ECONOMIC COSTS AND HEALTH BURDEN OF VISION PROBLEMS IN SINGAPORE

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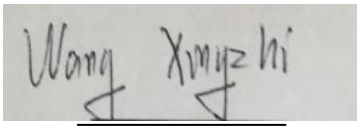
DECLARATION

I hereby declare that this thesis is my original work and it has been written by me in its entirety.

I have duly acknowledged all the sources of information which have been used in the thesis.

This thesis has also not been submitted for any degree in any university previously.



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Summary

Visual impairment (VI) is a public health problem with substantial disease burden worldwide. With the aging population, the prevalence of VI will increase dramatically, leading to a much heavier disease burden on individuals and society in the coming future. In order to alleviate the burden of VI, studies comprehensively and precisely measuring the disease burden from the economic and humanistic perspectives are essential for policy makers in resource allocation and preventative programs design.

For the economic burden of VI, majority of the studies are conducted in western countries, while in Asia, such studies are limited. Considering the high prevalence of VI in Asia that about 180.7 million people were visually impaired in 2010, it is necessary to explore the economic burden of VI. Meanwhile, generic health-related quality of life (HRQOL) is useful in the comparison between multiple health conditions and could be used in the cost-utility analysis (CUA), while studies exploring the impact of vision problems on generic HRQOL are limited. Compared with vision-specific quality of life, the limited usage of generic HRQOL instruments could be due to its general insensitivity.

Within this framework, several research questions concerning the economic and humanistic burden of vision problems were addressed. First, we estimated the direct medical costs from VI in Singapore. We found that VI imposed considerable direct costs at both individual and population levels in Singapore. Meanwhile, the direct

medical costs due to VI and four major eye diseases were likely to increase dramatically in the next decades. Second, we estimated the out-of-pocket expenditure and productivity loss of VI in Singapore. We found that VI had significant economic burden to the visually impaired patient and their families. Third, we measured the health burden associated with VI and compared the burden of VI with other four health conditions in Singapore. We found that VI was associated substantial health burden among Asians in Singapore. Fourth, we explored the effect of visual acuity (VA) on generic HRQOL among patients with VI in Singapore. We found that VA of the worse-seeing eye may have larger impact than that of the better-seeing eye on the health utility of visually impaired individuals. Fifth, we explored the effect of a vision 'bolt-on' item on the sensitivity of EQ-5D to the impact of vision problems. We found that the vision 'bolt-on' EQ-5D appeared to be more discriminative than the standard EQ-5D in measurement of vision problems.

These studies have provided new knowledge about the economic and humanistic burden of VI in Singapore. First, the economic and health burden of VI is substantial to visually impaired patients and their caregivers at both individual and population level in Singapore. The findings highlight the importance of VI prevention programs and provide detail information that could be used in the CUA of eye disease interventions in the future. Second, VA of the worse-seeing eye should be also used in the HRQOL studies, considering the larger impact of VA of the worse-seeing eye than that of the better-seeing eye on the health utility of visually impaired individuals.

Third, the vision ‘bolt-on’ EQ-5D shows more discriminative more than standard EQ-5D in measurement of vision problems and the sensitivity of the vision ‘bolt-on’ EQ-5D to vision change in interventional studies needs to be further investigated.

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List of Acronyms

AMD	Age-related macular degeneration
BMI	Body mass index
BMVA	Better eye-weighted mean visual acuity
BP	Blood pressure
BVA	Visual acuity in the better-seeing eye
CI	Confidence interval
CUA	Cost-utility analysis
DALY	Disability-adjusted life years
DR	Diabetic retinopathy
EQ-5D	European Quality of Life-5 Dimensions
HRQOL	Health-related quality of life
HUI	Health Utilities Index
ICD-10	International Classification of Diseases
IOP	Intraocular pressure
LogMAR	Logrithm of the minimum angle of resolution
MVA	Mean of visual acuity
MVH	Measurement and Valuation of Health Study
NEI-VFQ	National Eye Institute Visual Function Questionnaire
NICE	National Institute for Health and Care Excellence
OECD	Economic Co-operation and Development
OOP	Out-of-pocket
OR	Odds ratio
PACG	Primary angle-closure glaucoma
POAG	Primary angle-open glaucoma
QALY	Quality-adjusted life years
RE	Refractive error
SCES	Singapore Chinese Eye Study
SD	Standard deviation

SE	Standard error
SEED	Singapore Epidemiology of Eye Disease
SES	Socio-economic status
SF-6D	Short form 6 Dimensions
SG	Singapore
SiMES	Singapore Malay Eye Study
SINDI	Singapore Indian Eye Study
UCRE	Under-corrected refractive error
VA	Visual acuity
VF-14	Visual Function Index-14
VI	Visual impairment
VSQOL	vision-specific quality of life
WHO	World Health Organization
WMVA	Worse eye-weighted mean visual acuity
WVA	Visual acuity in the worse-seeing eye
YLD	Years lost due to disability
YLL	Years of life lost
Yrs	Years

List of Publications

Published papers

Wang X, Lamoureux E, Zheng Y, et al. Health burden associated with visual impairment in Singapore: the Singapore epidemiology of eye disease study. Ophthalmology. 2014; 121: 1837-42.

Luo N*, Wang X*, Ang M, et al. A vision 'bolt-on' item could increase the discriminatory power of the EQ-5D index score. Value in Health. 2015; 18: 1037-42.

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Chapter 1

Introduction

1 Visual Impairment

Visual impairment (VI) is a public health problem, which exerts substantial burden worldwide. According to the estimate from the World Health Organization (WHO), in 2010, about 285.39 million people were visually impaired worldwide, among whom 246.02 million people were in low vision and 39.37 million blindness (Pascolini and Mariotti, 2012). In Southeast Asia alone, about 27.91 million people were visually impaired in 2010, accounting for 9.8% of the total population in this area. Moreover, VI is the most prevalent cause of moderate and severe disability in the population aged 60 year and above, compared with other health conditions associated with disability (United Nations Population Fund, 2012). A study in Europe showed that VI, after memory loss, is the second top health concern in aging (International Federation on Aging, 2012).

VI is common in the elderly, because most eye diseases are age-related. People aged 40 and above constitute the majority of the VI population (Buhrmann et al., 2007). The prevalence rate of VI has been found to increase in each decade over the age of 40 in the Baltimore Eye Survey and the Los Angeles Latino Eye Study in the US (Tielsch et al., 1990; Varma et al., 2004). Similar trend has been found in studies in both eastern and western populations (Baasanhu et al., 1994; Zhao et al., 2010; Hyman et al., 2001; Wang et al., 2000; Iwase et al., 2006; Wong et al., 2008; Zheng et al., 2011). An Australia study even showed that the number of people with low vision and blindness increased by three-folds in each decade in people over the age of 40 (Taylor, 2006). With the rapid aging population, the burden of VI will increase dramatically. According to a Canadian Study, the prevalence of VI and number of people with VI is estimated to increase

by 56% and 97% from 2006 to 2031, respectively (Buhrmann et al., 2007). Even though the global age-standardized prevalence of blindness and VI in old people decreased from 3.0% and 14.3% in 1990 to 1.9% and 10.4% in 2010, due to the increasing population aging, the total number of people with VI and blindness remains increased (Stevens et al., 2013). For example, the number of old people with low vision has increased from 172 million in 1990 to 191 million in 2010 (Stevens et al., 2013).

1.2 Definition of Visual Impairment

VI is defined based on the presenting or best-corrected visual acuity (VA) in the better-seeing eye according to the US and the modified WHO definition (Tielsch et al., 1990; WHO, 2006). In the US definition, blindness is defined as VA of 20/200 or worse in the better-seeing eye and low vision as VA worse than 20/40 but better than 20/200 in the better-seeing eye. According to the modified WHO definition of VI or the International Classification of Diseases - 10 (ICD-10), there are 4 levels of vision status: normal vision (VA better or equal to 20/60), moderate VI (VA worse than 20/60 but better than or equal to 20/200), severe VI (VA worse than 20/200 but better than or equal to 20/400), and blindness (VA worse than 20/400). Moderate and severe VI could be combined as low vision.

1.3 Cause of Visual Impairment

Visual impairment is mainly caused by five eye conditions: cataract, glaucoma, diabetic retinopathy (DR), macular degeneration and under-corrected refractive error (UCRE). Globally,

the five eye diseases account for about 70% and 80% of low vision and blindness, respectively (Pascolini and Mariotti, 2012). The leading causes of low vision are UCRE (52.9%), cataract (18.4%), macular degeneration (3.1%), glaucoma (2.2%) and DR (1.9%). Cataract (33.4%) remains the leading cause of blindness, followed by UCRE (20.9%), glaucoma (6.6%), macular degeneration (6.6%) and DR (2.6%).

There are large differences in the causes of VI and blindness between regions. In 2010, the proportion range of blindness caused by cataract is from less than 15% in the high-income regions to more than 40% in South and Southeast Asia, and Oceania (Bourne et al., 2013; Keeffe et al., 2014). The proportion of blindness caused by macular degeneration is higher in regions with older populations, such as high-income regions (e.g. Asia Pacific, high income: 19.5%; North America, high income: 16.4%), Southern Latin America (19.5%), and Central (15.4%) and Eastern Europe (15.4% and 16.6%), while lower in regions such as south Asia (2.6%). The proportion of blindness caused by glaucoma is higher in tropical Latin America (15.5%) and lower in South Asia (4.7%), East and West Sub-Saharan Africa (4.0% and 4.4%), and Oceania (4.2%).The proportion of blindness caused by DR, ranging from 1.1% in east Asia to 4.3 % in high income Asia Pacific, does not notably vary among different regions. In terms of the causes of low vision, the proportion of low vision caused by UCRE is larger in south Asia (65.4%) than in other regions (43.2% to 48.1%). Meanwhile, cataract caused the smallest proportion of low vision in the highest-income regions (13.0% to 13.8%) and largest in south Asia (21.4%) and Southeast Asia (22.7%).

1.3.1 Age-Related Macular Degeneration

Age-related macular degeneration (AMD) is a deterioration of an eye's macula, a small oval-shaped pigmented area near the center of the retina in the human eye, and therefore leads to patient's central vision loss (Lim et al., 2012). With the aging process, small yellow deposits, which are called drusen, present beneath the retina. In the early AMD, medium sized drusen could be found and it does not much affect the vision status. In the late AMD, large drusen and damage to the macula leads to vision loss. There are two types of late AMD: dry (atrophic / non-neovascular) AMD and wet (exudative / neovascular) AMD. In dry AMD, the thinning macula leads to gradual vision loss. Currently, there is no treatment or medication for dry AMD. In wet AMD, with the growth of abnormal blood vessels underneath the retina and macular, fluid and blood may leak and cause damage to the macula. Compared with dry AMD, wet AMD may cause rapid and severe vision loss. Certain medication and treatment (e.g. anti-vascular endothelial growth factor injection therapy, and photodynamic therapy) have been developed to stop further vision loss. Nevertheless, current medication and treatment could not cure AMD or preclude recurrence. The risk factors of AMD mainly include age, smoking, genetic susceptibility and family history. For example, in the US, people aged 75 years and above are three times more likely to develop AMD, compared with those aged between 65 to 74 years old (Klein et al., 1991). Meanwhile, in UK, the risk of AMD related vision loss is two-fold in current smokers compared with that in non-smokers (Evans et al., 2005).

1.3.2 Cataract

Cataract refers to the clouding of the lens in the eye and the most common symptoms are blurry vision, faded colors, glare over light and double vision or multiple images (Asbell et al., 2005). Most cataracts are age-related that in Americans age 80 above, the percentage of people with cataract or cataract surgery is higher than 60% (Congdon et al., 2004). Apart from age, the risk factors of cataract mainly include smoking, diabetes, and ultraviolet exposure. In the treatment of cataract, cataract surgery has been proven to be cost-effective and therefore is widely used as the way to cure cataract (Baltussen et al., 2004; Frampton et al., 2014).

1.3.3 Diabetic Retinopathy

Diabetic retinopathy (DR) is the most common eye disease related with diabetes mellitus. It is caused by the micro aneurysms developed on the blood vessels inside the retina (Cheung et al., 2010). The fragile abnormal blood vessels could leak blood and fluid into the center of the eye, causing blurring vision. Meanwhile, the fluid leaking into the center of the macular leads to the swell of the macula, which is called macular edema. The severity of DR could be classified into five levels: mild non-proliferative DR, moderate non-proliferative DR, severe non-proliferative DR, proliferative DR, and clinically significant macular oedema. In the first 3 levels, blood vessels nourishing the retina are blocked, while in the latter two levels, abnormal, fragile new blood vessels grow along the retina and the surface of the vitreous gel. Nevertheless, macular edema could occur at any stage of DR and is more likely to occur with the progression of the disease. To prevent the progression of DR, treatment is mainly conducted for proliferative DR and clinically significant macular oedema. Proliferative DR is treated with laser surgery and a vitrectomy might be necessary in case of severe and persistent bleeding. Both treatment could

effectively reduce, but not cure the vision loss due to DR. The risk factors mainly include the presence of diabetes and the uncontrolled glucose or blood pressure level.

1.3.4 Glaucoma

Glaucoma is a group of diseases that damage the eye's optic nerve and, are often associated with increased intraocular pressure and decreased peripheral vision (Quigley, 2011). There are three types of glaucoma in adults: primary open-angle glaucoma (POAG), primary close-angle glaucoma (PACG), and secondary glaucoma. POAG is the most common type of glaucoma and is due to the slow fluid flow through the meshwork drain and the consequent increased intraocular pressure that damages the optic nerve and causes vision loss. The progression of POAG is slow and often has no symptoms until advanced stage. POAG is mainly treated with medication or surgery (laser surgery or conventional surgery) to lower the intraocular pressure. Unlike the open normal anterior chamber angle in POAG, in PACG, the anterior chamber angle is closed, leading to a sudden spiked intraocular pressure (IOP) elevation and subsequent damage to optic nerve and vision. Meanwhile, PACG is commonly associated with sudden intense eye pain, redness, nausea and vomiting, and therefore treated as a medical emergency that medication and laser surgery should be used immediately to prevent the disease progression, lower the IOP, prevent the damage to optic nerve, and protect vision (Schacknow and Samples, 2010). Secondary glaucoma is mainly a complication of other medical conditions (e.g. surgery, advanced cataract, eye injuries, and eye tumors). Medication and surgery are the common treatment for secondary glaucoma. Currently, there is no cure for glaucoma and the effect of glaucoma on people's life could be life-long, while early diagnosis and treatment may do help to

protect vision from severe vision loss. The risk factors of glaucoma include age, family history, and ethnicity, and may be slightly different among different types of glaucoma.

1.3.5 Under-Corrected Refractive Error

Refractive error (RE) refers to unappropriated light focusing on the retinal due to the optical defects and is a leading cause of vision loss. RE includes four types: myopia, hyperopia, astigmatism and presbyopia. Myopia refers to the too strong optical power of the eye for the corresponding axial length that light focuses in front of the retina, and is the most common type of RE (Morgan et al., 2012). The risk factors of myopia include genetics and environmental factors, such as reading and socioeconomic status. Hyperopia refers to the too weak optical power of the eye that light focuses behind the retina. Astigmatism refers to the optical defect caused by the differential refractive power along different ocular meridians. In people with astigmatism, the lines in particular direction appear to be less clearly, compared with lines at right angles. Presbyopia refers to the age-related decline in accommodation to lenses due to reduced focusing ability and is commonly seen in population older than 40. All types of RE could be easily corrected by eyeglasses, contact lenses and refractive surgery (Sakimoto et al., 2006).

1.4 Visual Impairment in Singapore

Singapore is a multi-ethnic country, in which Chinese, Indians and Malays comprise 96.7% of the total population in 2014 (Department of Statistics, 2014). Chinese constitute the majority of

the Singapore population at 74.3%, followed by 13.3% of Malays and 9.1% of Indians. Though the prevalence of major eye diseases (e.g., glaucoma and AMD) differs in ethnicities (Sommer et al., 1991), no significant differences in the prevalence of VI were found among the 3 ethnic groups. For Chinese, in the Tanjong Pagar Survey, the age-standardized prevalence rate of bilateral VI is 1.6% (low vision: 1.1%; blindness: 0.5%), according to the WHO definition of best-corrected visual acuity (Saw et al., 2004). For Malays, in the Singapore Malay Eye Study, the age-standardized prevalence rate of bilateral VI is 1.11% (low vision: 1.03%; blindness: 0.08%) and 0.52% (low vision: 0.47%; blindness: 0.05%), according to the US and WHO definition of best-corrected visual acuity, respectively (Wong et al., 2008). For Indians, in the Singapore Indian Eye Study (SINDI), the age-standardized prevalence rate of bilateral VI is 3.8% (low vision: 3.4%; blindness: 0.4%) and 1.8% (low vision: 1.6%; blindness: 0.2%), according to the US or WHO definition of best-corrected VA, respectively (Zheng et al., 2011). Compared with the prevalence rate of VI in populations in other countries, the prevalence rate of VI in Singapore is relatively row. For example, the prevalence rate of VI in Indians in Singapore is similar to those in the whites and Japanese, but lower than those in blacks, Chinese, Mongolians, and Indians living in Indian (Baasanhu et al., 1994; Zhao et al., 2010; Hyman et al., 2001; Tielsch et al., 1990; Varma et al., 2004; Wang et al., 2000; Iwase et al., 2006; Sapkota et al., 2006). Despite of the variations in methodologies and definitions among these studies, one possible reason for the relatively lower prevalence rate of VI in Singapore is the better knowledge and awareness of vision problems, better accessibility and affordability of the eye care system, and better eye care services and facilities provided in Singapore.

In Singapore, cataract, glaucoma, DR, AMD and UCRE are the leading causes of VI, which is in consistence with the findings in studies in Asia (Baasanhu et al., 1994; Li et al., 1999; Murthy et al., 2001; Dandona et al., 2001; Michon et al., 2002; Zainal et al., 2002). Cataract is the main cause of bilateral low vision in Chinese (58.8%) and Indians (60.0%), and bilateral blindness in Malays (65.2%) and Indians (65.7%). Meanwhile, UCRE is the main cause of bilateral low vision (52.2%) in Malays and glaucoma of bilateral blindness in Chinese (60.0%).

2 Disease Burden of Vision Problems

Disease burden refers to the burden that a disease imposes on society and is generally measured from clinical, economic and humanistic perspective (Reeder, 1995; Gunter, 1999; Kemp, 2006). Clinical burden is mainly measured by epidemiological indicators, such as prevalence, incidence, morbidity and mortality. Economic burden refers to direct, indirect and intangible costs associated with the disease. The economic burden studies are meaningful in that they may help to identify appropriate actions or strategies to reduce the cost of disease or injury (WHO, 2009). Humanistic burden refers the consequences of a disease on patient's functional status or quality of life (e.g. physical functioning, social functioning, well-being, and life satisfaction).

2.1 Economic Burden of VI

The economic burden of a health condition is measured by cost-of-illness study. In the cost-of-illness study, both the direct and indirect costs of the health condition are measured. In terms of vision problems, the economic burden of vision problems is significant and increases

dramatically over time. The worldwide economic burden of vision problems in 2010 is estimated to be $3.0 trillion (direct costs: $2.3 trillion; indirect costs: $652 billion). By the year 2020, the economic burden of vision problems is projected to be 3.6 trillion (direct costs: $2.8 trillion; indirect costs: $760 billion) (Access Economics, 2010). Same trends exist in regions and countries. In the US, the annual economic burden of vision problems among the population aged 40 and above is estimated to be $51.4 billion in 2004 and it increases to $111.1 billion in 2013 (Wittenborn and Rein, 2013). Meanwhile, in Australia, the annual economic burden of vision problems is estimated to increase from $9.8 billion in 2004 to $16.6 billion in 2009. In Canada, the annual economic burden of VI is estimated to be $15.8 billion in 2007, accounting for 1.19% of Canada's GDP, and is projected to be as much as $30.3 billion by 2032.

2.1.1 Cost-of-Illness Study

Cost-of-illness study measures the economic burden of diseases. The information from the cost-of-illness study highlights the magnitude of the impact of a disease on society (Finkelstein et al., 2003; Taylor and Sloan, 2000) and can help policy makers in resource allocation and strategy identification to better prevent or treat diseases (Miller et al., 1998; Warner et al., 1999). Cost-of-illness study generally measures direct and indirect costs. The definitions of direct and indirect costs are not consistent across studies. Generally speaking, direct costs measure the actual costs of resources related with a disease in the health care sector (Drummond et al., 2005), such as the costs due to inpatient and outpatient service, pharmaceuticals, vision care (optometry, ophthalmology and lenses), assistance program and research. Indirect costs measure the value of the lost productivity and mainly include costs due to productivity loss, informal care, tax

deduction, and transfer deadweight loss. Moreover, cost-of-illness study could be done from different perspective and reach different results. The perspectives may include society, health care system, business, government, and participants and families (Gold et al., 1996; Hodgson et al., 1994). Appropriate prospective identification should be based on research questions. For example, a study measuring the percentage of the costs of a disease on the government healthcare budget should be conducted from the perspective of the government, while another study concerning the individual costs of a disease to the patients or their families should be conducted from the perspective of patients and their families. Nevertheless, the most comprehensive measurement of the costs of a disease is estimated from the societal perspective.

There are two types of cost-of-illness studies: incidence-based and prevalence-based studies (Tarricone, 2006). Incidence-based studies estimate the lifetime costs, which measure the costs of a disease from onset to termination. Prevalence-based studies estimate the annual costs, which measure the costs of a disease in a period, regardless of the onset time. The prevalence-based studies are suitable to measure the current economic burden of a disease, while incidence-based studies are suitable to measure the cost changes when preventative programs are implemented. In comparison of the two kinds of studies, prevalence-based studies are more common in use, because less data, fewer assumptions, and less money are required to conduct the prevalence-based studies.

2.1.2 Direct Costs

Direct costs could be further classified as direct medical costs and direct non-medical costs (Drummond et al., 2005). Direct medical costs refer the costs of resources used for treating a particular disease, such as the costs due to inpatient and outpatient costs, while direct non-medical costs refer to the costs of the disease but not due to medical treatment. In patients with VI, direct non-medical costs include costs in supporting services, assistive devices, home care, residential care and transportation. The direct costs of VI are considerable. For example, the direct costs for vision problems in Australia are higher than those of coronary heart disease, stroke, depression, diabetes and asthma (Taylor et al., 2006). In Canada, the direct costs of VI ($8.6 billion) rank 1st in comparison of the direct costs of all kinds of diseases (Cruess et al., 2011).

2.1.2.1 Direct Medical Costs

Previous studies have shown that direct medical costs of VI are mainly due hospitalization, and medical service use in consultation, diagnosis and treatment (Clarke et al., 2003; Cruess et al., 2011; Frick et al., 2007; Frick et al., 2008; Morse et al., 1999; Roberts et al., 2010). In comparison, drug costs are not a major contributor to direct medical costs. For example, in Japan, the medical costs ($8.10 billion), composed of inpatient ($1.81 billion) and outpatient ($6.29 billion) medical expenditure, add up to 73% of the total health care costs ($11.09 billion) and 11.1% of the total economic costs ($72.81 billion). Comparatively, the costs of drugs ($1.40 billion) account for 12.6% of the total health costs and 1.9% of the total economic costs. Moreover, direct medical costs of VI are positively associated with the severity of VI that blindness has the largest costs. For example, the study measuring the impact of VI on costs in

Medicare beneficiaries with glaucoma shows that the annual mean costs per patient in 2007 are $8,157 for no vision loss, $13,162 for moderate VI, $15,312 for severe VI, and $18,670 for blindness.

The direct costs of eye diseases vary in different countries, considering the different prevalence rate of eye diseases and unit cost in diagnosis, consultation and treatment. According to the economic burden study in the US, UCRE ($16.1 billion) has the highest direct medical costs in 2011, followed by cataract ($10.7), physical disorders ($8.9 billion), retinal disorders ($8.7 billion) and glaucoma ($5.8 billion). In Canada, UCRE ($3.48 billion) remains to have the highest direct medical costs in 2007, while AMD ($898.9 million) has the second highest direct medical costs, followed by glaucoma ($549.0 million), cataract ($481.0 million) and DR ($205.7 million).

2.1.2.2 Direct Non-Medical Costs

In terms of the direct non-medical costs, home care assistance including assistive devices/aids, home modifications, and home-based nursing, is the main component (Frick et al., 2007; Rein et al., 2006; Schmier et al., 2009; Cruess et al., 2011; Wong et al., 2008; Roberts et al., 2010; Porz et al., 2010; Lafuma et al., 2006). Meanwhile, direct non-medical costs also increase with the severity of VI. For example, in the US study, the home health care costs from paid independent provider for blindness are $1200 more than that for low vision (Frick et al, 2007; Schmier et al., 2006; Schmier et al., 2009; Keeffe et al., 2009; Wong et al., 2008; Lafuma et al., 2006). Similar difference is also found in agency-sponsored home health care costs.

2.1.3 Indirect costs

Previous studies have shown that the substantial indirect costs of VI are even higher than the direct costs in some studies (Wittenborn, et al., 2013; Royal National Institute of Blind People, 2009). The indirect costs of VI are mainly due to productivity loss and informal care (Rein et al., 2006; Roberts et al., 2010; Lafuma et al., 2006; Brezin et al., 2005; Cruess et al., 2011, Frick et al., 2007). For example, in Japan, the costs due to productivity losses ($4.67 billion), including lower employment ($4.23 billion) and absenteeism ($0.38 billion), account for 35.6% of the indirect costs ($13.12 billion) and 6.4% of total economic costs ($72.81 billion). Meanwhile, the costs of informal care ($6.61billion) are even higher than productivity loss and together with productivity loss add up to 85.9% of the indirect costs and 16.5% of the total economic costs. Same as direct costs, indirect costs of VI also increase with the severity of VI, with the highest for blindness. For example, in the US, the annual informal care costs for blindness are $242 million, compared with $124 million for low vision (Frick et al., 2007).

2.2 Health-Related Quality of Life

VI, as a serious health condition, affects people's functioning and well-beings (Goldzweig et al., 2004; Ong et al., 2012; Lamoureux et al., 2008). Previous studies have shown that VI increases the risks of depression, falls, and injuries such as hip fractures (Dargent et al., 1996; Lamoureux et al., 2010). Notably, VI may also increase the risk of mortality by increasing the risks of injury, accident, or social and emotional problems leading to early death (McCaty et al., 2001; Freeman et al., 2005). To measure the impact of VI on people's functioning and well-beings, health

related quality of life (HRQOL) is widely used. HRQOL has a number of definitions and according to WHO, HRQOL is defined as "the optimum levels of mental, physical, role (e.g. work, parent, career, etc.) and social functioning, including relationships, and perceptions of health, fitness, life satisfaction and well-being" (Bowling, 1999). Compared with clinical outcome measure, HRQOL provides the unique information from patients' perspective about their perception of the effect of certain health conditions on multiple aspects of life. Meanwhile, HRQOL could improve patient care by widening the parameters of benefit, indicating the need for interventions, acting as prognostic indicators, aiding decision-making, and assisting resource allocation and healthcare policy (Fayers and Machin, 2007). HRQOL usually contains multi-dimensional assessments, such as physical, functional, psychological/emotional and social/occupational domains. There are three types of HRQOL scales: disease or condition specific measures, general or generic health profiles, and preference-based measures (Drummond et al., 2005).

Disease or condition specific measures concentrate on health outcomes specific to an individual disease, medical conditions, or patient population and thus have the advantages of better responsiveness to changes in the patient's condition and high acceptance of patients and physicians in a study. Nevertheless, disease or condition specific measures have two main disadvantages. First, specific measures could not be used to compare the effectiveness of programs in different disease areas. Second, the narrow focus of specific measures may sometimes fail to assess all the relevant dimension of the HRQOL of life of a certain disease. In terms of VI, vision-specific quality of life measures are widely used to measure the impact of VI

on HRQOL. The commonly used vision-specific HRQOL measures include the Visual Function Index (VF-14) and National Eye Institute visual Function Questionnaire (NEI-VFQ).

In comparison with disease or condition specific measures, general or generic health profiles comprehensively measure the HRQOL and could be applied across different patient population and disease areas. The widely used general health profiles include the Nottingham Health Profile, the Short Form (SF) 36 and the Sickness Impact Profile (Brazier et al., 1993; Bergner et al., 1981; Hunt et al., 1981). The main advantages of the widely used general health profiles are their proven validity and reliability. However, general health profiles couldn't be used to compare across different programs producing different types of outcomes, because they produce a profile of scores across different domains of the instrument rather than a single quality of life score, except the Sickness Impact Profile. Moreover, in the general health profile, the association between higher scores and preferred outcomes is not clear, because the scoring methods of the instruments are not based on individuals' preferences for the outcomes. Meanwhile, the score from general health profiles is not calibrated as death = 0 and perfect health = 1, and thus could not be combined with quantity of life.

Preference-based measures or utilities are the principal values representing the strength of an individual's preferences for specific health-related outcomes. Compared with specific measures and general health profiles, preference-based measures could generate a single index measure with death = 0 and perfect health = 1, and thus are widely used in the economic analysis, especially the cost-utility analysis (CUA). The preference / utility evaluation includes direct and

indirect methods. In direct method, utilities are measured directly from the individuals. There are three widely used techniques: the rating scale and its variants, the standard gamble, and the time trade-off. In indirect method, utilities are mainly assessed by generic HRQOL measures, such as Quality of Well-Being (QWB) (Kaplan et al., 1997), Health Utilities Index (HUI) (Feeny et al., 2004), European Quality of Life-5 Dimensions (EQ-5D) (Dolan, 1997), and Short Form 6 Dimensions (SF-6D) (Brazier et al., 1998). Among the generic HRQOL measures, EQ-5D has the advantage of simplicity and is recommended by National Institute for Health and Care Excellence (NICE, 2008) in the UK. Therefore, EQ-5D is used as the measure in majority of the studies exploring the impact of VI on generic HRQOL.

The health utility gained from generic HRQOL measures could be used in quality-adjusted life years (QALYs) calculation and further applied in the CUA. QALYs integrate the quantity of life and the quality of life into a single index and allow the comparison of the outcomes from different programs and interventions. QALYs are calculated as the time in the health state weighted by the utility score for the health state. For example, one intervention leads to a health state valued as 0.75 for four year and thus generates 3 QALYs. Similarly, another intervention leads to a health state valued as 0.50 for four years and thus generates 2 QALYs. Therefore, the first intervention generates additional 1 QALY. Apart from QALYs, disability-adjusted life years (DALYs) are also widely used as an alternative to QALYs (Murray, 1994). DALYs for a disease or health conditions include the Years of Life Lost (YLL) due to premature mortality and the Years Lost due to Disability (YLD) for people living with the disease or health condition. In the global burden of disease study, YLL is calculated as the number of death multiplied by standard

life expectancy at age of death in years, and YLD is calculated as the number of prevalent cases multiplied by the disability weight (Murray et al., 2012).

2.2.1 Impact of VI and Eye Diseases on Generic Health-Related Quality of Life

Previous studies have shown a substantial impact of VI on generic HRQOL. Studies in the Netherlands show that the effect of VI on generic HRQOL is larger than that of type 2 diabetes, coronary syndrome, and hearing impairment (Nispen et al., 2009; Langelaan et al., 2007). Moreover, increased severity of VI is significantly associated with the worsening EQ-5D index score and patients with VI are more likely to report problems in each dimension compared with the general Dutch population (Nispen et al., 2009; Langelaan et al., 2007). Similar findings are also found in other studies, mainly using EQ-5D as the generic HRQOL measure (Polack et al., 2007; Lotery et al., 2007; Polack et al., 2010; Thygesen et al., 2008; Smith et al., 2008). The impact of eye diseases on generic HRQOL is also explored in previous studies, in majority of which EQ-5D is used as the HRQOL measure.

For cataract, significant differences are observed between patients with cataract and the controls with normal vision (Polack et al., 2007; Polack et al., 2008; Polack et al., 2010). Nevertheless, the benefit of cataract surgery on generic HRQOL measured by EQ-5D index score varies. Some studies showed the responsiveness of the EQ-5D to the benefit of cataract surgery (Harwood et al., 2005; Sach et al., 2007; Ang et al., 2013), while others failed (Conner-Spady et al., 2005; Browne et al., 2007). In terms of the convergent validity, two studies have found a significant

association between VA and the higher probability of reporting problems in all EQ-5D dimensions except anxiety, while in the other two studies, no such finding was observed.

In terms of glaucoma, previous studies have shown that the EQ-5D index score is negatively associated with the severity levels of glaucoma and VI (Kobelt et al., 2006; Thygesen et al., 2008), even though the associations are not always significant (Aspinall et al., 2008 Montemayor et al., 2001). No other generic HRQOL measures have been used to measure the impact of glaucoma on generic HRQOL.

For AMD, patients with AMD have a significant reduction in generic HRQOL compared with general population (Lotery et al., 2007; Ruiz-Moreno et al., 2008; Soubrane et al., 2007). Moreover, significant difference in EQ-5D index score is found between patients with unilateral and bilateral AMD (Kim et al., 2010), while inconsistent finding exists in the difference in EQ-5D index score across different severity levels of VI. One study even shows that the EQ-5D index score for participants with normal vision is the worst, compared with that for participants with mild, moderate, and severe AMD (Soubrane et al., 2007). Nevertheless, studies exploring the association between the severity of AMD and the EQ-5D index score are limited.

Two studies show that EQ-5D index score has a significant difference between the two extreme groups (normal vision and blindness); however, the differences between the neighbor groups are frequently inconsistent (Lloyd et al., 2008; Smith et al., 2008). For example, the EQ-5D index

score in the VI group of 6/12 – 6/18 is worse than that in the neighbor groups of 6/6 – 6/9 and 6/24 – 6/36. Meanwhile, a study in Indian shows that only blindness is independently associated with the decline in EQ-5D index score, while other severity groups are not (Polack et al., 2015).

In conclusion, the results of studies using EQ-5D to measure the impact of VI and eye diseases on generic HRQOL are mixed. Most studies show that EQ-5D could successfully distinguish the differences between patients and controls (Tosh et al., 2012). Nevertheless, for construct validity, most of the studies show the little or no difference of EQ-5D index score across VI severity groups. Moreover, previous studies have identified the difference before and after the intervention, though most of them are not statistically significant. In terms of convergent validity, the results about the association between EQ-5D index score and VA measure are also mixed.

2.2.2 Vision-Specific Quality of life (VSQOL)

With the increasing emphasis on the full impact of VI on people's daily life, VSQOL is widely used. Among the various VSQOL instruments, the Visual Function Index (VF-14) and National Eye Institute Visual Function Questionnaire (NEI-VFQ) are most frequently used. VF-14 is originally developed to measure the functional impairment due to cataract (Steinberg et al., 1994) and afterward validated for VI (Chiang et al., 2013; Lamoureux et al., 2009; Lamoureux et al., 2008) and other eye diseases, including DR, UCRE, glaucoma, AMD and dry eye (Milne et al., 2012; Pan et al., 2014; Chan et al., 2013; Tong et al., 2010). VF-14 has also been translated and validated in multiple populations (Khadka et al., 2014; Chiang et al., 2011; Mousa et al., 2012).

All the studies have shown the significant association between the presences of vision problems and the deterioration of the VSQOL measured by VF-14 index score.

The original NEI-VFQ questionnaire contains 51 items and is firstly developed to provide a comprehensive visual function assessment (Mangione et al., 1998). Both VF-14 and NEI-VFQ require patients to rate their difficulties in performing the vision-related activities. Compared with VF-14, NEI-VFQ not only emphasizes patients' difficulty with tasks and symptoms, but also measures the effect of vision problems on other aspects of quality of life, such as dependency, emotional well-being, and social function. Nevertheless, the 51-item NEI VFQ questionnaire has a disadvantage of the long length, which may diminish participant rates and response reliability, and increase the data collection and management costs. To solve the problem, a shorter, 25-item version is developed to measure the most important dimensions of vision-related health status (Mangione et al., 2001). The NEI VFQ-25 contains 25 questions, related with 11 vision-related constructs and an additional single-item general health question. The NEI-VFQ-25 has been validated and widely used as the measure of VSQOL in the evaluation of the impact of multiple eye diseases or disease interventions, such as cataract, glaucoma, and retinal diseases, and in multiple populations (Stock et al., 2015; Abe et al., 2015; Takahashi et al., 2015; Gracitelli et al., 2015; Yuzawa et al., 2015).

3 Research Objectives

Vision problems have been shown to impose substantial economic and humanistic burden to the individuals and society; however such studies are limited in Singapore. Although understanding the economic burden of vision problems in Singapore is helpful to resource allocation and vision problem prevention, there are only three studies of direct medical costs of specific eye diseases, including acute PACG and myopia, found in literature. Apart from direct medical costs, productivity loss has been shown to account for a large amount of economic burden of vision problems, while no study has been done to measure the productivity loss of vision problems in Singapore. Moreover, the economic burden of a heath condition could be conducted from different perspective, providing unique cost information to each particular group. Therefore, the present project aims to address the economic burden of vision problems in Singapore from the perspective of healthcare system, and patients and their families.

In terms of humanistic burden, previous studies mainly focus on the impact of vision problems on VSQOL. There is a lack of studies on the impact of vision problems on generic HRQOL and the comparison between the health burdens of vision problems with other health conditions. EQ-5D is widely used as the measure of generic HRQOL because of its simplicity and is recommended by NICE. Nevertheless, EQ-5D is found to be insensitive to the impact of vision problems. Therefore, adding a vision 'bolt-on' item to the standard EQ-5D may solve the problem. Previous studies mainly focused on the valuation of the health utilities of all possible health states defined by the 'bolt-on' descriptive system, while the impact of the 'bolt-on' EQ-5D on sensitivity has not been conducted. Therefore, the present project aims to address the

health burden of vision problems in Singapore and evaluate a vision 'bolt-on' item on the sensitivity of EQ-5D to vision problems.

The specific objectives of the projects are summarized as below:

1. to measure the annual direct medical costs of VI in Singapore;

2. to measure the out-of-pocket (OOP) expenditure and productivity loss of VI in Singapore;

3. to assess the health burden associated with VI in Singapore;

4. to investigate the effect of VA on generic HRQOL in patients with VI;

5. to explore the effect of adding a vision dimension to the EQ-5D descriptive system;

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4 Organization of the Thesis

The thesis is organized in such a way that each of the subsequent chapters addresses each of the 5 specific aims.

The 2nd chapter reports the annual direct medical costs from VI and major eye diseases in Asian population. In this study, the annual direct medical costs of VI from the four major eye diseases in Singapore were described from the individual and national level using data from hospital financial department. The direct medical costs of VI and major eye diseases were also projected from 2015 to 2040.

The 3rd chapter reports the medical service utilization, OOP expenditure and productivity loss of VI in Singapore. In this study, data of the medical service utilization, OOP expenditure and productivity loss of VI were collected from face-to-face interview and estimated using regression models.

The 4th chapter reports the health burden associated with VI in Singapore. In this study, EQ-5D data from the Singapore Epidemiology of Eye Disease (SEED) were used to measure the HRQOL burden associated with VI and compare the burden with that associated with other 4 health conditions.

The 5th chapter reports the effect of VA on HRQOL among patients with VI in Singapore. In this study, generic HRQOL data from SEED study were analyzed using regression models to assess the effects of 5 different VA measures (VA in the better-seeing eye , better-weighted mean VA, mean VA, worse-weighted mean VA, and VA in the worse-seeing eye on visually impaired patients' EQ-5D index score. Meanwhile, age and socio-economic status were stratified in the data analysis.

The 6th chapter reports the effect of adding a vision dimension to the EQ-5D descriptive system, using data from the above economic burden of VI study. In the study, 16 pairs of mutually exclusive subgroups of individuals known to differ in vision status were defined and compared pairwise. The absolute mean difference and F-statistic were used as the measured of relative sensitivity in the comparisons of the EQ-5D index scores.

In the last chapter, the major findings of the project are summarized. Future work to address the research questions elicited in this project is also discussed.

Chapter 2

The Rising Economic Cost of Visual Impairment Due to Four Major Eye Disease in Asians: A Prospective Study of Direct Medical Costs in Singapore

2.1 Introduction

Visual impairment (VI) is a public health problem worldwide. According to the estimate from the World Health Organization (WHO) in 2010, about 285.39 million people were visually impaired, including 246 million with mild/moderate VI and 39.37 million with severe VI (Pascolini and Mariotti, 2012). Studies from Australia, Canada, Europe, Japan and the United States of America (USA) have described the heavy economic burden of VI on their society (Taylor et al., 2006; Cruess et al., 2011; Brezin et al., 2005; Roberts et al., 2010; Rein et al., 2006; Frick et al., 2007; Wittenborn, 2013). In Australia, for example, the economic costs of VI were estimated to be AUD$ 9.85 billion in 2006, higher than coronary heart disease, stroke, diabetes mellitus, or depression (Taylor et al., 2006).

In Asia, where about 45 million people were estimated to have significant VI in the southeast Asia region alone, few studies have described the economic burden of VI (Dilokthornsakul et al., 2014; Awan et al., 2012; Shamanna et al., 1998). With the aging population, the economic burden of VI is expected to increase in the near future, which highlights the importance to understand the economic burden of VI and plan for preventive programs. Singapore, a developed country with a multi-racial population comprising three major racial groups in Asia (i.e. Chinese, Indian, and Malay), represents a unique setting to study the economic burden of VI in Asians. To date, only direct costs of specific eye diseases such as acute primary angle-closure glaucoma (PACG) and myopia have been studied in Singapore (Wang and Chew, 2004; Lim et al., 2009; Zheng et al., 2013).

Therefore, in this study, we aimed to describe the annual direct medical costs of VI due to the

major eye diseases in Singapore and project the direct medical costs from 2015 to 2040.

2.2 Methods

Study subjects and procedures

Individuals with VI

Five hundred individuals with VI were recruited from the outpatient clinics in Singapore National Eye Center, the tertiary medical center for eye diseases in Singapore. The inclusion criteria were: 1) a clinical diagnosis of cataract, glaucoma, diabetic retinopathy (DR), or age-related macular degeneration (AMD) for at least 3 months; 2) visually impaired in both eyes; 3) 40 years old or above; 4) Singaporean or permanent resident; 5) able to communicate in English or Chinese, presence of a caregiver in case of language barrier; and 6) written informed consent. Quota sampling was used to recruit equal number of individuals with each of the four eye diseases. Patients, who were with VI and underwent cataract surgery within 1 year, were also eligible for the study. Patients of 40 years old or above were recruited because the investigated eye diseases in this study were not typical in younger persons.

The visually impaired individual's service utilization and expenditure data from the date of his/her first visit to SNEC till the date of interview were retrieved from the SNEC financial department (mean: 59.9 months; medium: 62.5 months; range: 3-136 months). Notably, the costs were estimated in dependent of government subsidy. This study for VI followed the principles of Declaration of Helsinki and the ethical approval was obtained from the Centralized Institutional Review Board (CIRB) of SingHealth.

Definitions of VI

In this study, presenting visual acuity (VA) was measured for each participant with a Snellen chart. The Snellen chart contains symbols to test VA (Chen et al., 2014). VI was classified into two levels according to the VA in the better-seeing eye: (1) mild/moderate VI (VA ≤6/12 to VA >6/60; and (2) severe VI (VA ≤6/60) (Tielsch et al., 1990).

Statistical Analysis

Annual direct medical costs of eye diseases and VI were estimated based on the cost data for the patients with VI. If the patients' costs data were available for more than 1 year, it would be traced back for 1 year from the date of interview. If the patients' costs data were available for less than 1 year, the annual costs were derived by multiplying the average costs per month by 12. Based on the data from the hospital financial department, the direct medical costs included three components: (1) consultation and examination; (2) treatment and procedure; and (3) medication. For total and each part of the costs, the ANOVA test was used to compare the costs across participants with different eye diseases, while the 2-sample t-test was used to compare the costs between mild/moderate and severe VI groups.

The annual direct medical costs of each major eye disease and VI in Singapore were calculated as the mean direct medical costs per capita multiplied by the projected number of individuals (i.e. population) with the condition in 2015 to 2040. The projected populations were estimated from a local study in which age- and ethnicity-specific prevalence data from the Singapore Epidemiology of Eye Diseases (SEED) study (Lavanya et al., 2009) and projected general population data were used to project the number of people seeking medical care due to various

eye conditions (Ansah et al., 2015). For each projected eye disease population, we adjusted its size by multiplying the prevalence rate of VI estimated from the SEED data. This is necessary as the study population of this study is patients with both eye diseases and VI. Further, we estimated the prevalence rates for subtypes of AMD (neovascular and non-neovascular AMD), glaucoma (primary open-angle glaucoma [POAG], PACG and secondary glaucoma), and DR (non-proliferative and proliferative DR) using the SEED data, and used them to determine the subpopulations of the eye diseases. We re-estimated the direct medical costs per capita for each subtype of the eye diseases and multiplied them with the corresponding subpopulation to derive the national-level direct medical costs. Costs for subtypes of the eye diseases were aggregated to provide the estimates for costs of the eye diseases. This subtype-weighted approach was used in the costs estimation because the prevalence rates of the eye disease subtypes in our sample and the projected future populations were different. Previous studies showed that costs of different subtypes or severities of the eye diseases varied (Lim et al., 2012; Cantor et al., 2010; Cheung et al., 2010; Happich et al., 2008).

An inflation rate of 3% and the average US dollar/Singapore dollar exchange rate of 1.25 in 2013 were used in the analysis. I was responsible for both the data collection and data analysis. All the analyses were conducted using SAS software version 9.2 (SAS Inc., Cary, NC) at a significance level of 0.05.

2.3 Results

The socio-demographic and health characteristics of recruited subjects are shown in Table 2.1. The mean ± standard deviation (SD) age of participants was 71.6 ± 9.8 years old. The proportion

of males was 47.6%. Majority of the patients was Chinese (88.0%). The mean ± SD VA in the better-seeing eye was 0.49 ± 0.31 and 76.6% of the participants were with mild/moderate VI. The mean ± SD total annual direct medical, consultation and examination, treatment and procedure, and medication costs per capita of those with VI in 2013 were S$7,090 ± 29,441, S$626 ± 845, S$2,114± 3,255, and S$4,350 ± 27,896, respectively.

Annual costs per capita for eye diseases and categories of VI are shown in Table 2.2. The direct medical costs of AMD (S$16,644 ± 56,406) were higher than those of glaucoma (S$6,222 ± 11,559), DR (S$2,767 ± 5,864) and cataract (S$2,727 ± 2,757) (p=0.0003). Medication costs were the major driver of direct medical costs for AMD and glaucoma, while treatment and procedure costs for cataract and DR. The annual direct medical costs of mild/moderate VI (S$5,449 ± 29,927 per capita) were significantly lower than those of severe VI (S$12,461 ± 38,431 per capita, p<0.0001). Medication costs accounted for the majority of direct medical costs for both mild/moderate VI (56.3%; S$3,068 out of S$5,449) and severe VI (68.6%; S$8,548 out of S$12,461). The treatment costs for both mild/moderate VI (S$1,796 per capita) and severe VI (S$3,153 per capita) were also considerable.

Projections of the number of individual with major eye diseases and VI for Singapore in 2015 to 2040 are shown Table 2.3. The number of individuals with major eye disease and VI would increase by at least 1.5 times in 2015 to 2040 (e.g. number of individuals with cataract and VI by about 1.7 times). In 2015, the number of individuals with cataract (20,846) was the highest, followed by AMD (17,738), DR (14,195), and glaucoma (7,940). Nevertheless, the increase rate of cataract was lower than that of the other three eye diseases and in 2040, the number of

individuals with DR (52,271) and AMD (52,105) was the highest, followed by cataract (35,456) and glaucoma (23,344).

Projections of the direct medical costs of major eye diseases and VI for Singapore in 2015 to 2040 are shown in Table 2.4. AMD had much higher direct medical costs than cataract, glaucoma and DR in this period. For example, in 2015, the direct medical costs of AMD (S$176.0 million) would be more than two times higher than those of cataract (S$60.3 million), glaucoma (S$44.4 million) and DR (S$56.5 million). The direct medical costs of each eye disease would increase by at least 3 times from 2015 to 2040 (e.g. direct medical costs of cataract by about 3.6 times). The direct medical costs of mild/moderate VI would be much larger than those of severe VI. For example, in 2015, the direct medical costs of mild/moderate VI would be S$333.3 million, 8.3 times more than those of severe VI (S$40.4 million). With the aging process, the medical costs of total VI costs would increase by about 5.6 times from S$373.8 million in 2015 to S$2103.0 million in 2040.

Table 2.1 Socio-demographic characteristics and costs for visual impairment in Singapore (n=500)

Age	
Mean (SD); Median (Range)	71.6 (9.8); 73.0 (41.0 - 98.0)
Gender	
Male	47.6%
Ethnicity	
Chinese	88.0%
Indian	5.4%
Malay	5.4%
Others	1.2%
Education	
No formal education	34.6%
Primary education	29.6%
Secondary education	35.8%
Employment status	
Working	19.8%
Not working	80.2%
Marital status	
Single	6.6%
Married	86.2%
Separated/divorced	1.4%
Widow	5.8%
Visual acuity in the better-seeing eye	
Mean (SD); Median (Range)	0.49 (0.31); 0.40 (0.30 - 3.00)
Mild/moderate VI	76.6%
Severe VI	23.4%
Annual total costs per capita (S$)	
Mean (SD); Median (Range)	7090 (29,441); 2,573 (58 - 474,951)
Annual consultation & examination costs per capita (S$)	
Mean (SD); Median (Range)	626 (845); 441 (0 - 8868)
Annual treatment & procedure costs per capita (S$)	
Mean (SD); Median (Range)	2,114 (3,255); 0 (0 - 29,443)
Annual medication costs per capita (S$)	
Mean (SD); Median (Range)	4,350 (27,896); 76 (0 - 453,731)

SD = standard deviation; S$ = Singapore dollars;

Table 2.2 Annual costs per capita in categories of major eye diseases and visual impairment (n=500)

	Direct medical costs		**Consultation & examination costs**		**Treatment & procedure costs**		**Medication costs**	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Diagnosis								
Cataract	2,727	2,757	606	724	1,949	2,398	172	475
Glaucoma	6,222	11,559	757	994	1,630	3,358	3,835	8,982
Diabetic retinopathy	2,767	5,864	500	674	1,526	2,454	740	4,522
Age-related degeneration	16,644	56,406	640	934	3,350	4,177	12,655	54,127
P value	0.0003		0.1168		<0.0001		0.001	
Visual impairment								
Mild/moderate VI	5,449	25,927	585	782	1,796	3,019	3,068	24,361
Severe VI	12,461	38,431	762	1,017	3,153	3,762	8,548	37,014
P value	<0.0001		0.0002		0.0021		<0.0001	

All costs are in thousand Singapore dollars;

SD = standard deviation; VI = visual impairment;

Table 2.3 Projection of the number of individuals with major eye diseases and visual impairment in 2015 to 2040

	2015	**2020**	**2025**	**2030**	**2035**	**2040**
Diagnosis						
Cataract	20,846	32,218	35,424	35,748	35,737	35,456
Glaucoma	7,940	11,752	15,605	18,899	21,521	23,344
Diabetic retinopathy	14,195	22,855	31,568	39,416	46,325	52,271
Age-related degeneration	17,738	29,070	38,228	44,786	49,359	52,105
Visual impairment						
Mild/moderate VI	57,662	91,066	114,742	131,857	145,241	154,960
Severe VI	3,057	4,829	6,084	6,991	7,701	8,216

VI = visual impairment;

Table 2.4 Projection of the direct medical costs of major eye diseases and visual impairment in 2015 to 2040

	2015	**2020**	**2025**	**2030**	**2035**	**2040**
Diagnosis						
Cataract	60.3	108.1	137.7	161.1	186.7	214.8
Glaucoma	44.4	82.8	132.6	192.0	261.5	342.1
Diabetic retinopathy	56.5	96.9	149.2	209.4	276.5	347.7
Age-related degeneration	176.0	334.4	509.8	692.4	884.7	1,082.6
Visual impairment						
Mild/moderate VI	333.3	610.3	891.4	1,187.6	1,516.4	1,875.6
Severe VI	40.4	74.0	108.1	144.0	183.9	227.4
Total costs	373.8	684.3	999.5	1,331.5	1,700.3	2,103.0

All in million Singapore dollars; Annual inflation rate: 3%;

VI = visual impairment;

2.4 Discussion

To our knowledge, this is the first study to estimate the economic burden of VI and major eye diseases at both individual and national levels in Singapore, a developed urban-state in Asia. Our study showed that VI imposed a substantial economic burden to the healthcare system of Singapore. For example, the median annual direct medical cost of VI per capita accounted for 9.5% of the median annual personal income in resident employed households in 2013 (Department of Statistics, 2013). The finding about the substantial economic burden of VI is consistent with the situations in other countries (Taylor et al., 2006; Cress et al., 2011; Brezin et al. 2005; Roberts et al., 2010; Rein et al., 2006; Frick et al., 2007). In our study, direct medical costs were estimated as costs for outpatient services, including consultation and examination, treatment and procedure, and medication. It should be noted that, because only direct medical costs occurred in the tertiary medical center were captured in the study, our cost estimates were lower than those estimates from previous studies, all of which investigated both direct and indirect costs (Taylor et al., 2006; Cruess et al., 2011; Roberts et al., 2010; Frick et al., 2007; Wittenborn, 2013). If only the direct medical costs of VI from outpatient service were considered, the costs of VI per capita estimated in our study were higher than those in studies conducted in other Asian countries (Roberts et al., 2010; Wang et al., 2013, Park et al., 2015). For example, the direct medical costs of VI per capital in Japan were $3,842 (equivalent to approximately S$4,802), account for 88.7% and 38.7% of the direct medical costs of mild/moderate and severe VI.

The findings in our study also provided a unique view of the economic burden of eye diseases in Singapore or broadly Asia. At the individual level, AMD had higher direct medical costs compared with cataract, DR and glaucoma. The high direct medical costs of AMD should be

mainly due to the high medication costs for neovascular AMD. The result is consistent with the finding in a Thailand study (9), but different from that in a French study in which consultation and examination costs were the major cost drivers (Bonastre et al., 2003). One possible reason for the difference was that the French study was conducted in 2000, which was before the approval of the expensive Anti-vascular Endothelial Growth Factor (VEGF) medications (e.g. ranibizumab and aflibercept). Similarly, medication costs accounted for the majority of the direct medical costs of glaucoma (Varma et al., 2011) and the higher medication costs of glaucoma than treatment costs should be due to the high costs of eye drops (Wong et al., 2008). Nevertheless, for both cataract and DR, treatment and procedure costs were the main cost drivers, because surgery, including laser and conventional surgery, is the main treatment for these two eye diseases (Cheung et al., 2010; Lundstrom et al., 2001). At the national level, the projected direct medical costs of AMD could remain at least two times higher than those of cataract, glaucoma and DR in 2015 to 2040. The result could not be simply compared with findings from other studies that the economic burden of eye diseases was estimated from the healthcare system perspective in our study, while the society perspective in majority of other studies (Taylor et al., 2006; Cruess et al., 2011; Wittenborn, 2013). Nevertheless, our study was consistent with a Canadian study that the estimated health system expenditure in people with vision loss was highest for AMD, followed by glaucoma, cataract and DR (Cruess et al., 2011). Apart from the high costs of medications, the high direct medical costs of AMD could also be due to late self-detection. Early AMD is painless and could progress slowly without self-detection until it progresses to late AMD, with obvious vision loss and symptoms (Cruess et al., 2011). Hence, patients with AMD seeking medical care are mainly those with late AMD which causes higher medical costs. The direct medical costs increased with the severity of VI, which was consistent

with the findings in previous studies (Frick et al., 2007; Bramley et al., 2008; Javitt et al., 2007). The results in our study highlight the importance of public health programs or strategies for early detection of major eye diseases and VI. Systematic screening and early treatment, which could delay or prevent the progression of eye diseases, are shown to be cost-effective means in healthcare resource utilization for eye diseases (Maberley et al., 2003; James et al., 2000). Moreover, more generous investment into research on more effective treatment or management strategies may also be a possible way to reduce the substantial economic burden of eye diseases and VI. For example, a new treatment of glaucoma was found to reduce the economic burden by delaying the disease progression from early stage ($623 per capita) to late stage ($2,511 per capita) (Lee et al., 2006).

There are some limitations in our study. First, only medical costs occurred in one tertiary medical center where participants were followed up were considered. Visually impaired individuals who were not seeking medical care were not included and, for those who were included, the medical costs occurred in other medical centers or primary care clinics were not captured. Therefore, the true medical costs per capita may be over- or under- estimated. Second, in calculating the medical costs of the eye diseases, only visually impaired individuals were considered. Therefore, the actual national-level direct medical costs for the studied eye diseases would be higher because those not visually impaired individuals would also seek medical care. Third, in calculating the medical costs of VI at the national level, only individuals whose VI was due to cataract, glaucoma, DR, or AMD were considered, failing to consider the individuals with VI caused by other eye diseases. Fourth, the number of patients with eye diseases between 2015 and 2040 in Singapore was projected using imperfect data available from 2012 to 2015 and thus

might not be accurate. Meanwhile, the inaccuracy could be also due to the innovations or breakthroughs in treatment of eye diseases and VI in the future (Kannnan et al., 2015; Gemenetzi et al., 2012).

In summary, the direct medical costs of VI are substantial at both individual and national levels in Singapore. Moreover, the economic burden due to the four major eye diseases and VI is likely to increase dramatically in the next three decades.

Chapter 3

Out-of-pocket Expenditure and Productivity Loss of Visual Impairment in Singapore

3.1 Introduction

Visual impairment (VI) is a public health problem worldwide. According to World Health Organization, about 285.39 million people were visually impaired in 2010, among whom 39.37 million were blind (Pascolini and Mariotti, 2012). Previous studies have shown that VI causes a substantial economic burden to the society (Wittenborn, 2013; Rein, 2013; Taylor et al., 2006; Roberts et al. 2010; Cruess et al. 2011; Economics 2009). In the United States, the annual costs of vision problems in 2013 were estimated to be $65.1 billion, which were only slightly lower than those of heart conditions, trauma, cancer and mental health disorders (Wittenborn, 2013; Rein, 2013). In Australia, the direct costs of vision problems were AUD$ 9.85 billion, ranking the 7th among various health conditions (Taylor et al., 2006).

Moreover, previous studies have shown that productivity loss, defined as the labor costs of lower income and reduced workforce participation, accounts for a large amount of economic burden of VI (Wittenborn, 2013; Rein, 2013). For example, in Australia, the productivity loss of individuals with VI was estimated to be AUD$1.78 billion in 2004, which was almost equal to the direct cost (AUD$ 1.82 billion) (Taylor et al., 2006).

The economic burden of VI estimated in previous studies is mainly from the perspectives of health care system, government and society, while the studies of out-of-pocket (OOP) expenditure of VI, defined as the expenditure borne by patients and their families, are limited (Organization for Economic Co-operation and Development, 2001; O'Connor et al., 2008; Wong et al., 2008). Compared with expenditure from other perspectives, OOP expenditure provides

more accurate and concise information of the health burden to the households, reflecting the affordability and equity of the health systems (Carpenter et al., 2015; Corrieri et al., 2010).

VI is also a serious public health issue in Singapore. According to the Singapore Epidemiology of Eye Disease study (SEED), the prevalence of VI was 4.4% and 3.8% in Malays and Indians aged 40 years and above, respectively (Wong et al., 2008; Zheng et al., 2011). With the aging population, the number of people with VI will increase dramatically. Studies investigating the economic burden of VI in Singapore were rare and mainly focused on the direct medical cost of specific eye diseases (Wang et al., 2004; Lim et al., 2009; Zheng et al., 2013). Our recent study showed that the direct medical costs of VI could be S$373.8 million in 2015 and increase by 5.6 times to S$2.10 billion in 2040 (Wang et al., 2015). Nevertheless, the heavy economic burden revealed in the study was from the perspective of healthcare system; no study has been conducted to estimate the OOP expenditure of VI or any eye disease. Moreover, no study has estimated the productivity loss of VI or any eye disease in Singapore.

In this study, we aimed to estimate the OOP expenditure and productivity loss of VI in Singapore.

3.2 Methods

A cross-sectional, questionnaire-based survey was conducted to assess the economic burden of 500 Singaporeans with VI and 500 Singaporeans without VI in the study. Individuals with VI were recruited from the outpatient clinics in Singapore National Eye Center, the tertiary medical center for eye diseases in Singapore, following certain inclusion criteria. Quota sampling was used to recruit equal number of individuals with each of the four eye diseases. After recruitment,

each individual and/or his/her caregiver was interviewed face-to-face in hospital by a trained research assistant using a set of standardized questionnaires including, in the order of administration, the vision 'bolt-on' EQ-5D questionnaire, the 14-item visual function questionnaire (VF-14), a healthcare utilization and expenditure questionnaire, and an employment questionnaire. Data collected using the EQ-5D and VF-14 questionnaires were used in a different study (see Chapter 6).

Among the 500 individuals without VI, 336 individuals were recruited from participants of the 2013 National Eye Care Day which provided free ophthalmologic examinations to registered members of the general public. The inclusion criteria were: 1) clinically confirmed absence of cataract, glaucoma, diabetic retinopathy (DR) and age-related macular degeneration (AMD); 2) aged 40 years or above; 3) Singapore citizen or permanent resident; 4) normal vision in both eyes; 5) able to communicate in English or Chinese; and 6) written informed consent. After recruitment, each individual or his/her caregiver was home visited and interviewed face-to-face by a trained interviewer using the same set of standardized questionnaires for individuals with VI. The remaining 164 individuals without VI were recruited from a convenience sample of communities and interviewed using the same inclusion criteria and procedures mentioned above except that normal vision and absence of the four eye diseases were based on self-report rather than clinical examination.

Data on the self-reported healthcare utilization, expenditure and the employment status were used in the analysis in Chapter 3. This study for VI followed the principles of Declaration of

Helsinki and the ethical approval was obtained from the Centralized Institutional Review Board (CIRB) of SingHealth.

Definitions of Visual Impairment and Eye Diseases

In the study, presenting VA was measured for each participant using a Snellen chart. VI was defined as VA ≤6/12 in the better-seeing eye (Tielsch et al. 1990, Zheng et al. 2011, Wong, Chong, et al. 2008). Four most common eye diseases including cataract, glaucoma, DR, and AMD were clinically diagnosed by the ophthalmologists and included in the study.

Healthcare Utilization and Expenditure

The standardized healthcare utilization and expenditure questionnaire used in this study assessed the healthcare utilization and expenditure information of individuals with and without VI in the past 3 months. The questionnaire consisted of 5 sections including inpatient services, emergency department services, outpatient services, other health care (e.g. message, acupuncture, bone setting), and health equipment. In each section, detailed information of healthcare utilization including reasons for seeking or using the services, healthcare service providers, and frequency of usage, was collected. Afterwards, information about the payment and payment type including health scheme and insurance, cash or credit card, and others, was collected. OOP expenditure was inquired for each healthcare service reported by the participants or their caregivers using the question of "how much in the bill was paid out-of-pocket using cash or credit card?"

Employment status

The employment status of participants and their caregivers in the past 1 month was assessed. For those who were working, their monthly wages, working hours, and absenteeism due to any health condition (for patients) or taking care of their clients (for caregivers) were inquired. For those who changed their employment status (from full-time to part-time, one job to another, stopping work) due to health reasons or caregiving responsibility, their last drawn monthly wages from the previous job were also inquired.

Statistical Analysis

The annual utilization and OOP expenditure due to any health problem were calculated for each individual as the healthcare utilization and expenditure in the past 3 months collected from the interview multiplied by 4. The calculation was conducted for each type of services and their total. Productivity loss was calculated as the percentage of the time of absenteeism due to health problems, multiplied by their monthly wages, and multiplied by 12. If an individual or his/her caregiver was unemployed or retired due to non-health reasons, the productivity loss was assumed to be 0. The utilization and OOP expenditure between individuals with and without VI were compared using the 2-sample t-test.

A 2-part model was used to estimate the healthcare utilization and OOP expenditure due to VI separately (Cantoni and Ronchetti, 2006). The first part was a logistic model that predicted the probability of positive utilization or expenditure, while the second part was a generalized linear model (GLM) with gamma family and log link for estimating the utilization or expenditure among those individuals who reported utilization or expenditure. In both the logistic regression model and GLM model with gamma family and log link, the independent variables included age

(40-59/60-79/80 above), gender (male/female), ethnicity (Chinese/non-Chinese), education (no formal education/primary education/secondary education), employment status (working/not working), marital status (married/not married), interview language (English/Chinese/others), and VI status (yes/no).

The average Canadian dollar/Singapore dollar and US dollar/Singapore dollar exchange rate of 1.21 and 1.25 in 2013 were used in the analysis, respectively. I was responsible for data collection and data analysis in the study. All the analyses were conducted using SAS software version 9.2 (SAS Inc., Cary, NC) at a significance level of 0.05.

3.3 Results

Characteristics of individuals with and without VI are shown in Table 3.1. For individuals with VI, the mean ± standard deviation (SD) age was 71.6 ± 9.8 years old and the proportion of males was 47.6%. Most individuals with VI were Chinese (88.0%), with primary or no formal education (64.2%), not working (80.2%), and married (86.2%). For individuals without VI, the mean ± SD age was 65.2 ± 7.5 years old and the proportion of males was 44.8%. Most individuals without VI were Chinese (87.2%), with secondary education (57.6%), not working (59.4%), and married (71.0%), and interviewed in Chinese (51.6%). Compared with individuals with VI, those without VI were younger, better educated, and more likely to work.

Annual healthcare utilization and OOP expenditure of individuals with and without VI are shown in Table 3.2. The annual healthcare utilization of individuals with VI was higher than that of individuals without VI. For example, the mean annual inpatient hospital admission number in individual with and without VI was 0.130 and 0.034, respectively ($p<0.0001$). After the

adjustment of covariates, the annual medical service utilization attributed to VI as indicated by the difference between individuals with and without VI was mainly due to outpatient clinic visits (marginal number of visits per person: 1.123) and other health care (marginal number of use per person: 0.394) (Table 3.2). The annual OOP expenditure of individuals with VI (S$3,047.40) was higher than those of individuals without VI (OOP expenditure: S$1,033.3), respectively (P<0.0001). Same trends were shown for all types of services (Table 3.2). After the adjustment of covariates, the annual OOP expenditure attributed to VI (S$2017.1) was mainly due to outpatient service costs (S$1259.4) and inpatient service costs (S$713.8).

Annual productivity loss of individuals with and without VI is shown in Table 3.3. The mean annual absenteeism time due to health problems in individuals with VI (89.4 hours) and their caregivers (136.9 hours) was higher than that in individuals without VI (5.0 hours) and their caregivers (1.0 hour), respectively (P<0.0001 for both). After adjusting for covariates, the productivity loss attributed to VI for patients and caregivers was 113.6 hours and 114.5 hours, respectively. Compared with patients (S$243.9), caregivers (S$555.1) had higher productivity loss due to VI.

Table 3.1 Characteristics of participants with and without visual impairment (n=1,000)

Characteristic	Individual with VI (n=500)		Individual without VI (n=500)		*P* value
Age(yrs), mean (SD)	71.6	(9.8)	65.2	(7.5)	<.0001
Gender					
Male	47.6	(238)	44.8	(224)	0.4096
Ethnicity					
Chinese	88.0	(440)	87.2	(436)	0.5809
Indian	5.4	(27)	6.0	(30)	
Malay	5.4	(27)	6.8	(34)	
Others	1.2	(6)	0	(0)	
Education					
No formal education	34.6	(173)	17.8	(89)	<0.0001
Primary education	29.6	(148)	24.6	(123)	
Secondary education	35.8	(179)	57.6	(288)	
Employment status					
Working	24.8	(124)	40.6	(203)	<0.0001
Not working	75.2	(376)	59.4	(297)	
Marital status					
Single	6.6	(33)	11.4	(57)	<0.0001
Married	86.2	(431)	71.0	(355)	
Separated/divorced	1.4	(7)	5.0	(25)	
Widow	5.8	(29)	12.6	(63)	
Interview language					
English	36.0	(180)	36.0	(220)	<0.0001
Chinese	64.0	(320)	51.6	(258)	
Others	0.0	(0)	4.4	(22)	

SD = standard deviation; VI = visual impairment; yrs = years

Table 3.2 Annual health service utilization and out-of-pocket expenditure of individuals with and without visual impairment (n=1,000)

Category	Individual with VI (n=500)		Individual without VI (n=500)		Marginal effect of VI (SE)	
	Mean	SD	Mean	SD		
Medical service utilization						
Inpatient care, no. of admission	0.130	0.567	0.034	0.181	0.098	(0.002)
Emergency department, no. of visits	0.046	0.253	0.020	0.178	0.034	(0.001)
Outpatient clinic, no. of visits	2.086	3.081	1.054	1.442	1.123	(0.005)
Other health care, no. of utilization	1.338	4.799	0.800	2.983	0.394	(0.006)
Health equipment, no. of purchase	0.212	0.489	0.116	0.350	0.033	(0.001)
Out-of-pocket expenditure, S$	3047.4	7234.4	1033.3	4302.0	2017.1	(21.6)
Inpatient service cost	1030.2	5139.6	333.8	3094.0	713.8	(16.7)
Emergency department service cost	77.0	1097.7	7.6	70.4	38.3	(1.4)
Outpatient service cost	1711.8	3521.4	512.3	2833.9	1259.4	(14.6)
Other health care	240.7	1702.6	171.2	923.5	64.3	(1.2)
Health equipment	64.7	287.3	16	167.3	9.4	(0.5)

No. = number; SD = standard deviation; SE = standard error; S$ = Singapore dollar; VI = visual impairment.

Table 3.3 Annual absenteeism and productivity loss of individuals with and without visual impairment (n=1,000)

Category	Individual with VI (n=500)		Individual Without VI (n=500)		Marginal effect of VI (SE)	
	Mean	SD	Mean	SD		
Absenteeism, hours						
Individual	89.4	301.9	5.0	25.5	113.6	(5.8)
Caregiver*	136.9	281.3	1.0	18.0	114.5	(2.5)
Productivity loss, S$	938.7	2040.8	53.2	296.8	915.3	(14.2)
Individual	242.7	1156.2	46.9	270.3	243.9	(13.9)
Caregiver	696.1	1761.0	6.3	125.0	555.1	(15.4)

SD = standard deviation; SE = standard error; S$ = Singapore dollar; VI = visual impairment

* If the individual has no caregiver, the absenteeism and productivity loss of the caregiver is 0.

3.4 Discussion

Our study showed that VI imposes substantial economic burden to the individuals and their families in Singapore – the annual OOP expenditure and productivity loss per capita due to VI was S$2017.1 and S$915.3, respectively, in 2013. To our knowledge, this is the first study to estimate the OOP expenditure and productivity loss of VI in Singapore. Moreover, previous cost-of-illness studies simply collected cost data from the individuals with the relevant condition. For example, in a study estimating the economic costs of myopia in Singapore, data were collected from adults aged over 40 years and with myopia (Zheng et al., 2013). In contrast, our study collected data from both the individuals with and without VI, thus providing more accurate estimates. This is because the economic burden due to VI is not limited to direct medical costs for vision problems. There are also medical costs for other health problems due to vision problems. Studies have demonstrated that poor vision increased the chance of falls, fractures and depression (Ivers et al., 2003; Noran et al., 2009; Ivers et al., 2002). Therefore, expenditures on other health problems caused by VI should also be considered when estimating the economic costs of VI. Nevertheless, it would be difficult for investigators or respondents to determine whether specific self-reported service utilization that occurred in the past is ascribed to VI. Thus, it is necessary to use individuals without VI as the reference group.

The result in our study that inpatient and outpatient services caused the majority of the OOP expenditure is consistent with previous studies (Kumar et al., 2015; Choi, 2015). The OOP expenditure of VI shown in our study is considerable. The mean annual OOP expenditure of VI is lower than that of VI (equal to SG$4,355) in Australia (Wong et al., 2008). In the Australian study, 150 visually impaired individuals completed diaries to record their daily personal vision-

related expenditure for up to a year. A large proportion of the OOP expenditure was related to transportation in the Australian study, which is not surprising as Australia has a much larger territory than Singapore which is an urban state with an area of 718.3 square kilometers only. The burden of the OOP expenditure measured by its percentage of the total household income or expenditure can be used to make cross-country comparisons (Organization for Economic Co-operation and Development, 2011). Based on our study and the published annual household expenditure (Singapore Department of Statistics, 2014), the OOP expenditure of VI accounts for 3.6% of household expenditure in Singapore, which is about the same as the average (3.2%) for the Organization for Economic Co-operation and Development (OECD) countries (Organization for Economic Co-operation and Development, 2011). Nevertheless, the economic burden of VI in Singapore is likely to increase dramatically in the future due to the rapidly aging population. According to Singapore Ministry of Health, the outpatient attendance rate of government-subsidized patients to department of ophthalmology in the major public hospitals increased 39.1% from 2002 to 2006 (Di, 2007). Therefore, policy makers might consider policies that will provide more subsidies for the inpatient and outpatient services for individuals with VI, especially those with low household income.

Our study shows that caregivers suffer from much more productivity loss compared with individuals with VI. The result is consistent with the finding in the Japanese study (Roberts et al. 2010). We found that the productivity loss of VI in Singapore is mainly due to absenteeism rather than completely loss of productivity. The estimated annual productivity loss of VI due to absenteeism (S$243.9 per capita) in Singapore is similar to that in Canada (Can$283.6, equivalent to approximately S$343.2) and Japan (US$234.6, equivalent to approximately

S$293.3) (Roberts et al., 2010, Cruess et al. 2011). In both the Canadian and Japanese studies, a human capital approach was used to estimate the productivity loss for individuals with VI for the entire population.

The major limitation of the study is the use of self-reported data. It is likely that respondents underreported service utilization due to recall bias. The use of a control group may not overcome this problem because individuals with VI should have underreported more than individuals without VI. Hence, the OOP expenditure and productivity loss due to VI might be underestimated in this study. Second, the healthy controls in the study were recruited from participants of a health screening event. They might be more health conscious and healthier than average members of the general population. As a result, the sampling bias might widen the actual difference in health service utilization and expenditure between individuals with and without VI. Third, only the productivity loss of the primary caregiver, defined as the caregiver who spent most time taking care of the patients, was considered, which might cause underestimation. Nevertheless, the vast majority of the patients had only one caregiver. Fourth, though 2-part model was used to adjust the covariates (e.g. age, gender and comorbidities) in the analysis, their effect on the OOP expenditure and productivity loss could not be completely ruled out.

In conclusion, our study demonstrated that VI has caused significant economic burden to patients and their families in Singapore. The significant economic burden of VI highlights the importance of financial assistance programs.

Chapter 4

Health Burden Associated with Visual Impairment in Singapore - The Singapore Epidemiology of Eye Disease Study

4.1 Introduction

Visual impairment (VI) is an important public health issue in Asia (Bourne et al., 2012). In Southeast Asia alone, about 45 million people have VI, among whom 12 million are blind (Resnikoff et al., 2004; Dandona et al., 2006). With the aging of the population, the burden of VI is anticipated to increase (Chiang et al., 2012; Gordois et al., 2012). Previous studies have shown that VI not only affects people's visual status but also has an impact on people's functioning and well-being (Goldzweig et al., 2004; Ong et al., 2012; Lamoureux et al., 2008). Hence, apart from visual acuity (VA), health-related quality of life (HRQOL) should also be measured in order to achieve a comprehensive assessment of the impact of VI on patients.

Both vision-specific and generic HRQOL instruments are used to measure the health burden of VI. Vision-specific quality of life (VSQOL) instruments such as the Vision Function Index Questionnaire (VF-14) (Steinberg et al., 1994) are more sensitive to vision problems than generic instruments such as the European Quality of Life Questionnaire (EQ-5D) (Brooks, 1996; Lotery et al., 2007). However, VSQOL instruments cannot generate a utility-based index score for calculation of quality-adjusted life years (QALYs) or comparison of the health burden associated with vision problems and other health conditions. The health burden of VI has been estimated using EQ-5D in several western and eastern populations (Lotery et al., 2007; Langelaan et al., 2007; van Nispen et al., 2009; Lin and Yu, 2012; Polack et al., 2008); however, the sample sizes of those studies are relatively small and therefore the

findings in those studies may not be generalizable to Asians in Singapore. In this study, we aimed to measure the impact of VI on generic HRQOL and to compare it with commonly seen health conditions in the three major ethnicities in Singapore.

4.2 Methods

4.2.1 Study Population

In this study, data from the Singapore Epidemiology of Eye Disease (SEED) Study were used, comprising three population-based eye studies: the Singapore Chinese Eye Study (SCES), the Singapore Indian Eye Study (SINDI), and the Singapore Malay Eye Study (SiMES). The three studies have been described in detail previously (Foong et al., 2007; Lavanya et al., 2009). In brief, an age-stratified random sampling was used to select ethnic Chinese, Indians, and Malays aged 40-80 years living in Singapore. The overall response rate was 75.6%: 72.8% for Chinese, 75.6% for Indians, and 78.7% for Malays. The SEED study adhered to the principles of Declaration of Helsinki and ethical approval was obtained from the Singapore Eye Research Institute Institutional Review Board.

4.2.2 Health-Related Quality of Life Measure

EQ-5D was used to assess the generic HRQOL. The EQ-5D contains five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Participants rated their health status in those dimensions on the day of survey as one of the three levels: no problems, some problems, or extreme problems. To measure the

utility or value of the health status of the participants, we used their responses to the five dimensions to calculate an index score ranging from -0.59 for the worst health state to 1.00 for perfect health (Dolan, 1997). In this interval scale used by the EQ-5D, the score of 0 means the value of the corresponding health states is as bad as death and negative scores indicate the corresponding health states are worse than death. In the three studies, trained research assistants conducted face-to-face interview in English, Chinese, Tamil, or Malay, depending on the participant's preference. Previous studies tested the validity and reliability of the EQ-5D questionnaire in English-speaking and Chinese-speaking Asian patients with rheumatic diseases in Singapore (Luo et al., 2003; Luo et al., 2003) as well as in local Malay- and Tamil-speaking patients (Wee et al., 2007). The EQ-5D demonstrated satisfactory validity and reliability in both local general and patient populations (Wee et al., 2007; Lee et al., 2013; Varma et al., 2006; Luo et al., 2009) including persons with vision problems (Au Eong et al., 2012; Ang et al., 2013).

4.2.3 Definitions of Visual Impairment (VI)

In all three eye studies, participants underwent extensive visual examinations, including VA testing and a detailed clinical slit lamp examination. The presenting VA for each participant was measured with a logarithm of the minimum angle of resolution (logMAR) chart (Lighthouse International, New York, NY) at a distance of 4m, with the participants wearing their habitual optical correction (e.g. spectacles or lenses). If the participants could read no number at 4m, they moved to 3, 2, or 1m,

consecutively. If they could read no number on the chart, the VA was measured as Counting Fingers, Hand Movement, Perception of Light, or No Perception of Light.

VI was classified as unilateral and bilateral VI and as mild/moderate, and severe. Mild/moderate VI was defined as VA <20/40 but >20/200 (logMAR >0.30 to <1.00) and severe VI as VA ≤20/200 (logMAR ≥1.00) (Tielsch et al., 1990). Unilateral VI was defined based on the VA of the better-seeing eye and classified the severity of bilateral VI into 6 categories (Zheng et al., 2011): (1) normal vision in both eyes, (2) normal vision in one eye, and mild/moderate VI in the other, (3) normal vision in one eye, and severe VI in the other, (4) mild/moderate vision impairment in both eyes, (5) severe VI in one eye, and mild/moderate VI in the other, (6) severe VI in both eyes.

4.2.4 Other Health Conditions

The presence or absence of four health conditions, including obesity, hypertension, diabetes, and hyperlipidemia, was determined for each participant. Obesity was defined as body mass index (BMI) ≥30; diabetes as random glucose ≥200mg/dl (11.1mmol/L), use of diabetic medication, or self-reports of physician diagnosis; hyperlipidemia as a total cholesterol level ≥239.4mg/dl (6.2mmol/L) or use of lipid-lowering drugs; and hypertension as systolic blood pressure (BP) ≥140mmHg, diastolic BP ≥90mmHg, or current use of antihypertensive medications. Blood pressure (BP) was measured twice (5 minutes apart). If there was more than 10mm Hg (systolic) and 5mm Hg (diastolic) difference in the BP measures, a third

measurement was performed and considered the BP as the mean between the 2 closest readings.

4.2.5 Statistical Analysis

Both univariate and multivariate analyses were performed to examine the association between the EQ-5D index score and VI. Firstly, ANOVA and chi-square tests were used to compare the socio-demographic characteristics across the three ethnicities and the EQ-5D index score across different subgroups of individuals with and without unilateral/bilateral VI. Secondly, multivariate linear regression models were used to examine the effect of unilateral/bilateral VI on the EQ-5D index score by controlling for socio-demographics that were found to be associated with HRQOL in a previous study[14]. As the distribution of the EQ-5D index score was skewed, the robust standard error estimator (Pullenayegum et al., 2010) was used in the multivariate linear regression analysis. In order to detect the differential effect of VI across ethnicities, a pooled analysis was performed with cross-product interaction terms between VI and ethnicity being added to the regression models. Thirdly, a binary logistic regression analysis was used to examine the association between the presence of EQ-5D health problems and the severities of unilateral/bilateral VI. In this analysis, responses to each EQ-5D item were coded into a binary variable (with problems/without problems) and analyzed it in a separate model. Lastly, the effects of VI and other health conditions (obesity, hypertension, diabetes, and hyperlipidemia) on the EQ-5D index score were estimated simultaneously in a multivariate linear regression model. In this

model, VI was classified into two categories (with VI/without VI) according to the VA of the better-seeing eye. In order to assess the total burden of VI and the other health conditions at the population level, the annual quality-adjusted life years (QALYs) loss per 100,000 persons were calculated for each condition using the formula below:

QALYs loss = disutility score X 1 year X 100,000 X prevalence rate, where disutility was the regression coefficient for the condition in the above-mentioned model and the prevalence rate was the observed proportion of cases with the condition in the SEED study. QALYs is an outcomes measure calculated as life years a person lives weighted by the person's quality of life measured by a utility-based measure such as the EQ-5D (Bravo et al., 2008; Jia et al., 2010). For example, one year in perfect health is one QALY, while two years in a health state of 0.75 is 1.5 QALYs.

Each ethnicity (Chinese, Indian, and Malay) was analyzed separately, using SAS software (version 9.2, SAS Institute, Inc., Cary, NC) at the significance level of 0.05.

4.3 Results

After excluding 3 Indian and 21 Malay participants with missing responses to EQ-5D, 3,353 Chinese, 3,397 Indian, and 3,259 Malay participants were included in the study. The socio-demographic and health characteristics of each ethnic group are described in Table 4.1. The mean ± SD age of Chinese, Indian and Malay subjects were 59.7 ± 9.9, 57.8 ± 10.1, and 58.7 ± 11.0 years, respectively. The proportion of males was 49.6%, 50.1%, and 48.8% in Chinese, Indians, and Malays, respectively. Significant

difference across the three ethnicities existed for all socio-demographic and health characteristics, except gender (P = 0.1671). The mean ± SD EQ-5D index score for Chinese (0.92 ± 0.12) was significantly higher than that for Indians (0.82 ± 0.23) and Malays (0.83 ± 0.19) (P< 0.0001).

The prevalence and EQ-5D index scores of participants with different severities of unilateral and bilateral VI are shown in Table 4.2. EQ-5D index score decreased with increasing severity of unilateral and bilateral VI in all three ethnicities (P <0.001 for all three ethnicities). For example, there was statistically significant difference in the EQ-5D index score between Chinese with normal vision in the better-seeing eye (0.93 ± 0.11), unilateral mild/moderate VI (0.90 ± 0.15), and unilateral severe VI (0.82 ± 0.22).

The effects of unilateral and bilateral VI on the EQ-5D index score after adjustment of covariates are described in Table 4.3. In terms of bilateral VI, Indians with mild/moderate VI in one eye and severe VI in the other (difference = -0.064, 95% confidence interval [CI] = -0.125 - -0.003), Indians with severe VI in both eyes (difference = -0.127, 95%CI = -0.237 - -0.017), and Malays with severe VI in both eyes (difference = -0.085, 95%CI = -0.148 - -0.022), had lower EQ-5D index score than their respective counterparts without VI. In terms of unilateral VI, Indians with mild/moderate VI (difference = -0.027, 95%CI = -0.052 - -0.002), Indians with severe VI (difference = -0.126, 95%CI = -0.236 - -0.016), and Malays with severe VI

(difference = -0.078, 95%CI = -0.137 - -0.019), had significantly lower EQ-5D index score than their respective counterparts without VI. Similar differences in the EQ-5D index score were also found in Chinese, although those were not statistically significant. For example, Chinese with unilateral severe VI (difference = -0.043, 95%CI = -0.086 - 0.001) and those with unilateral mild/ moderate VI (difference = -0.020, 95%CI = -0.047 - 0.007) had lower EQ-5D index score than those without VI. In the models testing for interaction between VI and ethnicity, significantly greater impact on Indians and Malays as compared to Chinese was observed for both bilateral VI (P = 0.0011) and unilateral VI (P = 0.0001).

The multivariate logistic regression analysis results for the EQ-5D dimensions of mobility, usual activities, pain/discomfort, and anxiety/depression are shown in Table 4.4. Self-care was not analyzed because very low proportion of participants reported such problems (1.1% in Chinese; 3.1% in Indians; 2.2% in Malays). After the adjustment of covariates, bilateral and unilateral VI were significantly associated with the reporting of problems with mobility and usual activities in all three ethnicities. For example, in Singapore Chinese, unilateral mild/moderate VI (OR = 2.08, 95%CI = 1.23-3.50), unilateral severe VI (OR = 4.94, 95%CI = 1.28-19.10), and bilateral severe VI (OR = 6.51, 95%CI = 1.59-29.58), were significantly associated with the reporting of problems in usual activities. In addition, bilateral (OR = 2.68, 95%CI = 1.11-6.50) and unilateral (OR = 2.54, 95%CI = 1.05-6.13) severe VI were also associated with the reporting of anxiety/depression in Indians.

The health burden of VI and four other health conditions measured by disutility and annual quality-adjusted life-years (QALYs) loss per 100,000 people are shown in Table 4.5. For all three ethnicities, the disutility score of VI (Chinese: 0.0239; Indian: 0.0297; Malay: 0.0272) was larger than that of obesity, hypertension, diabetes and hyperlipidemia. For example, in Chinese, the disutility score of VI was larger than that of obesity (0.0143), hypertension (0.0090), diabetes (0.0140), and hyperlipidemia (0.0027). The annual QALYs loss per 100,000 persons associated with VI (Chinese: 511.8; Indian: 608.8; Malay: 706.7) was higher than that of other conditions for all the three ethnicities. For example, in Chinese, the annual QALYs loss due to VI was larger than that of obesity (75.7), hypertension (506.4) and diabetes (212.2), and hyperlipidemia (127.4).

Table 4.1 Socio-demographic and health characteristics of the participants (n=10,009)

Variable	Chinese (n = 3,353)		Indian (n = 3,397)		Malay (n = 3,259)		*P* value
Age							
Mean (SD)	59.7	(9.9)	57.8	(10.1)	58.7	(11.0)	<0.0001
Gender							
Male	49.6	(1662)	50.1	(1703)	48.0	(1563)	0.1671
BMI (kg/m^2)							
Mean (SD)	23.7	(3.7)	26.2	(4.7)	26.4	(5.1)	<0.0001
Marital status							
Married	79.6	(2668)	78.2	(2656)	74.4	(2431)	<0.0001
Employment							
Employed	57.6	(1929)	57.8	(1963)	43.2	(1407)	<0.0001
Smoking status							
Current smokers	13.2	(442)	14.7	(499)	20.3	(661)	<0.0001
Education							
No formal education	22.6	(756)	17.9	(608)	29.8	(972)	
Primary education	31.0	(1038)	37.7	(1280)	43.2	(1409)	<0.0001
Secondary education	46.5	(1559)	44.4	(1508)	27.1	(883)	
Monthly personal income (S$)							
<1000	47.6	(1547)	49.3	(1631)	69.1	(2246)	
1000-2000	22.6	(736)	24.5	(810)	20.2	(654)	<0.0001
2000-3000	12.0	(390)	12.1	(399)	7.3	(237)	
>3000	17.8	(580)	14.2	(471)	3.4	(110)	
Other health conditions							
Obesity	5.3	(177)	17.1	(578)	20.9	(681)	<0.0001
Hypertension	59.2	(1984)	56.9	(1931)	69.2	(2256)	<0.0001
Diabetes	15.2	(487)	34.6	(1129)	24.5	(769)	<0.0001
Hyperlipidemia	47.2	(1527)	47.9	(1554)	41.2	(1328)	<0.0001
EQ-5D index score							
Mean (SD)	0.92	(0.12)	0.82	(0.23)	0.83	(0.19)	<0.0001

BMI = body mass index; EQ-5D = European Quality of Life-5 Dimensions; SD = standard deviation; S$ = Singapore dollar

Table 4.2 Prevalence and EQ-5D index score for different severities of unilateral and bilateral visual impairment (n=10,009)

Vision Category	Chinese (n = 3353)		Indian (n = 3397)		Malay (n = 3259)	
	Prevalence	Mean (SD)	Prevalence	Mean (SD)	Prevalence	Mean (SD)
Bilateral VI						
Normal vision in both eyes	53.9 (1805)	0.94 (0.10)	58.3 (1982)	0.84 (0.21)	53.6 (1753)	0.86 (0.16)
Mild or moderate VI in 1 eye, normal vision in the other	22.5 (754)	0.92 (0.13)	19.0 (646)	0.81 (0.23)	18.7 (612)	0.82 (0.20)
Severe VI in 1 eye, normal vision in the other	2.2 (75)	0.92 (0.13)	2.2 (76)	0.78 (0.29)	1.7 (55)	0.80 (0.19)
Mild or moderate VI in both eyes	18.0 (603)	0.90 (0.14)	16.5 (561)	0.78 (0.27)	19.7 (645)	0.80 (0.22)
Mild or moderate VI in 1 eye, severe VI in the other	2.7 (920	0.86 (0.21)	3.2 (108)	0.72 (0.34)	4.4 (144)	0.78 (0.22)
Severe VI in both eyes	0.7 (22)	0.82 (0.22)	0.8 (27)	0.63 (0.30)	1.8 (60)	0.72 (0.23)
P value	<0.0001		<0.0001		<0.0001	
Unilateral VI – better-seeing eye						
Normal vision	78.6 (2634)	0.93 (0.11)	79.5 (2704)	0.83 (0.21)	74.0 (2420)	0.84 (0.17)
Mild or moderate VI	20.7 (695)	0.90 (0.15)	19.7 (669)	0.77 (0.28)	24.1 (789)	0.80 (0.22)
Severe VI	0.7 (22)	0.82 (0.22)	0.8 (27)	0.63 (0.30)	1.8 (60)	0.72 (0.23)
P value	<0.0001		<0.0001		<0.0001	

EQ-5D = European Quality of Life-5 Dimensions; SD = standard deviation; VI = visual impairment.

Table 4.3 Effects of different severities of unilateral and bilateral visual impairment on EQ-5D index score in multivariate regression analysis (n=10,009)

Vision Category	Chinese		Indian		Malay	
	Beta	**95% CI**	**Beta**	**95% CI**	**Beta**	**95% CI**
Bilateral VI*						
Normal vision in both eyes (reference)						
Mild or moderate VI in 1 eye, normal vision in the other	-0.009	-0.023 - 0.005	-0.003	-0.025 - 0.019	-0.016	-0.034 - 0.002
Severe VI in 1 eye, normal vision in the other	-0.011	-0.035 - 0.013	-0.015	-0.046 - 0.016	-0.023	-0.056 - 0.010
Mild or moderate VI in both eyes	-0.016	-0.036 - 0.004	-0.021	-0.045 - 0.003	-0.019	-0.039 - 0.001
Mild or moderate VI in 1 eye, severe VI in the other	-0.031	-0.068 - 0.006	**-0.064**	-0.125 - -0.003	-0.028	-0.059 - 0.003
Severe VI in both eyes	-0.044	-0.089 - 0.001	**-0.127**	-0.237- -0.017	**-0.085**	-0.148 - -0.022
Unilateral VI – better-seeing eye*						
Normal vision (reference)						
Mild or moderate VI	-0.020	-0.047 - 0.007	**-0.027**	-0.052 - -0.002	-0.023	-0.052 - 0.006
Severe VI	-0.043	-0.086 - 0.001	**-0.126**	-0.236 - -0.016	**-0.078**	-0.137- -0.019

CI = confidence interval; EQ-5D = European Quality of Life-5 Dimensions; VI = visual impairment.

*Adjustment of age, gender, body mass index, income, education, employment status, smoking status and other health conditions; boldness: $P < 0.05$.

Table 4.4 Odds ratios (95% confidence interval) of different severities of unilateral and bilateral visual impairment in predicting EQ-5D health problems

Vision Category	Chinese				Indian				Malay			
	Mobility	**Usual activities**	**Pain / discomfort**	**Anxiety / depression**	**Mobility**	**Usual activities**	**Pain / discomfort**	**Anxiety / depression**	**Mobility**	**Usual activities**	**Pain / discomfort**	**Anxiety / depression**
Bilateral VI*												
Normal vision in both eyes (reference)												
Mild/moderate VI in 1 eye, normal vision in the other	1.52 (0.99-2.31)	1.66 (0.82-3.35)	1.09 (0.87-1.36)	1.23 (0.94-1.62)	1.12 (0.84-1.48)	1.33 (0.85-2.80)	0.92 (0.75-1.12)	1.13 (0.91-1.40)	1.26 (0.97-1.65)	1.29 (0.87-1.91)	1.04 (0.84-1.27)	1.09 (0.88-1.34)
Severe VI in 1 eye, normal vision in the other	2.19 (0.93-5.15)	1.72 (0.37-7.93)	0.75 (0.40-1.42)	0.71 (0.30-1.69)	**2.19** (1.21-3.95)	0.71 (0.21-2.41)	0.59 (0.35-1.00)	1.39 (0.82-2.36)	0.43 (0.17-1.13)	**2.80** (1.24-6.29)	1.55 (0.86-2.80)	1.37 (0.75-2.50)
Mild/moderate VI in both eyes	1.26 (0.81-1.97)	**2.59** (1.32-5.07)	0.90 (0.70-1.16)	1.06 (0.77-1.45)	**1.49** (1.12-1.97)	**1.62** (1.05-2.49)	0.85 (0.68-1.05)	1.18 (0.93-1.48)	1.26 (0.97-1.65)	**1.86** (1.29-2.68)	1.06 (0.86-1.31)	1.03 (0.82-1.28)
Mild/moderate VI in 1 eye, severe VI in the other	1.55 (0.73-3.28)	**3.53** (1.31-9.55)	1.53 (0.63-1.78)	1.26 (0.67-2.36)	**1.76** (1.08-2.89)	**2.76** (1.48-5.18)	0.75 (0.48-1.16)	1.32 (0.84-2.06)	**1.85** (1.21-2.82)	1.41 (0.78-2.55)	0.79 (0.54-1.16)	1.16 (0.78-1.71)
Severe VI in both eyes	**3.69**[&] (1.21-12.13)	**6.51** (1.59-26.58)	0.68 (0.22-2.15)	1.62 (0.51-5.14)	**3.85** (1.57-9.44)	**9.30** (3.53-24.53)	1.52 (0.62-3.75)	**2.68** (1.11-6.50)	**2.61** (1.44-4.72)	**6.80** (3.86-12.88)	1.44 (0.82-2.53)	1.16 (0.65-2.40)
Unilateral VI – better-seeing eye*												
Normal vision (reference)												
Mild/moderate VI	1.02 (0.71-1.46)	**2.08** (1.23-3.50)	0.90 (0.72-1.13)	1.01 (0.76-1.33)	**1.42** (1.11-1.81)	**1.66** (1.17-2.37)	0.87 (0.71-1.05)	1.14 (0.93-1.40)	**1.28** (1.02-1.60)	**1.50** (1.11-2.03)	0.98 (0.81-1.18)	1.01 (0.83-1.22)

Severe VI	2.87 (0.89-9.25)	**4.94** (1.28-19.10)	0.66 (0.21-2.08)	1.50 (0.48-4.71)	**3.55** (1.45-8.66)	**8.54** (3.29-22.18)	1.60 (0.65-3.94)	**2.54** (1.05-6.13)	**2.42** (1.36-4.34)	**5.75** (3.12-10.58)	1 .40 (0.80-2.45)	1.10 (0.63-1.93)

EQ-5D = European Quality of Life-5 Dimensions; VI = visual impairment.

*Adjustment of age, gender, body mass index, income, education, employment status, smoking status and other health conditions; only EQ-5D items significantly associated with VI included; boldness: $P < 0.05$.

[&]Odds ratio from logistic regression analysis.

Table 4.5 Annual quality-adjusted life-years (QALYs) loss per 100,000 persons associated with visual impairment and other health conditions

Ethnicity	Condition	Disutility*	Prevalence[#]	Annual QALYs loss (per 100, 000 people)
Chinese (n=3,353)	Obesity	-0.0143	5.3	75.7
	Hypertension	-0.0090	56.2	506.4
	Diabetes	-0.0140	15.2	212.2
	Hyperlipidemia[$]	-0.0027	47.2	127.4
	Unilateral VI	-0.0098	24.7	242.06
	Bilateral VI	-0.0239	21.4	511.8
Indian (n=3,397)	Obesity	-0.0133	17.1	228.2
	Hypertension	-0.0105	56.9	599.3
	Diabetes	-0.0169	34.6	585.4
	Hyperlipidemia[$]	-0.0064	47.9	306.6
	Unilateral VI	-0.0073	21.3	155.49
	Bilateral VI	-0.0297	20.5	608.8
Malay (n=3,259)	Obesity	-0.0124	20.9	258.3
	Hypertension	-0.0101	69.2	697.6
	Diabetes	-0.0166	24.5	407.8
	Hyperlipidemia[$]	-0.0013	41.2	53.6
	Unilateral VI	-0.0187	20.5	383.35
	Bilateral VI	-0.0272	26.0	706.7

VI = visual impairment

*Regression coefficient with adjustment of age, gender, body mass index, income, education, employment status and smoking status

[#]Calculated using data from the three ethnic cohorts

[$]Coefficient not statistically significant in the regression models

4.4 Discussion

To our knowledge, this is the first study to use EQ-5D instrument and QALYs to estimate the impact of VI on generic HRQOL and to compare the burden of VI and other health conditions in Singapore. Our study showed that unilateral and bilateral VI had an impact on generic HRQOL, which was also revealed in previous studies (Varma et al., 2006; Chia et al., 2003). Our study also showed that people with VI were more likely to experience problems in mobility and usual activities. This finding was consistent with the finding in Australia that visually impaired individuals' ability to maintain mobility and independence significantly decreased (Wang et al., 2003) and their need for community and family support was significantly high (Wang et al., 1999). We found that Singapore Indians with unilateral/bilateral severe VI reported more emotional problems than those without VI, similar to previous studies in India (Nirmalan et al., 2005; Fletcher et al., 1998). However, no such association was found in Chinese or Malays, suggesting that these two ethnicities might have better psychosocial adoption to vision problems than Indians. Previous studies of elderly with visual disorders found that psychosocial adaptation status was associated with mental health symptoms (Tolman et al., 2005; Wang and Chan., 2009).

Our study also demonstrated that the health burden of VI was larger than that of obesity, hypertension, diabetes, and hyperlipidemia. Similar results were found in two previous studies using EQ-5D as the measure of disease burden (Sullivan and Ghushchyan, 2006; Sullivan et al., 2011). In a US study, the disutility of VI was equal

to that of obesity, while much larger than that of the other three health conditions investigated here. In a UK study, the disutility of VI was smaller but close to that of obesity and diabetes, while much larger than that of hypertension and hyperlipidemia. Our finding that VI is a leading cause of disease burden is also supported by studies using WHO' s healthy years loss due to disability or ill health (YLDs) as the measure of disease burden (Murray, 1994). According to the Global Burden of Disease Study 2010, VI and diabetes mellitus were both the important causes of global health burden, while the other three health conditions were not (Vos et al., 2012). In a Dutch study, the burden of VI ranked the 2nd among the 47 diseases, much higher than diabetes mellitus (Melse et al., 2000). In Singapore, diabetes mellitus and vision problems, defined as bilateral low vision and blindness, ranked as the 1st and 8th leading causes of disability burden (in YLDs) while obesity, hypertension and hyperlipidemia were not among the 20 leading specific causes (Phua et al., 2009). This body of consistent evidence on the heavy burden of VI relative to other health conditions suggests that more resources could be allocated to programs and interventions likely to prevent VI.

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A major strength of our study is that our multi-ethnic Asian study population allowed us to study the ethnic difference in the impact of VI on generic HRQOL. VI seemed to impose higher burden on Indians and Malays than on Chinese. Bilateral severe VI had a significant impact on generic HRQOL in both Indians and Malays, while such impact was not found in Chinese. The annual QALYs loss per 100,000 people associated with VI for Indians and Malays was higher than that for Chinese. Moreover,

VI was associated with anxiety/depression in Indians but not in Chinese and Malays. The ethnic difference in the impact of VI on HRQOL suggests that eye health professionals in Singapore should pay more attention to visually impaired Indians as they may be at a higher risk of suffering from depression/anxiety than Singaporean Chinese and Malays. Our study findings also highlight the importance of developing public health strategies to promote awareness, prevention, and management of eye diseases among Indians and Malays, the two main minority groups of Singapore (Department of Statistics, Singapore, 2013). Last, the ethnic difference exhibited in our study suggests that ethnic difference should be examined when analyzing self-reported health outcomes related to vision problems in the multi-ethnic Singapore. Otherwise, important ethnic-specific differences might be overlooked.

The strength of this study includes the large samples of the three major Asian ethnicities and the clinical diagnoses of VI and other health conditions. There are some limitations in our study. First, due to the lack of visual field data, we only used the visual acuity to define VI. However, in most population-based studies, VA criterion only, and not the peripheral visual field criteria, is used to define VI (Ong et al., 2012; Varma et al., 2006; Zheng et al., 2011; Rahmani et al., 1996). Second, the health burden of only four health conditions were compared with that of VI, as only those four health conditions were clinically diagnosed in the SEED study. Third, using the UK scoring method for the EQ-5D might over- or under-estimate the burden of the studied conditions in absolute terms. There was no an EQ-5D scoring method

based on the health preferences of Singaporeans at the time of our study. However, it did not invalidate the comparisons across conditions or ethnicities. Fourth, although we controlled for the effects of some variables such as income level, education, and marital status in the multivariate analysis, confounding effects or selection bias could not be completely ruled out.

In summary, our study demonstrated that visual impairment is associated with substantial health burden in all the three Asian ethnicities living in Singapore. The relatively high burden of VI highlights the importance of VI prevention. The ethnic difference in this burden warrants further investigations.

Chapter 5

The Effect of Visual Acuity Measures Based on the Better- and Worse-seeing eyes on Health-related Quality of Life among Visually Impaired Individuals: the Singapore Epidemiology of Eye Disease (SEED) Study

5.1 Introduction

The visual acuity (VA) of an individual's better-seeing eye is usually used to indicate the overall severity of visual impairment (VI) in outcomes research of eye disease (Varma et al., 2006; McClure et al., 2009; Lin and Yu, 2012). This practice is probably based on the assumption that an individual's level of vision function is primarily determined by the individual's better-seeing eye. VA of the better-seeing eye is found to be positively associated with self-reported vision functioning (Varma et al., 2006; McClure et al., 2009; Lin and Yu, 2012).

VA of the better-seeing eye alone, however, may not be the optimal indicator for the effect of VI severity on general health related quality of life (HRQOL) which represents a broader health construct than vision function. This may be particularly true when the HRQOL measure used is utility-based, or reflecting the health preferences of patients or the general public. The published literature has shown that, while the better-seeing eye had a greater effect on self-rated health utility than the worse-seeing eye in some studies (Finger et al., 2013; Brown et al., 2001; Sahel et al., 2007), the opposite result was observed in other studies (Nease et al., 2000; Jampel et al., 2001). For example, health utility had a stronger correlation with VA in the worse-seeing eye than in the better-seeing eye in a study of patients with VI and angina (Nease et al., 2000).

Therefore, in this study, we aimed to ascertain the VA measure that best indicates the effect of VI on individuals' health utility. We compared the effect sizes of five VA measures based on the VA in the better- and worse-seeing eyes of visually impaired individuals on the preference-based EQ-5D-3L health index score.

5.2 Methods

Study Subjects

This study drew data from the Singapore Epidemiology of Eye Disease (SEED, 2004-11) study which comprised three ethnicity-specific eye studies: the Singapore Malay Eye Study (2004-2006), the Singapore Indian Eye Study, (2007-2009) and the Singapore Chinese Eye Study (2009-2011). Details of the study design have been described elsewhere (Foong et al., 2007; Lavanya et al., 2009). Briefly, an age-stratified (by 10-year age groups) random sampling methodology was used to select ethnic Chinese, Indians, and Malays 40 to 80 years of age living in Singapore. Participants went through a clinical examination and an interview to collect socio-demographic and medical data. The overall response rate was 75.6%: 72.8% for Chinese, 75.6% for Indians, and 78.7% for Malays. The SEED study adhered to the Declaration of Helsinki and was approved by the Singapore Eye Research Institute Institutional Review Board.

In the present study, the inclusion criteria were: 1) VI in at least one eye; 2) difference by at least one line in the VA of the two eyes; and 3) no missing data on the EQ-5D questionnaire. After excluding participants with normal vision or vision impaired to the same degree in both eyes, 3,183 participants were included in this study.

Measurement of Visual Acuity and Definitions of Visual Impairment (VI)

VA was measured using logarithm of the minimum angle of resolution (logMAR) number chart (Lighthouse International, New York, NY) at a distance of 4 meters and presenting VA was measured in the condition that participants wore their habitual optical correction (e.g. spectacles or lenses). If no number could be read at 4m, the participant was moved to 3, 2, or 1m, consecutively. If no number could be read on the chart, VA was assessed as Counting Fingers, Hand Movement, Perception of Light, or No Perception of Light. Based on presenting VA, VI was defined as logMAR >0.30 in either eye (Tielsch et al., 1990). Unilateral VI was defined as VI in one eye and normal vision on the other, while bilateral VI was defined as VI in both eyes.

Health-Related Quality of Life Measure

The EQ-5D questionnaire consists of 2 parts: a descriptive system and the EQ visual analog scale (VAS). The EQ-5D descriptive system comprises 5 items, each targeting a different health dimension including mobility, self-care, usual activities, pain/discomfort and

anxiety/depression. For each dimension, health problems that a respondent experiences on the day of survey are described as one of three levels: no problems, some problems and extreme problems. Hence, the EQ-5D-3L descriptive system defines a total of 243 (3^5) unique health states. Multiple algorithms are available for generating a utility-based index score for each of the EQ-5D described health states (Lee et al., 2009; Shaw et al., 2005; Tsuchiya et al., 2002; Dolan, 1997). In this study, we used the most widely used algorithm which reflects the health preferences of the generate UK population (Dolan, 1997). The score ranges from -0.59 to 1.00, with negative scores, 0, and 1 corresponding to health states considered worse than death, dead, and full health, respectively. The validity and reliability of the EQ-5D questionnaire have been previously tested in Singapore (Luo et al., 2003; Wee et al., 2007; Luo et al., 2009; Au et al., 2012; Ang et al., 2013).

Statistical Analyses

The effect of 5 VA measures on the EQ-5D index score was estimated using separate linear regression models. The measures were based on the VA of the better- and/or worse-seeing eyes, including VA in the better-seeing eye (BVA), VA in the worse-seeing eye (WVA), the mean VA of the two eyes (MVA), the better eye-weighted mean VA (BMVA, 0.75 * VA in the better-seeing eye + 0.25 * VA in the worse-seeing eye), and the worse-eye weighted mean VA (WMVA, 0.25 * VA in the better-seeing eye + 0.75 * VA in the worse-seeing eye), all measured on the logMAR scale. For each VA measure, the EQ-5D index score was regressed on the VA measure in a simple linear regression model. The regression coefficients

of the VA measures and the corresponding 95% confidence intervals (CIs) were used to compare the effect size of the VA measures.

The above mentioned linear regression analyses were conducted for individuals with unilateral and bilateral VI separately and, within each subgroup, for individuals with different ethnicity (Chinese, Indian, and Malay), age (≥ 65 years and <65 years) and socio-economic status (SES) (low and high). Low SES was defined as no formal education plus monthly personal income <S$1000.

In addition, logistic regression models were used to examine the association between the VA measures and reporting of health problems with the EQ-5D items. The response to each of the EQ-5D items was coded into a binary variable (1=moderate/extreme problems; 0=no problems) and was used as the dependent variable in the logistic regression models. For each EQ-5D item, five models in which only one of the VA measures was the independent variable were used to estimate the individual effect of the VA measures on self-reported problems in that dimension. I was responsible for data analyses in the chapter. Statistical analyses were performed with SAS software (version 9.2, SAS institute, Inc., Cary, NC).

5.3 Results

The mean ± standard deviation (SD) age of participants was 63.3 ± 10.2 years, the proportion of males was 49.6%, the mean ± SD of BVA was 0.30 ± 0.21, and WVA 0.71 ± 0.46. The mean ± SD of EQ-5D index score was 0.84 ± 0.21. Participants with unilateral VI (n=2,004) and bilateral VI (n=1,179) differed in all socio-demographic characteristics, VA measures, and EQ-5D index score (Table 5.1).

Table 5.1 Socio-demographic characteristics, visual acuity measure and EQ-5D index score for participants in the study (n=3,183)

Variable	All (n=3,183)	Unilateral VI (n=2,004)	Bilateral VI (n=1,179)	*P* value
Age				
Mean ± SD	63.3 ± 10.2	61.6 ± 9.9	66.3 ± 10.0	0.0566
Gender				
Male	49.60%	52.40%	44.87%	<0.0001
Monthly personal income (S$)				
<1000	67.28	60.14	79.43	<0.0001
1000-2000	18.27	21.2	13.28	
2000-3000	7.06	8.61	4.43	
>3000	7.39	10.04	2.86	
Education				
No formal education	33.84	26.86	45.71	<0.0001
Primary and below education	37.26	38.24	35.6	
Secondary and above education	28.9	34.9	18.69	
Low socio-economic status				
Yes	39.71	38.02	42.58	<0.0001
No	60.29	61.98	57.42	
VA in the better-seeing eye				
Mean ± SD	0.30 ± 0.21	0.17 ± 0.09	0.52 ± 0.19	<0.0001
Better eye-weighted mean VA				
Mean ± SD	0.40 ± 0.24	0.28 ± 0.12	0.62 ± 0.23	<0.0001
Mean of VA in both eyes				
Mean ± SD	0.51 ± 0.30	0.38 ± 0.19	0.73 ± 0.31	<0.0001
Worse eye-weighted mean VA				
Mean ± SD	0.61 ± 0.37	0.48 ± 0.28	0.83 ± 0.4	<0.0001
VA in the worse-seeing eye				
Mean ± SD	0.71 ± 0.46	0.58 ± 0.38	0.94 ± 0.50	<0.0001
EQ-5D index score				
Mean ± SD	0.84 ± 0.21	0.85 ± 0.20	0.81 ± 0.23	<0.0001

SD = standard deviation; S$ = Singapore dollar; VA= visual acuity; VI = visual impairment

The linear regression coefficient estimated using data from all participants with bilateral VI was, from high to low in absolute value, -0.095 for WMVA, -0.089 for WVA, -0.078 for MVA, -0.070 for BMVA, and -0.056 for BVA. In subgroup analysis, the rank order of the VA measures in terms of their regression coefficient values remained the same in ethnic Chinese/Indian participants (Table 5.2), participants <65 years old (Table 5.3), and participants in high SES (Table 5.5); in contrast, the rank order of the VA measures, from high to low based on their regression coefficient values, was BMVA, BVA, MVA, WMVA, and WVA in Malay participants, participants ≥65 years old, and participants in low SES (Tables 5.2-5.4). Nevertheless, there was no difference in the rank order of the regression coefficients for the VA measures across the three ethnic groups after the study sample was stratified by age (Table 5.3) or SES (Table 5.4). WVA and BMVA were associated with larger regression coefficient values than BVA and BMVA in participants <65 years old or in high SES, while the opposite was the case in participants ≥65 years old or in low SES, regardless of ethnicity. Further analysis showed that BVA and BMVA were associated with larger effect values on HRQOL than WVA and WMVA only in participants ≥65 years old and in low SES (Table 5.6). The trend that WVA and WMVA were associated with larger regression coefficient values than BVA and BMVA was observed in all other subgroups defined by age and SES: ≥65 years old and in high SES, <65 years old and in low SES, and participants <65 years old and in high SES (Table 5.6).

In participants with bilateral VI, the odds ratio (OR) of reporting problems was highest for WMVA/WVA, followed by, from high to low in OR, MVA, BMVA, and BVA. This was the

case for all the five health dimensions and also for all subgroups defined by age and SES except for participants ≥65 years old and in high SES (Table 5.6). For example, when all participants with bilateral VI were considered, the OR of reporting problems in mobility was 3.27 for WVA, 3.48 for WMVA, 2.66 for MVA, 2.11 for BMVA, and 1.80 for BVA. In participants ≥65 years old and in low SES, the OR for reporting problems in performing usual activities was, from high to low, 10.30 for BVA, 6.30 for BMVA, 3.43 for MVA, 2.33 for WMVA, and 1.85 for WVA.

Similar trends in the effect of the VA measures on the EQ-5D index scores and responses to the five health dimensions also exhibited in participants with unilateral VI (see Table 5.7-5.11).

Table 5.2 Unadjusted effects of VA measures on EQ-5D index score in participants with bilateral VI (n=1,179)

VA measure	All (n=1,179)			Chinese (n=391)			Indian (n=361)			Malay (n=427)		
	Beta	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**	
BVA	**-0.056**	**-0.082**	**-0.029**	**-0.048**	**-0.083**	**-0.012**	-0.055	-0.114	0.004	**-0.068**	**-0.131**	**-0.004**
BMVA	**-0.070**	**-0.103**	**-0.037**	**-0.063**	**-0.107**	**-0.019**	-0.071	-0.145	0.002	**-0.077**	**-0.125**	**-0.029**
MVA	**-0.078**	**-0.121**	**-0.035**	**-0.087**	**-0.143**	**-0.031**	-0.086	-0.182	0.011	-0.045	-0.108	0.018
WMVA	**-0.095**	**-0.134**	**-0.056**	**-0.099**	**-0.159**	**-0.040**	**-0.124**	**-0.242**	**-0.006**	-0.045	-0.094	0.003
WVA	**-0.089**	**-0.135**	**-0.044**	**-0.092**	**-0.138**	**-0.046**	**-0.102**	**-0.192**	**-0.012**	-0.042	-0.085	0.002

BVA = visual acuity in the better-seeing eye; BMVA = better eye-weighted mean visual acuity; CI = confidence interval; MVA = mean of visual acuity in both eyes; WMVA = worse eye –weighted mean visual acuity; WVA = visual acuity in the worse-seeing eye; Boldness: P <0.05;

Table 5.3 Unadjusted effects of VA measures on EQ-5D index score in participants with bilateral VI by age group and by ethnicity (n=1,179)

VA measure	All (n=1,179)			Chinese (n=391)			Indian (n=361)			Malay (n=427)		
	Beta	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**	
≥65 years	n=601			n=149			n=171			n=281		
BVA	**-0.100**	**-0.181**	**-0.019**	-0.071	-0.174	0.032	-0.097	-0.288	0.094	**-0.107**	**-0.209**	**-0.005**
BMVA	**-0.127**	**-0.224**	**-0.030**	-0.076	-0.184	0.032	-0.102	-0.321	0.118	**-0.146**	**-0.272**	**-0.021**
MVA	**-0.092**	**-0.168**	**-0.015**	-0.065	-0.153	0.024	-0.092	-0.239	0.055	-0.097	-0.195	0.000
WMVA	**-0.080**	**-0.148**	**-0.011**	-0.041	-0.113	0.030	-0.088	-0.217	0.041	-0.044	-0.105	0.017
WVA	-0.055	-0.110	0.001	-0.034	-0.093	0.026	-0.065	-0.156	0.026	-0.031	-0.080	0.018
<65 years	n=578			n=242			n=191			n=146		
BVA	-0.024	-0.059	0.012	-0.035	-0.079	0.010	-0.023	-0.085	0.039	-0.018	-0.089	0.053
BMVA	-0.043	-0.088	0.002	-0.055	-0.110	0.001	-0.042	-0.117	0.033	-0.031	-0.112	0.050
MVA	**-0.073**	**-0.142**	**-0.004**	**-0.090**	**-0.162**	**-0.018**	-0.079	-0.180	0.023	-0.045	-0.132	0.041
WMVA	**-0.116**	**-0.183**	**-0.050**	**-0.108**	**-0.207**	**-0.009**	-0.131	-0.272	0.010	-0.078	-0.202	0.047
WVA	**-0.095**	**-0.160**	**-0.031**	**-0.098**	**-0.194**	**-0.002**	-0.118	-0.244	0.008	-0.066	-0.172	0.040

BVA = visual acuity in the better-seeing eye; BMVA = better eye-weighted mean visual acuity; CI = confidence interval; MVA = mean of visual acuity in both eyes; WMVA = worse eye –weighted mean visual acuity; WVA = visual acuity in the worse-seeing eye;
Boldness: P <0.05;

Table 5.4 Unadjusted effects of VA measures on EQ-5D index score in participants with bilateral VI by social-economic status (n=1,179)

VA measure	All (n=1,179)			Chinese (n=391)			Indian (n=361)			Malay (n=427)		
	Beta	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**	
Low SES	n=502			n=165			n=112			n=225		
BVA	**-0.101**	**-0.189**	**-0.013**	-0.117	-0.235	0.001	-0.078	-0.282	0.127	-0.087	-0.203	0.029
BMVA	**-0.122**	**-0.226**	**-0.019**	-0.127	-0.259	0.005	-0.083	-0.326	0.160	-0.132	-0.280	0.017
MVA	**-0.085**	**-0.151**	**-0.019**	-0.092	-0.186	0.002	-0.056	-0.211	0.100	-0.053	-0.140	0.034
WMVA	**-0.056**	**-0.108**	**-0.005**	-0.070	-0.144	0.003	-0.040	-0.160	0.080	-0.034	-0.102	0.033
WVA	-0.036	-0.077	0.006	-0.056	-0.113	0.001	-0.030	-0.126	0.066	-0.024	-0.079	0.031
High SES	n=677			n=226			n=249			n=202		
BVA	-0.031	-0.071	0.009	-0.041	-0.096	0.015	-0.046	-0.150	0.058	-0.019	-0.083	0.046
BMVA	-0.043	-0.092	0.006	-0.055	-0.124	0.013	-0.065	-0.218	0.087	-0.025	-0.077	0.027
MVA	**-0.064**	**-0.127**	**0.000**	-0.083	-0.169	0.004	-0.095	-0.290	0.099	-0.043	-0.126	0.041
WMVA	**-0.132**	**-0.237**	**-0.027**	**-0.135**	**-0.269**	**-0.001**	-0.150	-0.434	0.134	-0.104	-0.254	0.046
WVA	**-0.098**	**-0.182**	**-0.014**	**-0.129**	**-0.241**	**-0.018**	-0.143	-0.392	0.105	-0.062	-0.175	0.052

BVA = visual acuity in the better-seeing eye; BMVA= better eye-weighted mean visual acuity; CI= confidence interval; MVA = mean of visual acuity in both eyes; SES = socio-economic status; WMVA = worse eye –weighted mean visual acuity; WVA = visual acuity in the worse-seeing eye;

Boldness: P <0.05;

Table 5.5 Unadjusted effects of VA measures on EQ-5D index score in participants with bilateral VI by socio-economic status and age group (n=1,179)

VA measure	≥65 & low SES (n=289)			<65 & low SES (n=213)			≥65 & medium/high SES (n=312)			<65 & medium/high SES (n=365)		
	Beta	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**	
BVA	**-0.142**	**-0.266**	**-0.018**	-0.018	-0.112	0.075	-0.024	-0.108	0.059	-0.035	-0.084	0.014
BMVA	**-0.131**	**-0.248**	**-0.014**	-0.035	-0.149	0.079	-0.042	-0.147	0.063	-0.069	-0.164	0.027
MVA	**-0.096**	**-0.185**	**-0.008**	-0.064	-0.176	0.049	-0.061	-0.166	0.043	-0.097	-0.213	0.019
WMVA	-0.070	-0.147	0.007	-0.083	-0.190	0.024	-0.086	-0.227	0.055	**-0.169**	**-0.301**	**-0.037**
WVA	-0.029	-0.072	0.014	-0.088	-0.196	0.021	-0.096	-0.249	0.057	**-0.138**	**-0.262**	**-0.013**

BVA = visual acuity in the better-seeing eye; BMVA= better eye-weighted mean visual acuity; CI= confidence interval; MVA = mean of visual acuity in both eyes; SES = socio-economic status; WMVA = worse eye –weighted mean visual acuity; WVA = visual acuity in the worse-seeing eye;

Boldness: P <0.05;

Table 5.6 Odds Ratios (95% confidence interval) of VA measures on each EQ-5D domain in participants with bilateral VI by socio-economic status and age group (n=1,179)

VA measure	All (n=1,179)					≥65 & low SES (n=289)					<65 or high SES (n=890)				
	Mobility	Self-care	Usual Activity	Pain/discomfort	Anxiety/depression	Mobility	Self-care	Usual Activity	Pain/discomfort	Anxiety/depression	Mobility	Self-care	Usual Activity	Pain/discomfort	Anxiety/depression
BVA	**1.80 (1.40-2.30)**	**1.89 (1.24-2.88)**	**1.83 (1.37-2.45)**	1.14 (0.90-1.44)	1.19 (0.93-1.52)	**3.90 (1.45-10.47)**	**11.53 (2.75-48.32)**	**10.30 (2.93-36.17)**	3.18 (1.01-10.03)	1.88 (0.63-5.57)	**1.61 (1.18-2.18)**	1.52 (0.77-3)	1.42 (0.96-2.10)	1.10 (0.83-1.46)	1.18 (0.87-1.60)
BMVA	**2.11 (1.55-2.88)**	**2.47 (1.46-4.16)**	**2.39 (1.59-3.59)**	1.19 (0.89-1.59)	1.28 (0.98-1.67)	**3.66 (1.46-9.18)**	**7.57 (2.26-25.36)**	**6.30 (2.33-17.05)**	1.85 (0.75-4.55)	1.52 (0.62-3.7)	**1.86 (1.27-2.73)**	1.88 (0.82-4.33)	1.60 (0.98-2.62)	1.13 (0.80-1.60)	1.25 (0.86-1.83)
MVA	**2.66 (1.78-3.98)**	**3.60 (1.84-7.06)**	**2.75 (1.72-4.40)**	1.31 (0.91-1.91)	**1.45 (1.04-2.03)**	**2.67 (1.32-5.37)**	**5.14 (1.78-14.88)**	**3.43 (1.63-7.21)**	1.32 (0.67-2.61)	1.27 (0.64-2.52)	**2.36 (1.42-3.90)**	**2.98 (1.03-8.61)**	**2.39 (1.26-4.54)**	1.29 (0.82-2.03)	1.54 (0.94-2.52)
WMVA	**3.48 (2.12-5.72)**	**5.58 (2.75-11.33)**	**4.83 (2.85-8.19)**	**1.56 (1.14-2.14)**	**1.80 (1.27-2.55)**	**2.09 (1.18-3.68)**	**2.53 (1.21-5.29)**	**2.33 (1.31-4.15)**	1.13 (0.66-1.92)	1.15 (0.67-1.98)	**3.62 (1.83-7.14)**	**6.86 (1.66-28.25)**	**7.25 (2.49-21.12)**	1.80 (0.98-3.32)	1.92 (0.99-3.70)
WVA	**3.27 (2.15-4.98)**	**4.56 (2.41-8.66)**	**3.73 (2.41-5.77)**	**1.88 (1.37-2.58)**	**2.20 (1.54-3.15)**	**1.77 (1.14-2.76)**	**1.96 (1.01-3.80)**	**1.85 (1.16-2.95)**	1.05 (0.75-1.47)	1.10 (0.72-1.66)	**3.55 (1.82-6.91)**	**5.81 (1.55-21.87)**	**5.82 (2.46-13.79)**	2.04 (0.99-4.20)	**2.38 (1.05-5.37)**

BVA: visual acuity in the better-seeing eye; BMVA: better eye-weighted mean visual acuity; MVA: mean of visual acuity in both eyes; SES: socio-economic status; WMVA: worse eye –weighted mean visual acuity; WVA: visual acuity in the worse-seeing eye;

Boldness: P <0.05;

Table 5.7 Unadjusted effects of VA measures on EQ-5D index score in participants with unilateral VI (n=2,004)

VA measure	All (n=2,004)			Chinese (n=753)			Indian (n=661)			Malay (n=590)		
	Beta	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**	
BVA	**-0.021**	**-0.043**	**0.002**	-0.019	-0.043	0.006	-0.027	-0.081	0.026	**-0.102**	**-0.141**	**-0.063**
BMVA	**-0.031**	**-0.061**	**-0.001**	-0.026	-0.059	0.007	-0.039	-0.110	0.032	**-0.146**	**-0.198**	**-0.094**
MVA	**-0.045**	**-0.089**	**-0.001**	-0.036	-0.084	0.012	-0.063	-0.166	0.040	-0.062	-0.136	0.012
WMVA	**-0.073**	**-0.108**	**-0.038**	**-0.088**	**-0.142**	**-0.033**	-0.110	-0.226	0.006	-0.034	-0.098	0.030
WVA	**-0.056**	**-0.106**	**-0.007**	**-0.073**	**-0.114**	**-0.031**	-0.080	-0.167	0.006	-0.023	-0.066	0.020

BVA = visual acuity in the better-seeing eye; BMVA = better eye-weighted mean visual acuity; CI = confidence interval; MVA = mean of visual acuity in both eyes; WMVA = worse eye –weighted mean visual acuity; WVA = visual acuity in the worse-seeing eye;

Boldness: P <0.05;

Table 5.8 Unadjusted effects of VA measures on EQ-5D index score in participants with unilateral VI by age group (n=2,004)

VA measure	All (n=2,004)			Chinese (n=753)			Indian (n=661)			Malay (n=590)		
	Beta	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**	
≥65	n=840			n=252			n=227			n=361		
BVA	**-0.124**	**-0.245**	**-0.002**	-0.108	-0.259	0.043	-0.123	-0.334	0.087	**-0.163**	**-0.323**	**-0.004**
BMVA	**-0.116**	**-0.221**	**-0.011**	-0.097	-0.239	0.045	-0.115	-0.320	0.091	**-0.157**	**-0.309**	**-0.005**
MVA	**-0.077**	**-0.147**	**-0.007**	-0.072	-0.187	0.042	-0.098	-0.283	0.088	-0.059	-0.160	0.042
WMVA	-0.050	-0.105	0.006	-0.047	-0.125	0.032	-0.073	-0.211	0.066	-0.029	-0.120	0.062
WVA	-0.032	-0.074	0.010	-0.034	-0.093	0.025	-0.057	-0.161	0.047	-0.016	-0.062	0.031
<65	n=1164			n=501			n=434			n=229		
BVA	-0.015	-0.046	0.017	-0.014	-0.065	0.036	-0.013	-0.076	0.051	-0.041	-0.107	0.024
BMVA	-0.027	-0.062	0.008	-0.025	-0.080	0.029	-0.029	-0.113	0.056	-0.056	-0.144	0.031
MVA	-0.038	-0.088	0.011	-0.032	-0.097	0.033	-0.049	-0.171	0.073	-0.066	-0.196	0.065
WMVA	**-0.090**	**-0.155**	**-0.025**	**-0.096**	**-0.181**	**-0.012**	-0.131	-0.321	0.059	-0.088	-0.239	0.063
WVA	**-0.133**	**-0.214**	**-0.053**	**-0.155**	**-0.259**	**-0.050**	-0.138	-0.344	0.068	-0.092	-0.254	0.070

BVA = visual acuity in the better-seeing eye; BMVA = better eye-weighted mean visual acuity; CI = confidence interval; MVA = mean of visual acuity in both eyes; WMVA = worse eye –weighted mean visual acuity; WVA = visual acuity in the worse-seeing eye;

Boldness: P <0.05;

Table 5.9 Unadjusted effects of VA measures on EQ-5D index score in participants with unilateral VI by social-economic status (n=2,004)

VA	All (n=2,004)			Chinese (n=753)			Indian (n=661)			Malay (n=590)		
measure	Beta	95 %CI		Beta	95 %CI		Beta	95 %CI		Beta	95 %CI	
Low SES	n=762			n=230			n=216			n=316		
BVA	**-0.130**	**-0.256**	**-0.003**	-0.087	-0.244	0.069	-0.183	-0.595	0.229	-0.190	-0.466	0.086
BMVA	**-0.105**	**-0.190**	**-0.019**	-0.051	-0.140	0.038	-0.136	-0.427	0.155	-0.169	-0.376	0.039
MVA	-0.050	-0.122	0.022	-0.041	-0.122	0.040	-0.066	-0.243	0.110	-0.076	-0.182	0.030
WMVA	-0.030	-0.087	0.026	-0.035	-0.095	0.026	-0.040	-0.162	0.083	-0.022	-0.093	0.050
WVA	-0.021	-0.063	0.021	-0.026	-0.071	0.020	-0.028	-0.121	0.066	-0.013	-0.067	0.041
High SES	n=1,242			n=523			n=445			n=274		
BVA	-0.016	-0.044	0.012	-0.011	-0.040	0.018	-0.010	-0.074	0.054	-0.026	-0.075	0.023
BMVA	-0.026	-0.063	0.012	-0.016	-0.054	0.023	-0.029	-0.115	0.057	-0.034	-0.100	0.032
MVA	-0.032	-0.087	0.023	-0.027	-0.083	0.030	-0.041	-0.168	0.085	-0.048	-0.145	0.049
WMVA	**-0.125**	**-0.215**	**-0.034**	**-0.106**	**-0.200**	**-0.012**	-0.151	-0.352	0.050	-0.063	-0.190	0.063
WVA	**-0.154**	**-0.260**	**-0.048**	**-0.191**	**-0.304**	**-0.078**	-0.170	-0.383	0.044	-0.081	-0.230	0.069

BVA = visual acuity in the better-seeing eye; BMVA= better eye-weighted mean visual acuity; CI= confidence interval; MVA= mean of visual acuity in both eyes; SES= socio-economic status; WMVA= worse eye –weighted mean visual acuity; WVA= visual acuity in the worse-seeing eye;

Boldness: P <0.05;

Table 5.10 Unadjusted effects of VA measures on EQ-5D index score in participants with unilateral VI by socio-economic status and age group (n=2,004)

VA measure	≥65 & low SES (n=383)			<65 & low SES (n=379)			≥65 & medium/high SES (n=412)			<65 & medium/high SES (n=830)		
	Beta	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**		**Beta**	**95 %CI**	
BVA	-0.159	-0.318	0.001	-0.012	-0.142	0.117	-0.013	-0.170	0.144	-0.046	-0.096	0.003
BMVA	-0.145	-0.291	0.001	-0.021	-0.126	0.084	-0.016	-0.120	0.089	-0.058	-0.120	0.003
MVA	-0.092	-0.204	0.020	-0.032	-0.143	0.080	-0.028	-0.110	0.055	**-0.107**	**-0.187**	**-0.027**
WMVA	-0.025	-0.098	0.047	-0.043	-0.168	0.083	-0.054	-0.162	0.053	**-0.173**	**-0.280**	**-0.066**
WVA	-0.016	-0.075	0.043	-0.049	-0.192	0.095	-0.063	-0.188	0.063	**-0.169**	**-0.277**	**-0.061**

BVA = visual acuity in the better-seeing eye; BMVA= better eye-weighted mean visual acuity; CI= confidence interval; MVA= mean of visual acuity in both eyes; SES= socio-economic status; WMVA= worse eye –weighted mean visual acuity; WVA= visual acuity in the worse-seeing eye;

Boldness: P <0.05;

Table 5.11 Odds Ratios (95% confidence interval) of VA measures on each EQ-5D domain in participants with unilateral VI by socio-economic status and age group (n=2,004)

VA measure	**All (n=2,004)**					**≥65 & lowSES (n=383)**					**<65 or high SES (n=1621)**				
	Mobility	Self-care	Usual Activity	Pain/discomfort	Anxiety/depression	Mobility	Self-care	Usual Activity	Pain/discomfort	Anxiety/depression	Mobility	Self-care	Usual Activity	Pain/discomfort	Anxiety/depression
BVA	**1.60 (1.22-2.11)**	**1.78 (1.13-2.79)**	**1.86 (1.42-2.44)**	1.22 (0.96-1.54)	1.14 (0.88-1.47)	**5.00 (1.12-22.36)**	3.97 (0.69-22.77)	**8.14 (2.07-31.97)**	1.78 (0.65-4.90)	1.85 (0.62-5.50)	**1.41 (1.01-1.97)**	1.58 (0.84-2.98)	1.49 (0.93-2.39)	1.19 (0.90-1.57)	1.04 (0.76-1.42)
BMVA	**1.99 (1.48-2.67)**	**2.17 (1.12-4.23)**	**2.34 (1.53-3.57)**	1.35 (0.99-1.84)	1.22 (0.87-1.71)	**4.43 (1.04-18.84)**	4.34 (0.65-28.87)	**8.87 (2.22-35.39)**	1.86 (0.61-5.69)	1.90 (0.60-6.05)	**1.70 (1.09-2.63)**	2.03 (0.80-5.16)	**2.14 (1.06-4.33)**	1.32 (0.86-2.03)	1.09 (0.72-1.65)
MVA	**2.72 (1.59-4.64)**	**3.18 (1.10-9.21)**	**3.56 (1.77-7.14)**	1.68 (0.89-3.16)	1.40 (0.85-2.30)	2.82 (0.97-8.25)	2.93 (0.59-14.67)	**6.44 (1.80-23.00)**	1.68 (0.69-4.10)	1.73 (0.70-4.24)	**2.65 (1.40-5.01)**	3.19 (0.82-12.36)	**2.98 (1.19-7.42)**	1.66 (0.80-3.45)	1.24 (0.68-2.27)
WMVA	**6.07 (3.92-9.40)**	**7.92 (2.22-28.24)**	**12.38 (6.19-24.78)**	**2.79 (2.05-3.81)**	1.54 (0.98-2.42)	1.80 (0.91-3.55)	2.05 (0.54-7.84)	**3.28 (1.04-10.34)**	1.40 (0.76-2.56)	1.50 (0.77-2.92)	**7.63 (2.52-23.11)**	**9.76 (1.47-75.92)**	**14.93 (3.09-72.02)**	**3.69 (1.49-9.16)**	2.05 (0.75-5.63)
WVA	**4.30 (2.49-7.44)**	**5.08 (1.93-13.36)**	**7.64 (4.69-12.44)**	**3.35 (2.54-4.40)**	**1.84 (1.40-2.40)**	1.48 (0.78-2.81)	1.71 (0.60-4.91)	2.37 (0.91-6.20)	1.27 (0.81-2.01)	1.37 (0.80-2.34)	**6.55 (2.33-18.37)**	6.98 (0.90-46.52)	**9.69 (2.09-44.9)**	**6.66 (2.01-21.99)**	**4.13 (1.07-15.92)**

BVA: visual acuity in the better-seeing eye; BMVA: better eye-weighted mean visual acuity; MVA: mean of visual acuity in both eyes; SES: socio-economic status; WMVA: worse eye –weighted mean visual acuity; WVA: visual acuity in the worse-seeing eye;

Boldness: P <0.05;

5.4 Discussion:

Our study demonstrated that the VA of both eyes of visually impaired individuals had an effect on their HRQOL and, more importantly, that the relative effect size of the individuals' better- and worse-seeing eyes varied with their socio-demographic characteristics. Specifically, while BVA had a larger effect than WVA on HRQOL in old individuals from low SES, WVA had a larger effect than BVA in young /middle-aged individuals and old individuals from high SES. To the best of our knowledge, this is the first time that the differential effect size of the better- and worse-seeing eyes on overall HRQOL is observed in the same study. Previous studies found that either BVA or WVA was more strongly associated than the other with utility-based HRQOL measures (Finger et al., 2013; Brown et al., 2001; Sahel et al., 2007; Nease et al., 2000; Jampel, 2001).

The differential effect size of the better- and worse-seeing eyes on the HRQOL of visually impaired individuals suggests that the effect of VA on an individual's functions and wellbeing varies with the individual's daily activities. The better-seeing eye is more important than the worse-seeing eye to old individuals in low SES could be because such individuals tend to do simple and easy daily activities such as household chores that rely more on the vision of their better-seeing eyes. On the other hand, the working young and old individuals in high SES may need a high level of vision acuity that is limited mainly by their worse-seeing eyes. Also, the worse-seeing eye should be a more important mental stressor than the better-seeing eye to such individuals because of their responsibilities and expectations. These hypotheses are supported by the differential association between the VA of both eyes and self-reported problems to the

individual EQ-5D health dimensions revealed in this study. The differential effect size of the two eyes may also reflect the temporal effect of visual impairment on individuals. It may be possible that when VA of the two eyes of an individual worsened in different degrees, the impact on HRQOL is mainly from the worse eye in the short term because of slow adaptation. However, the level of HRQOL is mainly determined by the better eye after the individual has leant how to live with his or her impaired vision.

Our study suggests that the current practice of using BVA alone as the measure of VI severity is not optimal. Conventionally, only BVA is used to study the association between vision and patient-reported outcomes (Varma et al., 2006; McClure et al., 2009; Lin and Yu, 2012), although BVA alone does not reflect the binocular visual function which is also contributed by WVA. Our study might also have implications on the ophthalmologic clinical practice: while the better-seeing eye should be given higher priority because it is a more important determinant of visual function than the worse-seeing eye, the potential benefit of treating the worse-seeing eye or preventing it from further worsening cannot be underestimated. There has been evidence supporting the HRQOL benefits associated the treatment of the worse-seeing eye. For example, association between improved patient-reported outcomes and treatment of neovascular age-related macular degeneration, regardless of the severity of the treated eye, was observed (Bressler et al., 2010; Finger et al., 2014); HRQOL benefits from the cataract surgery on the second eye, which is usually the worse-seeing eye are widely reported (Elliott et al., 2000; Castells et al., 2006; Desai et al., 1996; Lundstrom et al., 2001; Busbee et al., 2003). Moreover, by demonstrating that the worse-seeing eye might have a greater psychological effect than the

better-seeing eye, our study highlights the importance of psychosocial interventions to visually impaired patients (Senra et al., 2011; Senra et al., 2015).

The main limitation of the study is the use of only one utility measure (i.e. the EQ-5D health index) in only ethnic Asians with VI. Studies using other utility measures such as HUI3 and SF-6D and samples from other cultures are warranted to ascertain the generalizability of the findings reported in this paper. Moreover, the unmeasured variables other than age and SES are not tested in the study, though they could be the reason for the different impact of VA in the two eyes on the utility measure.

In summary, our study suggested that the visual acuity of the worse-seeing eye may have greater impact than that of the better-seeing eye on the overall health utility of visually impaired individuals. Therefore, the VA of the better-seeing eye alone appears to be suboptimal for outcome research of vision problems.

Chapter 6

A Vision ‘Bolt-On’ Item could Increase the Discriminatory Power of the EQ-5D Index Score

6.1 Introduction

Addition of new items, also referred to as 'bolt-on' items, has been explored as a means to improving the EQ-5D questionnaire (Hoeymans et al., 2005; Arrons and Krabbe 2011; Jansses et al., 2013; Longworth et al., 2014; Swinburn et al., 2013; Yang et al., 2014). 'Bolt-on' items usually take the same form of the EQ-5D items but target different health dimensions. The aim of this exercise is to increase the sensitivity of the EQ-5D in therapeutic areas where the performance of the standard version is suboptimal. For example, if the EQ-5D is not sensitive to the impact of eye diseases, addition of an item assessing vision problems may mitigate the problem.

Research on the 'bolt-on' items has focused on their measurement properties and valuation of the health states defined by the 'bolt-on' descriptive system. 'Bolt-on' items seem to enhance measurement. For example, studies showed that a cognition 'bolt-on' item captured additional health information when added to the EQ-5D (Hoeymans et al., 2005; Arrons and Krabbe, 2001). However, the effect of 'bolt-on' items on valuation of the resultant health states appeared to be complex (Jansses et al., 2013). While the utility values of all the possible health states (aka the 'value set') were successfully determined for a vision (Longworth et al., 2014) and a psoriasis (Swinburn et al., 2013) 'bolt-on' system, a sleep 'bolt-on' item was found to add no value to the EQ-5D (Yang et al., 2014). It was because the sleep problems described by the item had little impact on overall health utility compared to the health problems captured by the existing EQ-5D items. Therefore, the additional

information captured by ‘bolt-on’ items may not necessarily translate into a more sensitive utility-based health index.

One important question that has not yet been answered for the ‘bolt-on’ exercise is whether the utility-based index for the ‘bolt-on’ health states (hereafter referred to as ‘bolt-on’ index) is more sensitive than the standard EQ-5D index (hereafter referred to as ‘standard’ index) in empirical studies. The utility-based health index is a convenient outcome measure for medical decision making and cost-effectiveness analysis of health technologies, and it is a main reason for the popularity of the EQ-5D questionnaire. Like any new health-status measure, a ‘bolt-on’ index should be psychometrically validated before formal use. Therefore, the purpose of this study was to assess the discriminatory power or sensitivity to difference, of a vision ‘bolt-on’ index (Longworth et al., 2014) in terms of its ability to discriminate between individuals with different levels of vision problems. Through this study, we hope to evaluate the prospect of the ‘bolt-on’ exercise as an approach to developing new utility-based measures.

6.2 Methods

We used data from the burden-of-illness study for visual impairment (VI) in Singapore, which have been described in Chapter 2 and Chapter 3. In brief, health and economic burden of individuals with and without VI was assessed in a cross-sectional survey.

For individuals with VI, consecutive patients attending the specialist outpatient clinics in Singapore National Eye Centre, a tertiary eye centre which manages about half of all eye conditions in Singapore, were recruited following the inclusion criteria. After informed consent was obtained, each patient or his/her caregiver was interviewed face-to-face in the hospital by a bilingual research assistant using a battery of standardized questionnaires including, in the order of administration, the (3-level) vision 'bolt-on' EQ-5D questionnaire, the 14-item visual function questionnaire (VF-14) (Steinberg et al., 1994), and a health services utilization and expenditure questionnaire.

For individuals without VI, members of the general public who volunteered to be screened for eye diseases on the 2013 National Eye Care Day, which was conducted at the Singapore National Eye Centre, were recruited. Following informed consent, each subject was home visited and interviewed face-to-face by a trained interviewer using the same set of questionnaires for individuals with VI.

Definition of VI

In this study, VA was measured by a trained optometrist for each individual using a Snellen chart. VI was classified according to the VA in the better-seeing eye: (1) mild VI (VA ≤6/12 to >6/18); (2) moderate VI (VA ≤6/18 to >6/60); (3) severe VI (VA ≤6/60 to >6/120); and (4) blindness (VA≤6/120) (Tielsch et al., 1990; WHO, 2014).

Instruments

EQ-5D

The vision 'bolt-on' EQ-5D questionnaire comprises two parts: the 3-level EQ-5D descriptive system and a vision item. The EQ-5D descriptive system consists of 5 items, each for a different dimension including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Respondents were asked to describe their health status on the day of survey in those dimensions as no problems, some problems, or extreme problems. The vision item developed by Longworth and colleagues (Longworth et al., 2014) was used in this study. It consists of the heading of "Vision (using glasses or contact lenses if needed)" and the response options of "I have no problems seeing, I have some problems seeing, and I have extreme problems seeing". The vision item followed the EQ-5D items in the questionnaire and was administered immediately after the EQ-5D items in this study. Both the English and Chinese versions of the EQ-5D questionnaire were validated in local patients undergoing cataract surgery (Ang et al., 2013) and those with AMD (Au et al., 2012).

In this study, 4 published value sets were used to calculate EQ-5D index scores, including two value sets developed by Longworth and colleagues for predicting the vision 'bolt-on' index (EQ-5D[vision]) and the standard EQ-5D index (EQ-5D[core]), respectively, the value set developed in the UK's Measurement and Valuation of Health study (EQ-5D[MVH]) (Fayers and Machin, 2000), and a value set estimated in Singapore (EQ-5D[SG]) (Vickrey et al., 1997). The rationales for choosing the three EQ-5D indices were: EQ-5D[core] and EQ-5D[vision] were developed simultaneously using an identical study protocol; EQ-5D[MVH]

was developed using the health preferences of the same population as EQ-5D[vision]; EQ-5D[SG] was developed using the health preferences of the population from which the study sample was drawn. The characteristics of the Four EQ-5D value set were summarized in Table 6.1.

Table 6.1 Characteristics of the EQ-5D value sets used in the study

Characteristic	**EQ-5D[vision]**	**EQ-5D[core]**	**EQ-5D[MVH]**	**EQ-5D[SG]**
Sampling site	Yorkshire, UK	Yorkshire, UK	UK	Singapore
Sample size	157	155	2997	456
Score range	-0.072 – 1.000	-0.015 – 1.000	-0.594 – 1.000	-0.769 – 1.000
Number of health states valued	20	20	42	80

MVH, Measurement and Valuation of Health study; SG, Singapore.

EQ-5D[vision] and EQ-5D[core] were simultaneously developed using identical sampling, valuation, and data modeling procedures to study the impact of adding the vision dimension on the valuation of EQ-5D health states (Swinburn et al., 2013). Both value sets were estimated using time trade-off utility values of 20 health states directly measured from a general population sample drawn from Yorkshire, England (n=155 for EQ-5D[core] and 157 for EQ-5D[vision]). The values of EQ-5D[vision] range from -0.072 for the worst health state to 1.018 for the best health state. In this study, the only one >1 value for the best health state was truncated to 1.000, in order to achieve comparability with other EQ-5D value sets used. The range of EQ-5D[core] values is -0.015 to 1.000.

The EQ-5D[MVH] was estimated based on time trade-off valuation of 42 selected EQ-5D health states by a nationally representative sample (n=2,997) of the general UK population. The range of the values is -0.594 to 1.000. The EQ-5D[SG] was estimated using the time trade-off values from a general population sample (n=456) in Singapore. For estimating this value set, a total of 80 EQ-5D health states were valued using a modified MVH study protocol (Vickrey et al., 1997). The value range is -0.769 to 1.000. The main characteristics of the four EQ-5D index scores are summarized in Table 1.

VF-14

The VF-14 assesses the level of difficulty in performing activities of daily living due to vision problems. Each of the 14 items in this questionnaire measures one different vision problems using a 5-point Likert response scale ranging from 0 (no difficulty) to 4 (unable to

perform activity). The instrument has been validated in the Singaporean population previously (Lamoureux et al., 2009).

Statistical analysis

The discriminatory power of the 'bolt-on' index score was assessed by comparing the ability of the 'bolt-on' and standard index scores to discriminate between paired groups of individuals known to differ in VI severity or vision problems. For this purpose, 4 pairs of known groups were defined according to VI severity: no VI versus mild VI, mild VI versus moderate VI, moderate VI versus severe VI, and severe VI versus blindness; 12 pairs of known groups were defined using self-reported vision problems with VF-14, each pair for one different vision problem. Those vision problems included reading small print, reading newspapers, reading large print, recognizing people, seeing steps, reading traffic signs, doing handwork, filling forms, playing games, taking part in sports, cooking, and watching TV. Difficulty in car driving was assessed in VF-14 but was excluded from this analysis because very few participants drove or had driven a car. For each vision problem, the two known groups consisted of a group with problems (defined as reporting 'a little', 'some', or 'a great deal' of difficulty or 'unable' to perform the related activity) and a group without problems (defined as reporting 'no' difficulty in performing the related activity).

Discriminatory power was first assessed using the absolute mean difference in the index scores between the known groups defined by participants' VI severity and VF-14. A larger difference means greater utility gains and therefore a higher chance of drawing the

conclusion of cost-effectiveness when the index is used in a cost-utility analysis, thus indicating higher discriminatory power. Discriminatory power was also assessed in terms of the squared t-statistic derived from the two-sample t-test of the index scores between the known groups. The squared t-statistic (equivalent to the F-statistic from the ANOVA test in value) is widely used to assess the relative efficiency of patient-reported outcome measures (Fayers and Machin, 2000; Vickrey et al., 1997; Luo et al., 2009). A higher F-statistic value means higher likelihood for the measure to show statistical significance when used to compare groups. Hence, higher F-statistic values indicate higher discriminatory power. In this study, the F-statistic ratio of the two index scores was calculated for each pair of the known groups in such a way that a <1 ratio would mean that the 'bolt-on' index score is more discriminative. The ratio can be interpreted in terms of the relative sample size needed to achieve statistical significance (King et al., 2014). For example, a ratio of 0.5 means that the 'bolt-on' index can achieve the same statistical power as the standard index with only half of the sample size for the latter when they are used to compare the two groups.

The differences in the index scores between the known groups and their corresponding F-statistics were also estimated using multiple linear regression models in which the effect of age and gender was adjusted. The adjusted difference and F-statistic are better indicators than the unadjusted estimates of the sensitivity to change (or responsiveness) of the index scores in longitudinal studies. I was responsible for data collection and data analyses in the chapter. All analyses were conducted using SAS for Windows (version 9.2, SAS Institute, Inc., Cary, NC) at the significance level of 0.05.

6.3 Results

Sample characteristics

A total of 500 individuals with VI were recruited. The mean ± standard deviation (SD) age was 71.6 ± 9.8 years old and 47.6% was male. The majority of the individuals were Chinese (88.0%), with primary or no formal education (64.2%), not working (80.2%), and married (86.2%). The mean ± SD for EQ-5D[vision], EQ-5D[core], EQ-5D[MVH], and EQ-5D[SG] was 0.90 ± 0.15, 0.91 ± 0.15, 0.80 ± 0.27, and 0.74 ± 0.37, respectively. The full socio-demographic and health characteristics of individuals with VI are shown in Table 6.2.

A total of 336 individuals without VI participated in the study. The mean ± SD age was 63.1 ± 7.4 years old and 36.3% was male. The majority of them were Chinese (95.8%), with secondary education (68.2%), not working (58.3%), and married (77.4%). The mean ± SD for EQ-5D[vision], EQ-5D[core], EQ-5D[MVH], and EQ-5D[SG] was 0.97 ± 0.05, 0.96 ± 0.06, 0.90 ± 0.14, and 0.91 ± 0.14, respectively. Compared with individuals with VI, those without VI were significantly younger, better educated, more likely to work, and healthier according to the EQ-5D (Table 6.2).

Table 6.2 Characteristics of participants with and without visual impairment (n=836)

Characteristic	All (n=836)		Individuals with VI (n=500)		Individuals without VI (n=336)		P value*
Age (yrs), mean (SD)	68.2	(9.9)	71.6	(9.8)	63.1	(7.4)	<0.0001
Gender							
Male	43.1	(360)	47.6	(238)	36.3	(122)	0.0012
Ethnicity							
Chinese	91.4	(764)	88.0	(440)	96.4	(324)	0.0027
Indian	3.8	(32)	5.4	(27)	1.5	(5)	
Malay	4.1	(34)	5.4	(27)	2.1	(7)	
Others	0.7	(6)	1.2	(6)	0.0	(0)	
Education							
No formal education	25.6	(214)	34.6	(173)	12.2	(41)	<0.0001
Primary education	25.6	(214)	29.6	(148)	19.6	(66)	
Secondary education	48.8	(408)	35.8	(179)	68.2	(229)	
Employment status							
Working	28.6	(239)	19.8	(99)	41.7	(140)	<0.0001
Not working	71.4	(597)	80.2	(401)	58.3	(196)	
Marital status							
Single	8.3	(69)	6.6	(33)	10.7	(36)	0.3253
Married	82.7	(691)	86.2	(431)	77.4	(260)	
Separated/divorced	1.8	(15)	1.4	(7)	2.4	(8)	
Widow	7.3	(61)	5.8	(29)	9.5	(32)	
Interview language							
English	40.7	(340)	36.0	(180)	47.6	(160)	0.0008
Chinese	59.3	(496)	64.0	(320)	52.4	(176)	
EQ-5D index score, mean (SD)							
EQ-5D[vision]	0.93	(0.12)	0.90	(0.15)	0.97	(0.05)	<0.0001
EQ-5D[core]	0.93	(0.12)	0.91	(0.15)	0.96	(0.06)	<0.0001
EQ-5D[MVH]	0.84	(0.23)	0.80	(0.27)	0.90	(0.14)	<0.0001
EQ-5D[SG]	0.81	(0.31)	0.74	(0.37)	0.91	(0.14)	<0.0001

Mobility							
No problems	77.9	(651)	68.0	(340)	92.6	(311)	
Some problems	20.7	(173)	29.6	(148)	7.4	(25)	<0.0001
Extreme problems	1.4	(12)	2.4	(12)	0.0	(0)	
Self-care							
No problems	92.6	(774)	87.8	(439)	99.7	(335)	
Some problems	5.5	(46)	9.0	(45)	0.3	(1)	<0.0001
Extreme problems	1.9	(16)	3.2	(16)	0.0	(0)	
Usual activities							
No problems	86.0	(719)	78.2	(391)	97.6	(328)	
Some problems	10.8	(90)	16.4	(82)	2.4	(8)	<0.0001
Extreme problems	3.2	(27)	5.4	(27)	0.0	(0)	
Pain/discomfort							
No problems	61.7	(516)	60.2	(301)	64.0	(215)	
Some problems	35.9	(300)	36.4	(182)	35.1	(118)	0.0972
Extreme problems	2.4	(20)	3.4	(17)	0.9	(3)	
Anxiety/depression							
No problems	80.9	(676)	78.4	(392)	84.5	(284)	
Some problems	18.3	(153)	20.2	(101)	15.5	(52)	0.0111
Extreme problems	0.8	(7)	1.4	(7)	0.0	(0)	
Vision							
No problems	51.8	(433)	26.6	(133)	89.3	(300)	
Some problems	41.0	(343)	61.6	(308)	10.4	(35)	<0.0001
Extreme problems	7.2	(60)	11.8	(59)	0.3	(1)	

Note: the number inside the parentheses is the frequency and the number outside them is the proportion, unless otherwise specified.

*T-test or Chi-square test for the difference between individuals with VI and individuals without VI

SD, standard deviation; VI, visual impairment; yrs, years.

Absolute mean differences between known groups

All EQ-5D index scores decreased monotonically with increasing VI severity (Table 6.3). The mean differences in EQ-5D[SG] (range: 0.041 to 0.126) and EQ-5D[MVH] (range 0.028 to 0.070) for the 4 pairs of VI groups were larger than those in EQ-5D[vision] (range: 0.015 to 0.055) which were similar to or slightly larger than those in EQ-5D[core] (range: 0.017 to 0.036) (Figure 6.1). Similarly, the mean scores for individuals with a particular vision problem assessed by VF-14 were lower than those for individuals without that problem for all the four EQ-5D indices (Table 6.4). All the 12 vision problems are considered, the mean differences in EQ-5D[SG] (range: 0.178 to 0.387) and EQ-5D[MVH] (range 0.129 to 0.252) between the groups with and without a problem were larger than those in EQ-5D[vision] (range: 0.074 to 0.155) which were slightly but uniformly larger than those in EQ-5D[core] (range: 0.061 to 0.135) (Figure 6.3).

The trends in the mean between-group differences in the EQ-5D indices remained the same after adjusting for age and gender, although attenuated (Figures 6.2 and 6.4).

F-statistic ratios for known groups

The F-statistic ratio of EQ-5D[core], EQ-5D[MVH], and EQ-5D[SG] versus EQ-5D[vision] in the ANOVA tests for the groups known to differ in VI severity ranged from 0.415 to 0.667, 0.362 to 0.771, and 0.327 to 0.734, respectively (Figure 6.5).

Similarly, the F-statistic ratios derived from the comparisons of individuals with and without a vision problem were < 1 for all 12 vision problems for EQ-5D[core] and EQ-5D[MVH] versus EQ-5D; the F-statistic ratios for EQ-5D[SG] versus EQ-5D[vision] ranged from 0.829 to 1.006 (Figure 6.6). The F-statistic ratio values became smaller in all but one known-group comparisons after adjusting for the effect of age and gender (Figure 6.7 and 6.8); in the comparison of individuals with severe VI and those who were blind, the adjusted F-statistic ratio was 0.668, higher than the unadjusted value of 0.550.

Table 6.3 Mean (SD) EQ-5D index scores for different visual impairment groups (n=836)

Vision category	**n**	**EQ-5D[vision]**	**EQ-5D[core]**	**EQ-5D[MVH]**	**EQ-5D[SG]**
No VI	336	0.970 (0.048)	0.960 (0.058)	0.902 (0.139)	0.909 (0.136)
Mild VI	305	0.916 (0.114)	0.924 (0.113)	0.832 (0.220)	0.783 (0.308)
Moderate VI	78	0.902 (0.119)	0.907 (0.131)	0.804 (0.241)	0.742 (0.337)
Severe VI	39	0.860 (0.201)	0.876 (0.209)	0.753 (0.375)	0.680 (0.477)
Blindness	78	0.828 (0.218)	0.844 (0.218)	0.686 (0.369)	0.579 (0.496)
P value		<0.0001	<0.0001	<0.0001	<0.0001
F-statistic		31.39	18.73	17.65	25.19

MVH, Measurement and Valuation of Health study; VI, visual impairment; SD, standard deviation.

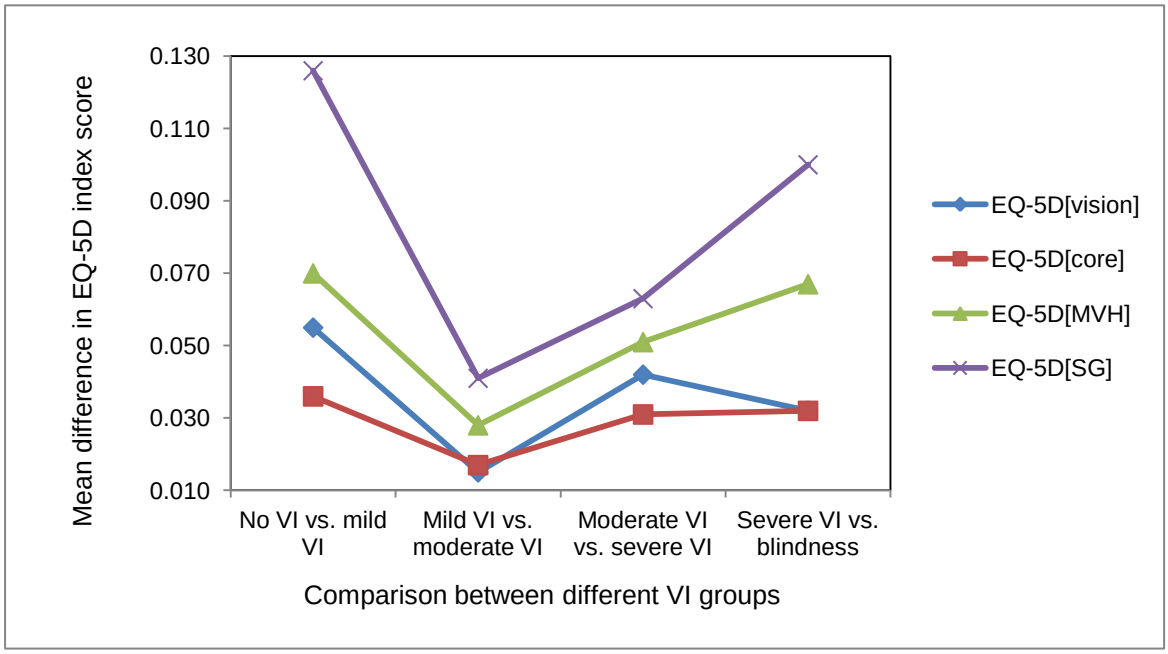
Table 6.4. Mean (SD) EQ-5D index scores for groups with and without a vision problem assessed by VF-14 (n=836)

	n	EQ-5D[vision]		EQ-5D[core]		EQ-5D[MVH]		EQ-5D[SG]	
Reading Small Print									
Without problems	337	0.970	(0.090)	0.964	(0.091)	0.917	(0.166)	0.912	(0.204)
With problems	499	0.896	(0.133)	0.903	(0.135)	0.788	(0.256)	0.734	(0.347)
Reading Newspaper									
Without problems	442	0.964	(0.089)	0.958	(0.090)	0.902	(0.173)	0.899	(0.207)
With problems	391	0.882	(0.141)	0.893	(0.145)	0.770	(0.269)	0.700	(0.369)
Reading Large Print									
Without problems	674	0.952	(0.085)	0.950	(0.088)	0.881	(0.178)	0.872	(0.216)
With problems	162	0.815	(0.183)	0.834	(0.188)	0.671	(0.335)	0.531	(0.456)
Recognizing People									
Without problems	696	0.949	(0.090)	0.946	(0.094)	0.874	(0.186)	0.862	(0.231)
With problems	140	0.811	(0.186)	0.833	(0.191)	0.670	(0.341)	0.530	(0.465)
Seeing Steps									
Without problems	671	0.953	(0.086)	0.951	(0.089)	0.884	(0.176)	0.873	(0.220)
With problems	165	0.815	(0.178)	0.831	(0.183)	0.662	(0.329)	0.531	(0.447)
Reading traffic signs									
Without problems	668	0.951	(0.089)	0.949	(0.092)	0.878	(0.184)	0.868	(0.226)
With problems	168	0.823	(0.177)	0.843	(0.182)	0.691	(0.326)	0.557	(0.447)
Doing Handwork									

Without problems	509	0.959	(0.078)	0.958	(0.079)	0.897	(0.162)	0.891	(0.199)
With problems	275	0.854	(0.165)	0.864	(0.168)	0.721	(0.303)	0.626	(0.411)
Filling Forms									
Without problems	556	0.958	(0.083)	0.955	(0.083)	0.891	(0.168)	0.886	(0.206)
With problems	272	0.859	(0.161)	0.871	(0.167)	0.736	(0.303)	0.641	(0.411)
Playing Games									
Without problems	547	0.946	0.095	0.946	(0.096)	0.873	(0.188)	0.858	(0.241)
With problems	168	0.829	0.179	0.844	(0.186)	0.688	(0.331)	0.567	(0.447)
Taking Part in Sports									
Without problems	535	0.943	0.098	0.944	(0.098)	0.869	(0.194)	0.851	(0.251)
With problems	166	0.831	0.177	0.846	(0.184)	0.693	(0.323)	0.569	(0.440)
Cooking									
Without problems	672	0.947	0.092	0.946	(0.095)	0.875	(0.184)	0.859	(0.235)
With problems	126	0.792	0.183	0.811	(0.191)	0.623	(0.344)	0.473	(0.460)
Watching TV									
Without problems	629	0.954	0.084	0.950	(0.088)	0.882	(0.176)	0.873	(0.216)
With problems	207	0.838	0.172	0.859	(0.178)	0.713	(0.321)	0.603	(0.439)

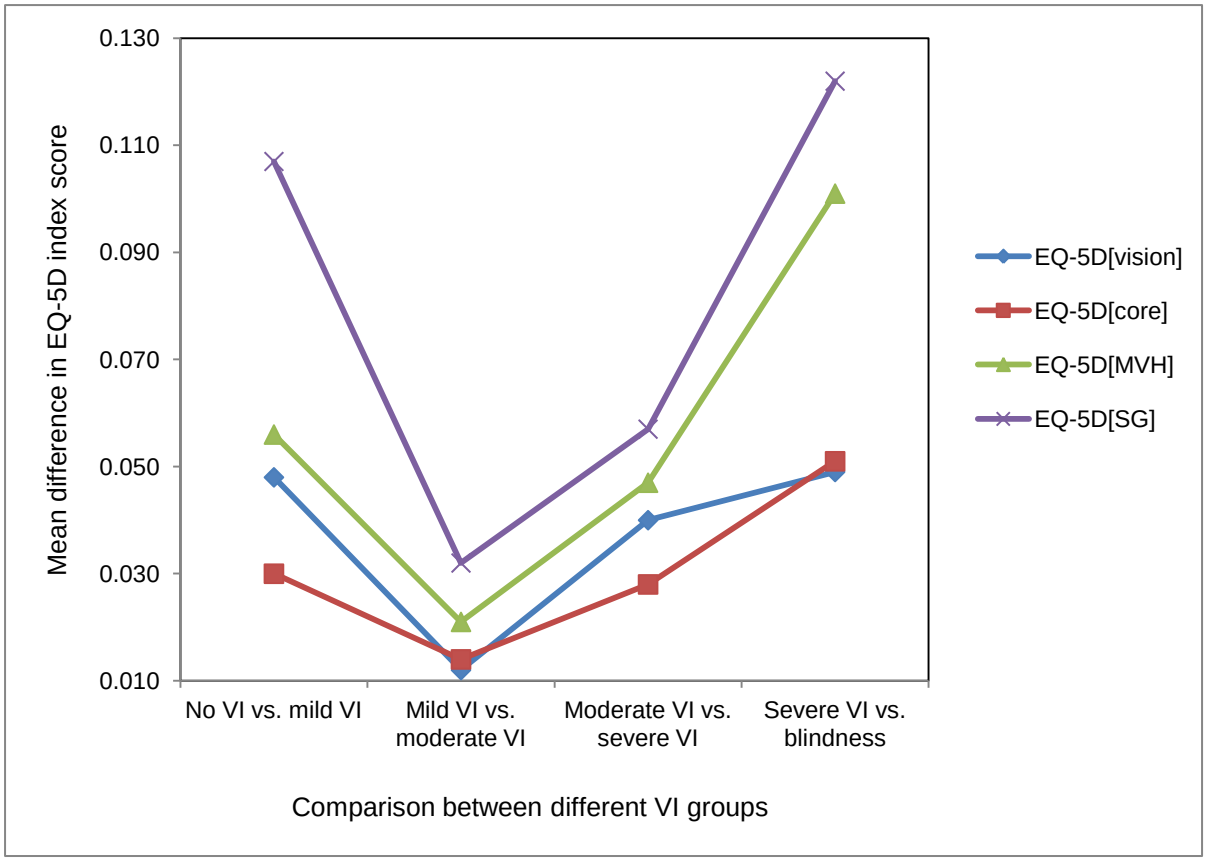
MVH, Measurement and Valuation of Health study; SD, standard deviation; SG, Singapore.

Figure 6.1 Unadjusted mean differences in EQ-5D index scores between different visual impairment groups



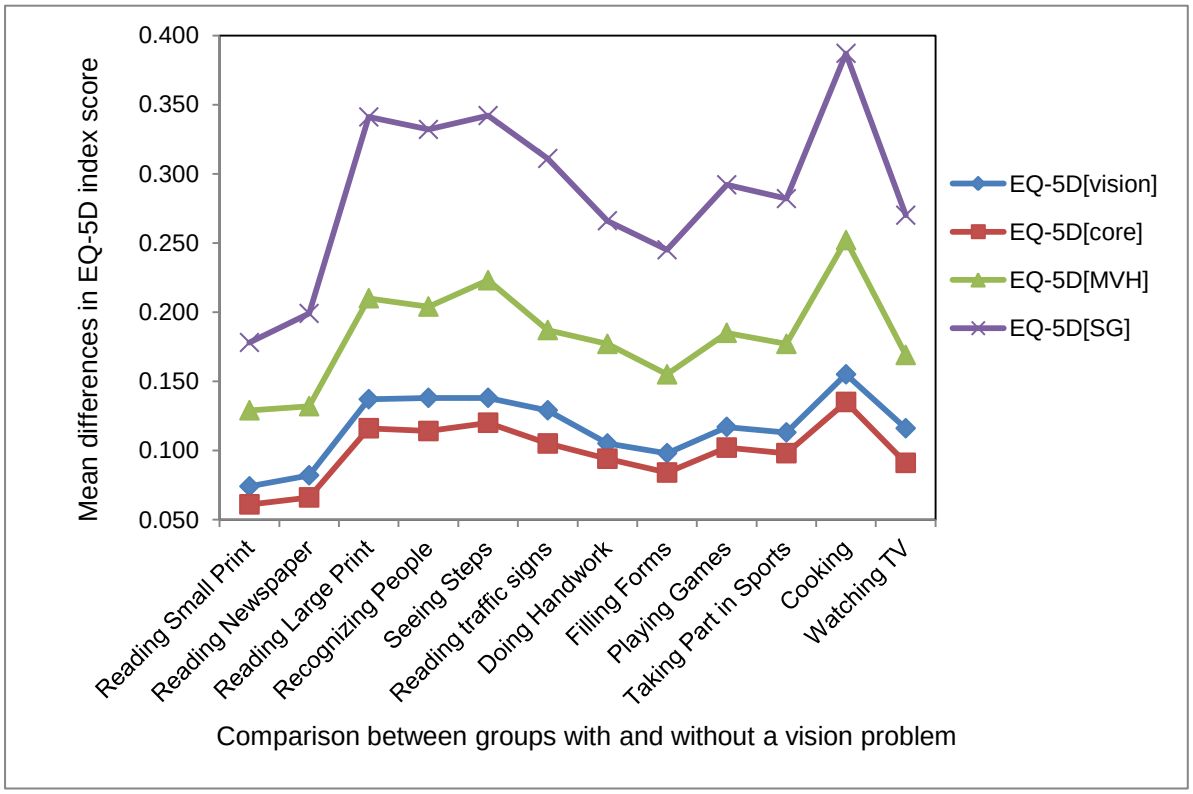
MVH, Measurement and Valuation of Health study; SG, Singapore; VI, visual impairment.

Figure 6.2 Adjusted mean differences in EQ-5D index scores between different VI groups



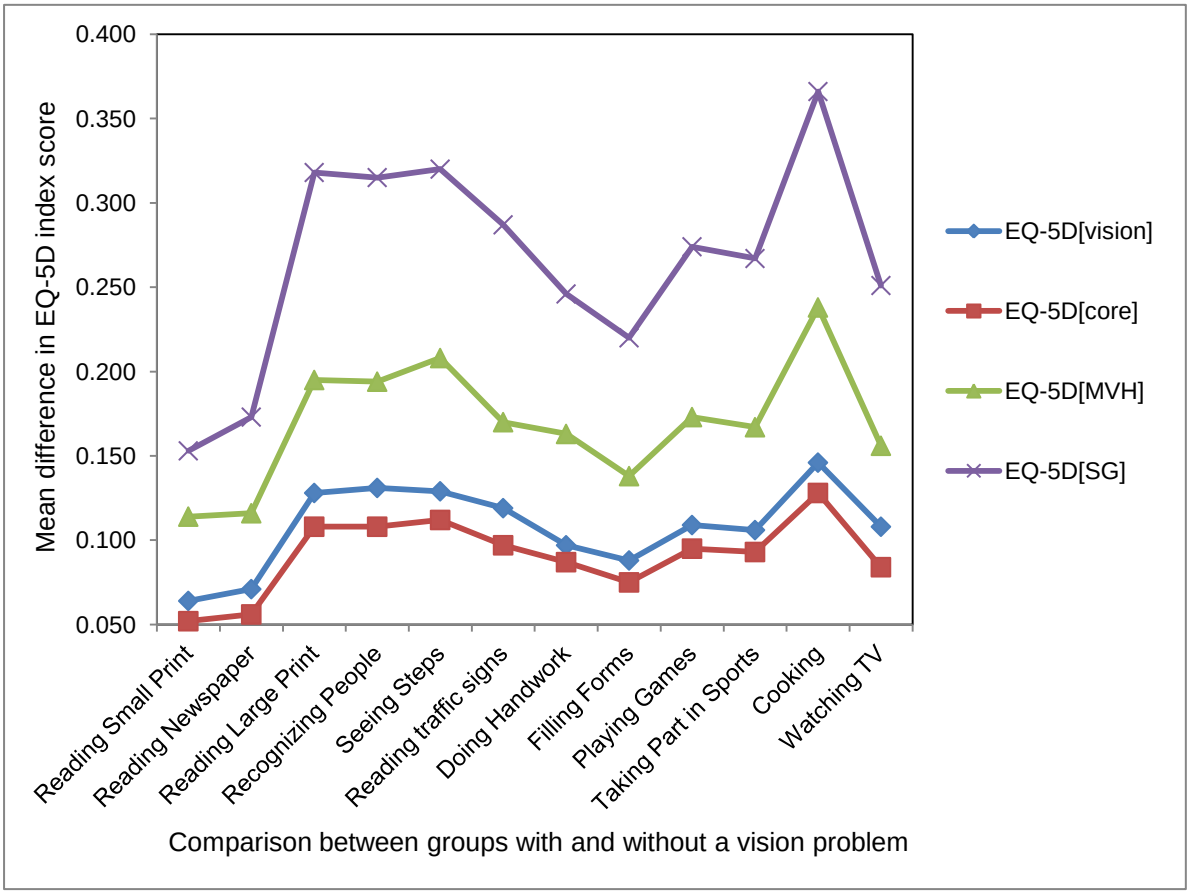
MVH, Measurement and Valuation of Health study; SG, Singapore; VI, visual impairment.

Figure 6.3 Unadjusted mean differences in EQ-5D index scores between groups with and without a vision problem assessed by the VF-14



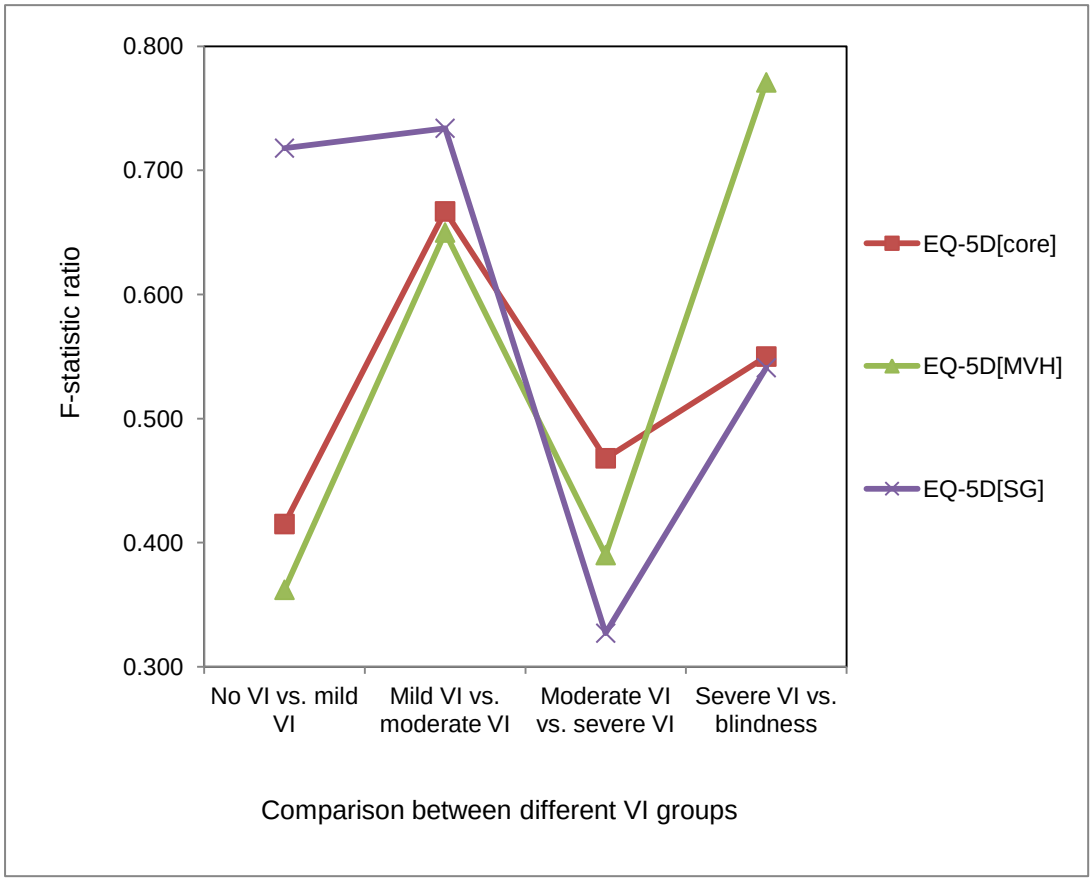
MVH, Measurement and Valuation of Health study; SG, Singapore.

Figure 6.4 Adjusted mean differences in EQ-5D index scores between groups with and without a vision problem assessed by the VF-14



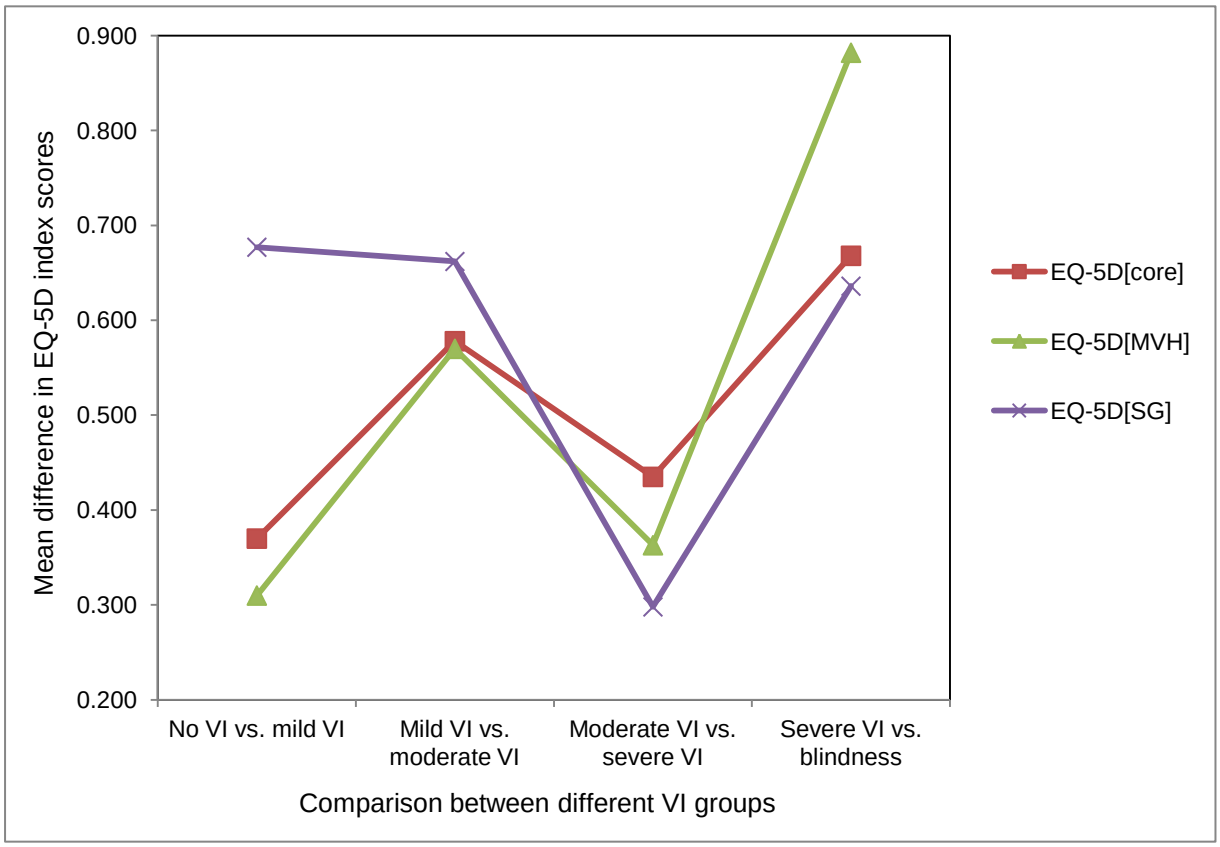
MVH, Measurement and Valuation of Health study; SG, Singapore; VI, visual impairment.

Figure 6.5 F-statistic ratios of unadjusted mean difference in EQ-5D index scores between different visual impairment groups



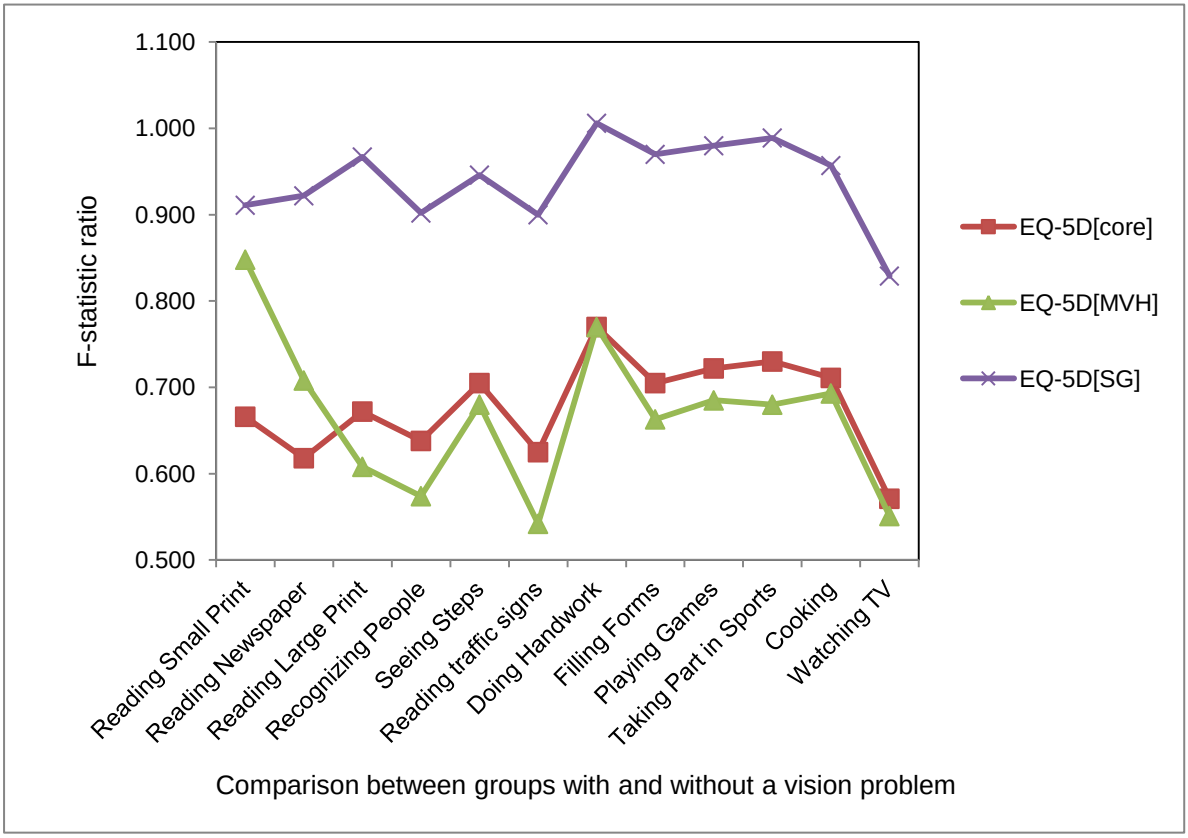
MVH, Measurement and Valuation of Health study; SG, Singapore; VI, visual impairment.

Figure 6.6 F-statistic ratio of adjusted mean difference in EQ-5D index scores between different VI groups



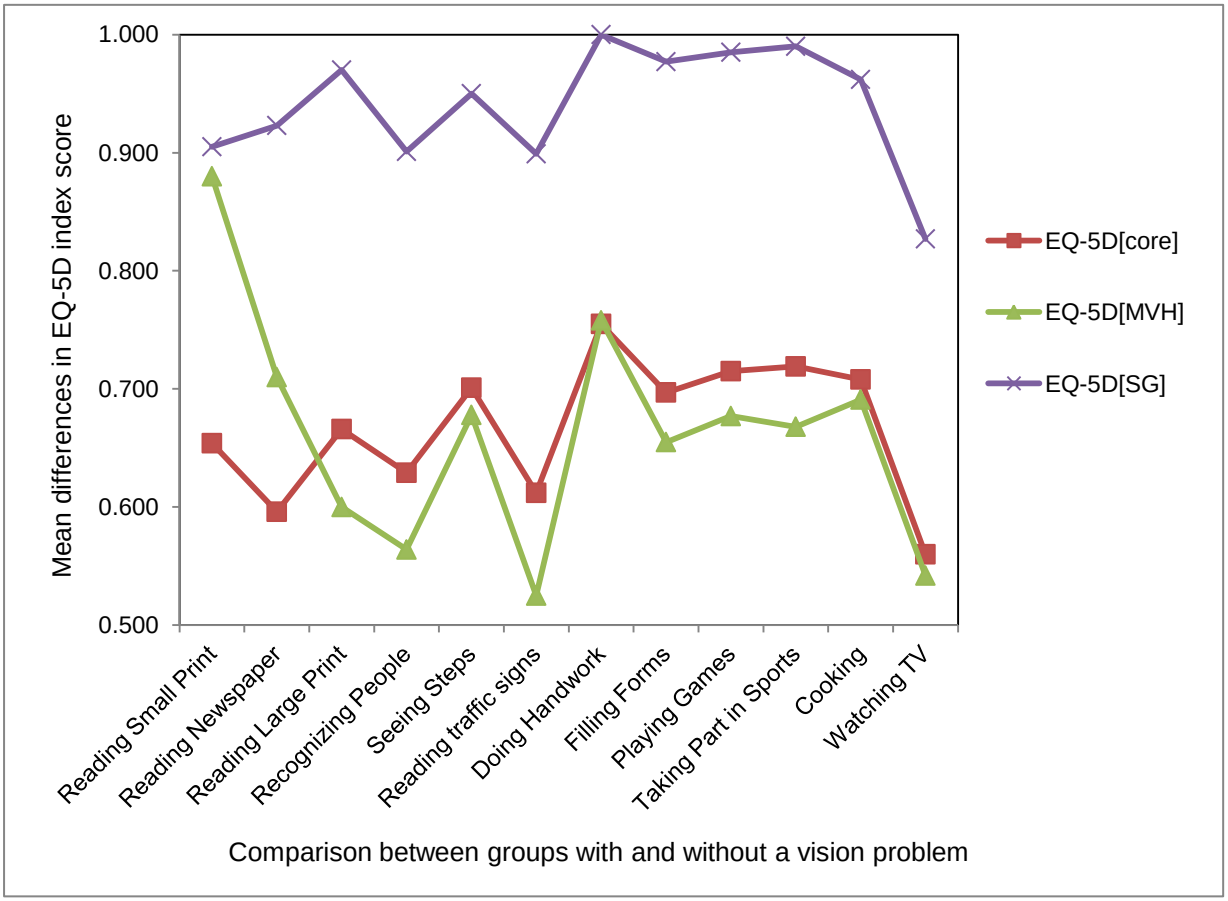
MVH, Measurement and Valuation of Health study; SG, Singapore; VI, visual impairment.

Figure 6.7 F-statistic ratios of unadjusted mean differences in EQ-5D index scores between groups with and without a vision problem assessed by the VF-14



MVH, Measurement and Valuation of Health study; SG, Singapore; VI, visual impairment.

Figure 6.8 F-statistic ratio of adjusted mean differences in EQ-5D index scores between groups with and without a vision problem assessed by the VF-14



MVH, Measurement and Valuation of Health study; SG, Singapore; VI, visual impairment.

6.4 Discussion

In this study, we found that the vision 'bolt-on' EQ-5D index score was more discriminative than the standard EQ-5D index score to different levels of visual problems. To the best of our knowledge, this is the first empirical study showing that a 'bolt-on' EQ-5D index score had higher discriminatory power than the standard EQ-5D index score. A previous study found that a cognition 'bolt-on' item might increase the sensitivity of the EQ-5D to change (or responsiveness) in the elderly population (Arrons and Krabbe, 2011). However, the preference-based EQ-5D index score was not assessed in that study. Hence, our study provided the first evidence for the value of the 'bolt-on' exercise in developing utility-based measures with better measurement properties.

The vision 'bolt-on' EQ-5D exhibited a larger difference than the standard EQ-5D in 14 of 16 comparisons of groups known to differ in vision status, suggesting that it would demonstrate greater gains than the latter for interventions that can improve vision acuity or function. Although the advantage in utility gains as indicated by adjusted mean absolute differences was small, it may still increase the chance of showing positive results in economic evaluation studies. For example, the utility gains of the EQ-5D[vision] and EQ-5D[core] were only between 0.01 and 0.03. If a new intervention can improve mildly impaired vision to normal vision and maintain it for 10 years, the incremental gains in QALYs for an individual treated by the intervention as compared to the usual care which can only maintain the current vision would be 0.48 and 0.30 based on the vision 'bolt-on' and standard EQ-5D, respectively,

according to our study. Assuming the incremental costs for the intervention as compared to usual care are $15,000, the point estimate of the incremental cost-effectiveness ratio (ICER) based on the 'bolt-on' and standard EQ-5D would be $31,250/QALY and $50,000/QALY, respectively. If the decision maker's willingness-to-pay threshold is $40,000/QALY, the use of the two index scores would lead to completely different conclusions. Therefore, the seemingly small advantage of the vision 'bolt-on' EQ-5D over the standard EQ-5D in economic evaluations should not be underestimated.

It should be noted that the 'bolt-on' index score may not always be advantageous to the standard EQ-5D index score in economic evaluations. In comparison of the EQ-5D[MVH, EQ-5D[SG] and EQ-5D[vision], the vision 'bolt-on' EQ-5D was not superior to the standard EQ-5D in generating larger between-group differences when the UK and Singapore value sets were used. An obvious reason for this result is the much wider ranges of the UK and Singapore value sets (Table 4.1). However, the result remained the same even after the two value sets were rescaled to the range of the vision 'bolt-on' value set. Therefore, the non-superiority of the vision 'bolt-on' system must have to do with the different ways in which those value sets were estimated. The design of the MVH, Singapore, and vision 'bolt-on' valuation studies differed in many important aspects such as target population, valuation procedure, and modeling strategy. Those have been shown to affect valuation of EQ-5D health states (Johnson et al., 2005; Rand-Hendriksen et al., 2012; Wang et al., 2014). Hence, an important implication of this result is that a 'bolt-on' EQ-5D might not necessarily result

in more positive cost-effectiveness outcomes than the standard EQ-5D when used in economic evaluations. How to increase the sensitivity of a 'bolt-on' system from its core system then? Our study suggests that one way to do it might be to estimate the value set of the new system using the same study protocol for the core system. Moreover, in two comparisons of individuals with different levels of VI, the absolute difference quantified by EQ-5D[vision] and EQ-5D[core] differed by only 0.002, with the standard EQ-5D being the more discriminative one. Although the difference is too small to affect the outcomes of economic evaluations, this result suggests that the vision 'bolt-on' item may not always increase the discriminatory power of the index score, especially when the difference between the groups and the sample size of the groups are both small. Despite this result, the 'bolt-on' EQ-5D is the first choice for use in economic evaluations since it is not disadvantaged in any condition.

Our study suggests that the 'bolt-on' index score would be more discriminative than the standard EQ-5D index score when they are used in studies aiming to detect statistically significant difference. Based on the F-statistic ratios, the 'bolt-on' index score is more likely than the standard EQ-5D index score (EQ-5D[MVH], EQ-5D[SG], and EQ-5D[core]) to show statistically significant results, which means a smaller sample size is needed when the 'bolt-on' index substitutes the standard EQ-5D index as the primary outcome measure in a clinical trial. This advantage of the 'bolt-on' index score was present in all the known-groups comparisons, including the two comparisons where the standard EQ-5D index score

demonstrated a lager absolute mean difference. This is not surprising as the F-statistic is a function of both the mean difference between groups and the standard deviation of the index scores (Fayers and Machin et al., 2000). When the mean difference is relatively small, a relatively higher F-statistic value is still possible if the corresponding standard deviation is small. The standard deviation of the 'bolt-on' index score was smaller than that for the standard EQ-5D index score for almost all of the comparison groups in this study. As the two indices use the common scale anchored by 0 (dead) and 1 (full health), this result means the 'bolt-on' index score could provide measurements with less error or higher reliability for the comparison groups. The higher F-statistic values suggest that, not only the vision 'bolt-on' item captured unique difference between known groups, it also meaningfully impacted on the index score. The F-statistic ratios also suggest that the advantage of the 'bolt-on' index score to the standard EQ-5D index score is greater in discriminating between different levels of VI than vision problems. This could be due to the fact that certain standard EQ-5D items such as the usual activities and the VF-14 captured some common information. As a result, the added value of the vision item to the EQ-5D is less when the target of measurement is defined by the VF-14. Taken all together, our study suggested that it would be more advantageous to use the vision 'bolt-on' EQ-5D than the standard EQ-5D in hypothesis-testing studies. This is good news as the performance of the standard EQ-5D in visual disorder was found to be mixed (Tosh et al., 2012).

The main limitation of this study is the use of experimental value sets which were estimated using a relatively small general population sample. There is currently no an official 'bolt-on' value set. Therefore, what we showed in the study is just the potential of the vision 'bolt-on' item in empirical studies, and the utility values reported in this paper should not be used in any formal economic evaluation. Secondly, it should be noted that discriminatory power is sensitivity to difference but not sensitivity to change or responsiveness, although higher discriminatory power may be a sign of better responsiveness. Hence, future studies are needed to assess the relative sensitivity of the 'bolt-on' and standard EQ-5D in interventional studies. Thirdly, this study was based on observation of a vision 'bolt-on' item in Asians with and without vision problems. Hence, the study findings might not be generalizable to other populations or 'bolt-on' items. Nevertheless, this study is well powered by a large sample of individuals and it has provided the first information about the potential of the 'bolt-on' exercise in the real world. Lastly, the "bolt-on" EQ-5D questionnaire only differs from the standard EQ-5D questionnaire by 1 question. Hence, its potential usefulness and clinical impact need to be explored further.

In conclusion, the vision 'bolt-on' EQ-5D appears to be more discriminative than the standard EQ-5D in measurement of vision problems. Future studies should investigate the extent to which the vision 'bolt-on' item can increase the sensitivity of the EQ-5D to vision change in interventional studies.

Chapter 7

Conclusions

7.1 Major findings

Five studies were conducted to determine the health and economic burden of visual impairment (VI) in Singapore. The major findings of these studies are as follows:

1. VI imposes considerable direct medical costs to the healthcare system now and in the next few decades in Singapore. AMD has the largest direct medical costs in both the individual and population levels, compared with the cataract, glaucoma, and diabetic retinopathy (DR).

2. VI also causes considerable out-of-pocket (OOP) expenditure and productivity loss in Singapore. Outpatient service is the main cause of medical service utilization and OOP expenditure. The productivity loss of caregivers is higher than that of the patients.

3. VI exerts substantial health burden in all three Asian ethnicities in Singapore. VI has a significant impact on health-related quality of life (HRQOL) and the health burden of VI measured by quality-adjusted life years (QALYs) per 100,000 people is higher than that of other health conditions.

4. The relative effect size of visual acuity (VA) in better-seeing and worse-seeing eye on the overall health utility is mediated by age and socio-economic status. VA in the better-seeing eye has a larger effect than VA in the worse-seeing eye only in those old (>65 years) and in low SES. Therefore, considering VA in the better-seeing eye alone in the HRQOL research of vision problems is suboptimal.

5. The vision ‘bolt-on’ EQ-5D seems to be more discriminative than the standard EQ-5D in the measurement of vision problems.

7.2 Contributions

The main contributions of the thesis to understanding the economic costs and health burden in Singapore are summarized as follows:

1. The economic burden and health burden of VI provide a comprehensive picture of the disease burden of VI in Singapore. The findings provide useful information for health professionals and policy makers to design and implement appropriate programs and strategies to prevent VI and reduce the disease burden of VI. Meanwhile, findings about the impact of VI on the health utilities and costs of VI could also be used in future cost-utility analysis of eye disease interventions.

2. The effect of VA in the better-seeing and worse-seeing eye on health utility in visually impaired individuals provides useful information for future the HRQOL research of vision problems. VA in the worse-seeing eye may be a more valuable measure in the HRQOL research of vision problems, compared with VA in the better-seeing eye.

3. The vision ‘bolt-on’ EQ-5D shows better discriminative power than the standard EQ-5D in the measurement of vision problems. The finding supports further development and testing of the vision ‘bolt-on’ EQ-5D in the cost-utility analysis of interventions for vision problems.

7.3 Future studies

New research questions from the findings and limitations in the studies are as follows:

1. Future studies need to estimate the direct medical costs of VI occurred in the medical centers apart from Singapore National Eye Center;
2. Future studies need to estimate the OOP expenditure and productivity loss of VI using more reliable data and more representative sample of individuals without VI as the control group.
3. Future studies need to study the impact of more health conditions on health utilities and compare it with VI in Singapore.
4. Future studies need to assess the effect of VA measures based on VA in the better-seeing and worse-seeing eye on utility measure in populations other than Asians.
5. Future studies need to build up an official 'bolt-on' value set based on the Singapore general population and assess the sensitivity of the 'bolt-on' EQ-5D to change or responsiveness in interventional studies.

Bibliography

Abe RY, Gracitelli CP, Diniz-Filho A, et al. Frequency Doubling Technology Perimetry and Changes in Quality of Life of Glaucoma Patients: A Longitudinal Study. American journal of ophthalmology. 2015; 160: 114-22 e1.

Alam K, Mahal A. Economic impacts of health shocks on households in low and middle income countries: a review of the literature. Globalization and health. 2014; 10: 21.

Ang M, Fenwick E, Wong TY, et al. Utility of EQ-5D to assess patients undergoing cataract surgery. Optometry and vision science: official publication of the American Academy of Optometry. 2013; 90: 861-6.

Ansah JP, De Korne D, Bayer S, et al. Future requirements for and supply of ophthalmologists for an aging population in Singapore. Hum Resour Health. 2015; 13: 86.

Arrons A, Krabbe P. Considering cognition as a bolt-on dimension for the EQ-5D. Discussion paper in the 28th Scientific Plenary Meeting of the EuroQol Group, Oxford, September 2011.

Aspinall PA, Johnson ZK, Azuara-Blanco A, et al. Evaluation of quality of life and priorities of patients with glaucoma. Investigative ophthalmology & visual science. 2008; 49: 1907–15.

Au Eong KG, Chan EW, Luo N, et al. Validity of EuroQOL-5D, time trade-off, and standard gamble for age-related macular degeneration in the Singapore population. Eye. 2012; 26: 379-88.

Awan H, Malik SM, Khan NU. The economic burden of blindness in Pakistan: a socio-economic and policy imperative for poverty reduction strategies. Indian journal of ophthalmology. 2012; 60: 358-64.

Baasanhu J, Johnson GJ, Burendei G, et al. Prevalence and causes of blindness and visual impairment in Mongolia: a survey of populations aged 40 years and older. Bulletin of the world health organization 1994; 72: 771– 6.

Bagust A, Beale S. Modelling EuroQol related health-related utility values for diabetic complications from CODE-2 data. Health Economics. 2005; 14: 217–30.

Bergner M, Bobbit R, Carter W, Gilson B. The Sickness Impact Profile: Development and final revision of a health status measure. Medical care. 1981; 8: 787–805.

Blind American Foundation of the Blind. Interpreting Bureau of Labor Statistics Employment Data. 2014.

Bonastre J, Le Pen C, Soubrane G, et al. The burden of age-related macular degeneration: results of a cohort study in two French referral centres. PharmacoEconomics. 2003; 21: 181-90.

Bourne R, Price H, Stevens G. Global burden of visual impairment and blindness. Archives of

ophthalmology. 2012; 130: 645-7.

Bourne RR, Stevens GA, White RA, et al. Causes of vision loss worldwide, 1990-2010: a systematic analysis. The lancet global health. 2013; 1: e339-49.

Bowling A. Health-related quality of life: a discussion of the concept, its use and measurement background: the quality of life. Presented to the adapting to change core course, September 1999. http://info.worldbank.org/etools/docs/library/48475/m2s5bowling.pdf. Accessed on Sep 25th, 2015

Bramley T, Peeples P, Walt JG, et al. Impact of vision loss on costs and outcomes in medicare beneficiaries with glaucoma. Archives of ophthalmology. 2008; 126: 849-56.

Bravo Vergel Y, Sculpher M. Quality-adjusted life years. Practical neurology. 2008; 8: 175-82.

Brazier J, Usherwood T, Harper R, et al. Deriving a preference-based single index from the UK SF-36 Health Survey. Journal of clinical epidemiology. 1998; 51: 1115-28.

Brazier, J. The SF-36 Health Survey Questionniare – a tool for economists. Heath economics.1993; 2: 213-15.

Bressler NM, Chang TS, Suner IJ, et al. Vision-related function after ranibizumab treatment by better- or worse-seeing eye: clinical trial results from MARINA and ANCHOR. Ophthalmology. 2010; 117: 747-56 e4.

Brezin AP, Lafuma A, Fagnani F, et al. Prevalence and burden of self-reported blindness and low vision for individuals living in institutions: a nationwide survey. Health and quality of life outcomes. 2005; 3: 27.

Brezin AP, Lafuma A, Fagnani F, et al. Prevalence and burden of self-reported blindness, low vision, and visual impairment in the French community: a nationwide survey. Archives of ophthalmology. 2005; 123: 1117–24.

Brooks R. EuroQol: the current state of play. Health Policy. 1996; 37: 53-72.

Brown MM, Brown GC, Sharma S, et al. A utility analysis correlation with visual acuity: methodologies and vision in the better and poorer eyes. International ophthalmology. 2001; 24: 123-7.

Brown MM, Brown GC, Sharma S, et al. Utility values and diabetic retinopathy. The American journal of ophthalmology. 1999; 128: 324–30.

Browne J, Jamiesin L, Lewsey J, et al. Patient Reported Outcome Measures (PROMs) in Elective Surgery: Report to the Department of Health. Available at https://www.lshtm.ac.uk/php/departmentofhealthservicesresearchandpolicy/assets/proms_report_12_dec_07.pdf. Accessed on Sep 10th, 2015:

Buhrmann R (2007). "Foundations for a Canadian vision health strategy: towards preventing avoidable blindness and promoting vision health. The National Coalition for Vision Health." Available at: http://www.visionhealth.ca. Accessed on Sep 25th, 2015

Buhrmann R HW, Beardmore, MA. Foundations for a Canadian vision health strategy: towards preventing avoidable blindness and promoting vision health. The National Coalition for Vision Health. Available at: http://wwwvisionhealthca. 2007. Accessed on Aug 20th, 2015

Busbee BG, Brown MM, Brown GC, et al. Cost-utility analysis of cataract surgery in the second eye. Ophthalmology. 2003; 110: 2310-7.

Cantor LB, Katz LJ, Cheng JW, et al. Economic evaluation of medication, laser trabeculoplasty and filtering surgeries in treating patients with glaucoma in the US. Current medical research and opinion. 2008; 24: 2905-18.

Carpenter A, Islam MM, Yen L, et al. Affordability of out-of-pocket health care expenses among older Australians. Health policy. 2015; 119: 907-14.

Castells X, Comas M, Alonso J, et al. In a randomized controlled trial, cataract surgery in both eyes increased benefits compared to surgery in one eye only. Journal of clinical epidemiology. 2006; 59: 201-07.

Chan EW, Chiang PP, Wong TY, et al. Impact of glaucoma severity and laterality on vision-specific functioning: the Singapore Malay eye study. Investigative ophthalmology & visual science. 2013; 54: 1169-75.

Chen FK, Agelis LE, Peh KK, et al. Factors Contributing to Discrepancy Between Visual Acuity Fractions Derived From a Snellen Chart and Letter Scores on the Early Treatment Diabetic Retinopathy Study Chart. Asia Pac J Ophthalmol. 2014; 3: 277-85.

Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. Lancet. 2010; 376: 124-36.

Chia EM, Mitchell P, Rochtchina E, et al. Unilateral visual impairment and health related quality of life: the Blue Mountains Eye Study. The British journal of ophthalmology. 2003; 87: 392-5.

Chiang PP, Marella M, Ormsby G, et al. Critical issues in implementing low vision care in the Asia-Pacific region. Indian journal of ophthalmology. 2012; 60: 456-9.

Chiang PP, Fenwick E, Marella M, et al. Validation and reliability of the VF-14 questionnaire in a German population. Investigative ophthalmology & visual science. 2011; 52: 8919-26.

Chiang PP, Zheng Y, Wong TY, et al. Vision impairment and major causes of vision loss impacts on vision-specific functioning independent of socioeconomic factors. Ophthalmology. 2013; 120: 415-22.

Choi S. Out-of-pocket expenditures and the financial burden of healthcare among older adults: by nativity and length of residence in the United States. J Gerontol Soc Work. 2015; 58: 149-70.

Clarke P, Gray A, Legood R, et al. The impact of diabetes-related complications on healthcare costs: results from the United Kingdom Prospective Diabetes Study (UKPDS Study No. 65). Diabetic Medicine. 2003; 20: 442–50.

Congdon NG, Friedman DS, Lietman T. Important causes of visual impairment in the world today. Jama. 2003; 290: 2057-60.

Conner-Spady BL, Sanmugasunderam S, Courtright P, et al. The prioritization of patients on waiting lists for cataract surgery: validation of the Western Canada waiting list project cataract priority criteria tool. Ophthalmic Epidemiology. 2005; 12: 81–90.

Corrieri S, Heider D, Matschinger H, et al. Income-, education- and gender-related inequalities in out-of-pocket health-care payments for 65+ patients - a systematic review. International journal for equity in health. 2010; 9: 20.

Cruess AF, Gordon KD, Bellan L, et al. The cost of vision loss in Canada. 2. Results. Canadian journal of ophthalmology. 2011; 46: 315–18.

Dandona L, Dandona R, Srinivas M, et al. Blindness in the Indian state of Andhra Pradesh. Investigative ophthalmology & visual science. 2001; 42: 908 –16.

Dandona L, Dandona R. What is the global burden of visual impairment? BMC medicine. 2006; 4: 6.

Department of Statistics MoTaI, Republic of Singapore. Census of Population 2010 Statistical Release1: Demographic Characteristics, Education, Language and Religion. 2011.

Department of Statistics, Republic of Singapore. Available at: http://www.singstat.gov.sg/statistics/browse-by-theme/household-income-tables. Accessed on March 16th, 2016.

Desai P, Reidy A, Minassian DC, et al. Gains from cataract surgery: visual function and quality of life. The British journal of ophthalmology. 1996; 80: 868-73.

Development of Singapore Labour Force Survey. Available at https://statsoecdorg/Indexaspx?DataSetCode=LFS_SEXAGE_I_R#. Accessed on Sep 24th, 2015.

Dilokthornsakul P, Chaiyakunapruk N, Ruamviboonsuk P, et al. Health resource utilization and the economic burden of patients with wet age-related macular degeneration in Thailand. International journal of ophthalmology. 2014; 7: 145-51.

Dolan P. Modeling valuations for EuroQol health states. Medical care. 1997; 35: 1095-108.

Drummond MF. Methods for the economic evaluation of health care programmes. 3rd edition. Oxford: Oxford University Press, 2005.

Access Economics. Future sight loss UK: the economic impact of partial sight and blindness in the UK adult population, executive summary. 2009.

Elliott DB, Patla AE, Furniss M, et al. Improvements in clinical and functional vision and quality of life after second eye cataract surgery. Optometry and vision science : official publication of the American Academy of Optometry. 2000; 77: 13-24.

Fayers PM, Machin D. Quality of life: Assessment, Analysis and Interpretation. Chichester: John Wiley & Sons, 2000.

Feeny D, Wu L, Eng K. Comparing short form 6D, standard gamble, and Health Utilities Index Mark 2 and Mark 3 utility scores: results from total hip arthroplasty patients. Qual Life Res. 2004; 13: 1659-70.

Finger RP, Fenwick E, Hirneiss CW, et al. Visual impairment as a function of visual acuity in both eyes and its impact on patient reported preferences. PloS one. 2013; 8: e81042.

Finger RP, Guymer RH, Gillies MC, et al. The impact of anti-vascular endothelial growth factor treatment on quality of life in neovascular age-related macular degeneration. Ophthalmology. 2014; 121: 1246-51.

Finkelstein EA, Fiebelkorn IC, and Wang G, National Medical Spending Attributable to Overweight and Obesity: How Much and Who's Paying? Health Affair. 2003; 22: W219- W26.

Fletcher A, Vijaykumar V, Selvaraj S, et al. The Madurai Intraocular Lens Study. III: Visual functioning and quality of life outcomes. American journal of ophthalmology. 1998; 125: 26-35.

Foong AW, Saw SM, Loo JL, et al. Rationale and methodology for a population-based study of eye diseases in Malay people: The Singapore Malay eye study (SiMES). Ophthalmic epidemiology. 2007; 14: 25-35.

Foong AWP, Saw SM, Loo JL, et al. Rationale and methodology for a population-based study of eye diseases in Malay people: The Singapore Malay eye study (SiMES). Ophthalmic epidemiology. 2007; 14: 25-35.

Frick KD, Walt JG, Chiang TH, et al. Direct costs of blindness experienced by patients enrolled in managed care. Ophthalmology. 2008; 115: 11–17.

Gemenetzi M, Yang Y, Lotery AJ. Current concepts on primary open-angle glaucoma genetics: a contribution to disease pathophysiology and future treatment. Eye. 2012; 26: 355-69.

Gold MR, Siegel JE, Russell LB, et al. Cost effectiveness in Health and Medicine. New York:

Oxford University Press, 1996.

Goldzweig CL, Rowe S, Wenger NS, et al. Preventing and managing visual disability in primary care: clinical applications. Jama. 2004; 291: 1497–502.

Gordois A, Cutler H, Pezzullo L, et al. An estimation of the worldwide economic and health burden of visual impairment. Global public health. 2012; 7: 465-81.

Gracitelli CPB, Abe RY, Tatham AJ, et al. Association Between Progressive Retinal Nerve Fiber Layer Loss and Longitudinal Change in Quality of Life in Glaucoma. Jama Ophthalmol. 2015; 133: 384-90.

Gunter MJ. The role of the ECHO model in outcomes research and clinical practice improvement. The American journal of managed care. 1999; 5: S217-24.

Happich M, Reitberger U, Breitscheidel L, et al. The economic burden of diabetic retinopathy in Germany in 2002. Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie. 2008; 246: 151-9.

Harwood RH, Foss AJ, Osborn F, et al. Falls and health status in elderly women following first eye cataract surgery: a randomised controlled trial. The British journal of ophthalmology. 2005; 89: 53–59.

Hodgson TA. Costs of Illness in Cost-Effectiveness Analysis: A Review of the Methodology. Pharmacoeconomics. 1994; 6: 536-52.

Hoeymans N, van Lindert H, Westert GP. The health status of the Dutch population as assessed by the EQ-6D. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2005; 14: 655-63.

Hunt SM, McKenna SP, McEwen J, et al. The Nottingham Health Profile: subjective health status and medical consultations. Social science & medicine Part A, Medical sociology. 1981; 15: 221-9.

Hyman L, Wu SY, Connell AM, et al, Barbados Eye Study Group. Prevalence and causes of visual impairment in The Barbados Eye Study. Ophthalmology. 2001; 108: 1751– 6.

International Federation on Aging. The high cost of low vision - the evidence on aging and the loss of sight. 2013.

Ivers R, Cumming R, Mitchell P. Poor vision and risk of falls and fractures in older Australians: the Blue Mountains Eye Study. New South Wales public health bulletin. 2002; 13: 8-10.

Ivers RQ, Cumming RG, Mitchell P, et al. Visual risk factors for hip fracture in older people. Journal of the American Geriatrics Society. 2003; 51: 356-63.

Iwase A, Araie M, Tomidokoro A, et al, Tajimi Study Group. Prevalence and causes of low vision and blindness in a Japanese adult population: the Tajimi Study. Ophthalmology 2006; 113: 1354–62.

James M, Turner DA, Broadbent DM, et al. Cost effectiveness analysis of screening for sight threatening diabetic eye disease. Bmj. 2000; 320: 1627-31.

Jampel HD. Glaucoma patients' assessment of their visual function and quality of life. Transactions of the American Ophthalmological Society. 2001; 99: 301-17.

Janssen B, Krabbe PFM, Lamers L, et al. The cognition dimension revisited: a detailed study on its added value and interaction with EQ-5D core dimensions. Discussion paper in the 30th Scientific Plenary Meeting of the EuroQol Group, Montréal, September 2013.

Javitt JC, Zhou Z, Willke RJ. Association between vision loss and higher medical care costs in Medicare beneficiaries costs are greater for those with progressive vision loss. Ophthalmology. 2007; 114: 238-45.

Jia H, Lubetkin EI. Trends in quality-adjusted life-years lost contributed by smoking and obesity. American journal of preventive medicine. 2010; 38: 138-44.

John Ansah DDK, Steffen Bayer, Pan Chong, Andrew Phua, Tiyagarajan Jayabaskar, Desmond Quek. Workforce planning for eye services in Singapore. Singapore Healthcare Management 2014. 2014; Available at http://www.singaporehealthcaremanagement.sg/Abstracts/Poster%20Exhibition/Documents/HR016%20-%20John%20P.%20Ansah%20(Pan%20Chong)_DUKE-NUS%20(SNEC).pdf.Accessed on Sep 24th, 2015

Johnraj MSP. Healthcare financing: how should Singapore's Ministry of Health shift costs from private pockets to the public purse. Case studies in public policy and public administration (Lee Kuan Yew School of Public Policy). 2013; http://lkyspp.nus.edu.sg/wp-content/uploads/2014/03/healthcare-financing-210314dlag.pdf Accessed on Sep 21th, 2015.

Johnson JA, Luo N, Shaw JW, et al. Valuations of EQ-5D health states: are the United States and United Kingdom different? Med Care. 2005; 43: 221-8.

Kannan R, Sreekumar PG, Hinton DR. Alpha crystallins in the retinal pigment epithelium and implications for the pathogenesis and treatment of age-related macular degeneration. Biochimica et biophysica acta. 2015.

Kaplan RM, Sieber WJ, Ganiats TG. The Quality of Well-Being Scale: Comparison of the interviewer-administered version with a self-administered questionnaire. Psychol Health. 1997; 12: 783-91.

Keeffe JE, Chou SL, Lamoureux EL. The cost of care for people with impaired vision in Australia. Archives of ophthalmoly. 2009; 127: 1377–81.

Kemp J. Is there a best outcome measurement for patients with asthma? Ann Allerg Asthma Im. 2006; 97: 432-39.

Khadka J, Huang J, Mollazadegan K, et al. Translation, cultural adaptation, and rasch analysis of the visual function (VF-14) questionnaire. Investigative ophthalmology & visual science. 2014; 55: 4413-20

Kim J, Kwak HW, Lee WK, et al. Impact of photodynamic therapy on quality of life of patients with age-related macular degeneration in Korea. Japanese journal of ophthalmology. 2010; 54: 325–30

King MT, Bell ML, Costa D, et al. The Quality of Life Questionnaire Core 30 (QLQ-C30) and Functional Assessment of Cancer-General (FACT-G) differ in responsiveness, relative efficiency, and therefore required sample size. Journal of clinical epidemiology. 2014; 67: 100-7.

Klein R, Klein BE, Linton KL. Prevalence of age-related maculopathy. The Beaver Dam Eye Study. Ophthalmology. 1992; 99: 933-43.

Kobelt G, Jonsson B, Bergstrom A, et al. Cost-effectiveness analysis in glaucoma: what drives utility? Results from a pilot study in Sweden. Acta ophthalmologica Scandinavica. 2006; 84: 363–71.

Kumar K, Singh A, Kumar S, et al. Socio-Economic Differentials in Impoverishment Effects of Out-of-Pocket Health Expenditure in China and India: Evidence from WHO SAGE. PloS one. 2015; 10: e0135051.

Lafuma A, Brezin A, Fagnani F, et al. Nonmedical economic consequences attributable to visual impairment: a nation-wide approach in France. The European journal of health economics. 2006; 7: 158–64.

Lamoureux EL, Chong E, Wang JJ, et al. Visual impairment, causes of vision loss, and falls: the Singapore Malay Eye Study. Investigative ophthalmology & visual science. 2008; 49: 528–33.

Lamoureux EL, Pesudovs K, Thumboo J, et al. An evaluation of the reliability and validity of the visual functioning questionnaire (VF-11) using Rasch analysis in an Asian population. Investigative ophthalmology & visual science. 2009; 50: 2607-13.

Lamoureux EL, Chong EW, Thumboo J, et al. Vision impairment, ocular conditions, and vision-specific function: the Singapore Malay Eye Study. Ophthalmology. 2008; 115:1973-81.

Lamoureux EL, Fenwick E, Moore K, et al. Impact of the severity of distance and near-vision impairment on depression and vision-specific quality of life in older people living in residential care. Investigative ophthalmology & visual science. 2009; 50:4103-9.

Lamoureux EL, Mitchell P, Rees G, et al. Impact of early and late age-related macular

degeneration on vision-specific functioning. The British journal of ophthalmology. 2011; 95:666-70.

Langelaan M, de Boer MR, van Nispen RM, et al. Impact of visual impairment on quality of life: a comparison with quality of life in the general population and with other chronic conditions. Ophthalmic epidemiology. 2007; 14: 119-26.

Lavanya R, Jeganathan VS, Zheng Y, et al. Methodology of the Singapore Indian Chinese Cohort (SICC) eye study: quantifying ethnic variations in the epidemiology of eye diseases in Asians. Ophthalmic epidemiology. 2009; 16: 325-36.

Lavanya R, Jeganathan VSE, Zheng YF, et al. Methodology of the Singapore Indian Chinese Cohort (SICC) Eye Study: Quantifying ethnic variations in the epidemiology of eye diseases in Asians. Ophthalmic epidemiology. 2009; 16: 325-36.

Lee CF, Ng R, Luo N, et al. The English and Chinese versions of the five-level EuroQoL Group's five-dimension questionnaire (EQ-5D) were valid and reliable and provided comparable scores in Asian breast cancer patients. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer. 2013; 21: 201-9.

Lee PP, Walt JG, Doyle JJ, et al. A multicenter, retrospective pilot study of resource use and costs associated with severity of disease in glaucoma. Archives of ophthalmology. 2006; 124: 12-9.

Lee YK, Nam HS, Chuang LH, et al. South Korean time trade-off values for EQ-5D health states: modeling with observed values for 101 health states. Value in health: the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2009; 12: 1187-93.

Li S, Xu J, He M, et al. A survey of blindness and cataract surgery in Doumen County, China. Ophthalmology. 1999; 106: 1602– 8.

Lien WD. Waiting times for new appointments at specialist outpatient clinics (soc) in restructured hospitals – orthopaedic surgery. Available at https://www.moh.gov.sg/content/dam/moh_web/Publications/Information%20Papers/2007/OP_Waiting%20Times_Orthopaedic%20Surgery-07.pdf. Accessed on Sep 25th, 2015.

Lim LS, Mitchell P, Seddon JM, et al. Age-related macular degeneration. Lancet. 2012; 379: 1728-38.

Lim MC, Gazzard G, Sim EL, et al. Direct costs of myopia in Singapore. Eye. 2009; 23: 1086-9.

Lin JC, Yu JH. Assessment of quality of life among Taiwanese patients with visual impairment. Journal of the Formosan Medical Association. 2012; 111: 572-9.

Lloyd A, Nafees B, Gavriel S. Health utility values associated with diabetic retinopathy. Diabetic medicine.2008; 25: 618–24.

Longworth L, Yang Y, Young T, et al. Use of generic and condition-specific measures of health-related quality of life in NICE decision-making: a systematic review, statistical modelling and survey. Health Technol Assess. 2014; 18: 1-224.

Lotery A, Xu X, Zlatava G, et al. Burden of illness, visual impairment and health resource utilisation of patients with neovascular age-related macular degeneration: results from the UK cohort of a five-country cross-sectional study. The British journal of ophthalmology 2007; 91:1303–7.

Lundstrom M, Stenevi U, Thorburn W. Quality of life after first- and second-eye cataract surgery: five-year data collected by the Swedish National Cataract Register. Journal of cataract and refractive surgery. 2001; 27: 1553-9.

Luo N, Chew LH, Fong KY, et al. Validity and reliability of the EQ-5D self-report questionnaire in Chinese-speaking patients with rheumatic diseases in Singapore. Annals of the Academy of Medicine, Singapore. 2003; 32: 685-90.

Luo N, Chew LH, Fong KY, et al. Validity and reliability of the EQ-5D self-report questionnaire in English-speaking Asian patients with rheumatic diseases in Singapore. Quality of life research: an international journal of quality of life aspects of treatment, care and rehabilitation. 2003; 12: 87-92.

Luo N, Johnson JA, Shaw JW, et al. Relative efficiency of the EQ-5D, HUI2, and HUI3 index scores in measuring health burden of chronic medical conditions in a population health survey in the United States. Med Care. 2009; 47: 53-60.

Luo N, Low S, Lau PN, et al. Is EQ-5D a valid quality of life instrument in patients with Parkinson's disease? A study in Singapore. Annals of the Academy of Medicine, Singapore. 2009; 38: 521-8.

Maberley D, Walker H, Koushik A, et al. Screening for diabetic retinopathy in James Bay, Ontario: a cost-effectiveness analysis. CMAJ: Canadian Medical Association journal = journal de l'Association medicale canadienne. 2003; 168: 160-4.

Mangione CM, Berry S, Spritzer K, et al. Identifying the content area for the 51-item National Eye Institute Visual Function Questionnaire: results from focus groups with visually impaired persons. Archives of ophthalmology. 1998; 116: 227-33.

Mangione CM, Lee PP, Gutierrez PR, et al. Development of the 25-item National Eye Institute Visual Function Questionnaire. Archives of ophthalmology. 2001; 119: 1050-8.

McClure TM, Choi D, Becker T, et al. The effect of visual impairment on vision-related quality of life in American Indian/Alaska Natives. Ophthalmic epidemiology. 2009; 16: 128-35.

Melse JM, Essink-Bot ML, Kramers PG, et al. A national burden of disease calculation: Dutch

disability-adjusted life-years. Dutch Burden of Disease Group. American journal of public health. 2000; 90: 1241-7.

Meng-Ting Wang KN, Shwu-Jiuan Sheu, Wei-Shi Yeh, Yu-Wen Lo, Wan-Ju Lee. Analysis of Excess Direct Medical Costs of Vision Impairment in Taiwan. Value in Health Regional Issue 2013; 2: 57-63.

Michon JJ, Lau J, Chan WS, et al. Prevalence of visual impairment, blindness, and cataract surgery in the Hong Kong elderly. The British Journal of Ophthalmology. 2002; 86: 133–9.

Miller LS, Zhang X, and Novotny T, et al. State Estimates of Medicaid Expenditures Attributable to Cigarette Smoking, Fiscal Year 1993. Public Health Reports. 1998; 113: 140-51.

Milne A, Johnson JA, Tennant M, et al., Measuring Health-Related Quality of Life for Patients with Diabetic Retinopathy. Rockville (MD), 2012.

Montemayor F, Sibley LM, Courtright P,et al. Contribution of multiple glaucoma medications to visual function and quality of life in patients with glaucoma. Canadian Journal of Ophthalmology. 2001; 36: 385–90.

Morse AR, Yatzkan E, Berberich B, et al. Acute care hospital utilization by patients with visual impairment. Archives of ophthalmology. 1999; 117: 943–9.

Mousa A, Al Ghamdi AH, Kalantan H, et al. Development and validation of an Arabic version of the Visual Functioning IndexVF-14 for cataract patients. Middle east African journal of ophthalmology. 2012; 19: 309-13.

Murray CJ, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012; 380: 2197-223.

Murray CJ. Quantifying the burden of disease: the technical basis for disability-adjusted life years. Bulletin of the World Health Organization. 1994; 72: 429-45.

Murthy GV, Gupta S, Ellwein LB, et al. A population-based eye survey of older adults in rural district of Rajasthan: I. Central vision impairment, blindness, and cataract surgery. Ophthalmology. 2001; 108: 679–85.

National Institute of Health and Care Excellence (NICE) (formerly the National Institute of Health and Clinical Excellence). NICE Guide to the Methods of Technology Appraisal. London: NICE; 2008.

Nease RF, Whitcup SM, Ellwein LB, et al. Utility-based estimates of the relative morbidity of visual impairment and angina. Ophthalmic epidemiology. 2000; 7: 169-85.

Nirmalan PK, Tielsch JM, Katz J, et al. Relationship between vision impairment and eye disease

to vision-specific quality of life and function in rural India: the Aravind Comprehensive Eye Survey. Investigative ophthalmology & visual science. 2005; 46: 2308-12.

Noran NH, Izzuna MG, Bulgiba AM, et al. Severity of Visual Impairment and Depression Among Elderly Malaysians. Asia-Pac J Public He. 2009; 21: 43-50.

O'Connor PM, Chou SL, Lamoureux EL, et al. Costs of vision impairment in childhood and youth: diary case studies. Optometry and vision science : official publication of the American Academy of Optometry. 2008; 85: 1106-9.

Organization for Economic Co-operation and Development (OECD). OECD Health Data 2001: A Comparative Analysis of 30 Countries, OECD, Paris, 2001, data sources, definitions an methods. Health statistics. 2001.

Organization for Economic Co-operation and Development (OECD). Health at a glance 2011. Available at http://wwwoecd-ilibraryorg/docserver/download/8111101ec054pdf?expires=1442977450&id=id&accname=guest&checksum=82BD6C5F49AEB97796A98BDFE5FB116D. Accessed on Sep 22th, 2015. 2011.

Ong SY, Cheung CY, Li X, et al. Visual impairment, age-related eye diseases, and cognitive function: the Singapore Malay Eye study. Archives of ophthalmology. 2012; 130: 895-900.

World Health Organization (WHO). World Health Statistics. http://wwwwhoint/gho/publications/world_health_statistics/en/. 2015; Access on Sep 13, 2015.

Pan CW, Chiang PP, Wong TY, et al. Ethnic differences in undercorrected refractive error in Asians. Optometry Vision Sci. 2014; 91:212-20.

Park HY, Ryu H, Kang HY, et al. Clinical and Economic Burden of Visual Impairment in an Aging Society of South Korea. Asia-Pacific journal of public health / Asia-Pacific Academic Consortium for Public Health. 2015; 27: 631-42.

Pascolini D, Mariotti SP. Global estimates of visual impairment: 2010. The British journal of ophthalmology. 2012; 96: 614-8.

Peter M. Fayers and David Machin. Quality of life. Second edition, 2007.

Phua HP, Chua AV, Ma S, et al. Singapore's burden of disease and injury 2004. Singapore medical journal. 2009; 50: 468-78.

Polack S, Alavi Y, Rachapalle Reddi S, et al. Utility values associated with diabetic retinopathy in Chennai, India. Ophthalmic epidemiology. 2015; 22: 20-7.

Polack S, Eusebio C, Fletcher A, et al. Visual impairment from cataract and health related quality of life: results from a case-control study in the Philippines. Ophthalmic Epidemiology. 2010; 17: 152–9.

Polack S, Eusebio C, Mathenge W, et al. The impact of cataract surgery on health related quality of life in Kenya, the Philippines, and Bangladesh. Ophthalmic epidemiology. 2010; 17: 387-99.

Polack S, Kuper H, Mathenge W, et al. Cataract visual impairment and quality of life in a Kenyan population. The British journal of ophthalmology. 2007; 91: 927-32.

Polack S, Kuper H, Wadud Z, et al A. Quality of life and visual impairment from cataract in Satkhira district, Bangladesh. The British journal of ophthalmology. 2008; 92: 1026–30.

Population trends, 2014; Department of Statistics, Ministry of Trade & Industry, Republic of Singapore; http://www.singstat.gov.sg/publications/publications-and-papers/population-and-population-structure/population-trends; Accessed on Sep 25th, 2015

Porz G, Scholl HP, Holz FG, et al. Methods for estimating personal costs of disease using retinal diseases as an example. Ophthalmology. 2010; 107: 216–20, 22.

Pullenayegum EM, Tarride JE, Xie F, et al. Analysis of health utility data when some subjects attain the upper bound of 1: are Tobit and CLAD models appropriate? Value Health. 2010; 13: 487-94.

Rahmani B, Tielsch JM, Katz J, et al. The cause-specific prevalence of visual impairment in an urban population. The Baltimore Eye Survey. Ophthalmology. 1996; 103: 1721-6.

Rand-Hendriksen K, Augestad LA, Dahl FA. A critical re-evaluation of the regression model specification in the US D1 EQ-5D value function. Population health metrics. 2012; 10: 2.

Reeder CE. Overview of pharmacoeconomics and pharmaceutical outcomes evaluations. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists. 1995; 52: S5-8.

Rein DB, Zhang P, Wirth KE, et al. The economic burden of major adult visual disorders in the United States. Archives of ophthalmology. 2006; 124: 1754-60.

Rein DB. Vision problems are a leading source of modifiable health expenditures. Investigative ophthalmology & visual science. 2013; 54: ORSF18-22.

Resnikoff S, Pascolini D, Etya'ale D, et al. Global data on visual impairment in the year 2002. Bulletin of the World Health Organization. 2004; 82: 844-51.

Roberts CB, Hiratsuka Y, Yamada M, et al. Economic cost of visual impairment in Japan. Archives of ophthalmology. 2010; 128: 766–71.

Ruiz-Moreno JM, Coco RM, Garcia-Arumi J, et al. Burden of illness of bilateral neovascular age-related macular degeneration in Spain. Current medical research and opinion. 2008; 24: 2103–11.

Saboo US, Amparo F, Abud TB, et al. Vision-Related Quality of Life in Patients with Ocular Graft-versus-Host Disease. Ophthalmology. 2015; 122: 1669-74.

Sach TH, Foss AJ, Gregson RM, et al. Falls and health status in elderly women following first eye cataract surgery: an economic evaluation conducted alongside a randomised controlled trial. The British journal of ophthalmology 2007; 91: 1675–1679

Sahel JA, Bandello F, Augustin A, et al. Health-related quality of life and utility in patients with age-related macular degeneration. Archives of ophthalmology. 2007; 125: 945-51.

Sapkota YD, Pokharel GP, Nirmalan PK, et al. Prevalence of blindness and cataract surgery in Gandaki Zone, Nepal. The British journal of ophthalmology. 2006; 90: 411– 6

Singapore Association of the Visually Handicapped (SAVH). SAVH Annual Report 2013/2014. 2013/2014.

Schmier JK, Covert DW, Matthews GP, et al. Impact of visual impairment on service and device use by individuals with diabetic retinopathy. Disability and rehabilitation. 2009; 31: 659–65.

Schmier JK, Halpern MT, Covert D, et al. Impact of visual impairment on use of caregiving by individuals with age-related macular degeneration. Retina. 2006; 26: 1056–62

Senra H, Barbosa F, Ferreira P, et al. Psychologic adjustment to irreversible vision loss in adults: a systematic review. Ophthalmology. 2015; 122: 851-61.

Senra H, Oliveira RA, Leal I. From self-awareness to self-identification with visual impairment: a qualitative study with working age adults at a rehabilitation setting. Clinical rehabilitation. 2011; 25: 1140-51.

Shamanna BR, Dandona L, Rao GN. Economic burden of blindness in India. Indian journal of ophthalmology. 1998; 46: 169-72.

Shaw JW, Johnson JA, Coons SJ. US valuation of the EQ-5D health states: development and testing of the D1 valuation model. Medical care. 2005; 43: 203-20.

Shepard DS, Undurraga EA, Halasa YA. Economic and disease burden of dengue in Southeast Asia. PLoS neglected tropical diseases. 2013; 7: e2055.

Singapore DoS. Report on the household expenditure survey 2012/13. http://wwwsingstatgovsg/publications/household-expenditure-survey Accessed on Sep 21th, 2015. 2014.

Smith DH, Johnson ES, Russell A. Lower visual acuity predicts worse utility values among patients with type 2 diabetes. Quality of life research. 2008; 17: 1277-84.

Sommer A, Tielsch JM, Katz J, et al. Racial differences in the cause-specific prevalence of blindness in east Baltimore. New England journal of medicine. 1991; 325: 1412–7.

Soubrane G, Cruess A, Lotery A, et al. Burden and health care resource utilization in neovascular age-related macular degeneration: findings of a multicountry study. Archives of ophthalmology. 2007; 125: 1249–54.

Steinberg EP, Tielsch JM, Schein OD et al. The VF-14: an index of functional impairment in cataract patients. Archives of Ophthalmology. 1994; 112: 630-38

Stevens GA., White RA, Flaxman SR, et al. Global prevalence of vision impairment and blindness: magnitude and temporal trends, 1990-2010. Ophthalmology 120(12): 2377-2384.

Stock MV, Vollman DE, Baze EF, et al. Functional Visual Improvement After Cataract Surgery in Eyes With Age-Related Macular Degeneration: Results of the Ophthalmic Surgical Outcomes Data Project. Investigative ophthalmology & visual science. 2015; 56: 2536-40.

Sullivan PW, Ghushchyan V. Preference-Based EQ-5D index scores for chronic conditions in the United States. Medical decision making: an international journal of the Society for Medical Decision Making. 2006; 26: 410-20.

Sullivan PW, Slejko JF, Sculpher MJ, et al. Catalogue of EQ-5D scores for the United Kingdom. Medical decision making: an international journal of the Society for Medical Decision Making. 2011; 31: 800-4.

Swinburn P, Lloyd A, Boye KS, et al. Development of a disease-specific version of the EQ-5D-5L for use in patients suffering from psoriasis: lessons learned from a feasibility study in the UK. Value Health. 2013; 16: 1156-62.

Takahashi GI, Otori Y, Urashima M, et al. Evaluation of Quality of Life in Japanese Glaucoma Patients and its Relationship With Visual Function. Journal of glaucoma. 2015.

Tarricone R: Cost-of-illness analysis: What room in health economics? Health policy. 2006; 77:51-63.

Taylor DH, Sloan FA, How Much Do Persons with Alzheimer's Disease Cost Medicare? Journal of the American Geriatrics Society. 2000; 48: 639-46.

Taylor HR, Pezzullo ML, Keeffe JE. The economic impact and cost of visual impairment in Australia. The British journal of ophthalmology. 2006; 90: 272-5.

Taylor HR. LXIII Edward Jackson Memorial Lecture: Eye care: dollars and sense. American journal of ophthalmology. 2007; 143: 1-8.

Thygesen J, Aagren M, Arnavielle S, et al. Late-stage, primary open-angle glaucoma in Europe: social and health care maintenance costs and quality of life of patients from 4 countries. Current

medical research and opinion. 2008; 24: 1763-70.

Tielsch JM, Sommer A, Witt K, et al, Baltimore Eye Survey Research Group. Blindness and visual impairment in an American urban population: the Baltimore Eye Survey. Archive of ophthalmology. 1990; 108: 286 –90.

Tolman J, Hill RD, Kleinschmidt JJ, et al. Psychosocial adaptation to visual impairment and its relationship to depressive affect in older adults with age-related macular degeneration. The Gerontologist. 2005; 45: 747-53.

Tong L, Waduthantri S, Wong TY, et al. Impact of symptomatic dry eye on vision-related daily activities: the Singapore Malay Eye Study. Eye (Lond). 2010; 24: 1486-91.

Tosh J, Brazier J, Evans P, et al. A review of generic preference-based measures of health-related quality of life in visual disorders. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2012; 15: 118-27.

Tsuchiya A, Ikeda S, Ikegami N, et al. Estimating an EQ-5D population value set: the case of Japan. Health economics. 2002; 11: 341-53.

van Nispen RM, de Boer MR, Hoeijmakers JG, et al. Co-morbidity and visual acuity are risk factors for health-related quality of life decline: five-month follow-up EQ-5D data of visually impaired older patients. Health and quality of life outcomes. 2009; 7: 18.

Varma R, Lee PP, Goldberg I, et al. An assessment of the health and economic burdens of glaucoma. American journal of ophthalmology. 2011; 152: 515-22.

Varma R, Wu J, Chong K, et al. Impact of severity and bilaterality of visual impairment on health-related quality of life. Ophthalmology. 2006; 113: 1846-53.

Varma R, Ying-Lai M, Klein R, et al. Prevalence and risk indicators of visual impairment and blindness in Latinos: the Los Angeles Latino Eye Study. Ophthalmology. 2004; 111: 1132– 40.

Vickrey BG, Hays RD, Genovese BJ, et al. Comparison of a generic to disease-targeted health-related quality-of-life measures for multiple sclerosis. Journal of clinical epidemiology. 1997; 50: 557-69.

Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012; 380: 2163-96.

Wang CW, Chan CL. Psychosocial adaptation status and health-related quality of life among older Chinese adults with visual disorders. Quality of life research: an international journal of quality of life aspects of treatment, care and rehabilitation. 2009; 18: 841-51.

Wang JC, Chew PT. What is the direct cost of treatment of acute primary angle closure

glaucoma? The Singapore model. Clinical & experimental ophthalmology. 2004; 32: 578-83.

Wang JJ, Foran S, Mitchell P. Age-specific prevalence and causes of bilateral and unilateral visual impairment in older Australians: the Blue Mountains Eye Study. Clinical & experimental ophthalmology. 2000; 28: 268 –73.

Wang JJ, Mitchell P, Cumming RG, et al. Visual impairment and nursing home placement in older Australians: the Blue Mountains Eye Study. Ophthalmic epidemiology. 2003; 10: 3-13.

Wang JJ, Mitchell P, Smith W, et al. Impact of visual impairment on use of community support services by elderly persons: the Blue Mountains Eye Study. Investigative ophthalmology & visual science. 1999; 40: 12-9.

Wang P, Li MH, Liu GG, et al. Do Chinese have similar health-state preferences? A comparison of mainland Chinese and Singaporean Chinese. The European journal of health economics : HEPAC : health economics in prevention and care. 2014.

Warner KE, Hodgson TA, Carroll CE. Medical Costs of Smoking in the United States: Estimates, Their Validity, and Their Implication. Tobacco Control. 1999; 8: 290-300.

Wee HL, Loke WC, Li SC, et al. Cross-cultural adaptation and validation of Singapore Malay and Tamil versions of the EQ-5D. Annals of the Academy of Medicine, Singapore. 2007; 36: 403-8.

WHO. ICD Upate and Revision Platform: Change the Definition of Blindness. Available from: http://www.who.int/blindness/Change%20the%20Definition%20of%20Blindness.pdf?ua=1. Accessed December 12, 2014.

Wittenborn JS RD. Cost of vision problems: the economic burden of vision loss and eye disorders in the United States. NORC at the University of Chicago Prepared for Prevent Blindness America, Chicago, IL, 2013. Available at: http://costofvision.preventblindness.org. Accessed on Aug 3rd, 2015.

Wong EY, Chou SL, Lamoureux EL, et al. Personal costs of visual impairment by different eye diseases and severity of visual loss. Ophthalmic Epidemiology. 2008; 15: 339–44.

Wong TY, Chong EW, Wong WL, et al. Prevalence and causes of low vision and blindness in an urban malay population: the Singapore Malay Eye Study. Archives of ophthalmology. 2008; 126: 1091-9.

World Health Organization. Magnitude and causes of visual impairment. Available at: http://www.who.int/mediacentre/factsheets/fs282/en/index.html. Accessed Sep 25th, 2015.

Wang XZ, Luo N, Lamoureux E, et al. The rising economic cost of visual impairment in Asians: a prospective study of direct medical costs in Singapore. The British journal of ophthalmology. 2015; Under review.

Yang Y, Brazier J, Tsuchiya A. Effect of adding a sleep dimension to the EQ-5D descriptive system: a "bolt-on" experiment. Medical decision making : an international journal of the Society for Medical Decision Making. 2014; 34: 42-53.

Yuzawa M, Fujita K, Wittrup-Jensen KU, et al. Improvement in vision-related function with intravitreal aflibercept: data from phase 3 studies in wet age-related macular degeneration. Ophthalmology. 2015; 122: 571-8.

Zainal M, Ismail SM, Ropilah AR, et al. Prevalence of blindness and low vision in Malaysian population: results from the National Eye Survey 1996. The British journal of ophthalmology. 2002; 86: 951– 6.

Zhao J, Ellwein LB, Cui H, et al. Prevalence of vision impairment in older adults in rural China: the China Nine-Province Survey. Ophthalmology. 2010; 117: 409 –16.

Zhao YJ, Tan LC, Li SC, et al. Economic burden of Parkinson's disease in Singapore. European journal of neurology: the official journal of the European Federation of Neurological Societies. 2011; 18: 519-26.

Zheng Y, Lavanya R, Wu R, et al. Prevalence and causes of visual impairment and blindness in an urban Indian population: the Singapore Indian Eye Study. Ophthalmology. 2011; 118: 1798-804.

Zheng YF, Pan CW, Chay J, et al. The economic cost of myopia in adults aged over 40 years in Singapore. Investigative ophthalmology & visual science. 2013; 54: 7532-7.

Appendices

The EQ-5D-3L questionnaire (as used in the Singapore Chinese Eye Study)

研究编号 Study ID:_____

问卷 – QUESTIONNAIRE

第二部分
Part 2

E. EQ-5D

请指明哪些句子最能形容您现在的健康状况。
Please indicate which statements best describe your own health state today

E1 {eqmobile} *(行动)-Mobility*

我在行走上没有问题 I have no problems in walking about ☐1
我在行走上有一些问题 I have some problems in walking about ☐2
我因行动受到限制而卧床 I am confined to bed ☐3

E2 {eqcare} *(自身照顾)-Self-care*

我在自身照顾上没有问题 I have no problems with self-care ☐1
我在替自己梳洗或更衣时有一些问题
I have some problems washing or dressing myself ☐2
我无法替自己梳洗或更衣 I am unable to wash or dress myself ☐3

E3 {eqacty} *一般活动（如工作、上课、家务、家庭或娱性活动)*-Usual activities

我在进行一般活动时没有问题
I have no problems with performing my usual activities ☐1
我在进行一般活动时有一些问题
I have some problems with performing my usual activities ☐2
我无法进行一般活动
I am unable to perform my usual activities ☐3

E4 {eqpain} *(痛楚/不适)-Pain/Discomfort*

我没有任何痛楚或不适 I have no pain or discomfort ☐1
我有中度的痛楚或不适 I have moderate pain or discomfort ☐2
我有严重的痛楚或不适 I have extreme pain or discomfort ☐3

E5 {eqanx} *(焦虑/忧郁)-Anxiety/Depression*

我没有感到焦虑或忧郁 I am not anxious or depressed ☐1
我感到一些焦虑或忧郁 I am moderately anxious or depressed ☐2
我极度焦虑或忧郁 I am extremely anxious or depressed ☐3

The vision "bolt-on" EQ-5D-3L questionnaire

I am now going to ask you some questions regarding your state of health today.

J1	In terms of mobility, would you say you…(READ OUT)?	Have no problems in walking about	1
		Have some problems in walking about	2
		Are confined to bed	3

J2	In terms of self-care, would you say you…(READ OUT)?	Have no problems with self-care	1
		Have some problems washing or dressing yourself	2
		Are unable to wash or dress yourself	3

J3	In terms of usual activities (e.g. work, study, housework, family or leisure activities), would you say you…(READ OUT)?	Have no problems with performing your usual activities	1
		Have some problems with performing your usual activities	2
		Are unable to perform your usual activities	3

J4	In terms of pain or discomfort would you say you…(READ OUT)?	Have no pain or discomfort	1
		Have moderate pain or discomfort	2
		Have extreme pain or discomfort	3

J5	In terms of anxiety or depression would you say you are…(READ OUT)?	Not anxious or depressed	1
		Moderately anxious or depressed	2
		Extremely anxious or depressed	3

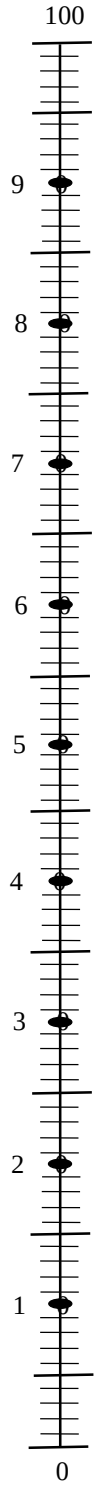
J6	In terms of vision, using glasses or contact lens if needed, would you say you have…(READ OUT)?	No problems seeing	1
		Some problems seeing	2
		Extremely problems seeing	3

SHOWCARD J7

J7	Using this scale where 0 means the worst state of health and 100 means the best state of health, how would you rate your own state of health today?	RECORD NO: _____

Best Imaginable

Health state



Worst Imaginable

Health state

The VF-14 questionnaire

I am now going to ask you a list of questions related to your vision (eyesight).

K1	Do you have any difficulty, even with glasses (i.e. spectacles) ***reading small print***, such as labels on medicine bottles, telephone book or food labels? If YES, PROBE: How much difficulty do you currently have? A little difficulty, a moderate amount of difficulty, a great deal of difficulty or unable to do the activity?	Yes, a little difficulty	1
		Yes, a moderate amount of difficulty	2
		Yes, a great deal of difficulty	3
		Yes, unable to do the activity	4
		No	5
		Not applicable	6

K2	Do you have any difficulty, even with glasses (i.e. spectacles) ***reading a newspaper*** *or* ***a book***? If YES, PROBE: How much difficulty do you currently have? A little difficulty, a moderate amount of difficulty, a great deal of difficulty or unable to do the activity?	Yes, a little difficulty	1
		Yes, a moderate amount of difficulty	2
		Yes, a great deal of difficulty	3
		Yes, unable to do the activity	4
		No	5
		Not applicable	6

K3	Do you have any difficulty, even with glasses (i.e. spectacles) **reading *a large-print book* or a large-print newspaper or numbers on a telephone**? If YES, PROBE: How much difficulty do you currently have? A little difficulty, a moderate amount of difficulty, a great deal of difficulty or unable to do the activity?	Yes, a little difficulty	1
		Yes, a moderate amount of difficulty	2
		Yes, a great deal of difficulty	3
		Yes, unable to do the activity	4
		No	5
		Not applicable	6

K4		Yes, a little difficulty	1
		Yes, a moderate amount of difficulty	2
		Yes, a great deal of difficulty	3
		Yes, unable to do the activity	4

	Do you have any difficulty, even with glasses (i.e. spectacles) ***recognizing people*** when they are close to you? If YES, PROBE: How much difficulty do you currently have? A little difficulty, a moderate amount of difficulty, a great deal of difficulty or unable to do the activity?	No	5
		Not applicable	6

K5	Do you have any difficulty, even with glasses (i.e. spectacles) ***seeing steps***, ***stairs*** *or* ***curbs (kerbs)***? If YES, PROBE: How much difficulty do you currently have? A little difficulty, a moderate amount of difficulty, a great deal of difficulty or unable to do the activity?	Yes, a little difficulty	1
		Yes, a moderate amount of difficulty	2
		Yes, a great deal of difficulty	3
		Yes, unable to do the activity	4
		No	5
		Not applicable	6
K6	Do you have any difficulty, even with glasses (i.e. spectacles) ***reading traffic signs, street signs*** or ***store signs***? If YES, PROBE: How much difficulty do you currently have? A little difficulty, a moderate amount of difficulty, a great deal of difficulty or unable to do the activity?	Yes, a little difficulty	1
		Yes, a moderate amount of difficulty	2
		Yes, a great deal of difficulty	3
		Yes, unable to do the activity	4
		No	5
		Not applicable	6

K7	Do you have any difficulty, ***doing fine handwork*** like sewing, knitting or carpentry because of your vision, even with glasses (i.e. spectacles)?	Yes, a little difficulty	1
		Yes, a moderate amount of difficulty	2
		Yes, a great deal of difficulty	3
		Yes, unable to do the activity	4
		No	5
		Not applicable	6

	If YES, PROBE: How much difficulty do you currently have? A little difficulty, a moderate amount of difficulty, a great deal of difficulty or unable to do the activity?		

K8	Do you have any difficulty, ***writing cheques*** or ***filling forms*** because of your vision, even with glasses (i.e. spectacles)?	Yes, a little difficulty	1
		Yes, a moderate amount of difficulty	2
		Yes, a great deal of difficulty	3
		Yes, unable to do the activity	4
		No	5
		Not applicable	6
	If YES, PROBE: How much difficulty do you currently have? A little difficulty, a moderate amount of difficulty, a great deal of difficulty or unable to do the activity?		

K9	Do you have any difficulty ***playing games*** such as chess, card games, mahjong because of your vision, even with glasses (i.e. spectacles)?	Yes, a little difficulty	1
		Yes, a moderate amount of difficulty	2
		Yes, a great deal of difficulty	3
		Yes, unable to do the activity	4
		No	5
		Not applicable	6
	If YES, PROBE: How much difficulty do you currently have? A little difficulty, a moderate amount of difficulty, a great deal of difficulty or unable to do the activity?		

K10	Do you have any difficulty ***taking part in sports*** like bowling, tennis, badminton, golf because of your vision, even with glasses?	Yes, a little difficulty	1
		Yes, a moderate amount of difficulty	2
		Yes, a great deal of difficulty	3
		Yes, unable to do the activity	4
		No	5
		Not applicable	6
	If YES, PROBE: How much difficulty do you currently have? A little difficulty, a moderate amount of difficulty, a great deal of difficulty or unable to do the activity?		

K11	Do you have any difficulty ***cooking*** because of your vision, even with glasses? If YES, PROBE: How much difficulty do you currently have? A little difficulty, a moderate amount of difficulty, a great deal of difficulty or unable to do the activity?	Yes, a little difficulty	1
		Yes, a moderate amount of difficulty	2
		Yes, a great deal of difficulty	3
		Yes, unable to do the activity	4
		No	5
		Not applicable	6

K12	Do you have any difficulty, even with glasses (i.e. spectacles), ***watching television?*** If YES, PROBE: How much difficulty do you currently have? A little difficulty, a moderate amount of difficulty, a great deal of difficulty or unable to do the activity?	Yes, a little difficulty	1
		Yes, a moderate amount of difficulty	2
		Yes, a great deal of difficulty	3
		Yes, unable to do the activity	4
		No	5
		Not applicable	6

K13	Do you currently drive a car?	Yes	1	**GO TO K14**
		No	2	**GO TO K16**

K14	How much difficulty do you have ***driving during the day*** because of your vision? Do you have…(READ OUT)?	No difficulty	1
		A little difficulty	2
		A moderate amount of difficulty	3
		A great deal of difficulty	4

K15	How much difficulty do you have ***driving at night*** because of your vision? Do you have…(READ OUT)?	No difficulty	1
		A little difficulty	2
		A moderate amount of difficulty	3
		A great deal of difficulty	4

Stop

K16	Have you ever driven a car?	Yes	1	**GO TO K17**
		No	2	**Stop**

K17	How long ago did you stop driving? Was it…(READ OUT)?	Less than 6 months ago	1
		6 to 12 months ago	2
		More than 12 months ago	3

K18	Why did you stop driving? Was it because of eyesight problem?	Vision	1
		Other illness	2
		Other reason	3

The healthcare utilization, expenditure and employment questionnaire

INTRODUCTION: Good morning/afternoon/evening, I am _____, from Singapore National Eye Center (SHOW INTERVIEWER CARD). On behalf of the Singapore Eye Research Institute (SERI), we are conducting a survey on the healthcare utilization and expenditure of Singaporeans with and without eye diseases (**SHOW LETTER FROM SERI**). We would appreciate it if you could help us by providing us the required information. Please be assured that all responses provided by you will be kept strictly confidential.

HEALTH SCHEMES & INSURANCE

A1	Do you have a Medisave account?	Yes	1	
		No	2	
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

A2	Are you currently covered by…(READ OUT)?	Medishield	1	**GO TO A3a**
		Private Shield Plan such as Incomeshield, PruShield	2	**GO TO A3b**
		Not covered by any Shield Plan	3	**GO TO A3a**
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

A3a	Are you currently covered by any…(READ OUT)?	Private Healthcare Insurance Plan that covers cost of inpatient services	1
		Private Healthcare Insurance Plan that covers cost of outpatient services	2
		Private Healthcare Insurance Plan that covers both cost of inpatient and outpatient services	3
		Have such Private Healthcare Insurance Plan but not sure of the coverage	4
		Not covered by such Private Healthcare Insurance Plan	5
		Don't Know (DO NOT READ OUT)	97
		Refused (DO NOT READ OUT)	99

GO TO A4

A3b	Apart from Private Shield Plan, are you currently covered by other …(READ OUT)?	Private Healthcare Insurance Plan that covers cost of inpatient services	1
		Private Healthcare Insurance Plan that covers cost of outpatient services	2
		Private Healthcare Insurance Plan that covers both cost of inpatient and outpatient services	3
		Have such Private Healthcare Insurance Plan but not sure of the coverage	4
		Not covered by such Private Healthcare Insurance Plan	5
		Don't Know (DO NOT READ OUT)	97
		Refused (DO NOT READ OUT)	99

A4		Yes	1
		No	2
		Don't Know (DO NOT READ OUT)	97

	Are you currently covered by ElderShield?	Refused (DO NOT READ OUT)	99

A5	Are you currently a holder of the Civil Service Card (CSC)?	Yes	1
		No	2
		Don't Know (DO NOT READ OUT)	97
		Refused (DO NOT READ OUT)	99

A6	Are you currently on Public Assistance (PA)?	Yes	1
		No	2
		Don't Know (DO NOT READ OUT)	97
		Refused (DO NOT READ OUT)	99

ACUTE CARE HOSPITAL/COMMUNITY HOSPITAL

B1	Did you at any time during the past 3 months stay at least one night in a hospital because of health problems?	Yes	1	**GO TO B2**
		No	2	**GO TO C1**
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

B2	How many times did you stay in a hospital (for at least one night for health problems) in the past 3 months?	RECORD NO:	___	**GO TO B3**
		DK (DO NOT READ OUT)	97	**GO TO C1**
		RF (DO NOT READ OUT)	99	

B3	I would like to know more details about each of your hospital admission in the past 3 months. Let's talk about your hospital admission. How many nights did you stay at the hospital?		Most Recent	2nd Most Recent	3rd Most Recent
		RECORD NUMBER	_____	_____	_____

B4	For this admission, which hospital did you stay in?		Most Recent	2nd Most Recent	3rd Most Recent
		Government Restructured Hospital			
		Alexandra Hospital	1	1	1
		Changi General Hospital	2	2	2
		Institute of Mental Health	3	3	3
		Khoo Teck Puat Hospital	4	4	4
		KK Women's and Children's Hospital	5	5	5
		National University Hospital	6	6	6
		Singapore General Hospital	7	7	7
		Tan Tock Seng Hospital	8	8	8
		National Heart Centre	9	9	9
		Community Hospital			
		Bright Vision Hospital	10	10	10
		Kwong Wai Shiu Hospital	11	11	11
		Ren Ci Hospital	12	12	12
		St Andrew' s Community Hospital	13	13	13
		St Luke's Hospital	14	14	14
		Thye Hua Kwan Hospital	15	15	15
		Private Hospital (Specify Name)	16 (_____)	16 (_____)	16 (_____)
		Others (Specify)	88 (_____)	88 (_____)	88 (_____)
		DK	97	97	97
		RF	99	99	99

IF GOVERNMENT RESTRUCTURED HOSPITAL (B4=1-9) – SEE SHADED AREA, GO TO B5

ELSE GO TO B6

B5	What class of ward did you stay in?		Most Recent	2nd Most Recent	3rd Most Recent
		A Class	1	1	1
		B1 Class	2	2	2
		B2 Class	3	3	3
		C Class	4	4	4
		DK (Do Not Read Out)	97	97	97
		RF (Do Not Read Out)	99	99	99

B6	How did you travel to the hospital?		Most Recent		2nd Most Recent		3rd Most Recent	
			Yes	No	Yes	No	Yes	No
		Ambulance	1	2	1	2	1	2
		Taxi	1	2	1	2	1	2
		Bus	1	2	1	2	1	2
		MRT	1	2	1	2	1	2
		Car	1	2	1	2	1	2
		Walk	1	2	1	2	1	2
		Others (Specify)	1 (_____)	2	1 (_____)	2	1 (_____)	2
		DK	1	2	1	2	1	2
		RF	1	2	1	2	1	2

B7	How much was spent on the transportation to the hospital?		Most Recent	2nd Most Recent	3rd Most Recent
		RECORD AMOUNT	$_____	$_____	$_____

B8	What were the medical conditions for which you sought treatment at the hospital?		Most Recent		2nd Most Recent		3rd Most Recent	
			Y	N	Y	N	Y	N
		Diabetes	1	2	1	2	1	2
		High blood pressure	1	2	1	2	1	2
		High blood cholesterol	1	2	1	2	1	2
		Heart attack /heart failure/ uneven heart rhythm	1	2	1	2	1	2
		Stroke	1	2	1	2	1	2
		Asthma	1	2	1	2	1	2
		Chronic obstructive pulmonary disease (COPD)	1	2	1	2	1	2
		Pneumonia	1	2	1	2	1	2
		Cough, cold, sore throat, fever	1	2	1	2	1	2
		Lower back pain	1	2	1	2	1	2
		Osteoporosis	1	2	1	2	1	2
		Rheumatism and arthritis	1	2	1	2	1	2
		Joint conditions	1	2	1	2	1	2
		Fractures	1	2	1	2	1	2
		Physical injuries	1	2	1	2	1	2

		Cataract	1	2	1	2	1	2
		Glaucoma	1	2	1	2	1	2
		Eye infection	1	2	1	2	1	2
		Hearing loss	1	2	1	2	1	2
		Schizophrenia	1	2	1	2	1	2
		Alzheimer's & other dementia	1	2	1	2	1	2
		Anxiety & depression	1	2	1	2	1	2
		Non cancer (benign) growth	1	2	1	2	1	2
		Cancer	1	2	1	2	1	2
		Other Medical Conditions (Specify:)	1 (____)	2	1 (____)	2	1 (____)	2
		DK	1	2	1	2	1	2
		RF	1	2	1	2	1	2
B9	How much was your hospital bill, excluding government subsidy?							

B10	How did you pay the hospital bill?

IF YES TO ANY HEALTH SCHEME/INSURANCE

B11	You mentioned that your hospital bill was paid using…(READ OUT HEALTH SCHEME/INSURANCE USED). How much was paid using these health scheme/insurance?

IF YES TO OUT-OF-POCKET USING CASH OR CREDIT CARD

B12	You mentioned that your hospital bill was paid out-of-pocket using cash or credit card. How much was paid using cash or credit card?

IF YES TO OTHERS

B13	How much was paid using ….(READ OUT OTHERS)?

	Most Recent			2nd Most Recent			3rd Most Recent		
Hospital Bill	**B9** $_____			**B9** $_____			**B9** $_____		
	B10		**B11**	**B10**		**B11**	**B10**		**B11**
	Y	N		Y	N		Y	N	
Health Scheme/Insurance									
Medisave	1	2	$_____ (A)	1	2	$_____ (A)	1	2	$_____ (A)
Medishield	1	2		1	2		1	2	
Private Insurance	1	2		1	2		1	2	
Medifund	1	2		1	2		1	2	
Civil Service Card	1	2		1	2		1	2	

Other Health Scheme/Insurance (Specify)	1 (____)	2		1 (____)	2		1 (____)	2	
			B12			**B12**			**B12**
Out-of-Pocket <u>Using Cash or Credit Card</u>									
Self	1	2	$_____ (B)	1	2	$_____ (B)	1	2	$_____ (B)
Family Member/Relative	1	2		1	2		1	2	
Friend	1	2		1	2		1	2	
Others (Specify)	1 (_____)	2		1 (_____)	2		1 (_____)	2	
			B13			**B13**			**B13**
Others (Specify)	1 (_____)	2	$_____ (C)	1 (_____)	2	$_____ (C)	1 (_____)	2	$_____p__ (C)
DK	1	2		1	2		1	2	
RF	1	2		1	2		1	2	
TOTAL (A+B+C)			**$_____**			**$_____**			**$_____**

INTERVIEWER TO CHECK : TOTAL (A+B+C)=B9

EMERGENCY DEPARTMENT SERVICES

C1	Let's now talk about emergency department in a hospital. Did you at any time during the past 3 months receive medical care in a hospital emergency department that did not result in hospitalization (i.e. not directly admitted to hospital)?	Yes	1	**GO TO C2**
		No	2	**GO TO D1**
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

C2	In the past 3 months, how many times did you receive medical care in a hospital emergency department that did not result in hospitalization?	RECORD NO:	___	**GO TO C3**
		DK (DO NOT READ OUT)	97	**GO TO D1**
		RF (DO NOT READ OUT)	99	

			Most Recent	2nd Most Recent	3rd Most Recent
C3	I would like to know more details about each of your visit to the hospital emergency department that did not result in hospitalization. Let's talk about your…….(READ OUT RECENCY) visit to the hospital emergency department. Which hospital emergency department did you visit?	**Government Restructured Hospital**			
		Alexandra Hospital	1	1	1
		Changi General Hospital	2	2	2
		Institute of Mental Health	3	3	3
		Khoo Teck Puat Hospital	4	4	4
		KK Women's and Children's Hospital	5	5	5
		National University Hospital	6	6	6
		Singapore General Hospital	7	7	7
		Tan Tock Seng Hospital	8	8	8
		Private Hospital (Specify)	9 (_____)	9 (_____)	9 (_____)
		Others (Specify)	88 (_____)	88 (_____)	88 (_____)
		DK	97	97	97
		RF	99	99	99

			Most Recent		2nd Most Recent		3rd Most Recent	
			Y	N	Y	N	Y	N
C4	How did you travel to the hospital emergency department?	Ambulance	1	2	1	2	1	2
		Taxi	1	2	1	2	1	2
		Bus	1	2	1	2	1	2
		MRT	1	2	1	2	1	2
		Car	1	2	1	2	1	2
		Walk	1	2	1	2	1	2
		Others (Specify)	1 (_____)	2	1 (_____)	2	1 (_____)	2
		DK	1	2	1	2	1	2
		RF	1	2	1	2	1	2

C5	How much was spent on the transportation to the hospital emergency department?		Most Recent	2nd Most Recent	3rd Most Recent
		RECORD AMOUNT	$_____	$_____	$_____

			Most Recent		2nd Most Recent		3rd Most Recent	
C6	What were the medical conditions for which you sought treatment at the hospital emergency department?		Yes	No	Yes	No	Y	N
		Diabetes	1	2	1	2	1	2
		High blood pressure	1	2	1	2	1	2
		High blood cholesterol	1	2	1	2	1	2
		Heart attack /heart failure/ uneven heart rhythm	1	2	1	2	1	2
		Stroke	1	2	1	2	1	2
		Asthma	1	2	1	2	1	2
		Chronic obstructive pulmonary disease (COPD)	1	2	1	2	1	2
		Pneumonia	1	2	1	2	1	2
		Cough, cold, sore throat, fever	1	2	1	2	1	2
		Lower back pain	1	2	1	2	1	2
		Osteoporosis	1	2	1	2	1	2
		Rheumatism and arthritis	1	2	1	2	1	2
		Joint conditions	1	2	1	2	1	2
		Fractures	1	2	1	2	1	2
		Physical injuries	1	2	1	2	1	2
		Cataract	1	2	1	2	1	2
		Glaucoma	1	2	1	2	1	2
		Eye infection	1	2	1	2	1	2
		Hearing loss	1	2	1	2	1	2
		Schizophrenia	1	2	1	2	1	2
		Alzheimer's & other dementia	1	2	1	2	1	2
		Anxiety & depression	1	2	1	2	1	2
		Non cancer (benign) growth	1	2	1	2	1	2
		Cancer	1	2	1	2	1	2
		Other Medical Conditions (Specify)	1 (____)	2	1 (____)	2	1 (____)	2
		DK	1	2	1	2	1	2
		RF	1	2	1	2	1	2

C7	How much was the bill for your visit to the hospital emergency department, excluding government subsidy?

C8	How did you pay the bill?

IF YES TO ANY HEALTH SCHEME/INSURANCE

C9	You mentioned that the bill was paid using…(READ OUT HEALTH SCHEME/INSURANCE USED). How much was paid using these health scheme/insurance?

IF YES TO OUT-OF-POCKET USING CASH OR CREDIT CARD

C10	You mentioned that the bill was paid out-of-pocket using cash or credit card. How much was paid using cash or credit card?

IF YES TO OTHERS

C11	How much was paid using ….(READ OUT OTHERS)?

	Most Recent			2nd Most Recent			3rd Most Recent		
Emergency Dept Bill	**C7** $_____			**C7** $_____			**C7** $_____		
	C8		**C9**	**C8**		**C9**	**C8**		**C9**
	Y	N		Y	N		Y	N	
Health Scheme/Insurance									
Private Insurance	1	2	$_____ (A)	1	2	$_____ (A)	1	2	$_____ (A)
Civil Service Card	1	2		1	2		1	2	
Other Health Scheme/Insurance (Specify)	1 (____)	2		1 (____)	2		1 (____)	2	
Out-of-Pocket Using Cash or Credit Card			**C10**			**C10**			**C10**
Self	1	2	$_____ (B)	1	2	$_____ (B)	1	2	$_____ (B)
Family Member/Relative	1	2		1	2		1	2	
Friend	1	2		1	2		1	2	
Others(Specify)	1 (____)	2		1 (____)	2		1 (_____)	2	
			C11			**C11**			**C11**
Others (Specify)	1 (____)	2	$_____ (C)	1 (____)	2	$_____ (C)	1 (_____)	2	$_____ (C)
DK	1	2		1	2		1	2	
RF	1	2		1	2		1	2	
TOTAL (A+B+C)			**$_____**			**$_____**			**$_____**

INTERVIEWER TO CHECK : TOTAL (A+B+C)=C7

OUTPATIENT SERVICES

D1	Let's now talk about visits to government polyclinics and private GP clinics. Did you at any time in the <u>past 3 months</u> receive medical care at a polyclinic or private GP clinic?	Yes	1	**GO TO D2**
		No	2	**GO TO D13**
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

D2	In the <u>past 3 months</u>, how many times did you visit a polyclinic or private GP clinic to receive medical care?	RECORD NO:	___	**GO TO D3**
		DK (DO NOT READ OUT)	97	**GO TO D13**
		RF (DO NOT READ OUT)	99	

			Most <u>Recent</u>	2nd Most <u>Recent</u>	3rd Most <u>Recent</u>
D3	I would like to know more details about each of your visit to a polyclinic/private GP clinic in the past 3 months. Let's talk about your…(READ OUT RECENCY) visit. For this visit, did you receive medical care at a polyclinic or private GP clinic?	Polyclinic	1	1	1
		Private GP Clinic	2	2	2
		DK (DO NOT READ OUT)	97	97	97
		RF (DO NOT READ OUT)	99	99	99

IF PRIVATE GP CLINIC – SEE SHADED AREA, GO TO D4,

			Most <u>Recent</u>	2nd Most <u>Recent</u>	3rd Most <u>Recent</u>
D4	For your visit to the private GP clinic, did you enjoy subsidized rate on your bill under the Community Health Assist Scheme (CHAS)?	Yes	1	1	1
		No	2	2	2
		DK (DO NOT READ OUT)	97	97	97
		RF (DO NOT READ OUT)	99	99	99

			Most <u>Recent</u>		2nd Most <u>Recent</u>		3rd Most <u>Recent</u>	
			Y	N	Y	N	Y	N
D5	How did you travel to the polyclinic/private GP clinic (INTERVIEWER TO READ OUT ACCORDINGLY)?	Ambulance	1	2	1	2	1	2
		Taxi	1	2	1	2	1	2
		Bus	1	2	1	2	1	2
		MRT	1	2	1	2	1	2
		Car	1	2	1	2	1	2
		Walk	1	2	1	2	1	2
		Others (Specify)	1 (___)	2	1 (____)	2	1 (___)	2
		DK (DO NOT READ OUT)	1	2	1	2	1	2
		RF (DO NOT READ OUT)	1	2	1	2	1	2

			Most <u>Recent</u>	2nd Most <u>Recent</u>	3rd Most <u>Recent</u>

D6	How much was spent on the transportation to travel to the polyclinic/private GP clinic (INTERVIEWER TO READ OUT ACCORDINGLY)?	RECORD AMOUNT	$_____	$_____	$_____

			Most Recent		2nd Most Recent		3rd Most Recent	
			Y	N	Y	N	Y	N
D7	What were the medical conditions for which you sought treatment at the polyclinic/private GP clinic (INTERVIEWER TO READ OUT ACCORDINGLY)	Diabetes	1	2	1	2	1	2
		High blood pressure	1	2	1	2	1	2
		High blood cholesterol	1	2	1	2	1	2
		Heart attack /heart failure/ uneven heart rhythm	1	2	1	2	1	2
		Stroke	1	2	1	2	1	2
		Asthma	1	2	1	2	1	2
		Chronic obstructive pulmonary disease (COPD)	1	2	1	2	1	2
		Pneumonia	1	2	1	2	1	2
		Cough, cold, sore throat, fever	1	2	1	2	1	2
		Lower back pain	1	2	1	2	1	2
		Osteoporosis	1	2	1	2	1	2
		Rheumatism and arthritis	1	2	1	2	1	2
		Joint conditions	1	2	1	2	1	2
		Fractures	1	2	1	2	1	2
		Physical injuries	1	2	1	2	1	2
		Cataract	1	2	1	2	1	2
		Glaucoma	1	2	1	2	1	2
		Eye infection	1	2	1	2	1	2
		Hearing loss	1	2	1	2	1	2
		Schizophrenia	1	2	1	2	1	2
		Alzheimer's & other dementia	1	2	1	2	1	2
		Anxiety & depression	1	2	1	2	1	2
		Non cancer (benign) growth	1	2	1	2	1	2
		Cancer	1	2	1	2	1	2
		Other Medical Conditions (Specify)	1 (_____)	2	1 (_____)	2	1 (_____)	2
		DK	1	2	1	2	1	2
		RF	1	2	1	2	1	2

D8	For your visit to the polyclinic/private GP clinic (INTERVIEWER TO READ OUT ACCORDINGLY), how much was your bill, excluding government subsidy?

D9	How did you pay the bill?

IF YES TO ANY HEALTH SCHEME/INSURANCE

D10	You mentioned that your bill was paid using…(READ OUT HEALTH SCHEME/INSURANCE USED). How much was paid using these health scheme/insurance?

IF YES TO OUT-OF-POCKET USING CASH OR CREDIT CARD

D11	You mentioned that your bill was paid out-of-pocket using cash or credit card. How much was paid using cash or credit card?

IF YES TO OTHERS

D12	How much was paid using ….(READ OUT OTHERS)?

	Most Recent			**2nd Most Recent**			**3rd Most Recent**		
Amount of Bill	**D8** $_____			**D8** $_____			**D8** $_____		
	D9		**D10**	**D9**		**D10**	**D9**		**D10**
	Y	N		Y	N		Y	N	
Health Scheme/Insurance									
Medisave	1	2		1	2		1	2	
Private Insurance	1	2		1	2		1	2	
Medifund	1	2	$_____	1	2	$_____	1	2	$_____
Civil Service Card	1	2	(A)	1	2	(A)	1	2	(A)
Other Health Scheme/Insurance (Specify)	1 (____)	2		1 (____)	2		1 (____)	2	
Out-of-Pocket Using Cash (including Credit Card)			**D11**			**D11**			**D11**
Self	1	2		1	2		1	2	
Family Member/Relative	1	2	$_____	1	2	$_____	1	2	$_____
Friend	1	2	(B)	1	2	(B	1	2	(B)
Others (Specify)	1 (____)	2		1 (_____)	2		1 (_____)	2	
			D12			**D12**			**D12**
Others (Specify)	1 (____)	2	$_____ (C)	1 (____)	2	$_____ (C)	1 (____)	2	$_____ (C)
DK	1	2		1	2		1	2	
RF	1	2		1	2		1	2	
TOTAL (A+B+C)			**$_____**			**$_____**			**$_____**

INTERVIEWER TO CHECK: TOTAL (A+B+C) =D8

D13	Let's now talk about visits to specialist outpatient clinics. Did you at any time	Yes	1	**GO TO D14**
		No	2	**GO TO E1**

	during the past 3 months receive medical care at a specialist outpatient clinic?	Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

D14	In the past 3 months, how many times did you receive medical care at a specialist outpatient clinic?	RECORD NO:	___	**GO TO D15**
		DK (DO NOT READ OUT)	97	**GO TO E1**
		RF (DO NOT READ OUT)	99	

D15	I would like to know more details about each of your visit to the specialist outpatient clinic in the past 3 months. Let's talk about your…(READ OUT RECENCY) visit to a specialist outpatient clinic. Which hospital or medical centre is the specialist outpatient clinic located at?		Most Recent	2nd Most Recent	3rd Most Recent
		Government Restructured Hospital			
		Alexandra Hospital	1	1	1
		Changi General Hospital	2	2	2
		Institute of Mental Health	3	3	3
		Khoo Teck Puat Hospital	4	4	4
		KK Women's and Children's Hospital	5	5	5
		National University Hospital	6	6	6
		Singapore General Hospital	7	7	7
		Tan Tock Seng Hospital	8	8	8
		National Cancer Centre	9	9	9
		National Heart Centre	10	10	10
		Singapore National Eye Centre	11	11	11
		National Skin Centre	12	12	12
		Private Hospital (Specify)	13 (_____)	13 (_____)	13 (_____)
		Others (Specify)	88 (_____)	88 (_____)	88 (_____)
		DK (DO NOT READ OUT)	97	97	97
		RF (DO NOT READ OUT)	99	99	99

D16	How did you travel to the specialist outpatient clinic located at…(READ OUT ANSWER IN D15)?		Most Recent		2nd Most Recent		3rd Most Recent	
			Y	N	Y	N	Y	N
		Ambulance	1	2	1	2	1	2
		Taxi	1	2	1	2	1	2
		Bus	1	2	1	2	1	2
		MRT	1	2	1	2	1	2
		Car	1	2	1	2	1	2
		Walk	1	2	1	2	1	2
		Others (Specify)	1 (_____)	2	1 (____)	2	1 (____)	2
		DK (DO NOT READ OUT)	1	2	1	2	1	2
		RF (DO NOT READ OUT)	1	2	1	2	1	2

D17	How much was spent on the transportation to the specialist outpatient clinic?		Most Recent	2nd Most Recent	3rd Most Recent
		RECORD AMOUNT	$_____	$_____	$_____

			Most Recent		2nd Most Recent		3rd Most Recent	
			Y	N	Y	N	Y	N
D18	What were the medical conditions for which you sought treatment at the specialist outpatient clinic?	Diabetes	1	2	1	2	1	2
		High blood pressure	1	2	1	2	1	2
		High blood cholesterol	1	2	1	2	1	2
		Heart attack /heart failure/ uneven heart rhythm	1	2	1	2	1	2
		Stroke	1	2	1	2	1	2
		Asthma	1	2	1	2	1	2
		Chronic obstructive pulmonary disease (COPD)	1	2	1	2	1	2
		Pneumonia	1	2	1	2	1	2
		Cough, cold, sore throat, fever	1	2	1	2	1	2
		Lower back pain	1	2	1	2	1	2
		Osteoporosis	1	2	1	2	1	2
		Rheumatism and arthritis	1	2	1	2	1	2
		Joint conditions	1	2	1	2	1	2
		Fractures	1	2	1	2	1	2
		Physical injuries	1	2	1	2	1	2
		Cataract	1	2	1	2	1	2
		Glaucoma	1	2	1	2	1	2
		Eye infection	1	2	1	2	1	2
		Hearing loss	1	2	1	2	1	2
		Schizophrenia	1	2	1	2	1	2
		Alzheimer's & other dementia	1	2	1	2	1	2
		Anxiety & depression	1	2	1	2	1	2
		Non cancer (benign) growth	1	2	1	2	1	2
		Cancer	1	2	1	2	1	2
		Other Medical Conditions (Specify)	1 (_____)	2	1 (_____)	2	1 (_____)	2
		DK (DO NOT READ OUT)	1	2	1	2	1	2
		RF (DO NOT READ OUT)	1	2	1	2	1	2

D19	For your visit to the specialist outpatient clinic, how much was the bill, excluding government subsidy?

D20	How did you pay the bill?

IF YES TO ANY HEALTH SCHEME/INSURANCE

D21	You mentioned that the bill was paid using…(READ OUT HEALTH SCHEME/INSURANCE USED). How much was paid using these health scheme/insurance?

IF YES TO OUT-OF-POCKET USING CASH OR CREDIT CARD

D22	You mentioned that the bill was paid out-of-pocket using cash or credit card. How much was paid using cash or credit card?

IF YES TO OTHERS

D23	How much was paid using ….(READ OUT OTHERS)?

	Most Recent			2nd Most Recent			3rd Most Recent		
Amount of Bill	**D19** $_____			**D19** $_____			**D19** $_____		
	D20		**D21**	**D20**		**D21**	**D20**		**D21**
	Y	N		Y	N		Y	N	
Health Scheme/Insurance									
Medisave	1	2		1	2		1	2	
Private Insurance	1	2		1	2		1	2	
Medifund	1	2		1	2		1	2	$_____
Civil Service Card	1	2	$_____	1	2	$_____	1	2	
Other Health Scheme/Insurance (Specify)	1 (____)	2		1 (____)	2		1 (____)	2	
Out-of-Pocket Using Cash or Credit Card)			**D22**			**D22**			**D22**
Self	1	2		1	2		1	2	
Family Member/Relative	1	2		1	2		1	2	
Friend	1	2	$_____	1	2	$_____	1	2	$_____
Others (Specify)	1 (____)	2		1 (____)	2		1 (__)	2	
			D23			**D23**			**D23**
Others (Specify)	1 (____)	2	$_____ (C)	1 (____)	2	$_____ (C)	1 (____)	2	$_____ (C)
DK	1	2		1	2		1	2	
RF	1	2		1	2		1	2	
TOTAL (A+B+C)			**$_____**			**$_____**			**$_____**

INTERVIEWER TO CHECK: TOTAL (A+B+C)=D19

HEALTH SUPPLEMENTS/TREATMENT

E1		Yes	1
		No	2
		Don't Know (DO NOT READ OUT)	97

	In the past 3 months, did you take any health supplements or herbal medicine (e.g. vitamins, cordyceps)?	Refused (DO NOT READ OUT)	99

E2a	In the past 3 months, did you visit a TCM (Traditional Chinese Medicine) physician?	Yes	1	**GO TO E2b**
		No	2	**GO TO E3a**
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

E2b	In the past 3 months, how many times did you visit a TCM physician?	RECORD:	_____	time(s)

E2c	On average, how much was the cost for each visit to the TCM physician, including consultation and medicine?	RECORD: $_____

E3a	In the past 3 months, did you go for acupuncture?	Yes	1	**GO TO E3b**
		No	2	**GO TO E4a**
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

E3b	In the past 3 months, how many times did you go for acupuncture?	RECORD:	_____	time(s)

E3c	On average, how much was the cost for each acupuncture session?	RECORD: $_____

E4a	In the past 3 months, did you go for massage?	Yes	1	**GO TO E4b**
		No	2	**GO TO E5a**
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

E4b	In the past 3 months, how many times did you go for massage?	RECORD:	_____	time(s)

E4c	On average, how much was the cost for each massage session?	RECORD: $_____

E5a		Yes	1	**GO TO E5b**
		No	2	**GO TO E6a**

	In the <u>past 3 months</u>, did you go for Tui-Na/Bone-setting?	Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

E5b	In the <u>past 3 months</u>, how many times did you go for Tui-Na/Bone-setting?	RECORD:	_____	time(s)

E5c	On average, how much was the cost for each Tui-Na/bone-setting treatment?	RECORD: $_____

E6a	In the <u>past 3 months</u>, did you go for foot reflexology?	Yes	1	**GO TO E6b**
		No	2	**GO TO F1a**
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

E6b	In the <u>past 3 months</u>, how many times did you go for foot reflexology?	RECORD:	_____	time(s)

E6c	On average, how much was the cost for each foot reflexology session?	RECORD: $_____

HEALTH AIDS/EQUIPMENT

F1a	Let's now talk about health aids/equipment. In the <u>past 3 months</u>, did you use a *magnifier*?	Yes	1	**GO TO F1b**
		No	2	**GO TO F2a**
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

F1b	Is the *magnifier* purchased, on loan or donated by someone?	Purchased	1	**GO TO F1c**
		On loan	2	**GO TO F2a**
		Donated by someone	3	
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

F1c	How much does the *magnifier* cost?	RECORD : $ _____

F1d	Who paid for the magnifier? Was it..(READ OUT)?		Yes	No
		Yourself	1	2
		Family member/relative	1	2
		Friend	1	2
		Others (Specify:_____)	1	2

F2a	In the <u>past 3 months</u>, did you use a *walking frame or a walking stick*?	Yes	1	**GO TO F2b**
		No	2	**GO TO F3a**
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

F2b	Is the *walking frame/walking stick* purchased, rented, on loan or donated by someone?	Purchased	1	**GO TO F2c**
		Rented	2	**GO TO F2e**
		On loan	3	**GO TO F3a**
		Donated by someone	4	
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

F2c	How much does the *walking frame/walking stick* cost?	RECORD : $ _____

F2d	Who paid for the *walking frame/walking stick*? Was it..(READ OUT)?		Yes	No	
		Yourself	1	2	**GO TO F3a**
		Family member/relative	1	2	
		Friend	1	2	
		Others (Specify:_____)	1	2	

F2e		$_____ per hour	1
		$ _____ per day	2
		$ _____ per week	3

	How much is the rental of the *walking frame/walking stick*?	$ _____ per month	4

F3a	In the <u>past 3 months</u>, did you use a *wheelchair*?	Yes	1	**GO TO F3b**
		No	2	**GO TO G1**
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

F3b	Is the *wheelchair* purchased, rented, on loan or donated by someone?	Purchased	1	**GO TO F3c**
		Rented	2	**GO TO F3e**
		On loan	3	**GO TO G1**
		Donated by someone	4	
		Don't Know (DO NOT READ OUT)	97	
		Refused (DO NOT READ OUT)	99	

F3c	How much does the *wheelchair* cost?	RECORD : $ _____

F3d	Who paid for the *wheelchair*? Was it..(READ OUT)?		Yes	No	**GO TO G1**
		Yourself	1	2	
		Family member/relative	1	2	
		Friend	1	2	
		Others (Specify:_____)	1	2	

F3e	How much is the rental of the *wheelchair*?	$_____ per hour	1
		$ _____ per day	2
		$ _____ per week	3
		$ _____ per month	4

EMPLOYMENT STATUS (RESPONDENT)

G1	Are you currently…(READ OUT)?	Working	1	**GO TO G2**
		Not working	2	**GO TO G9a**

G2	What is your occupation?	RECORD: _____

G3	Could you please tell me how much you earn per month?	Below $1,000	1
		$1,000 to $1,999	2
		$2,000 to $2,999	3
		$3,000 to $3,999	4
		$4,000 to $4,999	5
		$5,000 to $5,999	6
		$6,000 to $6,999	7
		$7,000 to $7,999	8
		$8,000 to $8,999	9
		$9,000 to $9,999	10
		$10,000 & above	11
		Don't Know (DO NOT READ OUT)	97
		Refused (DO NOT READ OUT)	99

G4	How many days do you work in a week?	RECORD : _____ days

G5	How many hours do you work per day?	RECORD : _____ hours

G6	In the <u>past month</u>, how many hours did you *miss work* because of health problem? *(Include hours missed on sick days, MC, time off, leave, times when went in late, left early etc. because of health problem)*	RECORD : _____ hours

G7	In the <u>past month</u>, how many extra hours did you have to work to catch up on tasks that you were unable to complete during normal working hours due to health problem?	RECORD : _____ hours

G8a	In the <u>past 3 months</u>, did you change job because of health problem?	Yes	1	GO TO G8b
		No	2	GO TO H1

G8b	In the <u>past 3 months</u>, how many times did you change job because of health problem?	RECORD : _____ times

G8c	How much did you earn per month for your previous job (s)? Let's talk about your…..(READ OUT RECENCY) previous job. How much did you earn per month for this job?

	Most Recent	2nd Most Recent	3rd Most Recent
Below $1,000	1	1	1
$1,000 to $1,999	2	2	2
$2,000 to $2,999	3	3	3
$3,000 to $3,999	4	4	4
$4,000 to $4,999	5	5	5
$5,000 to $5,999	6	6	6
$6,000 to $6,999	7	7	7
$7,000 to $7,999	8	8	8
$8,000 to $8,999	9	9	9
$9,000 to $9,999	10	10	10
$10,000 & above	11	11	11
Don't Know (DO NOT READ OUT)	97	97	97
Refused (DO NOT READ OUT)	99	99	99

GO TO H1

G9a	You mentioned that you are currently not working. Did you quit your job during the past 3 months because of health problem?	Yes	1	**GO TO G9b**
		No	2	**GO TO H1**

G9b	How long ago did you quit your job? Was it…(READ OUT)?	1 week or less ago	1
		Over 1 to 2 weeks ago	2
		Over 2 to 4 weeks ago	3
		Over 1 to 2 months ago	4
		Over 2 months ago	5

G9c	What was your occupation before you quitted the job?	RECORD : _____

G9d	Could you please tell me how much you earn per month for this job?	Below $1,000	1
		$1,000 to $1,999	2
		$2,000 to $2,999	3
		$3,000 to $3,999	4
		$4,000 to $4,999	5
		$5,000 to $5,999	6
		$6,000 to $6,999	7
		$7,000 to $7,999	8
		$8,000 to $8,999	9

		$9,000 to $9,999	10
		$10,000 & above	11
		Don’t Know (DO NOT READ OUT)	97
		Refused (DO NOT READ OUT)	99

CAREGIVER AVAILABILITY

H1	In the <u>past 3 months</u>, did anyone help you with any of the following daily activities because of your health problem? (INTERVIEWER TO READ OUT THE FOLLOWING ACTIVITIES, ONE AT A TIME)

	Yes	No	DK	RF		
Accompanying you to see a doctor	1	2	3	4		**IF YES TO ANY, GO TO H2a**
Doing light housework	1	2	3	4		
Assisting you with some routine activities e.g. getting in and out of bed or chair, bathing, dressing, using toilet	1	2	3	4		
Taking medicine	1	2	3	4		**ELSE, GO TO J1**
Others (Specify: _____)	1	2	3	4		

H2a	Who helped you with these daily activities because of your health problem? *INTERVIEWER: RECORD ANSWER IN COLUMN H2a below*

IF ONLY MAID MENTIONED, TRANSFER ANSWER TO H2b - GO TO J1

IF ONLY ONE FAMILY MEMBER/RELATIVE/FRIEND MENTIONED, TRANSER ANSWER TO H2b - GO TO I1

IF MORE THAN ONE FAMILY MEMBER/RELATIVE/FRIEND MENTIONED, ASK H2b

H2b	You mentioned that your…(READ OUT ANSWER IN H2a) helped you with these daily activities because of your health problem. Who spends most time helping you with these daily activities?

	H2a.		H2b. Main Caregiver
	Yes	No	
Maid	1	2	1
Spouse	1	2	2
Child	1	2	3
Grandchild	1	2	4
Brother	1	2	5
Sister	1	2	6
Neighbour/friend	1	2	7
Others (Specify:_____)	1	2	8

EMPLOYMENT STATUS (CAREGIVER)

I1	Let's now talk about your caregiver, that is, your….(**READ OUT ANSWER IN**	Working	1	**GO TO I2**
		Not working	2	**GO TO I9a**

I2	What is his/her occupation?	RECORD: _____

I3	Could you please tell me how much he/she earns per month?	Below $1,000	1
		$1,000 to $1,999	2
		$2,000 to $2,999	3
		$3,000 to $3,999	4
		$4,000 to $4,999	5
		$5,000 to $5,999	6
		$6,000 to $6,999	7
		$7,000 to $7,999	8
		$8,000 to $8,999	9
		$9,000 to $9,999	10
		$10,000 & above	11
		Don't Know (DO NOT READ OUT)	97
		Refused (DO NOT READ OUT)	99

I4	How many days does he/she work in a week?	RECORD : _____ days

I5	How many hours does he/she work per day?	RECORD : _____ hours

I6	In the <u>past month</u>, how many hours did he/she *miss work* because of taking care of you and helping you with your activities? *(Include time off, leave, times when went in late, left early etc. because of your health problem)*	RECORD : _____ hours

I7	In the <u>past month</u>, how many extra hours did he/she has to work to catch up on tasks that he/she was unable to complete during normal working hours due to taking care of you and helping you with your activities?	RECORD : _____ hours

I8a	In the <u>past 3 months</u>, did he/she change job because of taking care of you and helping you with your activities?	Yes	1	GO TO I8b
		No	2	GO TO J1

I8b	In the <u>past 3 months</u>, how many times did he/she change job because of taking care of you and helping you with your activities?	RECORD : _____ times

I8c	How much did he/she earn per month for his/her previous job (s)? Let's talk about his/her…..(READ OUT RECENCY) previous job. How much did he/she earn per month for this job?

	Most Recent	2nd Most Recent	3rd Most Recent
Below $1,000	1	1	1
$1,000 to $1,999	2	2	2
$2,000 to $2,999	3	3	3
$3,000 to $3,999	4	4	4
$4,000 to $4,999	5	5	5
$5,000 to $5,999	6	6	6
$6,000 to $6,999	7	7	7
$7,000 to $7,999	8	8	8
$8,000 to $8,999	9	9	9
$9,000 to $9,999	10	10	10
$10,000 & above	11	11	11
Don't Know (DO NOT READ OUT)	97	97	97
Refused (DO NOT READ OUT)	99	99	99

GO TO J1

I9a	You mentioned that your caregiver is currently not working. Did he/she quit his/her job during the past 3 months because of taking care of you and helping you with your activities?	Yes	1	GO TO I9b
		No	2	GO TO J1

I9b	How long ago did he/she quit his/her job? Was it…(READ OUT)?	1 week or less ago	1
		Over 1 to 2 weeks ago	2
		Over 2 to 4 weeks ago	3
		Over 1 to 2 months ago	4
		Over 2 months ago	5

I9c	What was his/her occupation before he/she quitted the job?	RECORD : _____

I9d	Could you please tell me how much he/she earns per month for this job?	Below $1,000	1
		$1,000 to $1,999	2
		$2,000 to $2,999	3
		$3,000 to $3,999	4
		$4,000 to $4,999	5
		$5,000 to $5,999	6
		$6,000 to $6,999	7
		$7,000 to $7,999	8
		$8,000 to $8,999	9
		$9,000 to $9,999	10
		$10,000 & above	11
		Don’t Know (DO NOT READ OUT)	97
		Refused (DO NOT READ OUT)	99

DEMOGRAPHICS

L1	What is your current marital status?	Single, i.e. Never married	1
		Married	2
		Separated/Divorced	3
		Widowed	4
		Don't Know (DO NOT READ OUT)	97
		Refused (DO NOT READ OUT)	99

L2	What is your highest educational qualification attained?	No formal qualification/Lower Primary	1
		Primary	2
		Lower Secondary	3
		Secondary	4
		Upper Secondary	5
		Polytechnic Diploma	6
		Professional Qualification & Other Diploma	7
		Degree	8
		Postgraduate	9

L3	Do you currently smoke regularly, that is, at least once a week?	Yes	1	**GO TO L5**
		No	2	**GO TO L4**
		Don't Know (DO NOT READ	97	
		Refused (DO NOT READ OUT)	99	**GO TO L5**

L4	Did you smoke regularly before, that is, at least once a week?	Yes	1
		No	2
		Don't Know (DO NOT READ OUT)	97
		Refused (DO NOT READ OUT)	99

L5	RECORD LANGUAGE OF INTERVIEW	English	1
		Mandarin	2
		Malay	3
		Tamil	4
		English & Mandarin	5
		English & Malay	6
		English & Tamil	7
		Others (Specify:_____)	8

Name of Respondent: _____ IRID : | | | | |

Address: _____

Contact Number : _____ Date of Interview: _____ INT_ID | | | | |