missing
18-17 (brother) How many full brothers have you had, that is alive or dead? …………. ☐ DK ☐ Missing
18-18 (sister) How many full sisters have you had, that is alive or dead? …………. ☐ DK ☐ Missing
18-19 (cousin) How many are still alive? …………. ☐ DK ☐ Missing
18-20 (child) How many are still alive? …………. ☐ DK ☐ Missing

22
19. Lifestyle Assessment

Smoking

19-1 (smoken) Have you ever smoked cigarettes, cigars or a pipe regularly? (regularly being at least weekly) □ Y □ N □ go to 19-6 □ DK □ Missing 9

If yes, which of the following have you regularly smoked:

**age smoked from**Average amount per week

<table>
<thead>
<tr>
<th>Code</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>age (yrs)</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>age (yrs)</td>
</tr>
</tbody>
</table>

19-2a (cigarettes) Cigarettes? □ Y □ N □ go to 19-6 □ DK □ Missing 9

*code...........

(Roll-your-own)

19-2b (cigarettes) Cigarettes? □ Y □ N □ go to 19-6 □ DK □ Missing 9

*code...........

(Roll-your-own)

19-2c (pipe) Pipe? □ Y □ N □ go to 19-6 □ DK □ Missing 9

*code...........

19-2d (cigar) Cigars? □ Y □ N □ go to 19-6 □ DK □ Missing 9

*code...........

19-3 (stopsmoke) Have you given up smoking? □ Y □ N □ go to 19-5 □ DK □ Missing 9

19-4 (pastcig) How much did you usually smoke per week just before you stopped? □ Y □ N □ go to 19-6

packs of manufactured cigs (20 per pack)

packets of hand-rolled cigs

cigars

packets of pipe tobacco

19-5 (cursmig) How much do you smoke per week currently?

packs of manufactured cigs (20 per pack)

packets of hand-rolled cigs

cigars

packets of pipe tobacco

19-6 (spouse) Is your husband/wife/partner:

□ a current smoker? □ go to 19-7 □ spouse deceased □ go to 19-12

□ an ex-smoker? □ go to 19-9 □ divorced □ go to 19-12

□ a never smoker? □ go to 19-18 □ no spouse/partner □ go to 19-18

don't know □ go to 19-18 □ missing □ go to 19-18

If spouse an ex-smoker,

19-7 (excig) On average how much do you think your husband/wife/partner smokes per week?

packs of manufactured cigs (20 per pack)

packets of hand-rolled cigs

cigars

packets of pipe tobacco

19-8 (exsmoyear) What year did he/she start smoking?

(if already smoking when married give year of marriage) □□□□□□□□□□□□□□□□□□□□

19-9 (excig) On average how much do you think your husband/wife/partner smoked per week just before he/she stopped?

packs of manufactured cigs (20 per pack)

packets of hand-rolled cigs

cigars

packets of pipe tobacco

19-10 (exsmoyear) What year did he/she start smoking?

(if already smoking when married give year of marriage) □□□□□□□□□□□□□□□□□□□□

19-11 (stop) When did he/she stop smoking? □ Gave up in □□□□□□□□□□□□□□□□□□□□

□ go to 19-18
If spouse deceased or divorced,

19-12 (desc1) At the time of death/divorce, was your husband/wife/partner a smoker? □ go to 19-13 ⌐ an ex-smoker? □ go to 19-15 ⌐ don't know □ go to 19-18 ⌐ a never smoker? □ go to 19-18 ⌐ missing □ go to 19-18

If deceased/divorced spouse a smoker,

19-13 (desc1) At the time of death/divorce, on average how much do you think your husband/wife/partner smoked per week? □ packs of manufactured cigs (20 per pack) □ packets of hand-rolled cigs □ cigars □ packets of pipe tobacco

19-14 (desc2) What year did he/she start smoking? □ (year) (if already smoking when married give year of marriage)

19-14a (desc2) In what year did he/she die? (or in what year did you separate?) □ (year) go to 19-18

If deceased/divorced spouse an ex-smoker,

19-15 (desc3) On average, how much do you think your husband/wife/partner smoked per week just before they stopped? □ packs of manufactured cigs (20 per pack) □ packets of hand-rolled cigs □ cigars □ packets of pipe tobacco

19-16 (desc4) What year did he/she start smoking? □ (year) (if already smoking when married give year of marriage)

19-17 (desc5) When did he/she stop smoking? Gave up in □ (year)

Alcohol

I would like to ask you some questions to see whether alcohol causes eye problems or whether it has any benefits for the eyes.

19-18 (aka) How often do you have an alcoholic drink?

never □ go to 19-21 □ 5-6 days a week □ 8 □ 5 days a week □
< once a week □ go to 19-21 □
1-2 days a week □ go to 19-21 □
3-4 days a week □
missing □ go to 19-21 □

19-19 (alctype) What do you mostly drink?

light beer □
fortified wine □
beer □
others □
wine □
don't know □
spirits □
missing □

19-20 (alcoons) On days when you have a drink, how many drinks do you usually have?

1-2 □ go to 19-21 □ 13 or more □
3-4 □
don't know □
5-8 □
missing □
9-12 □

19-21 (algens) Has there ever been a time in your life when you regularly drank four or more alcoholic drinks a day?

□ Y □ N □ DK □ 8 □ Missing

Mobile Telephone Use

I am now going to ask you about your use of mobile phones.

19-22 (aasb) Do you currently use a mobile phone? □ Y □ N □ go to 20-1 □ DK □ 8 □ Missing

19-23 (mobys) If yes, for how many years have you used it? □ yrs □ DK □ 8 □ Missing

19-24 (earnumb) Which ear do you normally hold it to?

□ right □ left □ both □ DK □ 8 □ Missing
20. Mini–Mental State Exam

The next set of questions are about memory. They may seem a bit childish but this is a standard questionnaire that we are asking everyone. Some of the questions are difficult, so don’t be surprised if you have trouble with some of them.

**Points**

<table>
<thead>
<tr>
<th>20-1</th>
<th>(year)</th>
<th>What is the year?</th>
<th>....../1</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-2</td>
<td>(season)</td>
<td>What is the season?</td>
<td>....../1</td>
</tr>
<tr>
<td>20-3</td>
<td>(date)</td>
<td>What is the date?</td>
<td>....../1</td>
</tr>
<tr>
<td>20-4</td>
<td>(day)</td>
<td>What is the day?</td>
<td>....../1</td>
</tr>
<tr>
<td>20-5</td>
<td>(month)</td>
<td>What is the month?</td>
<td>....../1</td>
</tr>
<tr>
<td>20-6</td>
<td>(state)</td>
<td>Where are we? State?</td>
<td>....../1</td>
</tr>
<tr>
<td>20-7</td>
<td>(country)</td>
<td>Country?</td>
<td>....../1</td>
</tr>
<tr>
<td>20-8</td>
<td>(own)</td>
<td>City/town?</td>
<td>....../1</td>
</tr>
<tr>
<td>20-9</td>
<td>(house)</td>
<td>Clinic Address?</td>
<td>....../1</td>
</tr>
<tr>
<td>20-10</td>
<td>(floor)</td>
<td>Floor?</td>
<td>....../1</td>
</tr>
</tbody>
</table>

**20-11 (recall)** I am going to name three objects. After I have said them, I want you to name them again in a few minutes. Give one point for each correct answer. Then repeat the objects up to 6 times until the participant learns all three.

APPLE   TABLE   HORSE

**20-12 (reason)** Can you subtract 7 from 100, then subtract 7 from the answer you get and keep subtracting 7 until I ask you to stop? (93, 86, 79, 72, 65). Give one point for each correct answer. Stop after five answers if subject refuses or cannot do this, ask them to spell WORLD backwards.

**20-13 (recall)** What were those three objects I asked you to remember? Give one point for each correct answer

**20-14 (language)** Please name these objects (point to a pencil and a watch) Give one point for each correct answer

**20-15 (language)** Now I would like you to repeat a phrase after me: “No ifs, ands, or buts”.

**20-16 (language)** Now I would like you to: 
Take the paper in your right hand.
Fold the paper in half.
Put the paper on the floor.
Give one point for each correct action

**20-17 (language)** Please read the words on this bit of paper and do what it says: ‘CLOSE YOUR EYES’

**20-18 (language)** Please write a sentence of your own choice. (The sentence should contain a subject and an object and should make sense. Ignore spelling errors when scoring)

**20-19 (language)** Please copy the design that you see printed on this paper. (Give one point if all sides and angles are preserved and if the intersecting sides form a quadrangle)

**20-20 (numerical)** Was the subject unable to complete 20-17 because of visual impairment? yes...........☐1 no...........☐2 unsure...........☐8 missing...........☐9

**20-21 (numerical)** Was the subject unable to complete 20-18 or 20-19 because of arthritis? yes...........☐1 no...........☐2 unsure...........☐8 missing...........☐9
CLOSE YOUR EYES
What was the gross income (including pensions and allowances) that you receive each week from all sources?
(count all income including: family allowance, parenting payment, unemployment benefits, rental assistance, pensions, student allowance, maintenance (child support), worker’s compensation, superannuation, wages, salary, overtime, commissions and bonuses, interest received, dividends, rents received (less expenses of operation), business or farm income (less expenses of operation). Do not deduct tax, superannuation, health insurance).

- $1,000 or more per week ($52,000 or more per year) ........................................... [ ] 1
- $700 - 999 per week ($36,400 - $51,599 per year) ........................................... [ ] 2
- $400 - 699 per week ($20,800 - $36,399 per year) ........................................... [ ] 3
- $200 - 399 per week ($10,400 - $20,799 per year) ........................................... [ ] 4
- $160 - 199 per week ($8,320 - $10,399 per year) ........................................... [ ] 5
- $120 - 159 per week ($6,240 - $8,319 per year) ........................................... [ ] 6
- $1 - 119 per week ($1 - $6,239 per year) ........................................................ [ ] 7
- Nil income ........................................................................................................ [ ] 8
- Negative income ............................................................................................ [ ] 9
- Don't know ..................................................................................................... [ ] 88
- Refused ........................................................................................................... [ ] 99

20-23 [hndetail1]  source 1: .................................................................................. code: 

20-24 [hndetail2]  source 2: .................................................................................. code: 

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21. Clinical Measurements 1

Chair Stand
C-1 (stand) Do you think it would be safe for you to try to stand up from a chair without using your arms? Yes ☐ 2

Demonstrate the chair stand for the participant.

“Please fold your arms across your chest and sit so that your feet are on the floor. Try to stand up without using your arms.”

Place the back of the chair against the wall to steady it. Stand next to the participant to provide assistance in case of lost balance. If unable to rise without using arms, say:

“Try to stand up using your arms to push off.”

C-2 (attempts) Number of attempts to rise: (inc. rocking, weight shifting) ______________ attempts

C-3 (stand) Participant rises:

Without arms ☐ 0 With arms ☐ 1

Dynamometer
C-4 (hand) Are you right- or left-handed?

Right ☐ 6 Left ☐ 1 Ambidextrous ☐ 2 Ambidextrous Left ☐ 3 Unknown ☐ 8

Demonstrate dynamometer, telling the participant:

"Point it straight at the floor and squeeze it as hard as you can."

The dynamometer is presented to participant, test the dominant hand first, then the non-dominant hand. Repeat for a total of two trials on each hand.

C-5 (dynamometer) 1st trial dominant ________ kg Not done ☐ 8
C-6 (dynamometer) 2nd trial non-dominant ________ kg Not done ☐ 8
C-7 (dynamometer) 1st trial non-dominant ________ kg Not done ☐ 8
C-8 (dynamometer) 2nd trial non-dominant ________ kg Not done ☐ 8

C-9 (dynamometer) Test is:

Reliable ☐ 0 Unreliable ☐ 1 Unable ☐ 7 No time ☐ 8

While seated ☐ 2 Refused ☐ 9

Body Mass Index
C-10 (height) Height ________ metres
C-11 (table) reliable ☐ 1 unreliable ☐ 2 specify: ______________________________ code:__________________
not done ☐ 3 specify: ______________________________ code:__________________
C-12 (w) Weight ________ kilograms
C-13 (w) reliable ☐ 1 unreliable ☐ 2 specify: ______________________________ code:__________________
not done ☐ 3 specify: ______________________________ code:__________________

Waist ratio
C-14 (w) Waist ________ cm
C-15 (w) reliable ☐ 1 unreliable ☐ 2 specify: ______________________________ code:__________________
not done ☐ 3 specify: ______________________________ code:__________________

Measured walk
We are going to observe how you normally walk. If you use a cane or other walking aid and would feel more comfortable with it, then you may use it.

This is our walking course. I want you to walk to the stop sign at your usual speed, just as if you were
walking down the street to go to the store. I will walk with you.  
When I want you to start, I will say "Ready? Begin."

C-16 (gainaid) Aids used for walk:
- No aid □  
- Arm □  
- Wheelchair □  
- Not done □  
- Walker □  
- Unable □  
- Quad cane □  
- Refused □  
- Other cane □  
- Off-site □  

C-17 (gainmne) Time for walk: ______________ sec

### 22. Disability

**General** - To be completed by the examiner

<table>
<thead>
<tr>
<th>Does the participant:</th>
<th>Yes</th>
<th>No</th>
<th>Don't know</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>22-1 (mp) have a hearing impairment?</td>
<td>□ 1</td>
<td>□ 2</td>
<td>□ 8</td>
<td>□ 9</td>
</tr>
<tr>
<td>22-2 (mp) have walking difficulties</td>
<td>□ 1</td>
<td>□ 2</td>
<td>□ 8</td>
<td>□ 9</td>
</tr>
<tr>
<td>22-3 (mp) use a cane/crutches/walker</td>
<td>□ 1</td>
<td>□ 2</td>
<td>□ 8</td>
<td>□ 9</td>
</tr>
<tr>
<td>22-4 (mp) use a wheel chair</td>
<td>□ 1</td>
<td>□ 2</td>
<td>□ 8</td>
<td>□ 9</td>
</tr>
<tr>
<td>22-5 (mp) have SOB/cough continuously</td>
<td>□ 1</td>
<td>□ 2</td>
<td>□ 8</td>
<td>□ 9</td>
</tr>
<tr>
<td>22-6 (mp) have a language problem</td>
<td>□ 1</td>
<td>□ 2</td>
<td>□ 8</td>
<td>□ 9</td>
</tr>
<tr>
<td>22-7 (mp) have a speech but not a language problem</td>
<td>□ 1</td>
<td>□ 2</td>
<td>□ 8</td>
<td>□ 9</td>
</tr>
<tr>
<td>22-8 (mp) appear demented</td>
<td>□ 1</td>
<td>□ 2</td>
<td>□ 8</td>
<td>□ 9</td>
</tr>
</tbody>
</table>

22-9 (mp) Who mainly answered the questionnaire?
- participant □ 1  
- sibling □ 1  
- other □ 7  
- □ 7 specify…………/code….  
- spouse □ 2  
- other relative □ 8  
- DK □ 8  
- son/daughter □ 1  
- friend □ 8  
- Missing □ 8

22-10 (mp) The overall quality of the interview was:
- reliable □  
- unreliable □  
- DK □  
- missing □  

---

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23. Olfaction Test  
(The San Diego Odour Identification Protocol)

I would now like to test your sense of smell and to detect changes in your ability to recognise everyday odours.

**Picture identification**

The odours that you will identify by smell are all pictured on this sheet. I would first like you to name the items pictured. Starting in the upper left hand corner, would you please name the pictures from left to right in the first row.

(staff) Do you have a stuffy nose or a cold at present?  □Y □N □DK □Missing

I would now like to present to you some of the odours pictured here to smell. An odour may be presented more than once. When I present the odours, I will first ask you to close your eyes and then I will place the odour under your nose and ask you to smell. I will then tell you when you can open your eyes and you can either point to the odour on the picture board or say the name of the odour that you smelled.
### Odour Identification Score Sheet

<table>
<thead>
<tr>
<th>Picture Recognition</th>
<th>Odour Identification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Odourants</strong></td>
<td><strong>Odourants</strong></td>
</tr>
<tr>
<td><strong>Recording key</strong></td>
<td><strong>Recording key</strong></td>
</tr>
<tr>
<td>370</td>
<td>370</td>
</tr>
<tr>
<td><strong>0= incorrect</strong></td>
<td><strong>0= incorrect</strong></td>
</tr>
<tr>
<td><strong>1= correct</strong></td>
<td><strong>1= correct</strong></td>
</tr>
<tr>
<td><strong>9= don’t know</strong></td>
<td><strong>9= don’t know</strong></td>
</tr>
<tr>
<td><strong>1= trial 1</strong></td>
<td><strong>1= trial 1</strong></td>
</tr>
<tr>
<td><strong>2= trial 2</strong></td>
<td><strong>2= trial 2</strong></td>
</tr>
<tr>
<td><strong>Response</strong></td>
<td><strong>Response</strong></td>
</tr>
<tr>
<td><strong>Any</strong></td>
<td><strong>Any</strong></td>
</tr>
<tr>
<td>a. chewing gum</td>
<td>1. peanut-butter</td>
</tr>
<tr>
<td>b. chicken</td>
<td>2. chocolate</td>
</tr>
<tr>
<td>c. vegemite</td>
<td>3. coffee</td>
</tr>
<tr>
<td>d. toothpaste</td>
<td>4. honey</td>
</tr>
<tr>
<td>e. eucalyptus</td>
<td>5. talcum powder</td>
</tr>
<tr>
<td>f. pineapple</td>
<td>6. vegemite</td>
</tr>
<tr>
<td>g. talcum powder</td>
<td>7. cinnamon</td>
</tr>
<tr>
<td>h. mustard</td>
<td>8. mustard</td>
</tr>
<tr>
<td>i. banana</td>
<td>Presentation Order</td>
</tr>
<tr>
<td>j. coffee</td>
<td>Kit Number</td>
</tr>
<tr>
<td>k. bread</td>
<td>Room Temp</td>
</tr>
<tr>
<td>l. lemon</td>
<td>Examiner Initials</td>
</tr>
<tr>
<td>m. popcorn</td>
<td>Olfaction Notes</td>
</tr>
<tr>
<td>n. soap</td>
<td></td>
</tr>
<tr>
<td>o. pizza</td>
<td></td>
</tr>
<tr>
<td>p. honey</td>
<td></td>
</tr>
<tr>
<td>q. watermelon</td>
<td></td>
</tr>
<tr>
<td>r. peanut-butter</td>
<td></td>
</tr>
<tr>
<td>s. strawberry</td>
<td></td>
</tr>
<tr>
<td>t. cinnamon</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Trial 1</strong></th>
<th><strong>Trial 2</strong></th>
<th><strong>Response</strong></th>
<th><strong>Any</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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## Station 2

### 24. Lensometer / Autorefractor

#### Glasses

- **E-1** (typical) **current glasses**
  - unifocal...☐ 1
  - bifocal...☐ 2
  - multifocal...☐ 3
  - separate pairs...☐ 4
  - no glasses...☐ 5
  - glasses not brought...☐ 6
  - DK...☐ 7
  - missing...☐ 8

#### Lens Analyzer

- **current glasses**:

<table>
<thead>
<tr>
<th>E-2</th>
<th>RIGHT</th>
<th>LEFT</th>
</tr>
</thead>
<tbody>
<tr>
<td>(ReedOS)</td>
<td>sph.</td>
<td>(LsoreDS)</td>
</tr>
<tr>
<td>E-3</td>
<td>(ReedDC)</td>
<td>cyl.</td>
</tr>
<tr>
<td>E-4</td>
<td>(Reexan)</td>
<td>axis.</td>
</tr>
<tr>
<td>E-5</td>
<td>(Reexal)</td>
<td>reading add.</td>
</tr>
</tbody>
</table>

- **E-8** *(random)*
  - axis. ............................
  - (Lsorean)  
  - axis. ............................

**Autorefractor**

(attach printout)

#### separate readers, if worn:

<table>
<thead>
<tr>
<th>E-6</th>
<th>RIGHT</th>
<th>LEFT</th>
</tr>
</thead>
<tbody>
<tr>
<td>(ReedOS)</td>
<td>sph.</td>
<td>(LsoreDS)</td>
</tr>
<tr>
<td>E-7</td>
<td>(ReedDC)</td>
<td>cyl.</td>
</tr>
</tbody>
</table>
25. Visual fields and grading

<table>
<thead>
<tr>
<th>Visual field test</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>VF-1 24-2 SITA</td>
<td>[ref] completed 1 not completed 2 reason.................... correction used</td>
<td>[ref] completed 1 not completed 2 reason.................... correction used</td>
</tr>
<tr>
<td>VF-2 Frequency Doubling Test</td>
<td>[ref] performed 1 not performed 2</td>
<td>[ref] performed 1 not performed 2</td>
</tr>
<tr>
<td>VF-3 Confrontation</td>
<td>[ref] performed 1 not performed 2</td>
<td>[ref] performed 1 not performed 2</td>
</tr>
</tbody>
</table>

26. A-Scan non contact biometry (IOL master)

<table>
<thead>
<tr>
<th>26-1 A-scan (IOL Master)</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[ref] performed 1 not performed 2</td>
<td>[ref] performed 1 not performed 2</td>
</tr>
</tbody>
</table>

27. Clinical Measurements II

**Peak Expiratory Flow**

<table>
<thead>
<tr>
<th>Test</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-10 (ref) 1st trial</td>
<td>Not done</td>
<td>8</td>
</tr>
<tr>
<td>C-11 (ref) 2nd trial</td>
<td>Not done</td>
<td>8</td>
</tr>
<tr>
<td>C-12 (ref) 3rd trial</td>
<td>Not done</td>
<td>8</td>
</tr>
<tr>
<td>C-13 (ped) Test is:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reliable</td>
<td>0</td>
<td>Unable</td>
</tr>
<tr>
<td>Unreliable</td>
<td>1</td>
<td>No time</td>
</tr>
<tr>
<td>While seated</td>
<td>2</td>
<td>Refused</td>
</tr>
</tbody>
</table>
# Station 3

Please place BP cuff on right arm.
Ask patient to uncross his/her legs.

## 28. Eye Disease

We would like to ask you some questions regarding your eye health.

### Cataract

28-1 (cat) Have you ever been told by a doctor that you have a cataract?
- □ Y
- □ N  
- go to 28-2  
- □ DK
- □ Missing

28-2 (cat) If yes, in which eye?
- right eye... □  
- left eye...... □

<table>
<thead>
<tr>
<th>Cataract</th>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>28-3 In what year were you first told?</td>
<td>[rectop]</td>
<td>[leastyr]</td>
</tr>
</tbody>
</table>
| 28-4 Have you had an operation for cataract? | [rectop]
- Yes
- No
- DK
- Missing |
| 28-5 If yes, in what year? | [leastyr] |
| 28-6 Which eye doctor removed your cataract? | [rectop] |
| 28-7 Have you had YAG laser to improve your vision after cataract surgery? | [rectYAO]
- Yes
- No
- DK
- Missing |
| 28-8 If yes, in what year? | [rectYAOy] |

### Macular Degeneration

28-9 (AMD) Have you ever been told by a doctor that you have macular degeneration?
- (hardening of the arteries at the back of the eye or retinal degeneration)
- □ Y
- □ N  
- go to 28-10  
- □ DK
- □ Missing

28-10 (AMD) If yes, in which eye?
- right eye... □  
- left eye...... □

<table>
<thead>
<tr>
<th>Macular degeneration</th>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>28-11 In what year were you first told?</td>
<td>[rectAMDyr]</td>
<td>[leastAMDyr]</td>
</tr>
</tbody>
</table>
| 28-12 Have you had laser treatment for macular degeneration? | [rectAMDlsy]
- Yes
- No
- DK
- Missing |
| 28-13 If yes, in what year did you first have laser treatment? | [leastlsy] |
| 28-14 Which eye doctor performed the laser treatment? | [leastlsy] |

---

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### Glaucoma

28-15 (gla) Have you ever been told by a doctor that you have glaucoma?  
- □ Y ☐ N ☐ go to 28-23 ☐ DK ☐ Missing

28-16 (gleyr) If yes, in what year were you first told? ..........(year)

28-17 (glurn) Have you used eyedrops or other medications for glaucoma?  
- □ Y ☐ N ☐ go to 28-21 ☐ DK ☐ Missing

28-18 (glreyr) If yes, in what year did you start using these medications? ..........(year)

28-19 (glrsvr) For how many years? .............. yrs

28-20 (glmdr) Which eye doctor first put you on treatment for glaucoma?   

28-21 (glmnur) Have you had an operation or laser treatment for glaucoma?  
- □ Y ☐ N ☐ go to 28-23 ☐ DK ☐ Missing

28-22 (glunyr) If yes, in what year? ...........(year)

### Diabetes

28-23 (dbed) Have you ever been told by a doctor that you have eye disease or eye damage related to your diabetes (diabetic retinopathy)?  
- □ Y ☐ N ☐ go to 28-29 ☐ DK ☐ Missing

28-24 (dmdyr) When were you first told?....................................................yrs ago

28-25 (dhees) Have you ever had laser treatment for your diabetic eye disease?  
- □ Y ☐ N ☐ go to 28-29 ☐ DK ☐ Missing

<table>
<thead>
<tr>
<th>If yes,</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(날시)</td>
<td>(날시)</td>
</tr>
</tbody>
</table>

28-26 Which eye was treated?  
- [☐] Yes ☐ No ☐ DK ☐ Missing  
- [☐] 1. 2. 3. 9

28-27 How many years ago?  
- [☐] Yes ☐ No ☐ DK ☐ Missing  
- [☐] 1. 2. 3. 9

28-28 Which eye doctor performed the laser treatment?  

28-29 (dlsrck) Which eye doctor performed the laser treatment?  

-----------------------------------------------

35 374
## Eye trauma

**28-29** (EYE) Have you had any **serious eye injuries** requiring doctor's care?

- [ ] Y 1
- [ ] N 2 go to 28-35
- [ ] DK 8
- [ ] Missing 9

**28-30** (SIDE) If yes, which eye was affected?

- [ ] right 1
- [ ] left 2
- [ ] Both 3
- [ ] DK 8
- [ ] Missing 9

<table>
<thead>
<tr>
<th>Trauma</th>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>28-31 ...was this due to being hit by a blunt object? (like a fist, ball, or dashboard of a car)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[ ] [ ] [ ] [ ] Missing</td>
<td>[ ] [ ] [ ] [ ]</td>
<td></td>
</tr>
<tr>
<td>(EYE) When? ........... years ago</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specify Mechanism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(SIDE) When? ........... years ago</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specify Mechanism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28-32 ...was this from a sharp object? (glass, knife or something that penetrated the eye)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[ ] [ ] [ ] [ ] Missing</td>
<td>[ ] [ ] [ ] [ ]</td>
<td></td>
</tr>
<tr>
<td>(EYE) When? ........... years ago</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specify Mechanism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(SIDE) When? ........... years ago</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specify Mechanism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28-33 ...was it due to a chemical burn? (like acid or lye)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[ ] [ ] [ ] [ ] Missing</td>
<td>[ ] [ ] [ ] [ ]</td>
<td></td>
</tr>
<tr>
<td>(EYE) When? ........... years ago</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specify Mechanism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(SIDE) When? ........... years ago</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specify Mechanism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28-34 ...did you have to stay in a hospital overnight or longer because of it?</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>[ ] [ ] [ ] [ ] Missing</td>
<td>[ ] [ ] [ ] [ ]</td>
<td></td>
</tr>
</tbody>
</table>

## Other Eye Conditions

**28-35** (RETI) Have you ever been told that you have a **problem in the retina** or the **back of the eye** eg retinal detachment, vessel blockage or bleeding?

- [ ] Y 1
- [ ] N 2 go to 28-38
- [ ] DK 8
- [ ] Missing 9

**28-36** (REDE) **If yes, specify** (which eye and condition)

<table>
<thead>
<tr>
<th>Code</th>
</tr>
</thead>
</table>

**28-37** (REYE) How many years ago were you first told? ........... years ago ............ age

**28-38** Any **other eye problems or surgery** I haven't asked you about?

<table>
<thead>
<tr>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Code</td>
</tr>
</tbody>
</table>
22. Clinical Measurements III
Pulse Rate:
C-10 (pr) Pulse rate is .........................beats per second
C-11 (prreq) Pulse is regular □1 irregular □2
C-12 (prel) reliable □1 unreliable □2 specify.............................
not done □3 specify.............................

Blood pressure:
C-13 (mmBP) I am now going to check your blood pressure. Indicate which arm used.
R. □1 L. □2 specify.............................
Not done..... □3 specify.............................
C-14 (cuffBP) Have you had caffeine/nicotine in last 4 hours? □Y □N □DK □Missing
C-15 (cuff) Cuff size: small □1 adult □2 large □3
C-16 (sysBP) systolic BP......................mmHg
C-17 (diopBP) diastolic BP.....................mmHg
C-18 (tymBP) reliable □1 unreliable □2 specify.............................
not done □3 specify.............................

30. Visual Acuity and Subjective Refraction
I am now going to test your vision with your glasses, if you wear them.

Logmar visual acuity score or E – equivalent
Measure at 2.4 metres (8 ft) with best distance correction; if unable to see any letters, then try at one metre

E-9 What distance was chart read?  R (Red✓) 2.4m........ □1  L (Lt✓) 2.4m........ □1
1.2m........ □2 1.2m........ □2
E-10 Current Distance Glasses (curved) yes........... □1 no........... □2

2.4m Right eye no correct Left eye no correct
6/60 H V Z D S ........... H V Z D S ........... 5
6/48 N C V K D ........... N C V K D ........... 10
6/36 C Z S H N ........... C Z S H N ........... 15
6/30 O N V S R ........... O N V S R ........... 20
6/24 K D N R O ........... K D N R O ........... 25
6/19 Z K C S V ........... Z K C S V ........... 30
6/15 D V O H C ........... D V O H C ........... 35
6/12 O H V C K ........... O H V C K ........... 40
6/9.5 H Z C K O ........... H Z C K O ........... 45
6/7.5 N C K H D ........... N C K H D ........... 50
6/6 Z H C S R ........... Z H C S R ........... 55
6/4.8 S Z R D N ........... S Z R D N ........... 60
6/3.8 H C D R O ........... H C D R O ........... 65
6/3.0 R D O S N ........... R D O S N ........... 70
<table>
<thead>
<tr>
<th></th>
<th>Right eye</th>
<th></th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-11 (RmaxVA)</td>
<td>Logmar VA</td>
<td></td>
<td>Logmar VA</td>
</tr>
<tr>
<td>E-12 (RPH)</td>
<td>Pinhole</td>
<td></td>
<td>Pinhole</td>
</tr>
</tbody>
</table>

If vision < 6/60

<table>
<thead>
<tr>
<th></th>
<th>Right eye</th>
<th></th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-13 (RpoorVA)</td>
<td>R .......</td>
<td>(LpooVA)</td>
<td>L .......</td>
</tr>
<tr>
<td></td>
<td>CF ........ □</td>
<td>CF ........ □</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HM ....... □</td>
<td>HM ....... □</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PL ........ □</td>
<td>PL ........ □</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NPL ........ □</td>
<td>NPL ........ □</td>
<td></td>
</tr>
</tbody>
</table>
**Logmar VA modified Sheridan-Gardiner**  (only if unable to read chart)

E-14  [R]SherG       [L]SherG       L  ...

E-15  [amblyo]  If one eye weaker (2 line difference) ask:

<table>
<thead>
<tr>
<th>right eye</th>
<th>yes</th>
<th>DK</th>
<th>no</th>
</tr>
</thead>
<tbody>
<tr>
<td>left eye</td>
<td>yes</td>
<td>miss</td>
<td></td>
</tr>
</tbody>
</table>

E-16  [visdis]  If visual disability, eg field defect or severe visual loss (< 6/60) in both eyes, ask:

<table>
<thead>
<tr>
<th>Have you sought help from:</th>
</tr>
</thead>
<tbody>
<tr>
<td>low vision clinic...</td>
</tr>
<tr>
<td>guide dogs...........</td>
</tr>
</tbody>
</table>

E-17  [denmVA]  Did mental disability or dementia prevent measurement of VA?

| Y | N | DK | Missing |

---

#### Visual Acuity with Best Subjective Refraction

<table>
<thead>
<tr>
<th>2.4m</th>
<th>Right eye</th>
<th>no. correct</th>
<th>Left eye</th>
<th>no. correct</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/60</td>
<td>H V Z D S</td>
<td>5</td>
<td>H V Z D S</td>
<td>5</td>
</tr>
<tr>
<td>6/48</td>
<td>N C V K D</td>
<td>10</td>
<td>N C V K D</td>
<td>10</td>
</tr>
<tr>
<td>6/36</td>
<td>C Z S H N</td>
<td>15</td>
<td>C Z S H N</td>
<td>15</td>
</tr>
<tr>
<td>6/30</td>
<td>O N V S R</td>
<td>20</td>
<td>O N V S R</td>
<td>20</td>
</tr>
<tr>
<td>6/24</td>
<td>K D N R O</td>
<td>25</td>
<td>K D N R O</td>
<td>25</td>
</tr>
<tr>
<td>6/19</td>
<td>Z K C S V</td>
<td>30</td>
<td>Z K C S V</td>
<td>30</td>
</tr>
<tr>
<td>6/15</td>
<td>D V O H C</td>
<td>35</td>
<td>D V O H C</td>
<td>35</td>
</tr>
<tr>
<td>6/12</td>
<td>O H V O C</td>
<td>40</td>
<td>O H V C K</td>
<td>40</td>
</tr>
<tr>
<td>6/9.5</td>
<td>H Z C K O</td>
<td>45</td>
<td>H Z C K O</td>
<td>45</td>
</tr>
<tr>
<td>6/7.5</td>
<td>N C K H D</td>
<td>50</td>
<td>N C K H D</td>
<td>50</td>
</tr>
<tr>
<td>6/6</td>
<td>Z H C S R</td>
<td>55</td>
<td>Z H C S R</td>
<td>55</td>
</tr>
<tr>
<td>6/4.8</td>
<td>S Z R D N</td>
<td>60</td>
<td>S Z R D N</td>
<td>60</td>
</tr>
<tr>
<td>6/3.8</td>
<td>H C D O R</td>
<td>65</td>
<td>H C D O R</td>
<td>65</td>
</tr>
<tr>
<td>6/3.0</td>
<td>R D O S N</td>
<td>70</td>
<td>R D O S N</td>
<td>70</td>
</tr>
</tbody>
</table>

E-18  [ReadVA]  Logmar VA  Right  [LsubVA]  Logmar VA  Left

#### Best Subjective Refraction

**RIGHT**

- Sph:
- Cyl:

**LEFT**

- Sph:
- Cyl:

E-19  [RandDS]  sph:
E-20  [RandDC]  cyl:
E-21  [Randacs]  axis:
E-22  [Randadd]  reading add:

**Logmar reading chart** (add age adjusted plus lens to trial frames)

E-23  [newva]  R:
E-24  [newvL]  L:
E-25  [aeotype]  both eyes:
### 31. GDX and HRT II

<table>
<thead>
<tr>
<th>camera</th>
<th>both</th>
<th>Right only</th>
<th>Left only</th>
<th>None</th>
<th>Reason for inability to take photograph</th>
</tr>
</thead>
<tbody>
<tr>
<td>31-1</td>
<td>HRT II</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

### 32. Slit lamp examination

#### Anterior Segment Abnormalities

<table>
<thead>
<tr>
<th></th>
<th>R eye</th>
<th>L eye</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>none</td>
<td>quest</td>
</tr>
<tr>
<td>L-1</td>
<td>Corneal Arcus</td>
<td>[Racrus]</td>
</tr>
<tr>
<td>L-2</td>
<td>Pterygium</td>
<td>[Rptery]</td>
</tr>
<tr>
<td>L-3</td>
<td>Pseudoxfiliation</td>
<td>[Rexfils]</td>
</tr>
<tr>
<td>L-4</td>
<td>Conjunctivochalasis</td>
<td>[Recalss]</td>
</tr>
<tr>
<td>L-5</td>
<td>Corneal opacities</td>
<td>[Recorps]</td>
</tr>
<tr>
<td>L-6</td>
<td>Other</td>
<td>[Relab1]</td>
</tr>
</tbody>
</table>

**L-8** (Multiple) Is the anterior chamber of the right eye judged occludable by slit lamp examination?

- [ ] Y: Stop - do not dilate right eye
- [ ] N
- [ ] DK
- [ ] Missing

**L-9** (Multiple) Is the anterior chamber of the left eye judged occludable by slit lamp examination?

- [ ] Y: Stop - do not dilate left eye
- [ ] N
- [ ] DK
- [ ] Missing
### IOP

<table>
<thead>
<tr>
<th>L-10</th>
<th>Time taken</th>
<th>(in seconds)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>L-11</th>
<th>Right eye</th>
<th>L-12</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-13</td>
<td>Was it...</td>
<td>L-14</td>
<td>Was it...</td>
</tr>
<tr>
<td></td>
<td>reliable</td>
<td></td>
<td>reliable</td>
</tr>
<tr>
<td></td>
<td>unreliable</td>
<td></td>
<td>unreliable</td>
</tr>
<tr>
<td></td>
<td>not done</td>
<td></td>
<td>not done</td>
</tr>
</tbody>
</table>

### Pachymetry

<table>
<thead>
<tr>
<th>L-15</th>
<th>Right eye 1st trial</th>
<th>Not done</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-16</td>
<td>Right eye 2nd trial</td>
<td>Not done</td>
</tr>
<tr>
<td>L-17</td>
<td>Right eye 3rd trial</td>
<td>Not done</td>
</tr>
<tr>
<td>L-18</td>
<td>Left eye 1st trial</td>
<td>Not done</td>
</tr>
<tr>
<td>L-19</td>
<td>Left eye 2nd trial</td>
<td>Not done</td>
</tr>
<tr>
<td>L-20</td>
<td>Left eye 3rd trial</td>
<td>Not done</td>
</tr>
</tbody>
</table>

### Iris Colour

(Use iris photograph reference standards. Do before pupil dilation)

<table>
<thead>
<tr>
<th>L-21</th>
<th>Right eye (iris)</th>
<th>Left eye (iris)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; std #1 (blue)</td>
<td>&lt; std #1 (blue)</td>
</tr>
<tr>
<td></td>
<td>&lt; std #2 (hazel/green)</td>
<td>&lt; std #2 (hazel/green)</td>
</tr>
<tr>
<td></td>
<td>&lt; std #3 (tan/brown)</td>
<td>&lt; std #3 (tan/brown)</td>
</tr>
<tr>
<td></td>
<td>&gt; std #3 (dark brown)</td>
<td>&gt; std #3 (dark brown)</td>
</tr>
<tr>
<td></td>
<td>cannot judge/not done</td>
<td>cannot judge/not done</td>
</tr>
</tbody>
</table>

### Dilation

Proceed with dilatation using Tropicamide 1% and Phenylephrine 10% in both eyes.

Note reason if dilating drops not instilled.
Station 4

30. Hearing Questionnaire

Thank you very much for coming to the Hearing Study today. I am going to ask you some questions about your hearing and other factors that can affect it. I will then conduct a number of hearing tests and will send you a report about these.

1. Hearing Loss
   HI-1 [heardloss] Do you feel you have a hearing loss?  □ Y  1 □ N  2 go to H1-11  □ DK  8  □ Missing  9
   HI-2 [whichear] Does it affect your:
       □ right ear alone  1 □ left ear alone  2
       □ both ears  3
       □ DK  8  □ Missing  9
   HI-3 [hears] For how long do you feel you’ve had a problem with your hearing? _____ years
   HI-4 [onset] Was the onset of the hearing loss gradual or sudden?
       □ gradual  1 □ sudden  2 □ DK  8  □ Missing  9
   HI-5 [notice] Did you or someone else first notice your hearing loss?
       □ self  1 □ spouse  2 □ relative  3
       □ friend  4 □ doctor  5 □ other person  6
       □ DK  8  □ Missing  9
   HI-6 [change] Do you feel that your hearing has changed since we last saw you for the hearing study?  □ Y  1  □ N  2 go to H2-1  □ DK  8  □ Missing  9
   HI-7 [details] Other details of hearing loss

---------

HI-8 [speak] Have you sought help or spoken to any professional about your hearing loss?  □ Y  1  □ N  2 go to H1-10  □ DK  8  □ Missing  9

HI-9 [contact] Which of the following have you contacted? multiple responses accepted
   □ family doctor  1 □ ENT doctor  2
   □ audiologist  3 □ hearing service/ hearing aid provider  4
   □ self help group (e.g. BHA, ATIA, SSSHH)  5 □ DK  8  □ Missing  9

HI-10 [supp] Have you received treatment or support services for your hearing loss from any of the following in the past? multiple responses accepted
  □ family doctor  1 □ ENT doctor  2
  □ audiologist  3 □ hearing service/ hearing aid provider  4
  □ self help group (e.g. BHA, ATIA, SSSHH)  5 □ DK  8  □ Missing  9

HI-11 [treat] Are you currently being treated or followed by a doctor for any hearing or ear condition?
  □ Yes, current  1 □ Yes, follow-up  2
  □ No  3 □ DK  8  □ Missing  9

42
2. Ear infections and other ear conditions

H2-1 [eucold] Have you had a head cold or sinus infection during last seven days?  
☐ Y 1 ☐ N 2 ☐ DK 8 ☐ Missing 9

H2-2 [coldnow] Do you have a cold now?  
☐ Y 1 ☐ N 2 ☐ DK 8 ☐ Missing 9

H2-3 [saurp] Since you last came to the hearing study, have you had any ear operations or treatment given?  
☐ Y 1 ☐ N 2 ☐ DK 8 ☐ Missing 9

Please specify________________________________________

3. Family history

Since the last time we examined your eyes or your hearing, have any of your close relatives developed a hearing loss?...including....

your father
H3-1 [father] ☐ Y 1 ☐ N 2 ☐ go to H3-4 ☐ DK 8 ☐ Missing 9
H3-2 [father] Details ____________________________

Onset? ☐ childhood 1 ☐ Before age 50 2 ☐ After age 50 3 ☐ DK 8 ☐ Missing 9

H3-3 [father] Details ____________________________

your mother
H3-4 [mother] ☐ Y 1 ☐ N 2 ☐ go to H3-7 ☐ DK 8 ☐ Missing 9
H3-5 [mother] Onset? ☐ childhood 1 ☐ Before age 50 2 ☐ After age 50 3 ☐ DK 8 ☐ Missing 9
H3-6 [mother] Details ____________________________

any brothers
H3-7 [brother] ☐ Y 1 ☐ N 2 ☐ go to H3-10 ☐ DK 8 ☐ Missing 9
H3-8 [brother] Onset? ☐ childhood 1 ☐ Before age 50 2 ☐ After age 50 3 ☐ DK 8 ☐ Missing 9
H3-9 [brother] Details ____________________________

any sisters
H3-10 [sister] ☐ Y 1 ☐ N 2 ☐ go to H3-13 ☐ DK 8 ☐ Missing 9
H3-11 [sister] Onset? ☐ childhood 1 ☐ Before age 50 2 ☐ After age 50 3 ☐ DK 8 ☐ Missing 9
H3-12 [sister] Details ____________________________
any children  □ Y 1  □ N 2  go to H4-1  □ DK 8  □ Missing 9
H3-13 [father]  Onset?  □ childhood 1  □ Before age 50 2  □ After age 50 3  □ DK 8  □ Missing 9
H3-15 [father]  Details __________________

4. Head injuries
H4-1 [heada]  Since your last assessment in this study, have you had any serious head injuries, whiplash or been knocked unconscious?  □ Y 1  □ N 2  □ DK 8  □ Missing 9
H4-2 [injdet]  Details (Including duration of LOC) __________________
H4-3 [concuss]  Since your previous assessment, has a doctor ever told you that you had concussion?  □ Y 1  □ N 2  □ DK 8  □ Missing 9

5. Hearing Aids and Devices
H5-1 [hearr]  Do you or have you ever worn a hearing aid of any type?  □ Y 1  go to H5-5  □ N 2  □ DK 8  □ Missing 9
H5-2 [horn]  Has a hearing aid been recommended to you in the past?  □ Y 1  □ N 2  go to H5-24  □ DK 8  □ Missing 9
H5-3 [hadked]  If you did not obtain a hearing aid, Why not?  go to H5 – 24 multiple responses accepted, consider all options below
□ too expensive 1  □ put off by others’ experience 5
□ concerned with appearance 2  □ other reason 6 (complete below)
□ considered you didn’t need one 3  □ not sure 7
□ too difficult (technical) to use 4  □ missing 9
H5-4 [hadked]  Details __________________
H5-5 [jacker]  How long have you been using your hearing aid?  □ less than 1 year 1  □ 1-5 years 2  □ 6-10 years 3
□ more than 10 years 4  □ DK 8  □ Missing 9
H5-6 [hainw]  Do you have your hearing aids now?  □ Y 1  □ N 2  go to H5-15  □ DK 8  □ Missing 9
H5-7 [heear]  Do you have one for each ear?  □ Y 1  □ N 2  □ DK 8  □ Missing 9
H5-8 [haseyl]  What style of hearing aid do you have now?
□ in the ear 1  □ in the canal 2  □ behind the ear 3
□ in the glasses 4  □ body aid 8  □ DK 8  □ Missing 9
H5-9 [hastrnd]  Details of hearing aid type/model __________________
H5-10 [hacoil]  Does your hearing aid have a telecoil switch?  □ Y 1  □ N 2  □ DK 8  □ Missing 9
H5-11 [havren]  Do you usually wear both, one or neither of your hearing aids?
□ both 1  □ one 2  □ neither 2  □ DK 8  □ Missing 9
H5-22 [hauze]  On average, how many hours per week do you wear at least one?
□ never 1  □ < 1 hr/week 2  □ < 1 hour/day 3
□ 1-4 hrs/day 4  □ 4-8 hrs/day 5  □ more than 8 hrs/day 6
□ DK 8  □ Missing 9

383
H5-13 [haptop] If you have hearing aids, but don’t wear them, why not? multiple responses accepted
  doesn’t help me to hear .......1 not working ........................................6
too uncomfortable ...........2 don’t like the appearance ...7
hearing aid whistles ...........3 other reason ............11 (complete below)
unable to put it on ..........4 not sure .....................8
batteries are too expensive ..5 missing .......................9

H5-14 [haptop] Details

H5-15 [haptop] How satisfied, on a scale of 1 to 10, were you with the clinical service you received at the time of fitting your hearing aid? (that is, professional, helpful, friendly) where 1 is ‘not at all satisfied’ and 10 is ‘very satisfied’.

Scale  1---2---3---4---5---6---7---8---9---10  number _____

H5-16 [hrepair] Has your hearing aid needed any repairs?
  □ Y 1  □ N 2  go to H5-18  □ DK 8  □ Missing 9

H5-17 [haptop] How satisfied, on a scale of 1 to 10, were you with any repair services to your hearing aid? (that is, professional, helpful, friendly) where 1 is ‘not at all satisfied’ and 10 is ‘very satisfied’.

Scale  1---2---3---4---5---6---7---8---9---10  number _____

H5-18 [haptop] Who provided your most recent hearing aid?
  □ hospital 1  □ government (private) 2  □ government (AHS/NAL) 3
  □ other 4  □ private (own funds) 5  □ DK 8  □ Missing 9

H5-19 [haptop] Who fitted you with your hearing aid?
  □ ENT doctor 1  □ audiologist 2  □ audiometrist/ hearing aid provider 3
  □ other 4  □ DK 8  □ Missing 9

Current Hearing Aids Check
If patient has hearing aids fitted currently, check

Right Aid working:  Yes  No  Left Aid working:  Yes  No
H5-20 [htaidsk]  1  2  H5-21 [htaidsk]  1  2
H5-22 [htaidsk] * If no, flat battery?  1  2  H5-212 [htaidsk] *If no, flat battery?  1  2

Notes/other faults in hearing aids

---

384
<table>
<thead>
<tr>
<th>Condition</th>
<th>right</th>
<th>left</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Study</td>
<td>H6-1[otot1] Yes No DK Missing □1... □2... □8... □9</td>
<td>H6-2[otot2] Yes No DK Missing □1... □2... □8... □9</td>
</tr>
<tr>
<td></td>
<td>Adequate view no wax □1</td>
<td>Adequate view no wax □1</td>
</tr>
<tr>
<td></td>
<td>Inadequate view due to wax □2</td>
<td>Inadequate view due to wax □2</td>
</tr>
<tr>
<td></td>
<td>View obscured by wax □3</td>
<td>View obscured by wax □3</td>
</tr>
<tr>
<td>TM perforation</td>
<td>H6-5[super1] Yes No DK Missing □1... □2... □8... □9</td>
<td>H6-6[super2] Yes No DK Missing □1... □2... □8... □9</td>
</tr>
<tr>
<td>Grommet</td>
<td>H6-7[grom1] Yes No DK Missing □1... □2... □8... □9</td>
<td>H6-8[grom2] Yes No DK Missing □1... □2... □8... □9</td>
</tr>
<tr>
<td>Exostosis</td>
<td>H6-9[exo1] Yes No DK Missing □1... □2... □8... □9</td>
<td>H6-10[exo2] Yes No DK Missing □1... □2... □8... □9</td>
</tr>
<tr>
<td>Comments</td>
<td></td>
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</table>

31. Hearing Examination

6. Otoscopy
7. Audiogram:  
(If NR at max. output: 888; if DNT: 999)

<table>
<thead>
<tr>
<th>Frequency</th>
<th>RAC</th>
<th>LAC</th>
<th>UBC</th>
<th>RBC</th>
<th>LBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>250Hz</td>
<td>H7°-1[re1]</td>
<td>H7°-2[ra1]</td>
<td>......</td>
<td>......</td>
<td>......</td>
</tr>
<tr>
<td>500Hz</td>
<td>H7°-3[ra2]</td>
<td>H7°-4[re2]</td>
<td>H7°-5[re3]</td>
<td>H7°-6[rn3]</td>
<td>H7°-7[rz3]</td>
</tr>
<tr>
<td>1000Hz</td>
<td>H7°-8[re3]</td>
<td>H7°-9[re4]</td>
<td>H7°-10[re5]</td>
<td>......</td>
<td>......</td>
</tr>
<tr>
<td>3000Hz</td>
<td>H7°-15[re7]</td>
<td>H7°-16[re8]</td>
<td>H7°-17[re8]</td>
<td>......</td>
<td>......</td>
</tr>
<tr>
<td>4000Hz</td>
<td>H7°-18[re8]</td>
<td>H7°-19[re9]</td>
<td>......</td>
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<tr>
<td>8000Hz</td>
<td>H7°-23[re10]</td>
<td>H7°-24[re11]</td>
<td>......</td>
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</tr>
</tbody>
</table>

Audiogram comments

8. Acoustic Impedance:

A. Tymps  
NR/absent: 888, DNT – 999; Unable to seal – 777; Artefact/negative – 222

<table>
<thead>
<tr>
<th>ME pressure</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>H8-1 [nqpress]</td>
<td>......</td>
<td>......</td>
</tr>
<tr>
<td>H8-2 [nqpress]</td>
<td>......</td>
<td>......</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>TM Compl.</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>H8-3 [compl]</td>
<td>......</td>
<td>......</td>
</tr>
<tr>
<td>H8-4 [compl]</td>
<td>......</td>
<td>......</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Cavity Volume</th>
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<th>Left</th>
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</thead>
<tbody>
<tr>
<td>H8-5 [cval]</td>
<td>......</td>
<td>......</td>
</tr>
<tr>
<td>H8-6 [cval]</td>
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</table>

B. ARTs

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<thead>
<tr>
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<th>Contra</th>
<th>Ipsi</th>
</tr>
</thead>
<tbody>
<tr>
<td>500Hz</td>
<td>H8°-7[an2]</td>
<td>H8°-8[ar2]</td>
</tr>
<tr>
<td>1000Hz</td>
<td>H8°-11[am3]</td>
<td>H8°-12[am3]</td>
</tr>
<tr>
<td>2000Hz</td>
<td>H8°-15[an4]</td>
<td>NOT TO TEST</td>
</tr>
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</table>
### C. AR Decay Test (at 1Khz – contralateral only)

<table>
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<tr>
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<th></th>
<th></th>
<th>Left</th>
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<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>H9=13[toe13]</td>
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</tr>
<tr>
<td>No decay</td>
<td>☐ 1</td>
<td>did not test ☐ 99</td>
<td>No decay</td>
<td>☐ 1</td>
<td>did not test ☐ 99</td>
</tr>
<tr>
<td>No sig decay</td>
<td>☐ 2</td>
<td>missing ☐ 9</td>
<td>No sig decay</td>
<td>☐ 2</td>
<td>missing ☐ 9</td>
</tr>
<tr>
<td>Decay</td>
<td>☐ 3</td>
<td></td>
<td>Decay</td>
<td>☐ 3</td>
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</tr>
</tbody>
</table>

### 9. OAE Study

**A: TEOAEs:**

Use NR:888 as necessary

**Whole Wave:**

<table>
<thead>
<tr>
<th>Probe</th>
<th>Contra</th>
<th>Ipsi</th>
</tr>
</thead>
<tbody>
<tr>
<td>500Hz</td>
<td>H9=9[toe12]</td>
<td>H9=10[toe12]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1000Hz</td>
<td>H9=13[toe13]</td>
<td>H9=14[toe13]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2000Hz</td>
<td>H9=10[toe14]</td>
<td>NOT TO TEST</td>
</tr>
<tr>
<td></td>
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<td></td>
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</tbody>
</table>

**Repro and SNR by Frequency:**

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<tr>
<th>Right Repro</th>
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<th>2000</th>
<th>3000</th>
<th>4000</th>
<th>5000</th>
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</thead>
</table>

<table>
<thead>
<tr>
<th>Left Repro</th>
<th>1000</th>
<th>2000</th>
<th>3000</th>
<th>4000</th>
<th>5000</th>
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|------------------|--------------|--------------|--------------|--------------|--------------|

|-----------------|--------------|--------------|--------------|--------------|--------------|

387
### Station 5

**Tests done:**

**PHOTOGRAPHY**

<table>
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<th>both</th>
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<th>Left only</th>
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<th>Reason for inability to take photograph</th>
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<tbody>
<tr>
<td>Topcon (Nuclear Lens)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
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<tr>
<td>Nitz (Cortical / PSC Lens)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Zeiss (fundus)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Canon (fundus)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

**OPTICAL COHERENCE TOMOGRAPHY (OCT)**

<table>
<thead>
<tr>
<th>both</th>
<th>Right only</th>
<th>Left only</th>
<th>None</th>
<th>Reason for inability to perform OCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>
### RIGHT EYE

<table>
<thead>
<tr>
<th>Lens</th>
<th>□ 1</th>
<th>□ 3</th>
<th>□ 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>phakic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aphakic, AC IOL...</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aphakic, no lens</td>
<td>□ 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>aphakic, PC IOL...</td>
<td></td>
<td>□ 4</td>
<td></td>
</tr>
<tr>
<td>emucleated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>missing</td>
<td></td>
<td></td>
<td>□ 6</td>
</tr>
</tbody>
</table>

- Posterior capsular opacity: □ Y □ N □ DK
- YAG Capsulotomy: □ Y □ N □ DK

### NUCLEAR WISC

<table>
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<tr>
<th>Grade</th>
<th>Number</th>
</tr>
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<tbody>
<tr>
<td>≤Std#1</td>
<td>1</td>
</tr>
<tr>
<td>≤Std#2</td>
<td>2</td>
</tr>
<tr>
<td>≤Std#3</td>
<td>3</td>
</tr>
<tr>
<td>≤Std#4</td>
<td>4</td>
</tr>
<tr>
<td>&gt;Std#4</td>
<td>5</td>
</tr>
<tr>
<td>Mature</td>
<td>6</td>
</tr>
<tr>
<td>Can’t grade</td>
<td>7</td>
</tr>
</tbody>
</table>

**Indicate with a “A1” the presence of cortical cataract or PSC in the following lens quadrants**

<table>
<thead>
<tr>
<th>PSC</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>Central circle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Please complete the following table by either circling the appropriate number or inserting a percentage.**

<table>
<thead>
<tr>
<th>Condition</th>
<th>absent</th>
<th>present</th>
<th>questionable</th>
<th>If VA is 6/12 or worse estimate % visual loss due to factors below</th>
<th>percent of total loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hard macular drusen</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>emucleation</td>
<td></td>
</tr>
<tr>
<td>soft macular drusen</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>amblyopia</td>
<td></td>
</tr>
<tr>
<td>Visible pigment</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>cataract</td>
<td></td>
</tr>
<tr>
<td>Geographic atrophy</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>AMD</td>
<td></td>
</tr>
<tr>
<td>Neovascular AMD</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>other retinal disease</td>
<td></td>
</tr>
<tr>
<td>Diabetic retinopathy</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>glaucoma</td>
<td></td>
</tr>
<tr>
<td>Retinal vein occlusion</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>other optic nerve disease</td>
<td></td>
</tr>
<tr>
<td>Asteroid hyalosis</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>Corneal disease</td>
<td></td>
</tr>
<tr>
<td>Titled disc</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>vitreous media</td>
<td></td>
</tr>
<tr>
<td>Myopic retinopathy</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>unsure</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
<td>other</td>
<td></td>
</tr>
</tbody>
</table>

---

389
LEF T EYE

- Phakic
- Aphakic, no lens
- Aphakic, PC IOL
- Aphakic, AC IOL
- Eunucleated
- Missing

Posterior capsular opacity

YAG Capsulotomy

<table>
<thead>
<tr>
<th>NUCLEAR WISC</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>central circle</th>
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<tbody>
<tr>
<td>≤ Std#1</td>
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</tr>
<tr>
<td>≤ Std#3</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ Std#4</td>
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<td></td>
<td></td>
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<tr>
<td>&gt; Std#4</td>
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</tr>
<tr>
<td>Mature</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can't grade</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Indicate with a "AI" the presence of cortical cataract or PSC in the following lens quadrants

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>central circle</th>
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<tbody>
<tr>
<td>PSC</td>
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<td></td>
</tr>
</tbody>
</table>

Please complete the following table by either circling the appropriate number or inserting a percentage

<table>
<thead>
<tr>
<th>Condition</th>
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<th>present</th>
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</thead>
<tbody>
<tr>
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<td>1</td>
<td>2</td>
<td>3</td>
<td>enucleation</td>
<td></td>
</tr>
<tr>
<td>soft macular drusen</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>amblyopia</td>
<td></td>
</tr>
<tr>
<td>Visible pigment</td>
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<td>2</td>
<td>3</td>
<td>cataract</td>
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<td>2</td>
<td>3</td>
<td>AMD</td>
<td></td>
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<tr>
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<td>2</td>
<td>3</td>
<td>other retinal disease</td>
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<tr>
<td>Diabetic retinopathy</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>glaucoma</td>
<td></td>
</tr>
<tr>
<td>Diabetic retinopathy</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>other optic nerve disease</td>
<td></td>
</tr>
<tr>
<td>Retinal vein occlusion</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>corneal disease</td>
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<tr>
<td>Asteroid hyalosis</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>vitreous media</td>
<td></td>
</tr>
<tr>
<td>Tiled disc</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>unsure</td>
<td></td>
</tr>
<tr>
<td>Myopic retinopathy</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>other</td>
<td></td>
</tr>
</tbody>
</table>

Other
Appendix B: References


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