Patterns and Risk Factor Profiles of Visual Loss in a Multiethnic Asian Population: The Singapore Epidemiology of Eye Diseases Study

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• PURPOSE: To describe the pattern and risk factor traits associated with visual loss (defined as either visual impairment [VI] or blindness) in a multiethnic Asian cohort of Malay, Indian, and Chinese individuals living in Singapore.

• METHODS: A total of 10 020 participants from the Singapore Epidemiology of Eye Diseases Study were examined between 2004 and 2011. All underwent standardized examinations. VI (visual acuity <20/40 to ≥20/200) and blindness (visual acuity <20/200) were defined based on the US definition, better-seeing eye. Singapore Population Census 2010 was used to calculate age-standardized prevalence. Multiple logistic regression analysis was performed to determine the independent and joint risk factors associated with visual loss.

• RESULTS: Malay individuals had higher age-standardized prevalence of best-corrected and presenting VI (5.4% and 19.9%, respectively) than Indian (3.6% and 18.0%) and Chinese individuals (3.3% and 17.2%). Cataract was the main cause for presenting and best-corrected blindness; cataract and diabetic retinopathy were the top causes for best-corrected VI, consistently observed across the 3 ethnic groups. Older age, female sex, lower socioeconomic status, diabetes, systemic comorbidities, and cognitive impairment were independently associated with increased risk of best-corrected visual loss (all $P \leq .027$). Individuals aged ≥60 years with diabetes were 12.7 times (95% confidence interval, 8.39–19.23) likely to have best-corrected visual loss, compared with younger, nondiabetic individuals. Lower income and education explained 58.1% and 23.2% of best-corrected visual loss in this population, respectively.

• CONCLUSION: In this urban multiethnic Asian population, we identified common traits associated with visual loss across Malay, Indian, and Chinese individuals. These results will be useful for the planning and designing of eye health services and strategies for Asia's rapidly developing populations living in urban communities. NOTE: Publication of this article is sponsored by the American Ophthalmological Society. (Am J Ophthalmol 2019;206:48–73. © 2019 Published by Elsevier Inc.)

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VISUAL LOSS, DEFINED AS EITHER VISUAL IMPAIRMENT (VI) or blindness, is a major public health problem,[1] and is among the top 3 most common impairments in terms of years lived with disability.[2] Visual loss is associated with reduced quality of life, increased risk of frailty, and mortality.[3–5] Globally, it was estimated that 36 million people were blind and 400 million suffered from VI in 2015.[1]

Asia alone accounts for approximately 60% cases of VI and blindness worldwide.[1,6] Furthermore, Asia accounts for most of the most common eye diseases; for example, 35% (59 million) of age-related macular degeneration (AMD)[7] and 60% (39 million) of glaucoma cases globally.[8] Taken together, there is an increase and possibly disproportionate burden of visual loss and age-related eye diseases on Asian individuals. This burden is likely to further increase in the next decade, given the rapid aging trends in Asia.[9,10] Hence, there is a need to have a granular understanding of the patterns of VI and blindness among Asian individuals, and the major factors associated with visual loss.

In the past 2 decades, there have been multiple population-based epidemiological studies and surveys in Asia that have provided considerable information on the patterns and trends of VI and blindness in disparate countries from Cambodia,[11] China,[12–22] India,[23–29] Japan,[30,31] Korea,[32] Nepal,[33] Singapore,[34] Pakistan,[35] Sri Lanka,[36] and Taiwan[37] (Supplementary Table 1). However, 3 major gaps remain.

LACK OF EVALUATION ON ETHNIC DIFFERENCES AMONG ASIAN INDIVIDUALS

THE INFLUENCE OF ETHNICITY ON HEALTH IS MYRIAD, affecting not only the incidence, severity, and prognosis of diseases but also the utilization of health services.[38–40] Ethnicity affects health through complex gene-environment and

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behavior-environment interactions, and research on multiethnic populations has been advocated by renowned health organizations such as the American Heart Association and the National Health Service Scotland.[41,42]

In Singapore, previous studies also showed the importance of evaluating ethnic differences when studying systemic diseases. For example, Singapore's National Health Survey previously observed Indian and Malay individuals to have higher prevalence of diabetes compared with Chinese,[43] thus leading to further postulation that prevalence of diabetic-related complications, such as diabetic retinopathy (DR), also may differ across ethnic groups in Singapore. Furthermore, a previous multiethnic coronary heart disease study on diabetic Singaporeans also reported ethnicity to be independently associated with coronary heart disease–related morbidity.[44] Collectively, these examples further emphasize the relevance of evaluating ethnic comparison in a country with multiethnic composition such as Singapore.

In the aspect of VI and blindness, previous multiethnic studies in the United States provided important insights into the understanding of the relative burden, risk factors, and impact of visual loss between white and African American individuals.[45–47] Findings from the US multiethnic studies rendered an extrapolated basis to hypothesize that ethnic variations also may be observed among Asian individuals as well, especially given the heterogeneity across different Asian ethnic groups.

However, currently, there is a palpable lack of evaluation on ethnic differences among Asian individuals on the risk of VI and blindness. Most previous studies have mainly focused on evaluations of specific individual ethnic groups (eg, Chinese, Indian), and few have evaluated possible ethnic difference among Asian individuals. This is mainly because the sampled population was typically more homogeneous by ethnicity. Thus, direct comparisons of ethnic variations (eg, Chinese vs Indian) between these previous Asian studies cannot be made accurately because of the inherent variations in population characteristics across these studies. Hence, ethnic comparison among Asian individuals remains an unaddressed knowledge gap.

In this regard, Singapore offers a unique opportunity to study variations among the 3 main Asian ethnic groups: Chinese, Indian, and Malay. Previous work had also observed differences in genetic ancestral profile across these 3 groups,[48] further justifying the rationale for ethnic comparison. On the other hand, genetic ancestral analyses showed that Singaporean Indian individuals well resemble Southern Indian,[49] Singaporean Chinese resemble Southern Han Chinese,[49] and Singaporean Malay individuals genetically resemble Peninsular Malaysian Malay and Indonesian Malay individuals.[50] Taken together, this indicates that evaluation of these 3 ethnic groups in Singapore also may provide useful proxy information on Malay, Indian, and Chinese individuals residing in other Asian countries.

Interesting previous observations on inherent differences among the 3 ethnic groups include the following examples. The eyes of Chinese individuals have been observed to have longer axial length and are more likely to be myopic,[51,52] Indian individuals have thinner cornea and higher intraocular pressure,[52] Malay individuals are more likely to be hypertensive,[52] and Indian individuals are more likely to have diabetes.[53] Furthermore, Chinese have a higher prevalence of AMD[52] and primary angle closure glaucoma.[8,54–56] Indian individuals have higher prevalence of DR compared with Malay and Chinese individual.[53] Consistent with these observations, early registry studies in Singapore also have shown ethnicity as an important risk factor for acute angle closure glaucoma, cataract surgery, and retinal detachment.[57–59] Considering the heterogeneity in genetic, ocular, and systemic profiles across the 3 ethnicities, it is therefore plausible to hypothesize that the patterns of VI and blindness may naturally differ across ethnic groups in Asia. Taken together, this further highlights the need for comprehensive evaluation in this aspect. As Malay, Indian, and Chinese individuals account for approximately 45% of the world population, with a global estimate of approximately 3.5 billion persons,[9] data on VI and blindness on these 3 main representative ethnic groups in Asia is crucial.

LACK OF ASIAN URBAN STUDIES ON VI AND BLINDNESS

A SECOND KNOWLEDGE GAP EXISTS WITH THE RAPID URBANization of Asian populations. Most previous Asian studies in the past 2 decades have understandably been focused on rural regions and communities (Supplementary Table 1). In fact, only a handful of studies from Korea, Japan, and Taiwan[30–32,37] have evaluated the trends of visual loss in urban regions. Hence, there remains currently a significant underrepresentation of Asian studies from urban communities. This is especially relevant with the current rapid development and urbanization in Asian countries. Furthermore, given that the rate of aging is more marked in urban regions compared with rural regions in Asia,[9] and the concomitant increases in the prevalence of age-related systemic chronic diseases associated with urbanization (eg, hypertension, diabetes),[60,61] the number of elderly in urban communities is expected to further increase and to be accompanied with corresponding increase in VI cases.

Because of the differences in environmental exposures, accessibility to eye care, and lifestyle profiles between urban and rural communities, it is likely that findings from urban study may offer new insights that are different from previous rural reports. Furthermore, within urban populations, there is generally a "wider socioeconomic

spectrum" and thus greater socioeconomic inequality and disparity compared with rural populations. As lower socioeconomic status had been shown to be associated with poorer eye care accessibility and utility,[62] evaluation in an urban setting provides a good opportunity to further identify socioeconomic factors associated with visual loss, further providing concrete evidence in this aspect to better inform policy makers in designing relevant social plans and policies.

CURRENT KNOWLEDGE GAPS ON RISK FACTORS ASSOCIATED WITH VI AND BLINDNESS

FINALLY, PREVIOUS POPULATION-BASED STUDIES MAINLY focused on reporting the prevalence and causes of visual loss, with very few that have evaluated comprehensively the entire domains of demographic, systemic, socioeconomic, and lifestyle profiles associated with VI and blindness. In fact, even risk factor evaluation on visual loss also has not been extensively reported in Western landmark population-based studies, such as Beaver Dam Eye Study,[63] Blue Mountains Eye Study,[64] and the Rotterdam Eye Study.[65] This is partly because of the limited/incomplete capture of relevant systemic or socioeconomic data or insufficient sample size in previous studies. Altogether, this presents as a missed opportunity, as insights into the characteristics associated with visual loss will potentially aid in formulation of more effective interventional strategies to combat VI and blindness.

Furthermore, although a limited number of studies have evaluated the independent effects of demographic and other factors on VI and blindness,[13,22] most previous analyses were brief and none have comprehensively explored joint and combined effects of various demographic, systemic, socioeconomic, and lifestyle factors with VI and blindness. Questions that could be addressed include the following: are older people with diabetes and hypertension at higher risk of visual loss than younger people without systemic comorbidities? Joint effect analysis provides more holistic and detailed risk factor profiling; such information will be informative in fine-tuning risk stratification for visual loss.

THE SINGAPORE EPIDEMIOLOGY OF EYE DISEASES STUDY

THE SINGAPORE EPIDEMIOLOGY OF EYE DISEASE (SEED) study is a world-leading epidemiology research program, commenced in 2004. The overall aim of the SEED study is to establish a "data portal" and information source on epidemiology of Asian eye diseases that covers the entire spectrum of prevalence, incidence, risk factors, and impact of major Asian eye diseases, based on the 3 major ethnic groups (Malay, Indian, Chinese) in Singapore. Evaluation of this multiethnic Asian population as a whole and ethnic differences among the ethnic groups, are 2 pivot points for SEED. Singapore is the ideal "population laboratory" for this purpose because of its geographic compactness and the inclusive reach of the local government's policies and urbanization. The SEED study was modeled after earlier landmark population-based eye studies with strong scientific reputations, namely the Beaver Dam Eye Study (United States, commenced in 1987), and the Blue Mountains Eye Study (Australia, commenced in 1992). Standardized protocols from SEED were modified from these 2 predecessors; this created a unique opportunity to articulate ocular research findings from Singapore among the global elites of population-based eye studies.

The SEED study is one of the few very well characterized cohorts internationally with a rich reservoir of data that is not only limited to eye diseases, but also encompasses systemic disease data, bio-samples, high-quality digital imaging data, data on quality of life assessment, and genetic markers. To date, the SEED program has resulted in many novel findings and generated close to 350 publications. Data collected from the SEED study also have been used by national and international agencies (eg, the Ministry of Health of Singapore, World Health Organization, the Global Burden of Disease program[66,67]), health bodies to formulate clinical guidelines (eg, 2014 Ministry of Health Diabetes Guidelines,[68] 2016 Asia Pacific Glaucoma Guidelines, 2016 American Diabetes Association Guidelines,[69] 2017 International Council of Ophthalmology Diabetic Eye Care Guidelines[70]), and have provided estimates of eye disease burden to set up Singapore's national DR screening,[71] and to assist the local government's planning for future health care manpower (future ophthalmology and optometry manpower[72]) in Singapore.

The SEED study is currently the single largest population-based comprehensive eye study comprising 10 033 adults aged 40 years and older, composed of Malay, Indian, and Chinese individuals, the 3 major ethnic groups in Asia. Standardized setting and examinations were performed across the 3 ethnic groups, thus providing a unique and unprecedented opportunity to compare data across these 3 ethnic groups in a common geographic and socioeconomic environment. To date, this has not been done in any other population-based studies worldwide. The unique design of the SEED study in an urban setting, coupled with a large sample and wide range of well-characterized data, will help to adequately address the previously mentioned knowledge gaps, and may provide new insights into the trends and patterns of racial differences in VI and blindness among Asian individuals.

Previously, we had only published prevalence of VI and blindness, separately for Malay, Indian, and Chinese individuals.[73–75] In this current thesis, we highlight areas that

were not published/done previously, and more important, new areas that can now be explored in this thesis, given the large, unprecedented combined data of the 3 ethnic groups. First, we previously did not evaluate the overall trends and ethnic difference of VI and blindness across the 3 major Asian ethnic groups in Singapore. To date, this has not been done in any other population-based studies as well. Second, we previously also did not evaluate/publish systemic and socioeconomic factors that are independently associated with visual loss. With the broad range of systemic and socioeconomic data captured in our SEED study, we are poised to provide new insights in these aspects. Third, presence of multiple comorbidity of systemic diseases is common in aging populations. Nevertheless, evaluation in this area is often limited by power/sample size. Hence, the potential impact of multiple comorbidity on visual loss has not been reported in other studies. By combining the 3 population-based data from SEED, we now have better statistical power to comprehensively evaluate the combined effects of ethnicity, socioeconomic risk factors, and multimorbidity of systemic diseases on visual loss. Findings in this area are particularly relevant for aging populations in urban communities.

• **CENTRAL HYPOTHESES:** Based on the previously mentioned knowledge gaps and rationale, a few hypotheses were formulated. First, given the differences in lifestyle, socioeconomic profiles, and cultural facets across the 3 ethnic groups, coupled with observations from previous reports that indicated differences in health awareness and health-seeking behavior across ethnic groups,[76,77] we hypothesized that Malay individuals have a higher prevalence of VI and blindness, whereas Chinese have the lowest prevalence among the 3 groups. Second, we hypothesized that lower socioeconomic indicators and presence of systemic diseases, such as diabetes, are associated with higher odds of prevalent VI and blindness. Third, we postulated that presence of combined measures of ethnicity, socioeconomic risk factors, and multiple comorbidity of systemic diseases increases the odds of VI and blindness.

• **OBJECTIVE OF THESIS AND POTENTIAL IMPACT:** The objective of this thesis was twofold. First, we attempted to describe and examine ethnic differences in patterns and causes of VI and blindness in a multiethnic Asian population of Malay, Indian, and Chinese individuals living in an Asian urban community. Second, we sought to assess the independent and joint effects of demographic, systemic, socioeconomic, and lifestyle factors on VI and blindness in this multiethnic Asian population.

This thesis provides the first large population-based summary of pattern, trends, and factors associated with VI and blindness in a multiethnic Asian cohort that represents the 3 major ethnic groups in Asia. Findings from this thesis will be particularly relevant to the increasing number of individuals with visual loss in Asia due to rapid aging.[1] In addition, independent and joint effect analysis of risk factors associated with visual loss may provide new knowledge to better stratify and identify individuals who are at higher risk of having visual loss, thus aiding public health officials in formulating more targeted vision-screening strategies. Overall, findings from this thesis will be useful and relevant in the planning and designing of eye health services for Asia's rapidly developing urban communities. Collectively, these data will directly and indirectly contribute to the World Health Organization (WHO)'s VISION 2020 goal of reducing VI and blindness.[78]

METHODS

• **STUDY DESIGN:** The SEED study is a population-based cross-sectional study, comprising 3 major ethnic groups in Singapore: Malay (the Singapore Malay Eye Study, year 2004 to 2006), Indian (the Singapore Indian Eye Study, year 2007 to 2009), and Chinese (the Singapore Chinese Eye Study, year 2009 to 2011). Details of the study design and methodology of the SEED study have been described in detailed previously.[79,80] In brief, the SEED study was conducted in the southwestern part of Singapore (Figure 1), using a standardized study protocol across the 3 ethnic groups of subjects. According to the Singapore census of 2000, the southwest region was unique in providing a fair distribution of the local population in terms of age, housing types, ethnic diversity, and socioeconomic status. In addition, the southwestern part of Singapore was selected mainly because of the following potential advantages. First, in this area, there were sufficient numbers of Malay, Indian, and Chinese individuals to obtain our original intended sample size. Second, the selected districts lay along the track line of Singapore's subway train, which allowed for a direct commute to the study clinic. Third, the study area covered approximately 110.4 sq km (42.6 sq mile) or 15.8% of the country's total land area of 699.4 sq km (270.0 sq mile), which covered a large sector of all populated areas in Singapore.

Age-stratified random sampling strategy was adopted in each ethnic group to select adults aged 40 to 80 years. A total of 5600 Malay residents, 6350 Indian residents, and 6752 Chinese residents were originally selected from Singapore's Ministry of Home Affairs. Ethnicity was defined and categorized based on the ethnicity indicated on each individual's National Registration Identity Card. From here, a list of eligible individuals was then identified. Ineligible individuals were defined as those who had permanently moved out from the stated residential address, had not lived at the given address in the past 6 months, or were deceased or terminally ill. A total of 4168 Malay, 4497 Indian, and 4605 Chinese individuals were identified as eligible individuals and invited to participate in the

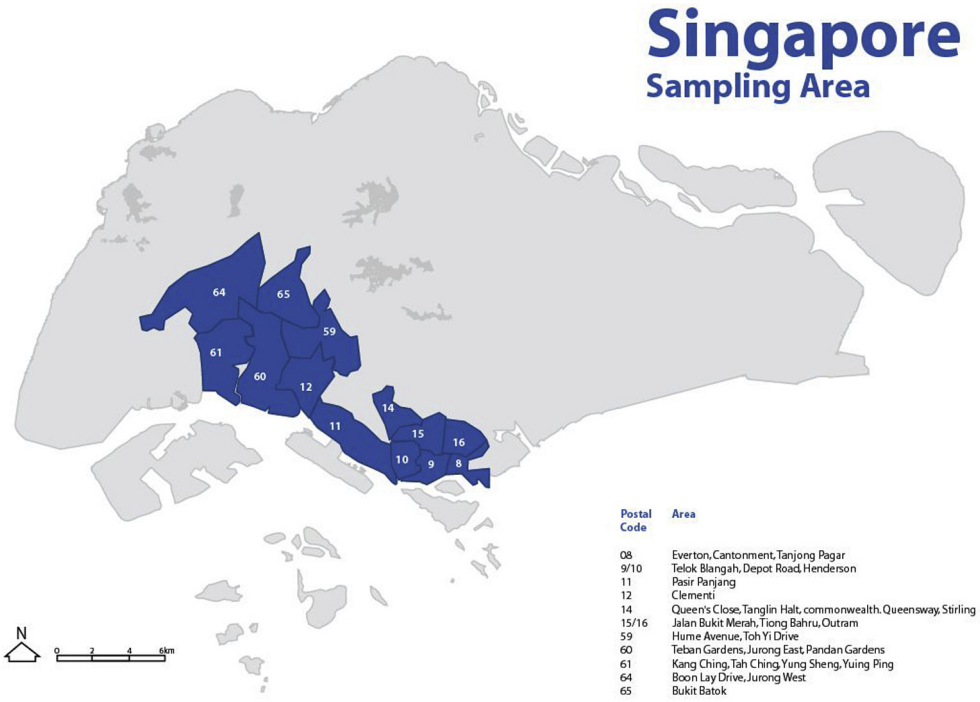

FIGURE 1. Study sampling area of the Singapore Epidemiology of Eye Diseases Study.

study; of which 3280 Malay (78.7% response rate), 3400 Indian (75.6% response rate), and 3353 Chinese (72.8%) individuals participated and underwent the study examinations. In each ethnic cohort, nonparticipants on average were slightly older than participants ($P < .001$ for all), but there were no significant sex differences between the 2 groups ($P > .05$ for all). Details on the sampling and enrollment of subjects are illustrated in Figure 2. The study was approved by the Singapore Eye Research Institute Institutional Review Board. All participants gave a written informed consent and the conduct of the study adhered to the Declaration of Helsinki. All subjects underwent standardized ocular, systemic examinations and interview at the Singapore Eye Research Institute.

• **OCULAR EXAMINATION AND VISUAL ACUITY TESTING:** All study participants underwent a detailed ocular examination, including visual acuity (VA) measurement, subjective refraction, slit lamp examination, intraocular pressure measurement, dilated fundus examination, and fundus photography. Digital fundus photography was performed using a 45-degree digital retinal camera (Canon CR DGi with a SLR digital camera back; Canon, Tokyo, Japan) after pupil dilation. Macular- and optic disc–centred fundus photos were captured for each eye.

The presenting VA (PVA) with habitual correction, and best-corrected VA (BCVA) after subjective refraction were recorded using an Early Treatment of Diabetic Retinopathy Study logarithm of Minimum Angle of Resolution number chart (Lighthouse International) at a distance of 4 m.[79] When no numbers could be read at 4 m, the participant was moved to 3, 2, or 1 m, consecutively. When no number could be read at even 1 m, VA was then assessed as counting fingers, hand movements, perception of light, or no perception of light.

• **DEFINITIONS OF VI AND BLINDNESS:** Overall, both the United States and the modified WHO definitions were used to define VI and blindness. According to the US definition, VI was defined as VA <20/40 but ≥20/200 in the better-seeing eye, and blindness was defined as VA <20/200 in the better-seeing eye. Based on the WHO definition, VI was defined as VA <20/60 but ≥20/400 in the better-seeing eye, and blindness was defined as VA <20/400 in the better-seeing eye. We used a modified definition to classify individuals with VA of counting fingers or worse as blind. All subjects were also further categorized into 5 mutually exclusive categories: (1) bilateral blindness; (2) bilateral VI (VI in one eye and VI/blindness in the other eye); (3) unilateral blindness; (4) unilateral VI; and (5) normal vision in both eyes. Of note, unilateral VI and unilateral blindness cases were defined based on the worse-seeing eye, with the fellow eye having normal vision.

• **ASSESSMENT ON CAUSES OF VI AND BLINDNESS:** Primary causes of VI or blindness were ascertained on the basis of clinical history, examination, disease definition, and clinical judgment. Undercorrected refractive error was

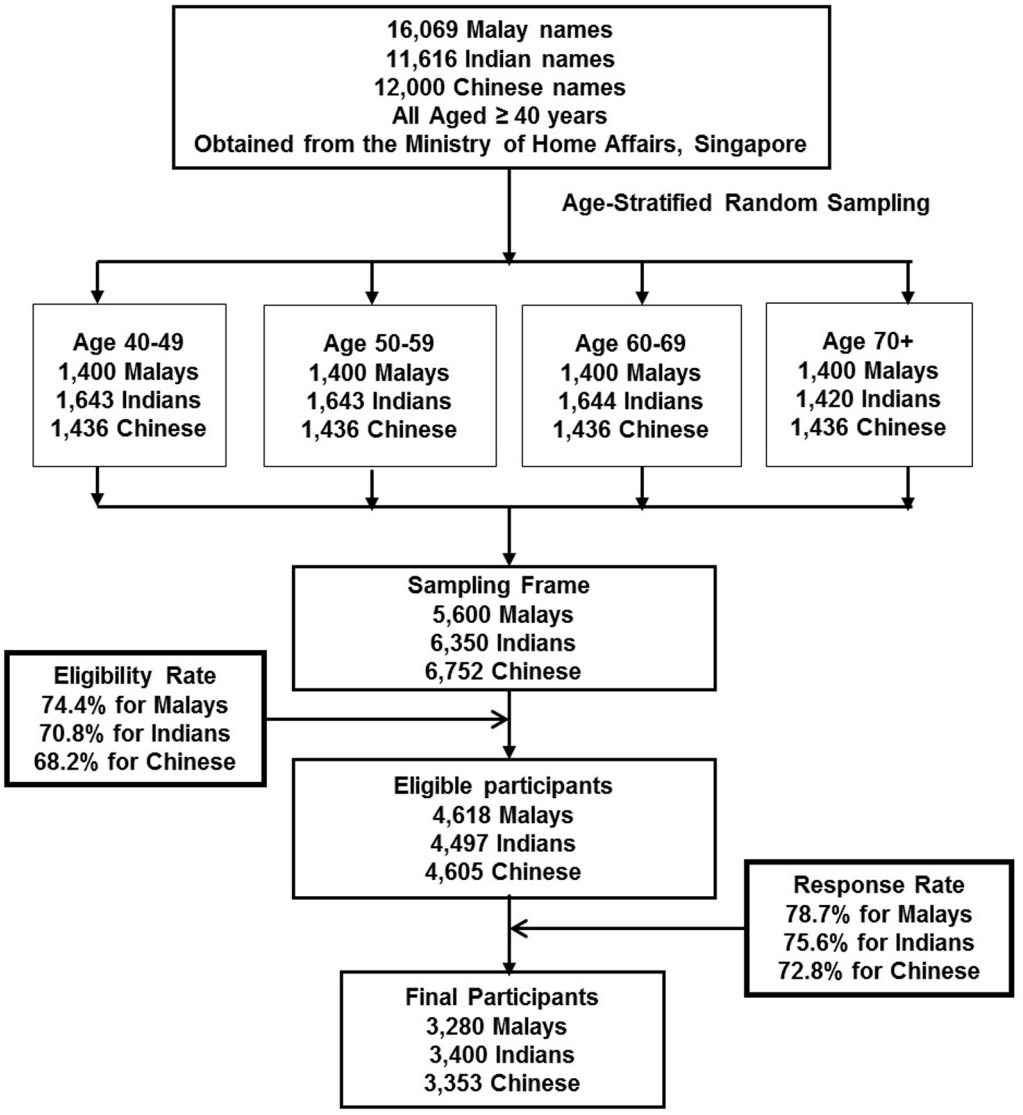

FIGURE 2. Selection and exclusion processes to form the final study population of the Singapore Epidemiology of Eye Diseases Study.

defined when BCVA was at least 2 lines (in logarithm of Minimum Angle of Resolution chart) better than PVA. Glaucoma was diagnosed according to the International Society of Geographical and Epidemiological Ophthalmology scheme.[81] AMD was graded from retinal photographs using the Wisconsin Age-related Maculopathy grading system.[82] DR was graded from retinal photographs using a modification of the Arlie House classification system for the Early Treatment Diabetic Retinopathy Study.[83] Cataract was determined from slit lamp examination and graded based on the using the Lens Opacities Classification System III.[84] All retinal photographs were sent to the University of Sydney for grading of retinopathy, cataract, and other retinal diseases. These were all graded by a single grader, with adjudication performed by 2 experts in retinal diseases and photo grading, when necessary (Prof Paul Mitchell and Prof Jiejin Wang, collaborators from the University of Sydney).

If there was more than 1 condition in the same eye, the main cause of VI and blindness was further determined, based on the severity of the underlying eye diseases. For example, in the case of intermediate cataract and mild DR, cataract would be indicated as the primary cause of VI.

• **QUESTIONNAIRE AND SYSTEMIC MEASUREMENTS:** Detailed interviewer-administered questionnaires were also performed to collect relevant medical history, socioeconomic status information (eg, education, income levels, type of housing), and lifestyle-related information (eg, cigarette use, alcohol consumption), as reported previously.[80]

Cognitive assessment was performed for participants aged 60 and older, using the Abbreviated Mental Test (AMT), which consists of 10 questions of general cognitive function. Cognitive impairment was defined as an AMT score of 6 or less of 10 for the participants with 0 to 6 years of formal education, and an AMT score of 8 or less of 10 for those with more than 6 years of formal education.[85] Deafness was defined based on self-reported history of hearing loss.

Systolic and diastolic blood pressures (BPs) were measured using an automated sphygmomanometer (DinamapPro100V2; GE HealthCare, Little Chalfont, UK). BP was measured twice, with 5 minutes apart. A third measurement was taken if the previous 2 systolic BP readings differed by more than 10 mm Hg or the diastolic BP by more than 5 mm Hg. The mean between the 2 BP closest readings was then taken. Nonfasting blood samples were extracted from participants to determine levels of serum glucose, glycosylated haemoglobin (HbA1C), cholesterol, and serum creatinine. Body mass index (BMI) also was measured. Patients with hypertension were defined as having systolic BP ≥140 mm Hg, diastolic BP ≥90 mm Hg, use of antihypertensive medications, or self-reported physician-diagnosed hypertension. Diabetes was defined as having random glucose level of ≥11.1 mmol/L, HbA1c of ≥6.5 mmol/L, use of diabetic medications, or self-reported physician-diagnosed diabetes. Hyperlipidemia was defined as total cholesterol ≥6.2 mmol/L or use of lipid-lowering drugs. Cardiovascular disease (CVD) was defined as self-reported myocardial infarction or angina or stroke. Chronic kidney disease (CKD) was defined as having an estimated glomerular filtration rate <60 mL/min per 1.73 m^2, based on the US National Kidney Foundation Kidney Disease Outcome Quality Initiative Working Group definition.[86] Estimated glomerular filtration rate was estimated from serum creatinine level, using the CKD Epidemiology Collaboration equation.[87] Systemic comorbidities were defined as concurrent presence of hypertension, diabetes, hyperlipidemia, CKD, or CVD. BMI was measured as weight in kilograms divided by height in meters squared. BMI was further divided into subgroups based on the WHO classification: underweight (BMI <18.5), normal (18.5 ≤ BMI <25), overweight (25 ≤ BMI <30), or obese (BMI ≥30).

• **STATISTICAL ANALYSIS:** All statistical analyses were performed using R version 2.15.3 (R Development Core Team, 2013, Vienna, Austria). In descriptive analyses, to compare characteristics across the 3 ethnic groups, 1-way analysis of variance was performed for continuous variables, and χ^2 tests were used for categorical variables. To compare characteristics between individuals with VI and those without, independent *t*-test was performed for continuous variables, and χ^2 test was used for categorical variables. Prevalence estimates of VI and blindness for entire sample and respective ethnic groups were calculated and standardized to the 2010 Singapore Population Census 2010. Bootstrapping was performed to compare the standardized rate of VI and blindness across the 3 ethnicities, between sex groups, and between diabetic and nondiabetic groups.

Multiple logistic regression model was used to assess the associations among demographic, socioeconomic, and systemic factors with presenting and best-corrected bilateral visual loss (defined as bilateral VI or blindness, based on better-seeing eye and US definition) in overall SEED sample and respective ethnic groups. Statistical interactions among demographic, socioeconomic, and systemic factors were examined in separate models by including cross-product interaction terms in the corresponding logistic regression models. Furthermore, for factors that were statistically significant ($P < .05$), the adjusted odds ratio (OR) as determined from the multiple logistic regression models and the prevalence of exposure factors were used to calculate the population of attributable risk (PAR) for these factors.[88] Last, factors that were significant (as determined from the multiple logistic regression model) in at least 2 ethnic groups were further illustrated in bar graphs for comparison of PAR across ethnic groups.

RESULTS

OF THE TOTAL 10 033 STUDY PARTICIPANTS, 13 DID NOT have presenting VA measured, thus leaving 10 020 participants (3269 Malay, 3400 Indian, 3351 Chinese) included for presenting VA-related analysis. In addition, another 34 participants did not have subjective refraction taken, leaving 9986 participants (3235 Malay, 3400 Indian, 3351 Chinese) included for best-corrected VA-related analysis. Table 1 shows the characteristics of the overall study sample, and respective ethnic groups. The mean (SD) age of the overall sample was 58.9 (10.4) years. Among the 3 ethnic groups, Malay individuals were slightly older, had higher BMI profile, had higher prevalence of hypertension and CKD, and had higher proportions of current smokers and individuals of low socioeconomic status. On the other hand, Indian individuals had higher prevalence of diabetes and CVD.

For the whole SEED sample, based on PVA and US definition, the age-standardized prevalence of bilateral blindness was 0.9% (95% confidence interval [CI], 0.7%–1.1%), 18.4% (95% CI, 17.6%–19.2%) for bilateral VI, 1.8% (95% CI, 1.6%–2.1%) for unilateral blindness, and 18.5% (95% CI, 17.7%–19.4%) for unilateral VI (Table 2). Based on BCVA and US definition, the age-standardized prevalence of bilateral blindness was 0.3% (95% CI, 0.2%–0.4%), 4.2% (95% CI, 3.8%–4.5%) for bilateral VI, 1.6% (95% CI, 1.4%–1.9%) for unilateral blindness, and 6.8% (95% CI, 6.3%–7.3%) for unilateral VI (Table 2). Overall, women had higher prevalence of

TABLE 1. Demographic, Systemic, and Socioeconomic Characteristics of Participants in the Singapore Epidemiology of Eye Diseases Study.

	Overall (N = 10 020)	Malay (n = 3269)	Indian (n = 3400)	Chinese (n = 3351)	P[a]
Age (y)	58.9 (10.4)	59.2 (11.0)	57.8 (10.1)	59.7 (9.9)	< .001
Female gender, n (%)	5082 (50.7)	1698 (51.9)	1694 (49.8)	1690 (50.4)	.206
BMI, kg/m^2	25.4 (4.7)	26.4 (5.1)	26.2 (4.8)	23.7 (3.7)	< .001
BMI categories, n (%)					
Underweight (BMI < 18.5)	434 (4.4)	140 (4.3)	94 (2.8)	200 (6.0)	< .001
Normal (18.5 ≤ BMI < 25)	4697 (47.2)	1243 (38.3)	1381 (40.8)	2073 (62.3)	
Overweight (25 ≤ BMI <30)	3393 (34.1)	1184 (36.5)	1330 (39.3)	879 (26.4)	
Obese (BMI ≥30)	1435 (14.4)	680 (20.9)	578 (17.1)	177 (5.3)	
Diabetes, n (%)	2957 (29.5)	1045 (32.0)	1320 (38.8)	592 (17.7)	< .001
Hypertension, n (%)	6383 (63.9)	2289 (70.3)	2050 (60.4)	2044 (61.1)	< .001
History of CVD, n (%)	1081 (10.8)	364 (11.2)	483 (14.3)	234 (7.0)	< .001
CKD, n (%)	1213 (12.7)	715 (22.8)	273 (8.4)	225 (7.1)	< .001
Hyperlipidaemia, n (%)	4403 (45.4)	1323 (41.2)	1554 (47.9)	1526 (47.1)	< .001
Education level, n (%)					
Formal education	7676 (76.7)	2295 (70.3)	2786 (82.1)	2595 (77.5)	< .001
No formal education	2331 (23.3)	968 (29.7)	608 (17.9)	755 (22.5)	
Month income status, n (%)					
Income ≥ S$2000	2187 (22.3)	348 (10.7)	870 (26.3)	969 (29.8)	< .001
Income < S$2000	7616 (77.7)	2893 (89.3)	2441 (73.7)	2282 (70.2)	
Current smoker, n (%)					
Never smoked or past smoker	8402 (84.0)	2598 (79.7)	2895 (85.3)	2909 (86.8)	< .001
Current smoker	1603 (16.0)	662 (20.3)	499 (14.7)	442 (13.2)	
Alcohol consumption, n (%)	848 (8.5)	53 (1.6)	429 (12.6)	366 (10.9)	< .001
Living alone, n (%)	495 (5.0)	157 (4.8)	169 (5.0)	169 (5.1)	< .001
Housing category (%)					
≥ 5 room public housing flat	3064 (30.6)	517 (15.8)	1211 (35.7)	1336 (39.9)	< .001
3–4 room public housing flat	6204 (62.0)	2245 (68.8)	2021 (59.6)	1938 (57.9)	
1–2 room public housing flat	738 (7.4)	503 (15.4)	161 (4.8)	74 (2.2)	
Low socioeconomic status, n (%)[b]	627 (6.4)	437 (13.5)	132 (4.0)	58 (1.8)	< .001

BMI = body mass index; CVD = cardiovascular disease; CKD = chronic kidney disease.
Data presented are mean (standard deviation) or frequency (percentage), where appropriate.
[a]*P* value was based on analysis of variance test for continuous variables and chi-square tests for categorical variables.
[b]Defined as having primary or lower education, individual monthly income < SGD$2000, and residing in 1–2 room public housing flat.

bilateral VI and blindness (presenting and best corrected) compared with men. Similar trends were observed for VI and blindness based on WHO definition (albeit different rates than the ones based on US definition, Supplementary Table 2). For all categories of VI and blindness, the prevalence rates increased with older age groups (all *P* trend < .001, not shown in tables). This trend is particularly prominent for presenting and best-corrected bilateral VI, with exponential increase in prevalence rates from age group 60 to 69 to age group ≥70 years.

Table 3 shows the prevalence of blindness and VI, based on US definition, across the 3 ethnic groups. For presenting bilateral blindness, we observed that Malay individuals (1.4%) had higher age-standardized prevalence, compared with Indian (0.7%, *P* < .001) and Chinese (0.5%, *P* < .001) individuals. Malay individuals also had higher age-standardized prevalence of presenting bilateral VI (19.9%), compared with Indian (18.0%) and Chinese (17.2%) individuals. These ethnic differences in prevalence rates were consistently observed for all age groups. However, Indian and Chinese individuals (both 2.1%) had higher prevalence of unilateral blindness compared with Malay individuals (1.3%, both *P* < .001). Chinese individuals had higher prevalence of unilateral VI (20.9%) compared with Indian (18.0%, *P* < .001) and Malay individuals (16.5%, *P* < .001). On the other hand, based on BCVA, the prevalence of best-corrected bilateral blindness was similar across the 3 ethnicities. For best-corrected bilateral VI, Malay individuals (5.4%) had higher age-standardized prevalence, compared with Indian (3.6%, *P* < .001) and Chinese individuals (3.3%, *P* < .001). Indian individuals had higher prevalence of best-corrected unilateral blindness, compared with

TABLE 2. Prevalence of Blindness and VI in the Singapore Epidemiology of Eye Diseases Study, Based on the US Definition

		Based on Presenting Visual Acuity			Based on Best-Corrected Visual Acuity		
		All (N = 10 020)	Male (n = 4938)	Female (n = 5082)	All (n = 9986)	Male (n = 4927)	Female (n = 5059)
Vision status[a]	Age group, y	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Bilateral blindness	40–49	9 (0.4)	1 (0.1)	8 (0.6)	2 (0.08)	0 (0.0)	2 (0.2)
	50–59	14 (0.5)	6 (0.4)	8 (0.5)	4 (0.1)	3 (0.2)	1 (0.06)
	60–69	28 (1.1)	11 (0.8)	17 (1.4)	11 (0.4)	6 (0.5)	5 (0.4)
	70+	58 (3.2)	16 (1.6)	42 (4.9)	23 (1.3)	8 (0.8)	15 (1.8)
	Total	109 (1.1)	34 (0.7)	75 (1.5)	40 (0.4)	17 (0.4)	23 (0.5)
	Age standardized prevalence, % (95% CI)[b]	0.9 (0.7–1.1)	0.5 (0.4–0.8)	1.3 (1.0–1.6)	0.3 (0.2–0.4)	0.3 (0.2–0.4)	0.4 (0.2–0.6)
Bilateral VI[c]	40–49	220 (8.9)	80 (6.7)	140 (10.9)	15 (0.6)	6 (0.5)	9 (0.7)
	50–59	455 (14.5)	173 (11.9)	282 (16.8)	43 (1.4)	9 (0.6)	34 (2.0)
	60–69	655 (25.6)	284 (21.7)	371 (29.6)	129 (5.1)	47 (3.6)	82 (6.6)
	70+	823 (44.9)	409 (42.0)	414 (48.1)	357 (19.6)	148 (15.3)	209 (24.6)
	Total	2153 (21.5)	946 (19.2)	1207 (23.8)	544 (5.5)	210 (4.3)	334 (6.6)
	Age standardized prevalence, % (95% CI)[b]	18.4 (17.6–19.2)	15.7 (14.6–16.8)	21.0 (19.8–22.3)	4.2 (3.8–4.5)	3.0 (2.6–3.5)	5.3 (4.8–5.9)
Unilateral blindness	40–49	27 (1.1)	17 (1.4)	10 (0.8)	14 (0.6)	9 (0.8)	5 (0.4)
	50–59	41 (1.3)	18 (1.2)	23 (1.4)	39 (1.2)	17 (1.2)	22 (1.3)
	60–69	65 (2.5)	38 (2.9)	27 (2.2)	55 (2.2)	32 (2.4)	23 (1.9)
	70+	73 (4.0)	43 (4.4)	30 (3.5)	86 (4.7)	53 (5.5)	33 (3.9)
	Total	206 (2.1)	116 (2.4)	90 (1.8)	194 (1.9)	111 (2.3)	83 (1.6)
	Age standardized prevalence, % (95% CI)[b]	1.8 (1.6–2.1)	2.0 (1.7–2.5)	1.6 (1.3–2.0)	1.6 (1.4–1.9)	1.8 (1.5–2.2)	1.4 (1.1–1.8)
Unilateral VI	40–49	319 (12.9)	160 (13.4)	159 (12.4)	47 (1.9)	25 (2.1)	22 (1.7)
	50–59	588 (18.7)	268 (18.4)	320 (19.0)	118 (3.8)	49 (3.4)	69 (4.1)
	60–69	661 (25.8)	367 (28.0)	294 (23.5)	295 (11.6)	151 (11.5)	144 (11.6)
	70+	444 (24.2)	246 (25.2)	198 (23.0)	389 (21.4)	197 (20.4)	192 (22.6)
	Total	2012 (20.1)	1041 (21.1)	971 (19.1)	849 (8.5)	422 (8.6)	427 (8.4)
	Age standardized prevalence, % (95% CI)[b]	18.5 (17.7–19.4)	19.2 (17.9–20.4)	17.9 (16.7–19.1)	6.8 (6.3–7.3)	6.6 (5.9–7.3)	7.0 (6.3–7.7)

CI = confidence interval; VI = visual impairment.

Based on the US definition, VI was defined as VA <20/40 to ≥20/200. Blindness was defined as VA <20/200.

[a]Bilateral blindness and bilateral VI were defined based on better-seeing eye, whereas unilateral blindness and unilateral VI were defined based on worse-seeing eye.

[b]Standardized to Singapore population 2010 census.

[c]Bilateral VI includes participants with VI in one eye and VI/blindness in the other eye.

TABLE 3. Prevalence of Blindness and Visual Impairment (VI) in the Three Ethnic Groups of the Singapore Epidemiology of Eye Diseases Study, Based on the United States Definition

		Based on Presenting Visual Acuity			Based on Best-Corrected Visual Acuity		
		Malay (n = 3269)	Indian (n = 3400)	Chinese (n = 3351)	Malay (n = 3235)	Indian (n = 3400)	Chinese (n = 3351)
Vision status[a]	Age group, y	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Bilateral blindness	40–49	5 (0.6)	3 (0.3)	1 (0.1)	0 (0.0)	2 (0.2)	0 (0.0)
	50–59	4 (0.4)	5 (0.5)	5 (0.5)	0 (0.0)	3 (0.3)	1 (0.1)
	60–69	14 (1.8)	10 (1.1)	4 (0.4)	5 (0.7)	4 (0.5)	2 (0.2)
	70+	37 (5.1)	9 (1.9)	12 (1.9)	12 (1.7)	6 (1.3)	5 (0.8)
	Total	60 (1.8)	27 (0.8)	22 (0.7)	17 (0.5)	15 (0.4)	8 (0.2)
	Age standardized prevalence, % (95% CI)[b]	1.4 (1.0–1.8)	0.7 (0.5–1.1)	0.5 (0.3–0.9)	0.3 (0.2–0.6)	0.4 (0.2–0.7)	0.2 (0.1–0.4)
Bilateral VI[c]	40–49	77 (9.5)	81 (8.5)	62 (8.7)	7 (0.9)	5 (0.5)	3 (0.4)
	50–59	156 (16.3)	174 (16.2)	125 (11.3)	19 (2.0)	18 (1.7)	6 (0.5)
	60–69	212 (27.3)	233 (26.3)	210 (23.3)	49 (6.4)	51 (5.8)	29 (3.2)
	70+	344 (47.5)	181 (37.8)	298 (47.2)	179 (25.3)	66 (13.8)	112 (17.8)
	Total	789 (24.1)	669 (19.7)	695 (20.7)	254 (7.9)	140 (4.1)	150 (4.5)
	Age standardized prevalence, % (95% CI)[b]	19.9 (18.4–21.4)	18.0 (16.6–19.4)	17.2 (15.9–18.7)	5.4 (4.8–6.2)	3.6 (3.0–4.2)	3.3 (2.7–3.9)
Unilateral blindness	40–49	2 (0.3)	13 (1.4)	12 (1.7)	0 (0.0)	9 (0.9)	5 (0.7)
	50–59	8 (0.8)	16 (1.5)	17 (1.5)	7 (0.7)	21 (2.0)	11 (1.0)
	60–69	20 (2.6)	20 (2.3)	25 (2.8)	16 (2.1)	21 (2.4)	18 (2.0)
	70+	25 (3.5)	27 (5.6)	21 (3.3)	26 (3.7)	30 (6.3)	30 (4.8)
	Total	55 (1.7)	76 (2.2)	75 (2.2)	49 (1.5)	81 (2.4)	64 (1.9)
	Age standardised prevalence, % (95% CI)[b]	1.3 (1.0–1.7)	2.1 (1.7–2.7)	2.1 (1.6–2.6)	1.1 (0.8–1.5)	2.2 (1.8–2.8)	1.6 (1.2–2.1)
Unilateral VI	40–49	86 (10.6)	120 (12.5)	113 (15.9)	7 (0.9)	24 (2.5)	16 (2.3)
	50–59	156 (16.3)	195 (18.1)	237 (21.4)	35 (3.7)	44 (4.1)	39 (3.5)
	60–69	202 (26.0)	212 (23.9)	247 (27.4)	93 (12.1)	89 (10.0)	113 (12.6)
	70+	168 (23.2)	119 (24.8)	157 (24.9)	137 (19.4)	78 (16.3)	174 (27.6)
	Total	612 (18.7)	646 (19.0)	754 (22.5)	272 (8.4)	235 (6.9)	342 (10.2)
	Age standardized prevalence, % (95% CI)[b]	16.8 (15.5–18.3)	18.0 (16.6–19.5)	20. 9 (19.3–22.6)	6.2 (5.5–7.1)	6.2 (5.4–7.1)	7.8 (7.0–8.8)

CI = confidence interval; VI = visual impairment.

Based on the US definition, VI was defined as VA <20/40 to ≥20/200. Blindness was defined as VA <20/200.

[a]Bilateral blindness and bilateral VI were defined based on better-seeing eye, whereas unilateral blindness and unilateral VI were defined based on worse-seeing eye.

[b]Standardized to Singapore population 2010 census.

[c]Bilateral VI includes participants with VI in one eye and VI/blindness in the other eye.

TABLE 4. Causes of VI and Blindness in the Singapore Epidemiology of Eye Diseases Study, Based on Presenting Visual Acuity and the United States Definition.

	Bilateral VI[a]				Bilateral Blindness			
	Overall SEED (n = 2153)	Malay (n = 789)	Indian (n = 669)	Chinese (n = 695)	Overall SEED (n = 109)	Malay (n = 60)	Indian (n = 27)	Chinese (n = 22)
Causes	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Undercorrected refractive error	1202 (55.8)	458 (58.0)	337 (50.4)	407 (58.6)	17 (15.6)	10 (16.7)	2 (7.4)	5 (22.7)
Cataract	735 (34.1)	278 (35.2)	226 (33.8)	231 (33.2)	67 (61.5)	42 (70.0)	16 (59.3)	9 (40.9)
Diabetic retinopathy	56 (2.6)	17 (2.2)	29 (4.3)	10 (1.4)	5 (4.6)	2 (3.3)	1 (3.7)	2 (9.1)
Age-related macular degeneration	33 (1.5)	8 (1.0)	15 (2.2)	10 (1.4)	9 (8.3)	2 (3.3)	3 (11.1)	4 (18.2)
Posterior capsular opacity	28 (1.3)	4 (0.5)	15 (2.2)	9 (1.3)	0 (0)	0 (0)	0 (0)	0 (0)
Myopic maculopathy	19 (0.9)	3 (0.4)	11 (1.6)	5 (0.7)	1 (0.9)	0 (0)	0 (0)	1 (4.5)
Glaucoma	16 (0.7)	6 (0.8)	5 (0.7)	5 (0.7)	3 (2.8)	2 (3.3)	1 (3.7)	0 (0)
Epiretinal membrane	7 (0.3)	0 (0)	2 (0.3)	5 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)
Other maculopathy	13 (0.6)	1 (0.1)	12 (1.8)	0 (0)	2 (1.8)	0 (0)	2 (7.4)	0 (0)
Corneal opacity/scar	13 (0.6)	2 (0.3)	9 (1.3)	2 (0.3)	2 (1.8)	1 (1.7)	0 (0)	1 (4.5)
Pterygium	3 (0.1)	2 (0.3)	0 (0)	1 (0.1)	0 (0)	0 (0)	0 (0)	0 (0)
Retinal detachment	3 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	2 (1.8)	1 (1.7)	1 (0.9)	0 (0)
Amblyopia	8 (0.4)	2 (0.3)	5 (0.7)	1 (0.1)	1 (0.9)	0 (0)	1 (3.7)	0 (0)
Retinal vein occlusion	1 (0)	1 (0.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Ocular trauma	2 (0.1)	2 (0.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Aphakia	1 (0)	1 (0.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Others	13 (0.6)	3 (0.3)	2 (0.3)	8 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)

SEED = Singapore Epidemiology of Eye Disease; VI = visual impairment.
[a]Bilateral VI includes participants with VI in one eye and VI/blindness in the fellow eye.

Malay individuals (1.1%, $P < .001$). Chinese individuals had the higher prevalence of unilateral VI (7.8%) compared with Indian (6.2%, $P < .001$) and Malay individuals (6.2%, $P < .001$). Supplementary Table 3 shows the prevalence of blindness and VI across the 3 ethnic groups, based on WHO definition. In general, the trends in ethnic differences were similar to the trends based on US definition (Table 3).

Tables 4 and 5 show the causes of VI and blindness (US definition) in the SEED study for overall sample and respective ethnic groups. Based on PVA (Table 4), the leading causes of bilateral VI were undercorrected refractive error (1202 cases; 55.8%), cataract (735 cases; 34.1%), DR (56 cases; 2.6%), and AMD (33 cases; 1.5%). This distribution was similarly observed across the 3 ethnic groups (Figure 3). On the other hand, for presenting bilateral blindness, the leading causes were cataract (67 cases; 61.5%), undercorrected refractive error (17 cases; 15.6%), AMD (9 cases; 8.3%), and DR (5 cases; 4.6%). This was also similarly observed across the 3 ethnic groups, except for Indian individuals, in whom AMD was the second leading cause instead (Figure 4). After refractive correction (ie, based on BCVA, Table 5), the leading causes of bilateral VI were cataract (422 cases; 77.6%), DR (35 cases; 6.4%), myopic maculopathy (18 cases; 3.3%), and posterior capsular opacity (17 cases; 3.1%). Across the 3 ethnic groups, cataract and DR were consistently the top 2 causes of best-corrected bilateral VI (Figure 5). Of note, there was a disproportionately higher number of cataract cases in Malay individuals (n = 217; 85.4%), compared with Indian (n = 91; 65%) and Chinese individuals (n = 114; 76%). In addition, myopic maculopathy was the third leading cause for Indian (n = 9) and Chinese (n = 7 individuals), whereas there were only 2 cases of myopic maculopathy in Malay individuals. For best-corrected bilateral blindness, cataract remained to be the primary cause (65%); this was also consistent across the 3 ethnic groups (Figure 6).

Table 6 shows demographic, systemic, lifestyle, and socioeconomic factors associated with presenting bilateral visual loss (based on US definition) in the SEED study. Multiple logistic regression model demonstrated that older age (per decade, OR, 1.85; 95% CI, 1.73–1.98), female sex (OR, 1.42; 95% CI, 1.25–1.62), presence of CKD (OR, 1.22; 95% CI, 1.05–1.43), cognitive impairment (OR, 2.15; 95% CI, 1.75–2.63), smaller housing type (those residing in 1- to 2-room public flats; OR, 1.88; 95% CI, 1.50–2.36), lower income (monthly income less than SGD $2,000; OR, 1.47; 95% CI, 1.23–1.77), and no formal education (OR, 1.75; 95% CI, 1.54–1.99) were significantly associated with higher risk of presenting bilateral VI or blindness. Of these factors, older age, female sex, cognitive impairment, smaller housing type, and lower education level were consistently significant across the 3

TABLE 5. Causes of VI and Blindness in the Singapore Epidemiology of Eye Diseases Study, Based on Best-corrected Visual Acuity and the US Definition.

	Bilateral VI[a]				Bilateral Blindness			
	Overall SEED (n = 544)	Malay (n = 254)	Indian (n = 140)	Chinese (n = 150)	Overall SEED (n = 40)	Malay (n = 17)	Indian (n = 15)	Chinese (n = 8)
Causes	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Cataract	422 (77.6)	217 (85.4)	91 (65.0)	114 (76.0)	26 (65.0)	13 (76.5)	9 (60.0)	4 (50.0)
Diabetic retinopathy	35 (6.4)	11 (4.3)	16 (11.4)	8 (5.3)	2 (5.0)	0 (0)	1 (6.7)	1 (12.5)
Age-related macular degeneration	13 (2.4)	7 (2.8)	2 (1.4)	4 (2.7)	6 (15.0)	1 (5.9)	3 (20.0)	2 (25.0)
Posterior capsular opacity	17 (3.1)	3 (1.2)	7 (5.0)	7 (4.7)	0 (0)	0 (0)	0 (0)	0 (0)
Myopic maculopathy	18 (3.3)	2 (0.8)	9 (6.4)	7 (4.7)	0 (0)	0 (0)	0 (0)	0 (0)
Glaucoma	8 (1.5)	4 (1.6)	4 (2.9)	0 (0)	2 (5.0)	2 (11.8)	0 (0)	0 (0)
Epiretinal membrane	5 (0.9)	0 (0)	1 (0.7)	4 (2.7)	0 (0)	0 (0)	0 (0)	0 (0)
Other maculopathy	2 (0.4)	0 (0)	2 (1.4)	0 (0)	1 (2.5)	0 (0)	1 (6.7)	0 (0)
Corneal opacity/scar	7 (1.3)	2 (0.8)	5 (3.6)	0 (0)	1 (2.5)	0 (0)	0 (0)	1 (12.5)
Pterygium	2 (0.4)	1 (0.4)	0 (0)	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)
Retinal detachment	3 (0.6)	1 (0.4)	1 (0.7)	1 (0.7)	2 (5.0)	1 (5.9)	1 (6.7)	0 (0)
Amblyopia	6 (1.1)	2 (0.8)	2 (1.4)	2 (1.3)	0 (0)	0 (0)	0 (0)	0 (0)
Retinal vein occlusion	1 (0.2)	0 (0)	0 (0)	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)
Ocular trauma	2 (0.4)	2 (0.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Aphakia	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Others	3 (0.6)	2 (0.8)	0 (0)	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)

SEED = Singapore Epidemiology of Eye Disease; VI = visual impairment.
[a]Bilateral VI includes participants with VI in one eye and VI/blindness in the fellow eye.

ethnic groups (all $P \leq .046$). However, CKD was significant only in Indian individuals (OR, 1.58; $P = .003$) but not Malay and Chinese individuals. Of note, in this multiple regression model adjusting for multiple factors, ethnicity was not significantly associated with risk of presenting bilateral visual loss (all $P \geq .225$)

For best-corrected bilateral visual loss (Table 7), older age (per decade, OR, 2.90; 95% CI, 2.53–3.33), female sex (OR, 1.74; 95% CI, 1.37–2.20), Malay individuals (compared with Chinese; OR, 1.72; 95% CI, 1.32–2.23), presence of diabetes (OR, 1.43; 95% CI, 1.16–1.76), presence of CKD (OR, 1.38; 95% CI, 1.10–1.74), cognitive impairment (OR, 2.07; 95% CI, 1.60–2.68), ≥3 systemic comorbidities (OR, 2.05; 95% CI, 1.30–3.23), smaller housing type (OR, 1.51; 95% CI, 1.05–2.19), lower income (OR, 2.84; 95% CI, 1.47–5.49), and no formal education (OR, 1.81; 95% CI, 1.45–2.26) were significant associated risk factors. Of these factors, older age, female sex, cognitive impairment, lower education level, and diabetes (borderline significance for Malay individuals) were common risk factors across the 3 ethnic groups. On the other hand, CKD was significant only in Indian individuals (OR, 1.75; $P = .02$), and deafness was significant only in Malay individuals (OR, 5.51; $P = .016$). Systemic comorbidities were significant in both Malay and Indian individuals, with more prominent effect observed in Indian individuals.

Furthermore, among the previously mentioned significant factors, old age (≥60 years) had the highest PAR for presenting bilateral visual loss in the overall sample (28.9%), followed by lower income level (21.0%), lower education level (12.4%), female sex (11.9%), and cognitive impairment (7.5%) (Table 8). Comparing the PAR profile across ethnicities (Figure 7), the PAR of old age for presenting bilateral visual loss was higher in Malay (31.6%) and Chinese (34.4%) compared with Indian individuals (21.3%); PAR of female sex was substantially higher in Malay (19.0%) than in Indian (8.5%) and Chinese individuals (8.4%); PAR for cognitive impairment was substantially higher in Malay (11.7%) than in Chinese individuals (2.7%). The profile of PAR was largely similar for income, and education level throughout the 3 ethnic groups.

Similarly, when evaluating best-corrected bilateral visual loss (Table 8), old age had the highest PAR (65.1%), followed by lower income level (58.1%), lower education level (23.2%), female sex (22.3%), cognitive impairment (14.4%), and diabetes (11.3%). The PAR profiles of old age, female sex, cognitive impairment, and diabetes differ with ethnicity (Figure 8). Old age yielded higher PAR in Malay (71.6%) and Chinese (76.2%), compared with Indian individuals (46.3%). The PAR of female sex was higher in Malay (27.0%) and Indian individuals (27.9%), compared with Chinese individuals (9.1%).

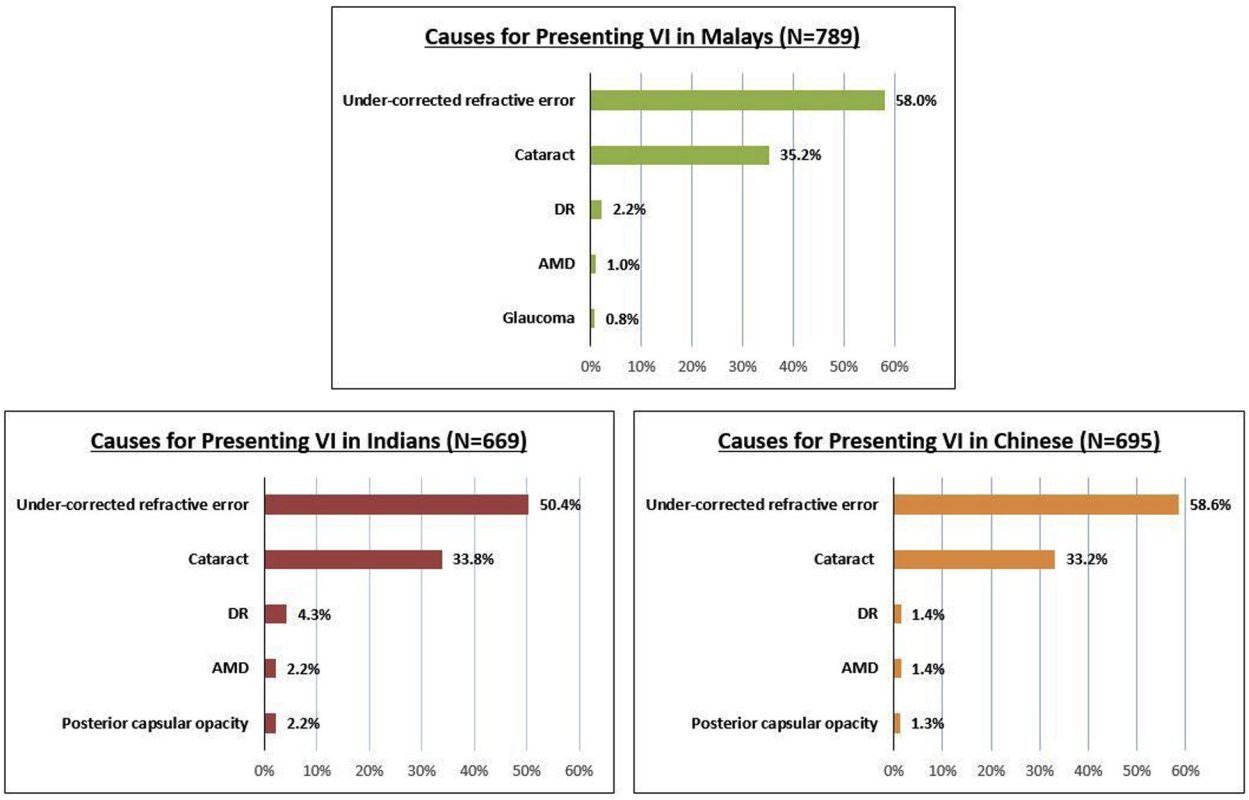

FIGURE 3. Comparison of top causes of presenting bilateral visual impairment (VI, US definition), across the 3 ethnicities in the Singapore Epidemiology of Eye Diseases Study. AMD = age-related macular degeneration; DR = diabetic retinopathy.

The PARs of diabetes (17.0%) and cognitive impairment (19.8%) were both highest in Indian compared with Malay and Chinese individuals.

In Table 9, we further assessed the joint effects of risk factors associated with best-corrected visual loss (while adjusted for the same set of covariates as Table 7). Significant interaction was observed between older age group (≥60 years) and specific systemic diseases on best-corrected bilateral VI or blindness (all *P* for interaction ≤ .003). Compared with individuals aged <60 years without diabetes, individuals aged ≥60 years with diabetes were 12.7 times (95% CI, 8.39–19.23) as likely to have best-corrected bilateral VI or blindness. On the other hand, older individuals with CKD were 14.13 times (95% CI, 9.85–20.26) more likely to have best-corrected bilateral VI or blindness, compared with younger individuals without CKD. In addition, compared with individuals aged <60 years without any systemic diseases, older individuals with 2 systemic comorbidities were 14.76 times (95% CI, 6.39–34.06) likely to have best-corrected bilateral visual loss; older individuals with 3 or more systemic comorbidities were 26.56 times (95% CI, 11.62–60.71) as likely to have best-corrected bilateral visual loss. Furthermore, we also observed significant interaction between diabetes and CKD on best-corrected bilateral visual loss (*P* interaction = .005). Compared with individuals without diabetes and CKD, diabetic individuals with concurrent CKD were 2.19 times as likely to have best-corrected bilateral visual loss (Supplementary Table 4). There were no significant interactions between demographic, systemic, or socioeconomic factors on presenting bilateral VI or blindness.

DISCUSSION

IN THIS THESIS, WE EVALUATED THE PREVALENCE AND causes of VI and blindness among adults aged ≥40 years in a multiethnic Asian population of Malay, Indian, and Chinese individuals living in Singapore. We showed that 18.4% and 0.9% had presenting bilateral VI and blindness, respectively; whereas 4.2% and 0.3% had best-corrected bilateral VI and blindness, respectively. Overall, Malay individuals had higher prevalence of bilateral VI and blindness compared with Indian and Chinese individuals. Prevalence of VI and blindness in SEED was slightly lower compared with most previous studies conducted in Asia, which mainly focused on rural regions. Uncorrected refractive error and cataract were the top causes for presenting VI and blindness; cataract and DR were the top causes for best-corrected VI

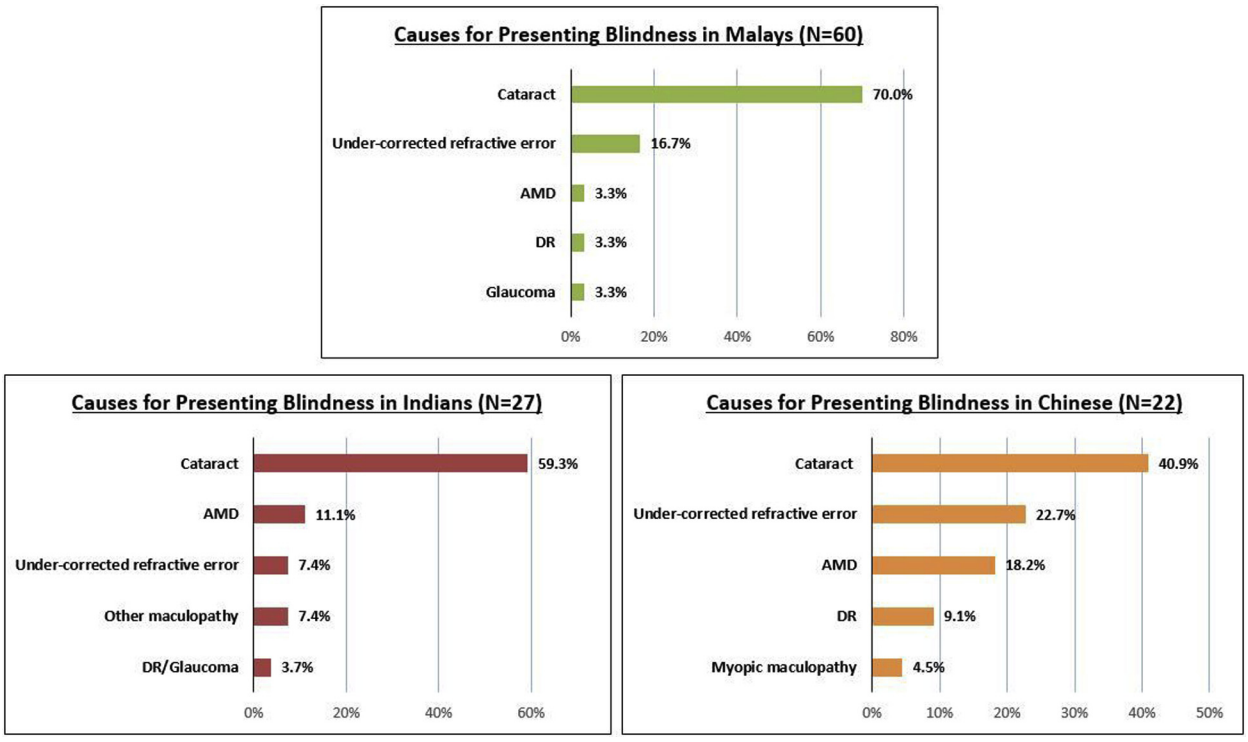

FIGURE 4. Comparison of top causes of presenting bilateral blindness (US definition), across the 3 ethnicities in the Singapore Epidemiology of Eye Diseases Study. AMD = age-related macular degeneration; DR = diabetic retinopathy.

and blindness; these were consistently observed across the 3 ethnic groups.

Although some previous studies provided preliminary information on risk factors associated with VI, findings from this thesis are the most comprehensive to date in this aspect, covering a wide range of relevant age-related systemic, demographic, and socioeconomic factors. Older age, female sex, lower socioeconomic status, diabetes, CKD, cognitive impairment, and systemic comorbidities were associated with higher risk of visual loss. Moreover, for the first time, we provided new findings on joint risk factor profiling, and identified that old age when combined with systemic comorbidities was associated with multifold risk of visual loss. This information are extremely useful to better risk-stratify high-risk subgroups and to aid in prioritization of health resource allocation, especially for the aging population. Last, we determined the PAR estimates of risk factors for visual loss, and identified that lower income and education had the highest modifiable attributable risks for visual loss. Such information will greatly help to guide policy makers in effectively identifying interventional areas and target for VI and blindness.

In totality, this thesis provides the first large population-based summary of trends and risk factors associated with VI and blindness in a multiethnic Asian population in Singapore, using multifaceted evaluations and analyses, and providing new insights on traits related to visual loss in Asians. These results will be useful and relevant in impacting the future planning and designing of eye health services and blindness prevention strategies for Asia's rapidly developing urban communities.

• **COMPARISON WITH OTHER ASIAN AND WESTERN STUDIES:** In our study, Malay individuals had higher age-standardized prevalence rates than Indian and Chinese individuals for presenting bilateral VI, blindness, and best-corrected bilateral VI. There were higher proportions of Malay individuals who had lower education and income and were residing in smaller public housing flats compared with Indian and Chinese individuals. Taken together, this suggests that more eye health awareness enhancement and social interventions need to be targeted on this group of individuals. Furthermore, a previous Singapore study reported less active health-seeking behavior (indicated by lower participation rate for health screenings) in Malay compared with Indian and Chinese individuals,[76] further suggesting that more "upstream interventions" need to be introduced and administered for Malay residents in Singapore.

Compared with other Asian studies conducted in the past 2 decades (Supplementary Table 1), prevalence rates of VI and blindness in SEED were generally lower. Specifically, when comparing the Singapore Chinese Eye Study with other Chinese studies, such as the Handan Eye Study and

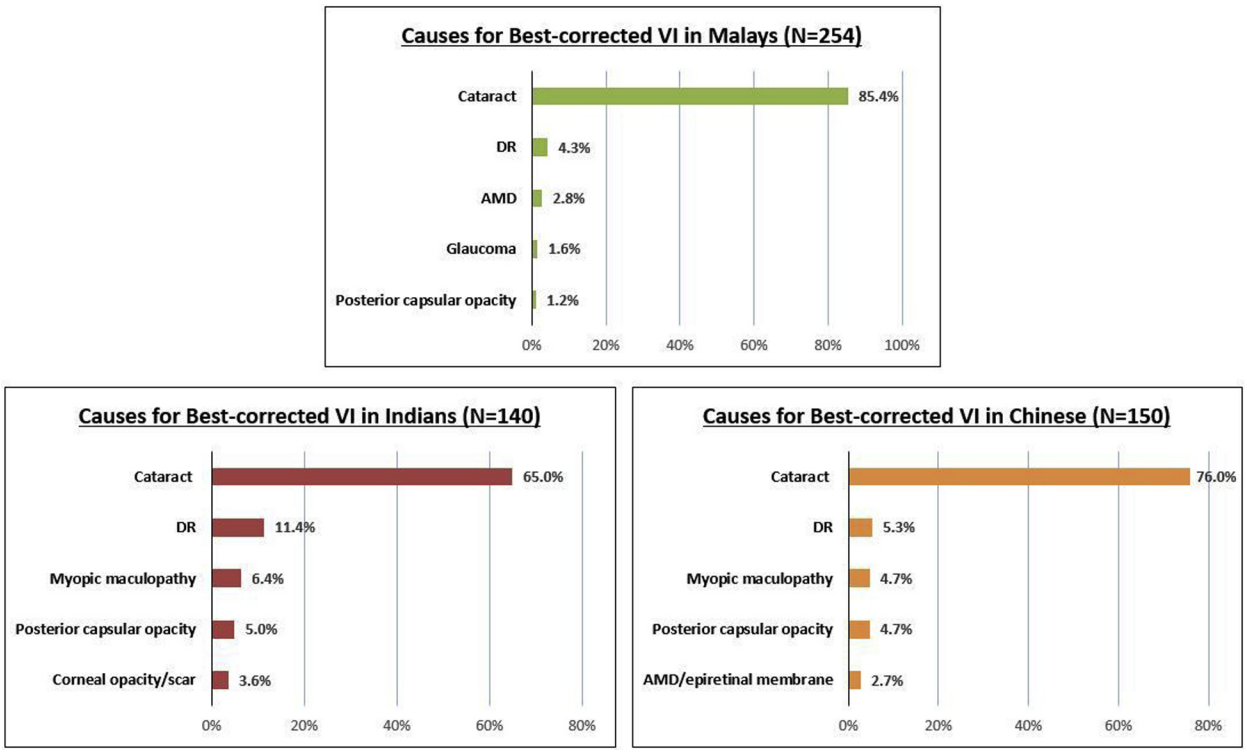

FIGURE 5. Comparison of top causes of best-corrected bilateral visual impairment (VI, US definition), across the 3 ethnicities in the Singapore Epidemiology of Eye Diseases Study. AMD = age-related macular degeneration; DR = diabetic retinopathy.

the China Nine Province Survey,[14–16,19,20,22] the prevalence of VI and blindness (for both presenting and best-corrected) was relatively lower for Singaporean Chinese. Similarly, Singaporean Indian individuals had lower rates of VI and blindness than other landmark population Indian studies, such as the Andhra Pradesh Eye Study[26] and the Central India Eye and Medical Study.[29] Overall, these differences are expected given the differences in accessibility and utilization of eye care services between Singapore and the previously mentioned areas/countries. On the other hand, when further comparing with other population-based studies in Western developed countries, the prevalence rates in SEED were largely similar to those reported in the Blue Mountains Eye Study,[64] Beaver Dam Eye Study,[63] and the Los Angeles Latino Eye Study.[65] In contrast, the Rotterdam Eye Study seemingly had slightly higher rates of best-corrected blindness (1.4%) and VI (7.3%), compared with SEED.[65] Nevertheless, it also should be noted that accurate comparisons across studies are limited by the inherent variations in population characteristics, and time period between studies. Thus, these observed differences also should also be interpreted with caution.

In terms of causes of visual loss, the overall leading causes for presenting VI in SEED were undercorrected refractive error, followed by cataract. Cataract was the top cause for presenting blindness. These were consistent across the 3 ethnic groups. Similarly, the Global Burden of Disease Study reported that undercorrected refractive error and cataract were the 2 common causes for presenting VI and blindness across countries in the high-income Asia Pacific region (developed countries), South Asia, East Asia, and Southeast Asia.[67] Taken together, it appears that undercorrected refractive error and cataract are the universal causes for presenting visual loss in most Asian regions, even in urban communities. Given that these 2 conditions are readily preventable, this calls for further scale-up in eye care services and health strategies to improve eye care accessibility and enhance the adequacy of eye care services for affected individuals, particularly among elderly individuals.

On the other hand, in SEED, cataract was the leading cause for best-corrected VI and blindness. Multiple Asian studies similarly reported cataract as the top cause for best-corrected blindness.[13,16,20,29,30,37] These collectively indicate that cataract is a universal cause for best-corrected VI and blindness for urban and rural regions. This further emphasizes the importance of continually improving accessibility to cataract surgery and optimal cataract surgery outcomes, which will in turn help to further reduce cataract-related VI and blindness.

Followed by cataract, DR and myopic maculopathy were the second and third leading causes for best-corrected VI. The high prevalence of diabetes in SEED (29.5%) possibly explains the substantial number of DR-related VI cases. This again highlights the impact of diabetes on VI,[89,90]

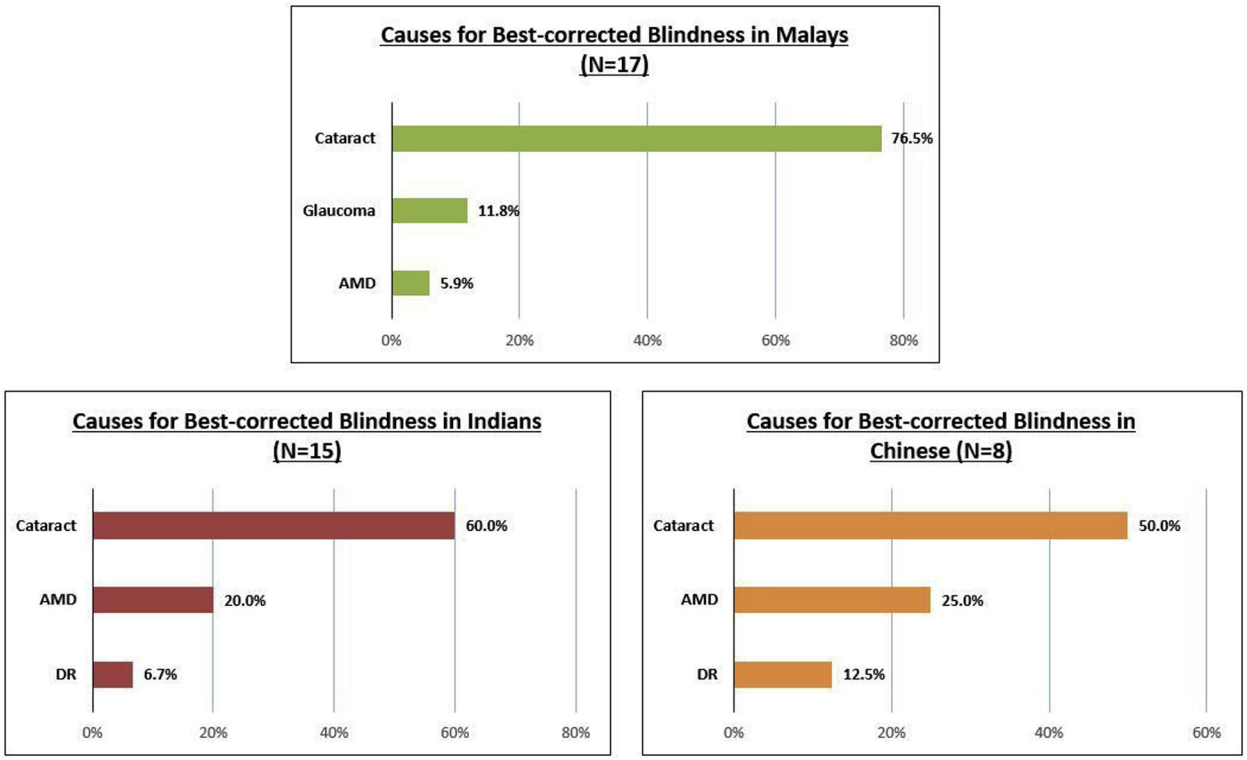

FIGURE 6. Comparison of top causes of best-corrected bilateral blindness (US definition), across the 3 ethnicities in the Singapore Epidemiology of Eye Diseases Study. AMD = age-related macular degeneration; DR = diabetic retinopathy.

further reinforcing the importance of greater awareness, compliance, and regular vision screening among diabetic individuals.[91] On the other hand, other Asian studies also reported myopic maculopathy as the leading cause for best-corrected VI after cataract.[13,37] This was not observed in other Western population studies,[63–65] further suggesting myopic maculopathy as an Asian-specific retinopathy.[92]

• **ASSOCIATIONS BETWEEN DEMOGRAPHIC AND SOCIOECONOMIC STATUS WITH VISUAL LOSS:** We found that older age and female sex were independently associated with increased risk of bilateral VI or blindness, for both presenting and best-corrected vision. This was similarly observed across the 3 ethnic groups. These findings also were consistent with that reported by previous studies in Asian and Western populations.[13,16,65,89] Notably, in our overall sample, old age (≥60 years) had the highest PAR for both presenting and best-corrected visual loss, further corroborating the significance of aging on the risk of visual loss.

In the aspects of socioeconomic status, smaller housing, lower income, and lower educational level were associated with both presenting and best-corrected visual loss in our study. This observation was largely similar across the 3 ethnic groups in our sample. Likewise, previous studies also reported that lower education level and lower income were associated with VI and blindness.[13,62,89] One possible explanation is that individuals with lower educational level may have limited awareness and lack of understanding of their own medical conditions, and thus less likely to go for routine vision screening, and have poorer compliance on follow-up even when referred to tertiary eye care for further treatment.[93] In addition, as reported previously, lower income is associated with poorer economic resources, which in turn may lead to poorer accessibility and utility of eye care services, subsequently resulting in suboptimal vision among economically disadvantaged groups in the long term.[89,94,95] Furthermore, lower education and income also had been shown to be linked with less active health-seeking behavior,[77] which may in part explain lower utility of health services among the disadvantaged groups as well. More important, visual loss, when untreated, is likely to further hinder individuals' work productivity and earning potential, potentially making these individuals more vulnerable to visual loss even for preventable or treatable causes, such as undercorrected refractive error and cataract. Hence, without appropriate interventions, socioeconomically disadvantaged individuals, especially elderly individuals, may continue to be mired with challenges associated with VI, and thus have poorer quality of life.

Of special note, our study in addition demonstrated that lower income and education were 2 of the highest modifiable attributable risk for presenting and best-corrected

TABLE 6. Factors Associated With Presenting Bilateral Visual Loss (US Definition) in the Singapore Epidemiology of Eye Diseases Study

	Presenting Bilateral Visual Loss as Outcome[a]							
	Overall Sample (N = 2262)[b]		Malay (n = 849)		Indian (n = 696)		Chinese (n = 717)	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Age (per decade)	1.85 (1.73–1.98)	< .001	2.01 (1.79–2.26)	< .001	1.61 (1.43–1.80)	< .001	2.04 (1.80–2.31)	< .001
Female	1.42 (1.25–1.62)	< .001	1.82 (1.44–2.28)	< .001	1.27 (1.00–1.59)	.046	1.28 (1.03–1.60)	.026
Ethnicity								
Chinese	Reference		—	—	—	—	—	—
Malay	1.06 (0.92–1.23)	.412	—	—	—	—	—	—
Indian	1.09 (0.95–1.26)	.225	—	—	—	—	—	—
Medical conditions								
Hypertension	0.99 (0.87–1.13)	.886	1.13 (0.88–1.45)	.324	0.92 (0.73–1.15)	.463	0.93 (0.74–1.18)	.576
Diabetes mellitus	1.02 (0.90–1.15)	.791	0.96 (0.79–1.17)	.720	1.09 (0.89–1.34)	.404	1.00 (0.78–1.28)	.977
Cardiovascular disease	1.09 (0.92–1.29)	.336	1.15 (0.87–1.52)	.317	1.05 (0.80–1.38)	.726	1.14 (0.80–1.63)	.474
Chronic kidney disease	1.22 (1.05–1.43)	.011	1.01 (0.81–1.26)	.926	1.58 (1.16–2.14)	.003	1.26 (0.90–1.76)	.174
Hyperlipidaemia	0.98 (0.87–1.10)	.704	1.06 (0.87–1.27)	.571	0.97 (0.79–1.18)	.731	0.88 (0.72–1.08)	.218
Systemic comorbidities[c]								
No systemic disease	Reference		Reference		Reference		Reference	
Any 1 systemic disease	0.93 (0.78–1.11)	.440	1.03 (0.73–1.44)	.877	1.07 (0.79–1.46)	.644	0.75 (0.56–1.00)	.052
Any 2 systemic diseases	0.98 (0.82–1.18)	.821	1.12 (0.79–1.60)	.520	1.15 (0.84–1.57)	.374	0.71 (0.53–0.97)	.029
≥ 3 systemic diseases	1.03 (0.85–1.24)	.775	1.12 (0.78–1.59)	.548	1.16 (0.85–1.59)	.355	0.82 (0.59–1.16)	.261
P-trend		.463		.449		.329		.318
Cognitive impairment[d]	2.15 (1.75–2.63)	<.001	2.80 (2.04–3.86)	<.001	1.93 (1.35–2.78)	<.001	1.52 (1.01–2.29)	.044
Deaf	1.86 (0.95–3.62)	.070	2.72 (0.89–8.33)	.080	2.41 (0.89–6.53)	.083	0.61 (0.10–3.54)	.580
BMI category								
Normal BMI	Reference		Reference		Reference		Reference	
Underweight	1.20 (0.93–1.55)	.163	1.16 (0.74–1.82)	.526	1.22 (0.72–2.06)	.454	1.17 (0.78–1.73)	.449
Overweight	0.87 (0.77–0.98)	.027	0.83 (0.67–1.02)	.081	0.85 (0.69–1.05)	.141	0.90 (0.71–1.13)	.352
Obese	0.83 (0.70–0.99)	.036	0.75 (0.58–0.97)	.027	0.86 (0.65–1.15)	.308	0.83 (0.53–1.30)	.414
Current smokers	1.15 (0.97–1.37)	.096	1.13 (0.86–1.50)	.381	1.16 (0.85–1.58)	.343	1.26 (0.93–1.71)	.142
Alcohol consumption	1.06 (0.85–1.32)	.615	0.61 (0.21–1.79)	.369	1.12 (0.82–1.54)	.470	0.94 (0.66–1.32)	.709
Housing type								
≥5 room public housing flat	Reference		Reference		Reference		Reference	
3–4 room public housing flat	1.33 (1.16–1.52)	< .001	1.19 (0.89–1.59)	.242	1.22 (0.98–1.52)	.075	1.52 (1.22–1.90)	< .001
1–2 room public housing flat	1.88 (1.50–2.36)	< .001	1.64 (1.15–2.33)	.006	1.58 (1.01–2.46)	.044	2.90 (1.64–5.14)	< .001
Living alone	0.83 (0.65–1.05)	.125	1.14 (0.75–1.73)	.533	0.70 (0.45–1.10)	.119	0.70 (0.45–1.08)	.107
Monthly income category								
≥ S$2000	Reference		Reference		Reference		Reference	
< S$2000	1.47 (1.23–1.77)	< .001	1.56 (0.97–2.50)	.067	1.36 (1.03–1.80)	.029	1.62 (1.22–2.17)	.001
Education category								
Formal education	Reference		Reference		Reference		Reference	
No formal education	1.75 (1.54–1.99)	< .001	1.64 (1.33–2.03)	< .001	1.80 (1.42–2.29)	< .001	1.66 (1.32–2.08)	< .001

BMI = body mass index; CI = confidence interval; OR= odds ratio.

[a]Inclusive of bilateral visual impairment and bilateral blindness, based on the better-seeing eye.

[b]In this model, ethnicity was also adjusted, in addition to covariates listed in table.

[c]Systemic comorbidities were classified based on the concurrent presence of 2 or more systemic conditions, namely, diabetes, hyperlipidemia, hypertension, chronic kidney disease, or cardiovascular disease. Evaluation of systemic comorbidities as exposure variable was performed in a separate model, where individual exposures of diabetes, hypertension, hyperlipidemia, chronic kidney disease, and cardiovascular disease were not included in the model.

[d]Cognitive impairment was assessed in a separate model, including only subjects aged 60 years and older, while adjusting for the same set of covariates as original main model.

TABLE 7. Factors Associated with Best-Corrected Bilateral Visual Loss (US Definition) in the Singapore Epidemiology of Eye Diseases Study

	Best-Corrected Bilateral Visual Loss as Outcome[a]							
	Overall Sample (N = 584)[b]		Malay (n = 849)		Indian (n = 696)		Chinese (n = 717)	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Age (per decade)	2.90 (2.53–3.33)	< .001	3.59 (2.86–4.51)	< .001	1.95 (1.54–2.46)	< .001	3.75 (2.83–4.96)	< .001
Female	1.74 (1.37–2.20)	< .001	2.03 (1.41–2.91)	< .001	1.94 (1.20–3.12)	.007	1.25 (0.81–1.93)	.308
Ethnicity								
Chinese	Reference		—	—	—	—	—	—
Malay	1.72 (1.32–2.23)	< .001	—	—	—	—	—	—
Indian	1.23 (0.93–1.63)	.149	—	—	—	—	—	—
Medical conditions								
Hypertension	1.14 (0.85–1.53)	.389	1.06 (0.67–1.69)	.795	1.57 (0.91–2.69)	.105	1.00 (0.57–1.77)	.994
Diabetes mellitus	1.43 (1.16–1.76)	.001	1.34 (0.99–1.81)	.055	1.51 (1.01–2.25)	.044	1.58 (1.02–2.44)	.039
Cardiovascular disease	1.08 (0.83–1.42)	.560	1.10 (0.74–1.65)	.631	1.03 (0.63–1.68)	.904	1.23 (0.70–2.19)	.472
Chronic kidney disease	1.38 (1.10–1.74)	.005	1.21 (0.89–1.65)	.218	1.75 (1.09–2.82)	.020	1.16 (0.69–1.92)	.577
Hyperlipidaemia	1.22 (0.99–1.50)	.059	1.43 (1.06–1.94)	.018	1.16 (0.77–1.75)	.478	0.95 (0.63–1.43)	.793
Systemic comorbidities[c]								
No systemic disease	Reference		Reference		Reference		Reference	
Any 1 systemic disease	1.32 (0.83–2.10)	.243	1.56 (0.66–3.67)	.31	2.25 (0.90–5.67)	.084	0.82 (0.40–1.70)	.592
Any 2 systemic diseases	1.18 (0.74–1.89)	.479	1.58 (0.68–3.70)	.29	2.23 (0.88–5.63)	.09	0.54 (0.26–1.15)	.113
≥ 3 systemic diseases	2.05 (1.30–3.23)	.002	2.37 (1.03–5.47)	.043	4.03 (1.64–9.86)	.002	1.12 (0.54–2.35)	.757
P-trend		<.001		.004		<.001		.44
Cognitive impairment[d]	2.07 (1.60–2.68)	<.001	1.85 (1.27–2.69)	.001	2.52 (1.51–4.19)	<.001	2.12 (1.25–3.60)	.006
Deaf	2.06 (0.87–4.89)	.101	5.51 (1.38–22.01)	.016	1.53 (0.38–6.26)	.552	1.27 (0.13–12.34)	.838
BMI category								
Normal BMI	Reference		Reference		Reference		Reference	
Underweight	1.31 (0.87–1.98)	.192	1.29 (0.68–2.45)	.433	1.63 (0.70–3.81)	.259	1.06 (0.52–2.19)	.865
Overweight	0.68 (0.54–0.86)	.001	0.76 (0.54–1.07)	.112	0.58 (0.37–0.90)	.014	0.66 (0.40–1.07)	.090
Obese	0.71 (0.52–0.97)	.029	0.78 (0.51–1.17)	.230	0.50 (0.28–0.90)	.020	0.93 (0.39–2.22)	.868
Current smokers	1.22 (0.87–1.70)	.244	1.13 (0.68–1.85)	.643	1.37 (0.69–2.74)	.368	1.37 (0.75–2.50)	.303
Alcohol consumption	1.00 (0.59–1.68)	.991	—	—	0.68 (0.29–1.59)	.377	1.37 (0.68–2.77)	.384
Housing type								
≥ 5 room public housing flat	Reference		Reference		Reference		Reference	
3–4 room public housing flat	1.14 (0.87–1.49)	.335	0.96 (0.58–1.57)	.861	1.15 (0.73–1.81)	.546	1.25 (0.78–1.98)	.351
1–2 room public housing flat	1.51 (1.05–2.19)	.027	1.37 (0.78–2.39)	.273	1.07 (0.48–2.37)	.871	2.08 (0.84–5.16)	.116
Living alone	0.86 (0.57–1.30)	.466	1.05 (0.58–1.88)	.883	0.49 (0.19–1.32)	.159	0.96 (0.43–2.10)	.910
Monthly Income category								
≥ S$2000	Reference		Reference		Reference		Reference	
< S$2000	2.84 (1.47–5.49)	.002	4.02 (0.54–29.95)	.174	2.86 (1.11–7.41)	.030	2.69 (0.93–7.76)	.067
Education category								
Formal education	Reference		Reference		Reference		Reference	
No formal education	1.81 (1.45–2.26)	< .001	1.73 (1.23–2.43)	.002	1.94 (1.27–2.96)	.002	1.71 (1.11–2.64)	.015

BMI = body mass index; CI = confidence interval; OR= odds ratio.

[a]Inclusive of bilateral visual impairment and bilateral blindness, based on the better-seeing eye.

[b]In this model, ethnicity was also adjusted, in addition to covariates listed in the table.

[c]Systemic comorbidities were classified based on the concurrent presence of 2 or more systemic conditions, namely, diabetes, hyperlipidemia, hypertension, chronic kidney disease, or cardiovascular disease. Evaluation of systemic comorbidities as exposure variable was performed in a separate model, where individual exposures of diabetes, hypertension, hyperlipidemia, chronic kidney disease, and cardiovascular disease were not included in the model.

[d]Cognitive impairment was assessed in a separate model, including only subjects aged 60 years and older, while adjusting for the same set of covariates as original main model.

TABLE 8. Population-Attributable Risk for Risk Factors Associated With Presenting and Best-corrected Bilateral Visual Loss (US Definition).

	PAR for Presenting Bilateral Visual Loss				PAR for Best-Corrected Bilateral Visual Loss			
	Overall	Malay	Indian	Chinese	Overall	Malay	Indian	Chinese
Old age (60 and older)	28.9	31.6	21.3	34.4	65.1	71.6	46.3	76.2
Ethnicity								
Chinese	—	—	—	—	Reference	—	—	—
Malay	—	—	—	—	17.6	—	—	—
Indian	—	—	—	—	4.0	—	—	—
Female	11.9	19.0	8.5	8.4	22.3	27.0	27.9	9.1
Medical conditions								
Diabetes mellitus	—	—	—	—	11.3	9.2[a]	17.0	10.0
Chronic kidney disease	2.4	0.2[a]	3.8	1.6[a]	7.8	6.4[a]	9.3	2.4[a]
Cognitive impairment[b]	7.5	11.7	7.3	2.7	14.4	13.3	19.8	11.0
Housing type								
1–2 room public housing flat	3.8	5.2	2.0	2.2	4.6	5.1[a]	0.5[a]	3.1[a]
Monthly income category								
< S$2000	21.0	24.1[a]	17.1	24.6	58.1	68.5[a]	58.9	55.8[a]
Education category								
No formal education	12.4	12.5	10.4	11.1	23.2	22.8	20.7	21.7

PAR = population-attributable risk.

Only factors that were significant in original multiple regression model (Tables 6 and 7) were included for PAR analysis. Best-corrected bilateral visual loss inclusive of bilateral visual impairment and bilateral blindness, based on the better-seeing eye. All values are percentages (%).

[a]Denotes not statistically significant in original ethnic-specific multiple logistic regression model.

[b]Cognitive impairment was assessed in a separate model, including only subjects aged 60 years and older.

visual loss, further indicating that these 2 factors are suitable targets for public health intervention in reducing VI and blindness even for urban communities. In addition, when comparing with ethnicity, lower income and education still stood out to have higher PAR for best-corrected visual loss. This potentially suggests that the risk of best-corrected visual loss is more likely attributed to environmental factors (ie, socioeconomic related) than genetic ancestral factors.

• SYSTEMIC DISEASES AND VISUAL LOSS: In the overall sample of our study, we observed that individuals with diabetes were 1.4 times as likely to have best-corrected bilateral visual loss. Consistent with this, we also observed that the prevalence rates of bilateral VI and blindness for both presenting and best-corrected vision were higher in diabetic individuals compared with nondiabetic individuals in SEED (all $P < .001$) (Supplementary Table 5). The association between diabetes and best-corrected visual loss was also consistently observed across Malay, Indian, and Chinese individuals. Previous studies similarly reported higher prevalence of VI among diabetic individuals, and highlighted diabetes as a significant risk factor for nonrefractive VI.[89,96–98] These observations in diabetes may be explained by the links between diabetes and several common age-related eye diseases, notably DR,[99,100] cataract,[101] AMD,[102] and glaucoma.[103,104] In fact, DR was noted as the second leading cause of best-corrected VI in our study, consistent across the 3 ethnic groups. Furthermore, 11.3% of risk of best-corrected visual loss was attributed to diabetes in our sample, with an even higher PAR among Indian individuals (17.0%). Taken together, given diabetes is a modifiable risk factor, this further reinforces the importance of early identification of prediabetes, prevention of diabetes, and optimal diabetes management. Current efforts in regular vision screening and retinal photo examination[71] among diabetic individuals should continue and increase, in a bid to detect VI and its underlying cause(s) at an early stage, allowing earlier interventions to be administered. This is especially important considering the growing prevalence of diabetes in urban communities.[105]

On the other hand, we also observed that CKD was associated with increased risk of both presenting and best-corrected bilateral visual loss. However, this association was observed only in Indian individuals (OR, 1.75). Similarly, in the Beijing Eye Study, Jonas and colleagues[106] did not find significant association between CKD and VA in Chinese individuals. In the face of limited literature in this aspect currently, our findings provide preliminary indication that CKD is an

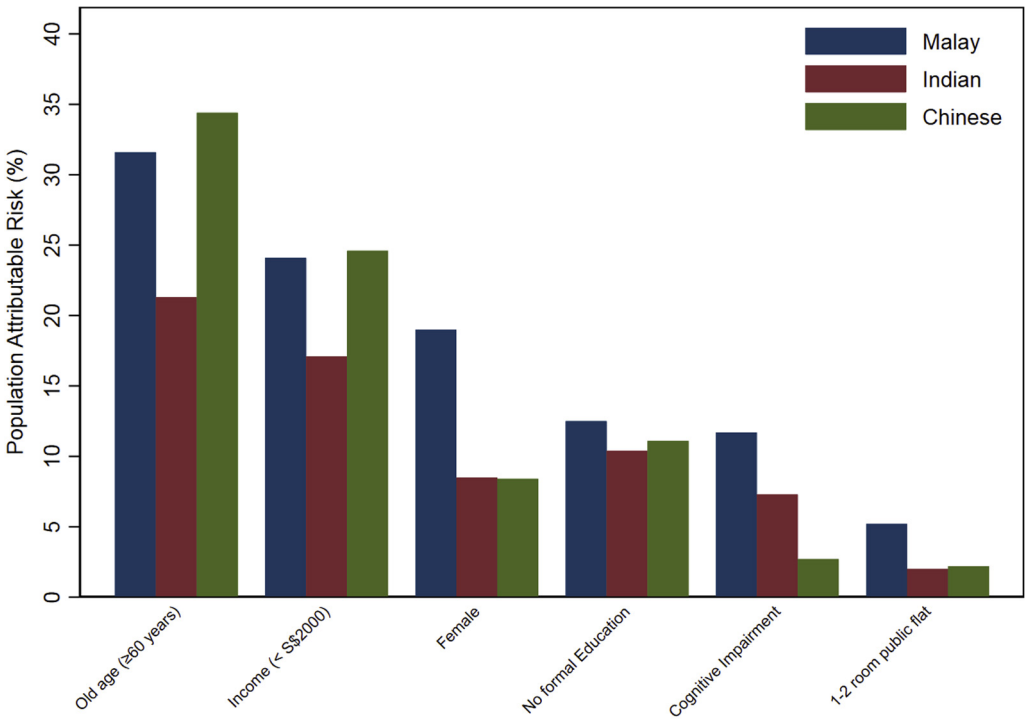

FIGURE 7. Population-attributable risk for risk factors associated with presenting bilateral visual loss (visual impairment or blindness).

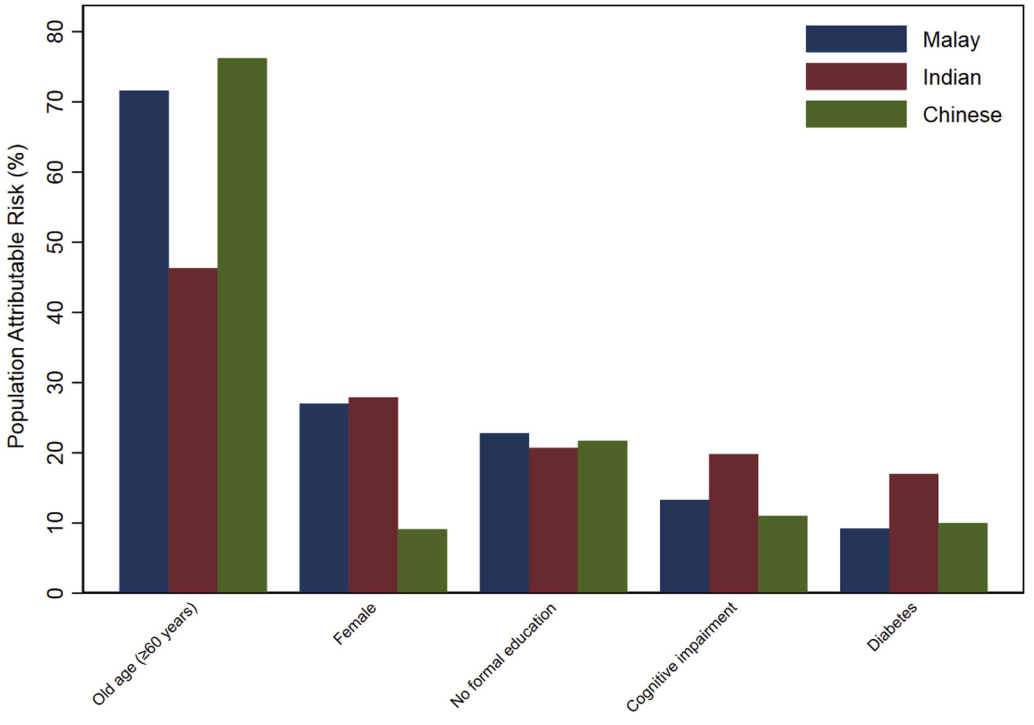

FIGURE 8. Population-attributable risk for risk factors associated with best-corrected bilateral visual loss (visual impairment or blindness).

TABLE 9. Stratum-specific Odds Ratio (95% Confidence Interval) of Best-corrected Bilateral Visual Loss (US Definition) in Categorical Groups of Age and Systemic Conditions

	Age Group, y		
	<60		≥60
Diabetes status			
Absent	1.00 (reference)		10.04 (6.76–14.92)[a]
Present	2.96 (1.76–5.01)[a]		12.70 (8.39–19.23)[a]
		P interaction = .003	
Chronic kidney disease status			
Absent	1.00 (reference)		8.37 (6.04–11.58)[a]
Present	4.83 (2.47–9.42)[a]		14.13 (9.85–20.26)[a]
		P interaction = .003	
Systemic comorbidities[b]			
No systemic disease	1.00 (reference)		12.58 (4.92–32.16)[a]
Any 1 systemic disease	2.28 (0.88–5.90)		16.79 (7.24 38.92)[a]
Any 2 systemic diseases	3.71 (1.43–9.65)[c]		14.76 (6.39–34.06)[a]
≥ 3 systemic diseases	9.51 (3.84–23.60)[a]		26.56 (11.62–60.71)[a]
		P interaction = .006	

Outcome variable was inclusive of bilateral visual impairment and bilateral blindness, based on better-seeing eye. Analysis was adjusted for age, sex, ethnicity, hypertension, cardiovascular disease, hyperlipidemia, deafness, body mass index, smoking status, alcohol consumption, housing type, living alone status, monthly income, and education.

[a]Denotes $P < .001$.

[b]Systemic comorbidities were classified based on the concurrent presence of 2 or more systemic conditions, namely, diabetes, hyperlipidemia, hypertension, chronic kidney disease, or cardiovascular disease. Evaluation of systemic comorbidities as exposure variable was performed in a separate model, where individual exposures of diabetes, hypertension, hyperlipidemia, chronic kidney disease and cardiovascular disease were not included in the model.

[c]Denotes $P < .05$.

independent risk factor for VI, a trait that may be unique to Indian individuals. Nevertheless, further studies, particularly longitudinal cohort, are warranted to better elucidate this.

In addition, we showed that systemic comorbidities (concurrent presence of any 3 conditions of diabetes, hypertension, hyperlipidemia, CKD, and CVD) were associated with higher risk of best-corrected bilateral visual loss. This was, again, particularly marked among Indian individuals (OR, 4.03). On this front, we further observed significant interaction effects between diabetes and CKD. Individuals with concomitant diabetes and CKD were 2.2 times as likely to have best-corrected bilateral visual loss, compared with individuals free of both diseases. One possible explanation is that diabetes and CKD are closely linked with common pathophysiology, particularly the mechanisms in microvascular complications.[107,108] Similar to diabetes, CKD was also previously reported to be associated with age-related eye diseases, such as DR, AMD, and glaucoma,[107] which are common causes of visual loss.

• **COGNITIVE IMPAIRMENT WITH VISUAL LOSS:** In addition, we observed that individuals with cognitive impairment were 2.1 times as likely to have both presenting and best-corrected bilateral visual loss. This finding was similarly observed by Jonas and colleagues[109] in the Beijing Eye Study, which reported that subjects with decreased cognitive function scores had poorer presenting VA and BCVA. Previous studies also indicated that age-related ocular diseases and features, such as retinal degeneration, tessellated fundus, and suboptimal electrophysiological responses, were correlated with cognitive decline.[109,110] In addition, severe forms of cognitive impairment, such as Alzheimer disease, had also been found to be associated with decreased vision, further corroborating a link between cognitive impairment and visual loss.[111] On the other hand, other prospective studies also reported that VI was associated with higher risk of incident cognitive impairment.[85,112–114] In this regard, due to the cross-sectional nature of our study, we are unable to determine the actual causal relationship between cognitive impairment and VI. This warrants further longitudinal studies.

• **JOINT EFFECTS OF AGE AND SYSTEMIC DISEASES ON VISUAL LOSS:** To the best of our knowledge, this is the first study that demonstrated significant interaction and effect modification between aging and systemic diseases on the risk of visual loss. Old age, combined with diabetes, CKD, or systemic comorbidities, was shown to have multifold risk of having best-corrected bilateral visual loss. This finding is especially relevant to the aging population in Asia and worldwide, particularly so for those residing in urban communities. Furthermore, this information may potentially

aid in the formulation of more targeted screening strategies for high-risk subgroups. Specifically, individuals aged ≥60 years with concurrent diabetes, CKD, or any 2 systemic comorbidities (in the form of diabetes, CKD, hypertension, CVD, or hyperlipidemia) should be warranted for even more regular vision screenings to identify VI or blindness at an earlier stage. In addition, these findings also may help to guide decisions on better prioritization of screening or intervention strategies, when faced with limited resources.

• **STRENGTH AND LIMITATIONS:** This thesis covers the 3 major ethnic groups in Asia (Malay, Indian, and Chinese), while adopting well-established and standardized examination methods and protocols across the 3 examined groups. This provides a unique and unprecedented opportunity to pool and compare data across the 3 ethnic groups in a relatively common geographic and socioeconomic environment. Other strengths of this thesis include large population-based samples that provide sufficient statistical power to comprehensively evaluate the independent and combined effects of multiple comorbidity measures of ethnicity, demographic, systemic, and socioeconomic risk factors on VI and blindness. Furthermore, the wide range of data collected in this study allowed for relevant confounding factors to be accounted for in the analysis, further substantiating the validity of our findings. Last, definition of VI and blindness (outcomes of interest) and diagnosis of eye diseases were defined according to international recommended criteria and guidelines, limiting the potential discrepancy and bias due to misclassification in our study.

Nevertheless, this thesis also has a few limitations. First, this study was cross-sectional in nature, thus causal inference may not be conclusively drawn from current findings. Second, our analysis focused only on Asian ethnicity; replication of our findings in other populations may be required to further test for generalization. Third, as automated perimetry was performed on only a subset of study participants identified to be glaucoma suspects, loss of visual fields was not included as part of the definition for blindness. Therefore, the prevalence of blindness due to glaucoma may have been underestimated. Fourth, as cataract accounted for most VI cases after refractive correction, it was possible that concurrent retinal diseases might have been masked by significant cataract, especially among elderly individuals. Last, as described in the Methods section, the nonparticipants were older than the attended participants, thus potential bias in this study sample may not be entirely ruled out.

• **FUTURE DIRECTIONS:** Findings from this thesis, in particular ethnic differences and risk factors for VI and blindness, may serve as good references for other population research groups in Asia and elsewhere. In addition, the direct and indirect economic impact of VI and blindness on communities and countries should be further analyzed and quantified comprehensively, to further provide holistic perspectives on the burden of visual loss. Such reports are currently well published for Western populations but still lacking for Asian populations. Further collaborations between research groups to combine data and to perform meta-analysis on VI remain necessary to advance the research and the understanding on the magnitude of VI in Asia, in particular urban communities where data remain scarce.

CONCLUSION

ASIA IS HOME TO THE WORLD'S LARGEST POPULATION AND accounts for the greatest burden of visual loss globally. In this multiethnic Asian population-based study in Singapore, we determined shared and unique traits associated with visual loss across Malay, Indian, and Chinese individuals. We further identified combined effects of age and systemic comorbidities on VI and blindness; and socioeconomic factors that had high modifiable attributable risks for visual loss. Collectively, these findings will be useful for the planning of eye health services, and designing of relevant interventions for Asia's rapidly developing urban communities, in a bid to reduce the burden of VI and blindness.

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