Prevalence of myopic macular degeneration worldwide: a systematic review and meta-analysis

Minjie Zou,1,2 Shibin Wang,3 Aiming Chen,4 Zhenzhen Liu,1 Charlotte Aimee Young,5 Yichi Zhang,6 Guangming Jin,1 Danying Zheng1

ABSTRACT

Purpose To investigate the prevalence of myopic macular degeneration (MMD) in the global population.

Methods All published literature of population-based studies on MMD prevalence worldwide were searched and only those with clear definitions to diagnose and classify MMD lesions by standardised grading methods were selected. Meta-analysis methods were used to calculate the pooled prevalence of MMD and its 95% CI in a random-effects model. The prevalence of MMD lesions would also be reported, together with the subgroup analysis of age, region and gender. Correlation between MMD prevalence and spherical equivalent levels and axial length were also evaluated.

Results 12 studies with 58 558 subjects were included in this meta-analysis. The pooled prevalence of MMD in the world population was 2.1% (95% CI: 1.3% to 3.3%). In the subgroup analysis, people with the following characteristics were at higher risk of developing MMD: female, urban life, living in Asia, older age, longer axial length and severer myopia.

Conclusions MMD is a serious public health concern worldwide, particularly in subjects who are women, subjects living in urban areas, subjects living in Asia, and subjects with longer axial lengths and severer myopia. Further studies from other continents/ethnicities are needed for comprehensive estimates of the prevalence of MMD globally.

INTRODUCTION

Myopia has been one of the leading causes of visual impairment worldwide and the prevalence of myopia has been increasing in the past decades. Predictably, 49.8% of the world population will have myopia and 9.8% will have high myopia by 2050, which will be a great economic myopia-related burden globally. Individuals with high myopia are at an increased potential risk of developing myopia-related blinding complications, the most common of which is myopic macular degeneration (MMD), which could cause a progressive decrease in visual acuity.1–3 MMD is one of the leading causes of blindness worldwide and usually causes a heavy economic burden to societies and individuals.3–5 MMD has been reported as the first to the third most important cause of visual loss in Asian populations, indicating much more effort is needed for the guidance of future solutions.1

Evaluating the magnitude of MMD is of great importance for health authorities to understand its harmful impact and to develop appropriate preventive strategies. Though several studies performed in different countries reported the prevalence of MMD4,7,10–12–20 due to differences in diagnostic, definition and study locations, the prevalence of MMD in the general population varied significantly between studies, ranging from 0.2% to 10.7%.5,15–19

Unfortunately, to the best of our knowledge, there has been no systematic review and meta-analysis in the prevalence of MMD published prior, which hinders people’s understanding of the disease burden of MMD. Therefore, a better understanding of the magnitude of MMD is needed. We performed this systematic review and meta-analysis to address the prevalence of MMD in worldwide populations and performed subgroup analysis by evaluating different potential risk factors in worldwide populations.

METHODS

Search strategy for literature

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. Publications reporting the prevalence of MMD among all populations worldwide were reviewed and assessed. Two investigators (GJ and MZ) searched the literature independently in both English (Embase, PubMed and Web of Science) and Chinese (SinoMed, WanFang and Chinese National Knowledge Infrastructure) databases until 19 July 2019. The search terms were as follows:

1. “Retinal Degeneration”[Mesh] [All fields] or “Macular Degeneration”[Mesh] [All fields] or “Retinal Diseases”[Mesh] [All fields] or “Retinal maculopathy” [All fields] or “Retinal complications”[All fields] or “Myopic macular degeneration” [All fields] or “Myopic maculopathy” [All fields]

2. “Refraction error” [Mesh] [All fields] or “Myopia” [Mesh] [All fields] or “Myopia, Degenerative” [Mesh] or “Pathological myopia” [All fields] or “pathologic myopia” [All fields] or “Epidemiology” [Mesh] [All fields] or “Cohort Studies” [Mesh] [All fields] or “Prevalence” [Mesh] [All fields] or “Cross-Sectional Studies” [Mesh] [All fields] or “Risk Factors” [Mesh] [All fields]


Study selection

Studies were included if they met the following criteria: (1) population-based study; (2) use...
recognised definitions and standardised grading method to diagnose and classify MMD lesions; (3) accessible full text in Chinese or English; (4) sample size ≥1000; (5) response rate ≥60%.7 13 14 17 18 Several internationally recognised definitions and standardised grading methods are used for pathologically myopia (PM) and PM Classification.7 13 14 17 18 Among the included studies, PM Classification developed by Vongphanit and the International Meta-Analyses of Pathological Myopia (META-PM) classification were the most used grading methods. According to PM Classification developed by Vongphanit, myopic retinopathy was graded into five categories including no myopic retinal lesion (category 0), tessellated fundus (category 1), diffuse chorioretinal atrophy (category 2), patchy chorioretinal atrophy (category 3) and macular atrophy (category 4). Four additional features to supplement these categories were defined as ‘plus’ lesions, namely lacquer cracks, myopic chorioidal neovascularisation, Fuchs’ spot and posterior staphyloma. 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, chorioidal neovascularisation (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. Studies using convenience sampling and those without details on the sampling method as well as studies focused on special populations (eg, patients with myopes) were also excluded.

Titles and abstracts of all initial searched results were screened independently by two investigators (GJ and MZ). If there was more than one publication based on the same study, the study with more complete information would be selected.

Data extraction and quality assessment
Two investigators (GJ and MZ) conducted the data extraction independently and any disagreements were resolved by a discussion with a third investigator (SW). The following information was extracted and tabulated: first author, study setting, sampling method, survey time, sample size, basic demographic data, and the prevalence of MMD and the specific lesions of pathological changes in MMD.

The quality of all selected articles was evaluated by two investigators (GJ and MZ) with a commonly used 8-item assessment tool. According to the quality evaluation tool, each study was given a score of 0–8. We consider a score of 7–8 as moderate quality and 0–3 as low quality. The coding of assessment has been described previously.22–24

Statistical analysis
The meta-analysis was conducted using the Comprehensive Meta-Analysis software V2 (Biostat, Englewood, New Jersey, USA). The prevalence of MMD and specific lesions of pathological changes in MMD with 95% CIs were calculated using random-effects models. Heterogeneity between studies was assessed by I² statistic, and I² > 50% was regarded as high heterogeneity. The age-specific pooled prevalence of MMD by 40–49, 50–59, 60–69 and >70 years old age groups was conducted. To explore the possible sources of heterogeneity associated with gender, place of residence (rural/urban), area (Asia/North America), survey year, refraction levels, grading systems and axial length levels, subgroup analyses were performed separately. In the subgroup analysis of the grading scheme, we chose the two most commonly used grading systems (International META-PM Classification and PM Classification developed by Vongphanit). Continuous variables were dichotomised using median splitting method in subgroup analyses. According to the principle of meta-analysis, I² > 50% indicates great heterogeneity and in this situation, the random-effect model is suggested for conservativeness and reliability. Publication bias was assessed by the Funnel plot and Beg tests. The significance level was set at p<0.05 (two-tailed). The funnel plot would be presented when the number of studies being meta-analysed is > 10.

RESULTS
Study selection and inclusion results with basic characteristics
Figure 1 shows the selection process of studies identified through the database search with 3954 initial records. Altogether, 12 studies (13 datasets as one study provided two cross-sectional with two different samples)20 with 58,558 subjects were included for qualitative synthesis. The basic characteristics of included studies are given in table 1. Of the 12 studies, 2 were in Chinese,12 13 and the remaining were in English.6 7 10 14-20 25 We included 28,356 individuals of five studies conducted in mainland China,6 12 13 16 18 1058 of one study in Taiwan China,14 7702 of two studies in Japan,17 20 8716 of one study in Singapore,7 4582 of one study in the USA,15 3583 of one study in Australia,10 and 4561 of one study in India.19 All included studies have clear definitions of the target population and the samples are representative of the general population. Only one study graded subjects with myopia and the remaining 11 studies have all subjects graded for MMD. Some included studies report MMD prevalence among all subjects,13 14–18 20 whereas others also present MMD prevalence among high myopic subjects.6 7 10 12 16 17 As for the grading in the included studies, seven studies had grading conducted by one investigator,6 12 14 15 18 19 among which four studies had a second examination when necessary,10 12 13 15 19 and the remaining studies had double grading.10 16 17 20 As several subgroup analyses (gender, age, spherical equivalent refraction levels and axial length levels) are not provided in all of the

Figure 1 Flowchart of the study selection process.
The prevalence of high myopia and MMD in the world population
The prevalence of high myopia ranged from 1.3% to 8.0%, whereas the prevalence of MMD ranged from 0.2% to 10.7% given in table 2. The pooled prevalence of high myopia was 3.0% (95% CI: 2.1% to 4.2%) as shown in the online supplementary figure 2 and the pooled prevalence of MMD was 2.1% (95% CI: 1.3% to 3.3%). A relevant forest plot was shown in the online supplementary figure 3. When it comes to MMD within high myopic subjects, the prevalence rate was 47.4% (95% CI: 24.3% to 71.7%) (online supplementary figure 4). As for sublesions of MMD, the pooled prevalence of staphyloma was 0.9% (95% CI: 0.6% to 1.4%), being the most frequent pathological lesions of MMD. Choriotinal atrophy at the posterior pole was also common, with a prevalence of 0.6% (95% CI: 0.1% to 2.3%). Other pathological lesions of MMD such as lacquer cracks and Fuchs’ spots were infrequent with prevalence rates of 0.3% (95% CI: 0.2% to 0.4%) and 0.2% (95% CI: 0.1% to 0.2%), respectively. MMD prevalence within high myopic subjects ranged from 25.3% to 71.4%. The age-specific and age-sex-specific prevalence of MMD is given in figure 2.

Subgroup analysis of the pooled prevalence of MMD
The pooled prevalence of MMD among different subgroups is shown in table 3. Online supplementary figures 5–12 show the forest plots of MMD prevalence by several subgrouping methods. In the subgroup of gender, the prevalence of MMD in women is higher than men with statistical significance (2.6%, 95% CI (1.6% to 4.3%) for women vs 1.9%, 95% CI (1.1% to 3.5%) for men, p<0.001).

As for the comparison between populations living in different areas, our results show that the prevalence of MMD in rural areas is significantly lower than that in urban districts. Meanwhile, people are at higher risk of having MMD in American and Australia than in Asia.

As for the subgroup analysis of axial length, the prevalence of MMD in subjects with an axia length longer than 26 mm is higher than subjects with an axial length shorter than 26 mm. Myopes with severer spherical equivalent (SE) refraction levels are more likely to suffer from MMD (p=0.08).

For the subgroup analysis of age group, the prevalence of MMD increased from 1.3% (95% CI, 1.0% to 1.7%) in the 40–49 age group to 4.5% (95% CI, 2.6% to 7.8%) in the 70+ age group (p<0.001). When comparing the prevalence of MMD in earlier studies versus later studies (1993–2006 vs 2007–2019), a time trend was found with the prevalence of MMD being higher in the later study group than earlier study group (1.3%, 95% CI (0.8% to 2.2%) vs 3.5%, 95% CI (1.9% to 6.3%)).

Different grading schemes also influenced the prevalence rate of MMD. The prevalence of studies using PM Classification by Vongphanit is much lower than that of International META-PM Classification (1.6%, 95% CI (1.0% to 2.6%) vs 4.7%, 95% CI (2.4% to 8.9%)).

In exploratory meta-regression analyses, significance was found between the prevalence rate of MMD and the following factors: response rate (slope=−1.170, p<0.0001), study quality score (slope=−0.222, p<0.0001), conducted year (slope=0.068, p=0.0001), male to female ratio (slope=−2.256, p<0.0001), and myopia degree (slope=−0.715, p<0.0001).

DISCUSSION
In the current study, 12 studies with 13 datasets conducted in different parts of the world (China, Taiwan China, Japan, India, Singapore, Australia, Japan, China, India, Singapore, Japan, China, Australia, and Singapore). The results showed that the prevalence of MMD is significantly higher in urban areas than in rural areas. This finding is consistent with previous studies that have reported higher prevalence rates of MMD in urban areas compared to rural areas. One possible explanation for this difference is that urban areas have a higher population density and a higher prevalence of myopia than rural areas. Myopia is a risk factor for the development of MMD, and the higher prevalence of myopia in urban areas may contribute to the higher prevalence of MMD in these areas.

The prevalence of MMD also varies by age group. The prevalence rate of MMD increases with age, with the highest prevalence rate in the 70+ age group. This finding is consistent with previous studies that have reported higher prevalence rates of MMD in older age groups. One possible explanation for this difference is that older individuals are more likely to have chronic conditions that increase the risk of developing MMD, such as hypertension and diabetes.

The prevalence of MMD also varies by sex. The prevalence rate of MMD is higher in women than in men. This finding is consistent with previous studies that have reported higher prevalence rates of MMD in women. One possible explanation for this difference is that women are more likely to have chronic conditions that increase the risk of developing MMD, such as hypertension and diabetes.

The prevalence of MMD also varies by axial length. The prevalence rate of MMD is higher in myopes with axial length longer than 26 mm than in myopes with axial length shorter than 26 mm. This finding is consistent with previous studies that have reported higher prevalence rates of MMD in myopes with longer axial lengths. One possible explanation for this difference is that myopes with longer axial lengths are more likely to have pathological changes in the retina and choroid that increase the risk of developing MMD.

Furthermore, different grading schemes also influence the prevalence rate of MMD. The prevalence of studies using PM Classification by Vongphanit is much lower than that of International META-PM Classification. This finding is consistent with previous studies that have reported lower prevalence rates of MMD in studies using PM Classification than in studies using International META-PM Classification. One possible explanation for this difference is that PM Classification may underestimate the prevalence rate of MMD, as it does not take into account the presence of subclinical lesions that may be present in individuals with myopia but do not cause visual symptoms.

In conclusion, the prevalence of MMD varies by location, age, sex, axial length, and grading scheme. Future studies should focus on understanding the factors that contribute to these differences in order to develop effective strategies for the prevention and treatment of MMD. Additionally, future studies should focus on understanding the mechanisms by which myopia increases the risk of developing MMD, in order to develop effective strategies for the prevention and treatment of MMD.
Table 2  Pooled prevalence of overall and sublesions of MMD

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>High myopia (%)</th>
<th>MMD (%)</th>
<th>MMD within high myopic subjects (%)</th>
<th>Male (%)</th>
<th>Female (%)</th>
<th>Staphyloma (%)</th>
<th>Lacquer cracks (%)</th>
<th>Fuchs’ spot (%)</th>
<th>Chorioretinal atrophy (%)</th>
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<tr>
<td>SEED</td>
<td>8716</td>
<td>6.0 (5.5 to 6.5)*</td>
<td>4.0 (3.6 to 4.4)</td>
<td>28.7 (25.0 to 32.7)</td>
<td>4.1 (3.5 to 4.7)</td>
<td>3.9 (3.4 to 4.5)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>The Shaanxi Eye Study</td>
<td>6815</td>
<td>–</td>
<td>1.3 (1.1 to 1.6)</td>
<td>–</td>
<td>1.1 (0.7 to 1.6)</td>
<td>2.2 (1.7 to 2.8)</td>
<td>1.0 (0.8 to 1.3)</td>
<td>0.3 (0.2 to 0.5)</td>
<td>0.1 (0 to 0.2)</td>
<td>0.3 (0.2 to 0.5)</td>
</tr>
<tr>
<td>The Yangxi Eye Study</td>
<td>4469</td>
<td>1.3 (1.0 to 1.7)†</td>
<td>1.4 (1.1 to 1.8)</td>
<td>–</td>
<td>1.6 (1.2 to 2.2)</td>
<td>1.7 (1.2 to 2.3)</td>
<td>0.2 (0.1 to 0.4)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>The Shihpai Eye Study</td>
<td>1058</td>
<td>4.2 (3.1 to 5.6)†</td>
<td>3.0 (2.1 to 4.2)</td>
<td>–</td>
<td>2.4 (1.5 to 3.9)</td>
<td>4.3 (2.7 to 6.8)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CHES</td>
<td>4582</td>
<td>8.0 (7.2 to 8.8)*</td>
<td>10.7 (9.8 to 11.6)</td>
<td>–</td>
<td>12.4 (10.8 to 14.2)</td>
<td>11.3 (10.1 to 12.6)</td>
<td>1.9 (1.5 to 2.3)</td>
<td>0.8 (0.6 to 1.1)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>The Handan Eye Study</td>
<td>6603</td>
<td>2.1 (1.8 to 2.5)*</td>
<td>0.9 (0.7 to 1.2)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.8 (0.6 to 1.0)</td>
<td>0.4 (0.3 to 0.6)</td>
<td>0.2 (0.1 to 0.3)</td>
<td>0.5 (0.4 to 0.7)</td>
</tr>
<tr>
<td>The Beijing Eye Study</td>
<td>4319</td>
<td>2.4 (2.0 to 2.9)</td>
<td>3.1 (2.6 to 3.7)</td>
<td>65.4 (58.8 to 71.5)</td>
<td>–</td>
<td>–</td>
<td>1.6 (1.3 to 2.0)</td>
<td>0.2 (0.1 to 0.4)</td>
<td>0.1 (0 to 0.3)</td>
<td>3.1 (2.6 to 3.7)</td>
</tr>
<tr>
<td>The Hisayama Eye Study (2005)</td>
<td>1892</td>
<td>1.5 (1.0 to 2.2)*</td>
<td>1.7 (1.2 to 2.4)</td>
<td>–</td>
<td>1.2 (0.6 to 2.3)</td>
<td>2.2 (1.5 to 3.2)</td>
<td>–</td>
<td>0.1 (0 to 0.4)</td>
<td>0.1 (0 to 0.4)</td>
<td>–</td>
</tr>
<tr>
<td>The Blue Mountain Eye Study</td>
<td>3583</td>
<td>2.7 (2.2 to 3.3)*</td>
<td>1.2 (0.9 to 1.6)</td>
<td>25.3 (16.9 to 36.0)</td>
<td>1.0 (0.6 to 1.6)</td>
<td>1.4 (1.0 to 2.0)</td>
<td>0.7 (0.5 to 1.0)</td>
<td>0.2 (0.1 to 0.4)</td>
<td>0.1 (0 to 0.3)</td>
<td>0.2 (0.1 to 0.4)</td>
</tr>
<tr>
<td>The Central India Eye and Medical Study</td>
<td>4561</td>
<td>–</td>
<td>0.2 (0.1 to 0.4)</td>
<td>–</td>
<td>0.1 (0.0 to 0.4)</td>
<td>0.3 (0.1 to 0.6)</td>
<td>–</td>
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<td>–</td>
</tr>
<tr>
<td>The Hisayama Eye Study (2012)</td>
<td>2874</td>
<td>2.5 (2.0 to 3.1)*</td>
<td>3.0 (2.4 to 3.7)</td>
<td>–</td>
<td>2.3 (1.6 to 3.3)</td>
<td>3.5 (2.7 to 4.5)</td>
<td>–</td>
<td>0.2 (0.1 to 0.5)</td>
<td>0.2 (0.1 to 0.5)</td>
<td>–</td>
</tr>
<tr>
<td>The Hisayama Eye Study (2017)</td>
<td>2936</td>
<td>3.0 (2.4 to 3.7)*</td>
<td>3.6 (3.0 to 4.3)</td>
<td>–</td>
<td>3.3 (2.5 to 4.4)</td>
<td>3.8 (3.0 to 4.8)</td>
<td>–</td>
<td>0.2 (0.1 to 0.4)</td>
<td>0.2 (0.1 to 0.4)</td>
<td>–</td>
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<tr>
<td>The Wuxi Eye Study</td>
<td>6150</td>
<td>3.7 (3.3 to 4.2)†</td>
<td>2.6 (2.2 to 3.0)</td>
<td>71.4 (55.2 to 76.9)</td>
<td>2.2 (1.7 to 2.8)</td>
<td>3.0 (2.5 to 3.8)</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Pooled Prevalence</td>
<td>58558</td>
<td>3.0 (2.1 to 4.2)†</td>
<td>2.1 (1.3 to 3.3)§</td>
<td>47.4 (24.3 to 71.7)§</td>
<td>4.2 (3.9 to 4.6)**</td>
<td>4.6 (4.3 to 4.9)††</td>
<td>0.9 (0.6 to 1.4)††</td>
<td>0.3 (0.2 to 0.4)§§</td>
<td>0.2 (0.1 to 0.2)¶¶</td>
<td>0.6 (0.1 to 2.3)***</td>
</tr>
</tbody>
</table>

*≤−5.0D. †≤−6.0D. §I²=97.995%, p<0.001.
¶I²=98.846%, p<0.001.
†I²=98.090%, p<0.001.
**I²=97.707%, p<0.001.
††I²=97.707%, p<0.001.
‡‡I²=98.846%, p<0.001.
§§I²=98.090%, p<0.001.
¶¶I²=97.707%, p<0.001.
***I²=98.454%, p<0.001.

CHES, the Chinese American Eye Study; MMD, myopic macular degeneration; SEED, the Singapore Epidemiology of Eye Disease.
Clinical science

Figure 2  Age-specific and age-sex-specific prevalence of MMD among the world population. (A) Age-specific prevalence of MMD. (B) Age-sex-specific prevalence of MMD. MMD, myopic macular degeneration.

Singapore, Australia and USA) were included, and the pooled prevalence of MMD in this meta-analysis was 2.1% (95% CI: 1.3% to 3.3%). Most of the included studies were from Asia. Though no meta-analysis of MMD has been published prior, the result is consistent with the traditional view that MMD is a frequently occurring ocular disease in the elderly population and the risk of developing MMD among high myopic subjects is much higher (47.4%, 95%CI: 24.3% to 71.7%). In the sublesions of MMD, staphyloma and choroidal atrophy at the posterior pole ranked the first and second most frequent pathological changes in MMD.

In the subgroup analysis of gender, the result indicates that MMD is more common in women than men, in accordance with most of the original investigations. A possible explanation lies in the anatomical differences between sexes and discrepancy in career choices between men and women which could have an impact on the pathogenesis of MMD.

Table 3  Subgroup analysis of myopic macular degeneration prevalence in the world population

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>No. of study/data</th>
<th>Pooled prevalence and 95% CI (%)</th>
<th>Heterogeneity, I² (%)</th>
<th>Q-value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Male</td>
<td>11</td>
<td>1.9 (1.1 to 3.5)</td>
<td>97.707</td>
<td>436.158</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>11</td>
<td>2.6 (1.6 to 4.3)</td>
<td>98.782</td>
<td>469.866</td>
<td></td>
</tr>
<tr>
<td>District</td>
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<tr>
<td>Urban</td>
<td>8</td>
<td>3.1 (1.8 to 5.2)</td>
<td>98.752</td>
<td>560.962</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rural</td>
<td>4</td>
<td>0.9 (0.5 to 1.4)</td>
<td>91.226</td>
<td>34.191</td>
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</tr>
<tr>
<td>Region</td>
<td></td>
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</tr>
<tr>
<td>Asia</td>
<td>11</td>
<td>1.9 (1.4 to 2.6)</td>
<td>96.553</td>
<td>290.110</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>USA and Australia</td>
<td>2</td>
<td>3.7 (0.4 to 26.5)</td>
<td>99.507</td>
<td>202.893</td>
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</tr>
<tr>
<td>Age (years)</td>
<td></td>
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<tr>
<td>40-49</td>
<td>3</td>
<td>1.3 (1.0 to 1.7)</td>
<td>0</td>
<td>1.190</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>50-59</td>
<td>7</td>
<td>2.0 (0.9 to 4.4)</td>
<td>97.830</td>
<td>276.453</td>
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<tr>
<td>60-69</td>
<td>8</td>
<td>3.0 (1.5 to 5.8)</td>
<td>97.833</td>
<td>323.001</td>
<td></td>
</tr>
<tr>
<td>70+</td>
<td>8</td>
<td>4.5 (2.6 to 7.8)</td>
<td>96.338</td>
<td>191.169</td>
<td></td>
</tr>
<tr>
<td>Axial length (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;26</td>
<td>3</td>
<td>0.9 (0.1 to 7.1)</td>
<td>95.796</td>
<td>47.571</td>
<td>0.001</td>
</tr>
<tr>
<td>≥26</td>
<td>3</td>
<td>8.4 (2.1 to 28.2)</td>
<td>96.696</td>
<td>60.529</td>
<td></td>
</tr>
<tr>
<td>SE refraction levels (diopters)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.00 to −5.99</td>
<td>4</td>
<td>0.5 (0.1 to 2.0)</td>
<td>95.527</td>
<td>67.068</td>
<td>0.08</td>
</tr>
<tr>
<td>≤−6.00</td>
<td>4</td>
<td>32.1 (16.9 to 52.2)</td>
<td>93.259</td>
<td>44.501</td>
<td></td>
</tr>
<tr>
<td>Conducted time</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1993–2006</td>
<td>7</td>
<td>1.3 (0.8 to 2.2)</td>
<td>95.658</td>
<td>138.200</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2007–2017</td>
<td>6</td>
<td>3.5 (1.9 to 6.3)</td>
<td>99.052</td>
<td>527.669</td>
<td></td>
</tr>
<tr>
<td>Grading system</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>5</td>
<td>1.6 (1.0 to 2.6)</td>
<td>96.159</td>
<td>104.132</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>M</td>
<td>4</td>
<td>4.7 (2.4 to 8.9)</td>
<td>99.024</td>
<td>307.388</td>
<td></td>
</tr>
</tbody>
</table>

M, International META-PM Classification; META-PM, meta analyses of pathologic myopia; SE, spherical equivalent; V, PM Classification by Vongphanit.
Specific living areas may contribute to the development of MMD, as results of this meta-analysis show that people living in cities are at higher risk of developing MMD than those in rural districts. Urban citizens tend to have a higher level of education, which is shown to have a strong correlation to more myopes and higher SE refraction levels, thus leading to the severity of MMD. Residents of Asia have a lower rate of MMD in comparison with those who dwell outside Asia. Lifestyle is considered as an important factor as genetic characteristics may be similar between Chinese Americans and Chinese born and raised locally. The axial length of different races could also contribute to the disparity, which will be discussed further. As there are only two studies using International META-PM Classification, it is more than three times that of the 40–49 age group. It has been proven by past research that increasing maculopathy severity has a strong association with older age.

The significant difference in the prevalence of MMD in four specific age groups should be highlighted. In the age-specific subgroup analysis, the prevalence of MMD in the 70+ age group is more than three times that of the 40–49 age group. It has been proven by past research that increasing maculopathy severity has a strong association with older age.

Analysis between studies conducted from 1993 to 2006 and from 2007 to 2019 shows that people in the latter subgroup tend to develop MMD in a higher frequency. Changes in lifestyle could be an important factor in the rise of prevalence. Other changes, such as the improvement of diagnostic methods or advances in ophthalmic devices, could also influence the epidemiology of MMD.

Studies using International META-PM Classification are found to have a higher MMD prevalence than those using PM Classification by Vongphanit. The most possible explanation for this disparity may be the difference in the definition of chorioretinal atrophy as the diagnostic criteria in PM Classification by Vongphanit is stricter than that in the International META-PM Classification as the definition of chorioretinal atrophy by Vongphanit also required the copresence of additional myopia-related signs which could assist in differentiating myopic chorioretinal atrophy from the atrophic signs of laser scars, age-related maculopathy or toxoplasmosis, whereas diffuse chorioretinal atrophy, patchy chorioretinal atrophy and macular atrophy were all considered to have MMD in META-PM Classification.

The strength of this meta-analysis lies in the large pooled sample size from wide geographical distribution. In addition, it is one of the few meta-analyses concerning the prevalence of MMD being published, which is needed for a better understanding of the present situation and more advanced clinical guidance. Moreover, the quality assessment of all included studies with clearly defined evaluation tools ensures the quality of this meta-analysis.

However, several limitations should be considered. First, although similar definitions of MMD were used in different studies, inconsistencies in the definition could affect the results to a certain extent. Second, some relevant information in subgroup analysis, such as axial length levels and SE refraction levels, was not available in all selected articles, which may influence the analysis process. Third, residents living in mainland China make up a large proportion of the total study population and could have an influence on the analysis result. In addition to Asia, only studies from the USA and Australia could be found. Consequently, the prevalence of MMD in regions such as Latin America, Africa and Europe would need to be explored for a deeper understanding of the disease.

In conclusion, this meta-analysis offers a comprehensive and up-to-date estimate of MMD among wide populations, with the subgroups of age, gender, district, region, axial length and SE refraction levels analysed. The results of this meta-analysis indicate that the prevalence of MMD remains high and with the discrepancy in different subgroups. Further studies are needed to explore potentially affected factors such as sex, lifestyle, different racial axial length and severity of myopia on the development of MMD. Because the majority of included studies were conducted in Asia, studies from other continents/ethnicities are needed for comprehensive estimates of the prevalence of MMD globally.

Contributors GJ and DZ: designed the study, initiated the collaborative project, revised the paper, MZ, SW and ZL: monitored data collection, wrote the statistical analysis plan and drafted the paper. AC, CAY and YZ: cleaned and analysed the data. GJ and DZ: administrative, technical or logistic support.

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ORCID iDs Minjie Zou http://orcid.org/0000-0001-7706-6662
Guangming Jin http://orcid.org/0000-0001-9994-6338

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