Prevalence, Risk Factors, and Impact of Myopic Macular Degeneration on Visual Impairment and Functioning Among Adults in Singapore

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PURPOSE. To determine the prevalence, risk factors, and impact of myopic macular degeneration (MMD) on visual impairment and functioning among adults in Singapore.

METHODS. A comprehensive eye examination, including subjective refraction, axial length, and visual acuity (VA) measurements, was performed in adults aged ≥40 years in the Singapore Epidemiology of Eye Diseases (SEED) study. From fundus photographs, MMD was graded using the International META-PM classification. Vision-specific functioning (VSF) was assessed with a validated visual-functioning questionnaire (VF-11) using Rasch analysis.

RESULTS. A total of 8716 phakic subjects were included in this analysis. The mean age (± SD) was 57.2 ± 9.5 years (33.5% Malay, 33.2% Indian, and 33.3% Chinese). The prevalence of myopia (spherical equivalent [SE] ≤ −0.5 diopters [D]) and high myopia (SE ≤ −5.0 D) was 35.7% and 6.0%, respectively. The age-standardized prevalence of MMD was 3.8% (95% confidence interval [CI], 3.4–4.3%). The prevalence of MMD was 7.7% among low to moderate myopes, and 28.7% among high myopes. The prevalence of MMD increased nonlinearly with SE and age. MMD was associated with older age, more myopic SE, and lower education. Subjects with Meta-PM categories 3 or 4 in the better-seeing eye had worse best-corrected VA (β, 0.19; 95%CI, 0.16–0.23) and poorer VSF (β, −9.7; 95%CI, −17.6 to −1.8) than those without MMD after multivariate adjustments.

CONCLUSIONS. Approximately 1 in 26 phakic adults in Singapore has MMD. Older age and myopic SE are major risk factors of MMD. MMD has a substantial impact on visual impairment and functioning.

Keywords: epidemiology, quality of life, vision-specific functioning, pathologic myopia

Myopia is a major public health problem worldwide.1–3 It has been estimated that nearly 23% (1406 million) and 3% (163 million) of the world population had myopia (spherical equivalent [SE] ≤ −0.5 diopters [D]) and high myopia (SE ≤ −5.0 D) in 2000.1 Individuals with high myopia are at increased risk of developing myopia-related blindness complications, such as myopic macular degeneration (MMD), posterior staphyloma, and retinal detachment, all of which can cause irreversible vision loss.1,2,4,5

Several population studies worldwide, including in Australia,6 China and Taiwan,7,9 Japan,10 and India,11 have assessed the prevalence of MMD in adult populations, reporting estimates ranging from 0.2% in rural India to 3.1% in China. However, there were varying definitions of MMD in these previous studies.4,12 The same definition of MMD by Curtin13 that included posterior staphyloma was used by the Blue Mountains Eye Study (N = 3583),6 the Beijing Eye Study (N = 4319),9 and the Handan Eye Study (N = 6603).8 In contrast, a slightly different definition of MMD that did not account for posterior staphyloma was adopted by the Shihpai Eye Study (N = 1058)9 and the Hisayama Study (N = 1892).10 Recently, the International Photographic Classification and Grading System for Myopic Maculopathy (META-PM) classification was proposed. Among these population-based studies, only the Central India Eye and Medical Study conducted in rural India (N = 4561)13 employed the International META-PM classification.14 Therefore, the use of inconsistent definitions of MMD has led to limited comparability of findings, highlighting the need to use a standardized international definition of MMD.3,12 Most studies
were also conducted in ethnically homogenous populations, and interethnic comparisons of MMD were limited.

MMD can result in irreversible loss of central vision and is one of the leading causes of blindness in countries worldwide. However, studies on the impact of MMD on vision in Asia have been limited to Chinese and Japanese populations. MMD was also associated with poorer vision-specific functioning (VSF) in clinic-based studies, but the association may be overestimated in selective clinic samples with more severe MMD cases. Furthermore, the impact of MMD on VSF has yet to be assessed in detail in population-based studies.

Using the International META-PM classification, we aimed to examine the prevalence of MMD among population-based samples of Chinese, Indians, and Malays living in Singapore and its impact on vision and VSF.

METHODS

Study Population

The Singapore Epidemiology of Eye Diseases (SEED) study is a population-based study conducted in Singapore from 2004 to 2011, comprising three major ethnic groups: Malays (recruitment conducted in 2004–2006), Indians (2007–2009), and Chinese (2009–2011). The study methodologies have been described elsewhere. In brief, an age-stratified random sampling frame selected 5600 Malays, 6350 Indians, and 6752 Chinese aged 40 to 80 years from the Ministry of Home Affairs. Of these, 4168 Malays, 4497 Indians, and 4605 Chinese were eligible to participate. Persons who had moved from the residential address, not lived there in the past 6 months, deceased, or terminally ill were ineligible. A total of 3280 Malays, 3400 Indians, and 3553 Chinese participated (response rates of 78.7%, 75.6%, and 72.8%, respectively; mean total numbers of eligible participants, 352 participants had missing or ungradable corrected visual acuity (BCVA) measurements were conducted on the same day by a trained optometrist. Blindness and VI were defined based on BCVA (to account for only unavoidable vision loss) of the better-seeing eye. In the US definition, the presence and severity of VI was categorized as no VI (BCVA 20/40 or better, logMAR < 0.50), VI (BCVA worse than 20/40 but better than 20/200, 0.30 < logMAR < 1.00), and blindness (BCVA of 20/200 or worse, logMAR ≥ 1.00).

Inclusion/Exclusion Criteria

Subjects with the following conditions were excluded from this study: (1) history of cataract surgery, aphakic or pseudophakic, and/or self-reported refractive surgery in both eyes (n = 765); (2) missing refraction data in both eyes (n = 90); and (3) combination of cataract surgery in one eye and missing refraction data in the other eye (n = 110). Of the 9068 eligible participants, 552 participants had missing or ungradable fundus photographs in both eyes. A total of 8716 phakic subjects comprising 2926 Malays, 2890 Indians, and 2900 Chinese were included in this study.

Visual Acuity Assessment

The monocular presenting visual acuity (PVA) was measured using the logarithm of the minimal angle of resolution (logMAR) chart (Lighthouse International, New York, NY, USA) at 4 m, with the participants wearing their habitual correction. If the largest number could not be read at 4 m, the chart was moved closer to the participant; then counting fingers, hand motion, or light perception was assessed. Subjective refraction and best-corrected visual acuity (BCVA) measurements were conducted on the same day by a trained optometrist.

Refractometry

Noncycloplegic autorefractometry was performed using an autorefractometer (model RK5; Canon, Inc., Ltd., Tochigiken, Japan). Refraction was then subjectively refined by the study optometrists. The fundus photographs of both eyes were graded using a standardized protocol, and the graders were masked to the subjects’ characteristics. Adjudication was performed by a retinal specialist (C-WW). Grading of pathologic lesions by the retinal specialist (C-WW) and three trained graders were compared; the k statistics showed high intergrader agreement (agreement of the Meta-PM categories were 0.94 [C-WW, YD] and 0.94 [C-WW, YD], and 0.88 [C-WW, C-WT]). Intergrader reliability was also high (k coefficient of 0.88 [YD, YD], 0.94 [YD, C-WT], and 0.94 [YD, C-WT]).

Definition of MMD

Based on the International META-PM classification, the presence of MMD was defined and classified into the following categories: no macular lesions (category 0); tessellated fundus only (category 1); diffuse chorioretinal atrophy (category 2); patchy chorioretinal atrophy (category 3); and macular atrophy (category 4). “Plus” lesions, which supplemented the Meta-PM categories, comprised lacquer cracks, choroidal neovascularization (CNV), and Fuchs spot. Based on fundus photograph grading, an eye was considered to have MMD if Meta-PM category 2, 3, 4, or any “plus” lesion was observed. The presence of optic disc abnormalities (optic disc tilt, peripapillary atrophy [PPA], and peripapillary intrachoroidal cavitation [ICC]) was also graded, although they are not part of the META-PM classification. Optic disc tilt was defined by an oval optic disc with a tilt ratio (minimum diameter to maximum diameter) of less than 0.75. PPA was defined using the classification by Curtin and Karlin. Peripapillary ICC was observed as an elevated, well-circumscribed, dome-shaped, yellow-orange lesion inferior to the optic disc along the inferior margin of the PPA.
Prevalence, Risk Factors, and Impact of MMD in Singapore

Risk Factor Assessment
Detailed questionnaires, administered by trained research staff through face-to-face interviews, were used to collect demographic information (age, sex, and race), socioeconomic characteristics (education level), general medical history, and lifestyle-related factors (smoker or nonsmoker) from participants in their preferred language (English or mother tongue). Education level was classified as primary/below education and secondary/above education. Body mass index was calculated as body weight (in kilograms) divided by body height (in meters) squared. Hypertension was defined as systolic blood pressure \( \geq 140 \text{ mm Hg} \), diastolic blood pressure \( \geq 90 \text{ mm Hg} \), physician-diagnosed hypertension, or self-reported history of hypertension. Diabetes mellitus was defined as random glucose of \( \geq 11.1 \text{ mM} \), diabetic medication use, or a physician-diagnosed history of diabetes. Hyperlipidemia was defined as total cholesterol \( \geq 6.2 \text{ mM} \) or self-reported use of lipid-lowering drugs. Cardiovascular disease was defined as history of previous myocardial infarction, angina, or stroke.

Assessment of Vision-Specific Functioning
The VF-11 scale\(^{27,28} \) consists of 11 questions (VF-11) about different aspects of vision-dependent activities to assess the level of difficulty in performing daily tasks involving near and distance vision.

Statistical Analysis
MMD grade and myopic refractive error in the worse eye were used in the analysis. The age-standardized prevalence rates of MMD were calculated by direct standardization of the study samples to the Singapore population, using the 2010 Singapore census. Associations of demographic and socioeconomic factors with MMD were assessed using multivariable-adjusted logistic regression models including covariates of age, ethnicity, sex, education, and, selected using stepwise backward methods. To determine optimal SE and age thresholds to detect individuals at risk of MMD, the sensitivity and specificity values were calculated for each predetermined cutoff. Simple practical thresholds were used.

Risk Factors of MMD
The prevalence of MMD increased in a nonlinear pattern with increasing age, SE, and AL (Fig. 1). Each curve was obtained using the logistic function, and there were no evident natural thresholds seen. Specifically, a gradual nonlinear increase in prevalence of MMD with older age was observed (Fig. 1A), and the prevalence of MMD increased gradually at lower myopic SE and shorter AL levels and plateaued at higher myopic SE and longer AL levels (S-shaped trend; Figs. 1B, 1C). Among the 350 participants with MMD, 41.1% had low myopia (\(-3.0 < \text{D} < \pm 0.5 \text{ D}\)), 16.0% had moderate myopia (\(-5.0 < \text{D} < \pm 3.0 \text{ D}\)), and 42.9% had high myopia (\(\text{SE} < \pm 5.0 \text{ D}\)). Within each age group, there was an increasing trend in prevalence of MMD with higher myopia severity (Fig. 2). Similarly, the prevalence of MMD increased with age within each myopia category. In participants with no, low, moderate, and high myopia, the prevalence of MMD was higher among those aged \(\geq 70\) years (0.0%, 31.1%, 47.7%, and 65.0%, respectively) than in those aged \(<70\) years (0.0%, 3.5%, 7.1%, and 25.7%, respectively).

The prevalence of MMD increased significantly with older age cutoff points (odds ratio [OR] of 3.6/5.0; 95%CI, 3.2–4.0, \(P < 0.001\)). Intraocular pressure, body
Table 1. Prevalence of Any Myopic Macular Degeneration (MMD), Meta-PM Categories, Bilateral MMD, and Unilateral MMD in Adults Aged 40 to 80 Years in the Singapore Epidemiology of Eye Diseases (SEED) Study Stratified by Age, Racial Groups, Sex, Myopia, and Axial Length Levels (N = 8716)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Any MMD, n = 350</th>
<th>Any MMD, n = 334</th>
<th>Any MMD, n = 16</th>
<th>Bilateral MMD, n = 237</th>
<th>Unilateral MMD, n = 113</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude rate</td>
<td>8716</td>
<td>350</td>
<td>334</td>
<td>16</td>
<td>113</td>
</tr>
<tr>
<td>Age-standardized rate</td>
<td>3.8 (3.4–4.3)</td>
<td>3.6 (3.4–4.1)</td>
<td>0.2 (0.1–0.3)</td>
<td>0.2 (0.1–0.3)</td>
<td>1.5 (1.1–1.5)</td>
</tr>
<tr>
<td>Age group, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–49</td>
<td>2457</td>
<td>35</td>
<td>1.0 (0.9–1.0)</td>
<td>0.2 (0.0–0.4)</td>
<td>0.7 (0.3–1.0)</td>
</tr>
<tr>
<td>50–59</td>
<td>3016</td>
<td>80</td>
<td>0.2 (0.0–0.2)</td>
<td>0.1 (0.0–0.2)</td>
<td>1.4 (0.9–1.8)</td>
</tr>
<tr>
<td>60–69</td>
<td>2195</td>
<td>106</td>
<td>0.1 (0.0–0.1)</td>
<td>0.1 (0.0–0.1)</td>
<td>1.5 (1.0–2.0)</td>
</tr>
<tr>
<td>70+</td>
<td>1068</td>
<td>129</td>
<td>0.4 (0.0–0.7)</td>
<td>0.9 (0.8–1.1)</td>
<td>2.2 (1.3–2.0)</td>
</tr>
<tr>
<td>P value for trend</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>2900</td>
<td>140</td>
<td>4.3 (3.4–5.2)</td>
<td>4.3 (3.5–4.5)</td>
<td>3.7 (2.5–4.8)</td>
</tr>
<tr>
<td>Malay</td>
<td>2926</td>
<td>145</td>
<td>1.9 (1.6–2.3)</td>
<td>1.7 (1.4–2.0)</td>
<td>1.2 (0.9–1.5)</td>
</tr>
<tr>
<td>Indian</td>
<td>2890</td>
<td>67</td>
<td>2.3 (2.1–2.6)</td>
<td>1.7 (1.4–2.0)</td>
<td>0.7 (0.4–1.0)</td>
</tr>
<tr>
<td>P value for between-race comparison</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4323</td>
<td>177</td>
<td>4.1 (3.5–4.7)</td>
<td>4.0 (3.4–4.5)</td>
<td>3.3 (2.2–4.5)</td>
</tr>
<tr>
<td>Female</td>
<td>4393</td>
<td>175</td>
<td>3.9 (3.3–4.5)</td>
<td>3.7 (3.2–4.3)</td>
<td>2.9 (2.4–3.5)</td>
</tr>
<tr>
<td>P value for between-sex comparison</td>
<td>0.71</td>
<td>0.55</td>
<td>0.2 (0.1–0.3)</td>
<td>0.2 (0.1–0.5)</td>
<td>0.9 (0.6–1.3)</td>
</tr>
<tr>
<td>Myopia levels</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No myopia, SE &gt; −0.5 D</td>
<td>5608</td>
<td>0</td>
<td>0.0 (0.0–0.0)</td>
<td>0.0 (0.0–0.0)</td>
<td>0.0 (0.0–0.0)</td>
</tr>
<tr>
<td>Low myopia, −3.0 D &lt; SE ≤ −0.5 D</td>
<td>2045</td>
<td>144</td>
<td>7.0 (5.9–8.2)</td>
<td>7.0 (5.9–8.2)</td>
<td>5.5 (4.4–6.6)</td>
</tr>
<tr>
<td>Moderate myopia, −5.0 D &lt; SE ≤ −3.0 D</td>
<td>540</td>
<td>56</td>
<td>10.4 (7.8–12.9)</td>
<td>10.0 (7.5–12.5)</td>
<td>7.6 (5.3–9.8)</td>
</tr>
<tr>
<td>High myopia, −8.0 D &lt; SE ≤ −5.0 D</td>
<td>556</td>
<td>61</td>
<td>17.1 (15.2–21.1)</td>
<td>16.0 (12.2–19.8)</td>
<td>11.5 (8.2–14.9)</td>
</tr>
<tr>
<td>Severe myopia, SE ≤ −8.0 D</td>
<td>167</td>
<td>89</td>
<td>53.3 (45.6–60.9)</td>
<td>47.5 (39.7–55.0)</td>
<td>2.9 (2.4–3.5)</td>
</tr>
<tr>
<td>P value for trend</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;26.5 mm</td>
<td>8217</td>
<td>219</td>
<td>2.7 (2.3–3.0)</td>
<td>2.6 (2.3–3.0)</td>
<td>2.2 (1.5–2.9)</td>
</tr>
<tr>
<td>≥26.5 mm</td>
<td>280</td>
<td>110</td>
<td>3.5 (3.5–4.5)</td>
<td>3.4 (3.4–4.1)</td>
<td>2.4 (1.8–2.8)</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Age-standardized rate (95%CI) compared with the 2010 Singapore population by direct standardization.

mass index, smoking, hypertension, diabetes, hyperlipidemia, and cardiovascular disease were not associated with MMD.

**Disc Lesions Associated With MMD**

Figure 3 shows the fundus photographs of eyes with various Meta-PM categories and associated disc lesions. The prevalence of optic disc tilt, PPA, and peripapillary ICC was 12.5%, 79.6%, and 0.1%, respectively, and the corresponding prevalence rates were 19.3%, 88.2%, and 0.4% among participants with myopia (N = 5108) and 61.5%, 36.2%, and 1.7% among participants with high myopia (N = 523). The prevalence of MMD was significantly higher among eyes with optic disc lesions than eyes without these lesions (all P values < 0.001; Fig. 4), and this association remained statistically significant in subgroups with low and moderate myopia (N = 2582) and with high myopia (N = 523). Among participants with MMD (N = 405), the prevalence of optic disc tilt, PPA, and peripapillary ICC was 43.1%, 100.0%, and 2.6%, respectively.

**Impact of MMD**

In the whole study population (N = 8716), there were 16 subjects with both MMD and bilateral VI or blindness. After excluding 3624 participants with ocular comorbidities, 5092 participants without ocular comorbidities were included for
the following analyses. Of the 5092 participants, 119 (2.3%) were identified as having MMD, of whom 26 (21.8%) had blindness or VI in at least one eye, and 93 (78.2%) had normal vision in both eyes, based on the US definition (Fig. 5). Among the 26 participants with blindness or VI in at least one eye, 23 had high myopia and the remaining 3 participants had low or moderate myopia.

The presence of any MMD was associated with poorer BCVA, but the presence of MMD in general was not significantly associated with poorer VSF compared to persons without MMD (Table 3). The mean BCVA of the better-seeing eye of participants with MMD was significantly worse (0.11; 95%CI, 0.1–0.12) than that of participants without MMD (0.016; 95%CI, 0.015–0.016; P < 0.001), after multivariate adjustments with PVA in model 2. Additionally, the mean BCVA of the better-seeing eye of participants with Meta-PM categories 3 or 4 was significantly worse (0.33; 95%CI, 0.30–0.36) than that of participants with Meta-PM category 2 (0.10; 95%CI, 0.09–0.11; P < 0.001). The presence of Meta-PM categories 3 or 4 in the better-seeing eye was found to be significantly associated with worse BCVA (P < 0.001) and poorer VSF (P = 0.02) compared to individuals with no MMD in the better-seeing eye. An independent association with Meta-PM categories 3 or 4 in the better-seeing eye was observed for 5 of 11 items in the VF-11, after multivariable adjustments in both models 1 and 2. In model 2, the presence of Meta-PM categories 3 or 4 had the largest effect on difficulty in playing games (β coefficient of −20.2; 95%CI, −29.6 to −8.8, P = 0.04), followed by difficulty in recognizing friends (β coefficient of −14.6; 95%CI, −22.2 to −7.0, P < 0.001), and difficulty in seeing stairs (β coefficient of −7.6; 95%CI, −14.7 to −0.4, P = 0.03).

**DISCUSSION**

The age-standardized prevalence of MMD was 3.8% in a phakic adult population in Singapore, and was higher in those of older age, higher myopic SE, and lower education level. There was a dose–response relationship between MMD and SE, and MMD was present even in low and moderate myopes. The detrimental impact of advanced grades of MMD on VI and VSF presents a potential public health issue.

**Prevalence of MMD**

The prevalence of MMD among adults in Singapore (3.8%) is one of the highest to be reported in recent studies, that is, the Beijing Eye Study (3.1%, N = 4519; aged ≥ 40 years), Handan Eye Study (0.9%, N = 6605; aged ≥ 50 years), Hisayama Eye Study in Japan (1.7%, N = 1892; aged ≥ 40 years), Central India Eye and Medical study in Rural India (0.2%, N = 4561; aged ≥ 30 years), Blue Mountains Eye Study in Australia (1.2%, N = 3583; aged ≥ 49 years), and Shihpai Eye Study in Taiwan (3.0%, N = 1038, aged ≥ 65 years). Our high prevalence of MMD could be related to the higher prevalence rates of myopia
and high myopia (35.7% and 6.0%, respectively), compared to that in the Blue Mountains Eye Study (16.8% and 2.7%, respectively) and Handan Eye Study (26.6% and 2.1%, respectively). However, the differences between prevalence rates among populations may also be due to varying definitions of MMD adopted, and different age compositions in each study population.

### Risk Factors of MMD

The age-related trend with MMD is well established in previous studies and is consistent with our findings, which places MMD as another important age-related eye disease. The MMD lesions are primarily degenerative and worsen with age. The age-related association with MMD may denote an

### Table 2. Univariate and Multivariate Analyses of Risk factors for Any Myopic Macular Degeneration (MMD) Among Adults Aged 40 to 80 Years in the Singapore Epidemiology of Eye Diseases (SEED) Study (N = 8716)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>N</th>
<th>n</th>
<th>Unadjusted OR* (95%CI)</th>
<th>P Value</th>
<th>Multivariate-Adjusted OR† (95%CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–49</td>
<td>2437</td>
<td>35</td>
<td>1.0 (reference)</td>
<td>-</td>
<td>1.0 (reference)</td>
<td>-</td>
</tr>
<tr>
<td>50–59</td>
<td>3016</td>
<td>80</td>
<td>1.9 (1.3–2.8)</td>
<td>0.002</td>
<td>4.9 (2.9–8.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>60–69</td>
<td>2195</td>
<td>106</td>
<td>3.5 (2.4–5.1)</td>
<td>&lt;0.001</td>
<td>16.4 (9.5–28.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>70+</td>
<td>1068</td>
<td>129</td>
<td>9.4 (6.4–15.8)</td>
<td>&lt;0.001</td>
<td>58.2 (32.8–103.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P value for trend</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indian</td>
<td>2890</td>
<td>67</td>
<td>1.0 (reference)</td>
<td>-</td>
<td>1.0 (reference)</td>
<td>-</td>
</tr>
<tr>
<td>Non-Indian</td>
<td>5826</td>
<td>283</td>
<td>2.2 (1.6–2.8)</td>
<td>&lt;0.001</td>
<td>1.5 (1.0–1.8)</td>
<td>0.10</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4323</td>
<td>177</td>
<td>1.0 (reference)</td>
<td>-</td>
<td>1.0 (reference)</td>
<td>-</td>
</tr>
<tr>
<td>Female</td>
<td>4393</td>
<td>173</td>
<td>1.0 (0.8–1.2)</td>
<td>0.71</td>
<td>1.0 (0.8–1.5)</td>
<td>0.96</td>
</tr>
<tr>
<td>Spherical equivalent, D</td>
<td>8716</td>
<td>350</td>
<td>1.5 (1.5–1.6)</td>
<td>&lt;0.001</td>
<td>1.8 (1.7–1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary/above education</td>
<td>3689</td>
<td>130</td>
<td>1.0 (reference)</td>
<td>-</td>
<td>1.0 (reference)</td>
<td>-</td>
</tr>
<tr>
<td>Primary/below education</td>
<td>5027</td>
<td>220</td>
<td>1.3 (1.0–1.6)</td>
<td>0.04</td>
<td>1.7 (1.3–2.4)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Univariate analysis.
† Multivariate analysis, adjusted for age, race, sex, spherical equivalent, and education level.

### FIGURE 3. Fundus photographs of eyes with myopic macular degeneration (MMD) Meta-PM categories and associated disc lesions. Top row (A1–A3) shows the photographs of eyes with Meta-PM category 2 (diffuse chorioretinal atrophy). Middle row (B1–B3) shows the photographs of eyes with Meta-PM category 3 (patchy chorioretinal atrophy). Bottom row (C1–C3) shows the photographs of eyes with Meta-PM Category 4 (myopic macular atrophy). Peripapillary atrophy was present in all eyes. (A2, C1, C2) show eyes with optic disc tilt. (A3) shows an eye with peripapillary intrachoroidal cavitation and lacquer crack.
association between the duration of myopia and MMD. The relatively high prevalence of MMD in subjects with low myopia suggests that age may be a surrogate for duration of myopia in an individual.

A higher risk of MMD was associated with greater myopic SE among adults in other studies. Similarly, our findings indicate that individuals with severe myopia levels have a high risk of MMD development, but MMD can develop in individuals with low and moderate myopia as well. The prevalence of MMD increased with severity of myopia in a dose–response pattern, which is similar to the results from the Handan Eye Study.

The prevalence of MMD was highest in Chinese compared to Malays and Indians in Singapore, which may be due to the higher prevalence of high myopia in Chinese (9.7%) compared to Malays (4.1%), and Indians (4.3%). Given a certain SE distribution after adjustments in the multivariate regression model, the risk of MMD was not significantly different in Indians compared to Chinese and Malays. Further investigations on the ethnic differences in prevalence of MMD are warranted.

Previous studies found no association between MMD and education, but we found one with lower education level. Low socioeconomic status and education levels were related to other age-related eye diseases, such as cataract and age-related...
TABLE 3. Differences in Best-Corrected Visual Acuity and Vision-Specific Functioning Scores From the Modified VF-11 Questionnaire With Myopic Macular Degeneration (MMD) and Corresponding Meta-PM Categories in Adults Without Ocular Comorbidities Aged 40 to 80 Years in the Singapore Epidemiology of Eye Diseases (SEED) Study (N = 5092) Using Linear Regression Models

<table>
<thead>
<tr>
<th>Variable</th>
<th>$N$</th>
<th>BCVA, logMAR Model 1</th>
<th></th>
<th>BCVA, logMAR Model 2</th>
<th></th>
<th>Vision-Specific Functioning Score Model 1</th>
<th></th>
<th>Vision-Specific Functioning Score Model 2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$\beta$ Coefficient</td>
<td>P</td>
<td>$\beta$ Coefficient</td>
<td>P</td>
<td>$\beta$ Coefficient</td>
<td>P</td>
<td>$\beta$ Coefficient</td>
<td>P</td>
</tr>
<tr>
<td>MMD in the better-seeing eye</td>
<td></td>
<td>(95%CI)</td>
<td></td>
<td>(95%CI)</td>
<td></td>
<td>(95%CI)</td>
<td></td>
<td>(95%CI)</td>
<td></td>
</tr>
<tr>
<td>No MMD</td>
<td>5008 Reference</td>
<td>Reference</td>
<td>-</td>
<td>Reference</td>
<td>-</td>
<td>Reference</td>
<td>-</td>
<td>Reference</td>
<td>-</td>
</tr>
<tr>
<td>MMD</td>
<td>84  0.06 (0.04–0.07)</td>
<td>&lt;0.001</td>
<td>0.04 (0.03 to 0.06)</td>
<td>&lt;0.001</td>
<td>-1.80 (–4.39 to 0.80)</td>
<td>0.18</td>
<td>-0.96 (–3.52 to 1.61)</td>
<td>0.46</td>
<td></td>
</tr>
<tr>
<td>MMD in the worse-seeing eye</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No MMD</td>
<td>4986 Reference</td>
<td>Reference</td>
<td>-</td>
<td>Reference</td>
<td>-</td>
<td>Reference</td>
<td>-</td>
<td>Reference</td>
<td>-</td>
</tr>
<tr>
<td>MMD</td>
<td>106 0.14 (0.10–0.17)</td>
<td>&lt;0.001</td>
<td>-0.01 (–0.04 to 0.02)</td>
<td>0.43</td>
<td>-2.24 (–4.63 to 0.15)</td>
<td>0.07</td>
<td>0.50 (–2.70 to 2.10)</td>
<td>0.81</td>
<td></td>
</tr>
<tr>
<td>Severity of MMD in the better-seeing eye</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No MMD</td>
<td>5008 Reference</td>
<td>Reference</td>
<td>-</td>
<td>Reference</td>
<td>-</td>
<td>Reference</td>
<td>-</td>
<td>Reference</td>
<td>-</td>
</tr>
<tr>
<td>Meta-PM category 2</td>
<td>76  0.04 (0.03–0.05)</td>
<td>&lt;0.001</td>
<td>0.03 (0.02 to 0.04)</td>
<td>&lt;0.001</td>
<td>-1.34 (–1.68 to 1.40)</td>
<td>0.34</td>
<td>-0.56 (–3.26 to 2.14)</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td>Meta-PM category 3 and 4</td>
<td>8  0.23 (0.19–0.27)</td>
<td>&lt;0.001</td>
<td>0.19 (0.16 to 0.23)</td>
<td>&lt;0.001</td>
<td>-13.64 (–21.68 to –5.61)</td>
<td>0.001</td>
<td>-9.71 (–17.64 to –1.79)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Severity of MMD in the worse-seeing eye</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No MMD</td>
<td>4986 Reference</td>
<td>Reference</td>
<td>-</td>
<td>Reference</td>
<td>-</td>
<td>Reference</td>
<td>-</td>
<td>Reference</td>
<td>-</td>
</tr>
<tr>
<td>Meta-PM category 2</td>
<td>98  0.12 (0.08–0.16)</td>
<td>&lt;0.001</td>
<td>-0.02 (–0.05 to 0.01)</td>
<td>0.17</td>
<td>-2.28 (–4.73 to 0.17)</td>
<td>0.07</td>
<td>-0.49 (–2.94 to 1.97)</td>
<td>0.70</td>
<td></td>
</tr>
<tr>
<td>Meta-PM category 3 and 4</td>
<td>8  0.40 (0.27–0.52)</td>
<td>&lt;0.001</td>
<td>0.13 (0.03 to 0.22)</td>
<td>0.008</td>
<td>-1.67 (–9.49 to 6.16)</td>
<td>0.68</td>
<td>2.36 (–5.43 to 10.16)</td>
<td>0.55</td>
<td></td>
</tr>
</tbody>
</table>

Ocular comorbidities include cataract, glaucoma, age-related macular degeneration, and diabetic retinopathy. Model 1 adjusted for age, race, sex, education, and spherical equivalent (SE). Model 2 adjusted for age, race, sex, education, SE, and presenting visual acuity in the better or worse eye accordingly. A high BCVA (logMAR) indicates poorer visual acuity, and a low BCVA better acuity. A high vision-specific functioning score indicates a high level of visual functioning, and a low score a low level of functioning.
Prevalence, Risk Factors, and Impact of MMD in Singapore

majority of the eyes with MMD in the Blue Mountains Eye
adulthood. Similar to our findings, PPA was detected in
pared to MMD atrophic lesions that tend to develop later in
lesions occur early during childhood or adolescence, com-

In addition, the impact of advanced MMD grades on VSF may
result in overestimation of negative SE values. The stratified
analyses showed that the risk of MMD increased with SE in
participants with cataract (OR of 1.6 per 1 D; 95%CI, 1.5–1.7),
and this association was also present in participants without
cataract (OR of 2.8, 95%CI, 1.9–4.1)43 and cataract surgery (OR of 2.1, 95%CI, 1.1–4.2).44 Furthermore,
the risks of cataract and cataract surgery increase with more
severe myopia levels.44,45 However, previous prevalence
studies on MMD also excluded subjects with history of cataract
surgery7,19 to reflect the true relationship between MMD and
SE among phakic participants without cataract surgery. Posterior
staphyloma is included in the definition of pathologic
myopia, but such anatomic abnormalities were not investigated
as optical coherence tomography images were not available in
7002 (80.3%) participants in this study. Therefore, the
detection of other myopia-related complications, for instance,
macular hole and macular schisis, was not possible. Subtle
lacquer cracks might be missed in fundus photographs without
the use of fluorescein angiography or indocyanine green
angiography. Lens-induced myopia shifts due to cataracts may
result in overestimation of negative SE values. The stratified
analyses showed that the risk of MMD increased with SE in
participants with cataract (OR of 1.6 per 1 D; 95%CI, 1.5–1.7),
and this association was also present in participants without
cataract (OR of 1.9 per 1 D; 95%CI, 1.8–2.1). As AL is not
affected by cataract, the high correlation between SE and AL (r
= -0.73) suggests that the effect of cataract-induced myopia
shifts on the association between SE and MMD is not large, if
present. Other risk factors of MMD, such as choroidal thickness
and family history of myopia, were not available in all adults.
Also, visual field data were not collected for all participants.
In addition, due to the cross-sectional design of our study,
the temporality of associations cannot be established and thus
inference of causal relationships of MMD is limited.

CONCLUSIONS

In conclusion, the age-standardized prevalence of MMD among
phakic adults in Singapore was one of the highest worldwide at
3.8%, and ranged between 2.3% and 4.6% across Chinese,
Malays, and Indians. Contrary to the association between
myopia and higher education level, MMD was associated with
lower education level, which may act as a proxy for low
socioeconomic status rather than an indicator of near work.
The risk of MMD is present not only in high myopes, but in low
and moderate myopes as well, especially in older age. These
findings suggest that closer monitoring of those with advanced
grades of MMD is crucial for appropriate management and for
instituting timely visual rehabilitation.16 Finally, the higher
prevalence of MMD among individuals with more severe
myopia levels highlights an urgent need for preventive myopia
control strategies in early life to delay the onset and
progression of myopia,\textsuperscript{47} which in turn lowers the risk of myopia-related vision-threatening complications in adulthood.\textsuperscript{49,50}

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**References**

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